The Royal Danish School of Pharmacy

Annual Report

2000-2001
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The Royal Danish School of Pharmacy: Strengthening our academic platform for tomorrow

The Royal Danish School of Pharmacy has signed a performance contract with the Ministry of Science, Technology and Innovation under which we agree to implement various teaching and research initiatives. A contract like this places everyone at the School of Pharmacy, staff as well as students, under an obligation to contribute continuously to our academic development. The contract also requires management to develop our human resources policy to keep the School in the
forefront and provide challenges and interesting work for everyone involved. Everyone is a player in and contributor to this complex and multifaceted process.

The performance contract provides a framework and objectives for the School. However, at the same time we must recognise that the School is on its way into a new academic era. Our working sphere, the field of pharmaceutical sciences is undergoing rapid change. Major transformations in this wide academic field, are coupled with the dramatic biomedical developments of the post-genomic period we now live in. As the only Danish pharmaceutical institution with research-based teaching, the School is at the hub of this accelerating process, which poses major structural and functional challenges. Although the new situation has enormous potential for the School, the prerequisite for realising these prospects is that we show the will and the strength to be effective players with external partners whose support is absolutely essential to the process of change.

Many more pharmacists needed
The powerful reinforcement of the fields of biology and biomedicine has resulted in a formidable expansion of the basic knowledge of medical science. The pharmaceutical disciplines often set the efficiency in the transformation of medical knowledge into new drugs and therapies. This factor has already created bottlenecks, particularly in the pharmaceutical industry, while the School is under pressure in terms of resources and recruitment. The forecast is that the need for pharmacists with MSc and PhD degrees in clinical pharmacy will grow dramatically in the years ahead. In addition we face mounting pressure from the pharmacy sector to meet their urgent need for pharmacists. In response we must make every effort to mobilise resources so that the School’s research capacity as well as MSc and PhD programmes can be exploited to the full. In the longer term, we must expand the School’s combined education and research capacity to match the rapid development of the research-based pharmaceutical industry and biotechnology sector. The School’s goal must be to live up to expectations to educate a sufficient number of key pharmaceutical experts at the MSc and PhD levels in all relevant branches of the pharmaceutical sphere.

Unrealistic to educate pharmacists at other sites
In order to increase the number of pharmacy graduates, it has been suggested to establish a pharmaceutical faculty at the University of Aarhus or University of Southern Denmark in Odense. The idea has merit on several grounds, as another institution to provide pharmaceutical education and research would be desirable, if implementation of a full programme were possible. However, such an initiative must be considered unrealistic, at any rate within the next decade or so. We simply do not have the teaching capacity, and the current difficulty in recruiting new students makes the idea of establishing additional pharmaceutical faculties unrealistic.

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ficulty in recruiting new students to the field presents a serious obstacle to initiatives of this kind. It is highly improbable that the universities in either Aarhus or Odense have envisioned establishing a new full-scale pharmaceutical department. The idea probably is to add biology masters’ programmes to their existing chemistry programmes in order to offer degrees targeted specifically at the pharmaceutical industry. However, establishing special sector-oriented pharmaceutical studies would create problems. The most obvious solution to the capacity problem would be to expand the School’s educational capacity by 25-30%. An expansion of such magnitude would require additional teaching facilities, new buildings to some extent, and the infusion of the requisite financial resources. We have a compelling need to make
The work on the focus areas mentioned above will largely fall to the Study Board, but will be accomplished by the management of the School of Pharmacy. In light of the diversity of the Study Board’s tasks, an ongoing assessment will be made of the extent to which they could be handled by the Programme Administration. Insofar as implementation of new and changed programme modules will imply changes in the departmental structure of the School, the Senate (Konsistorium) will naturally be involved in decision-making.

Closing down centres
In terms of research, the year under review was affected by the political decision to close down the two inter-institutional centres under the School, Drug Design and Transport and Neuroscience PharmaBiotec, at the end of their respective appropriation periods on 31 October and 31 December 2001. Other centres of corresponding inter-institutional character were also closed by political fiat. The two centres under the auspices of the School were closed despite the very positive international evaluation of their research results as well as the development and continuation of close cooperation with the drug industry generated by their activities. This complementary cooperation between industrial scientists and scientists at the School, based on mutual trust, is a strong facet of the School’s research profile.

In contrast, we are pleased that the Drug Design and Transport Centre has been granted sustenance funds for a four-year period corresponding to about 25% of the centre’s appropriation. Only two other centres that were closed down at other institutions were allocated sustenance funds on a similar level. Thus we find it positive that the precedent has been set for continuing and further developing the research training activities developed in cooperation with the drug industry within the framework of the two centres under the School.

Good research development
Research continues to develop well at the School, with the group of younger scientists increasingly mastering and managing its course. In 2001 many junior as well as senior scientists attracted research funds from external sources. These research resources have major impact on all academic development at the School as well as for the international status of the individual scientist. It is not possible to list all of those who have helped put the School on the international research map. However, special mention must be made of Professor Mikael Begtrup, who received the prestigious Chemistry Award from the Carlsberg Foundation, and Anders Asbjørn Jensen, assistant research professor, who was awarded the PhD Prize by the Danish Academy of Natural Sciences. Finally I would like to mention Dung Ngoc Do, precision instrument maker and a graduate of the School, who received a distinguished bronze medal and well-deserved royal handshake for his apprenticeship project.

In order to combine and reinforce research at the School and continue to profile research both nationally and internationally, the decision has been made to set up a number of strategic focus areas at the School. This new initiative is expected to lead to a limited number, perhaps four to six, of detailed plans along these guidelines, and to develop a new educational structure that will stimulate a dynamic interplay between pharmacy degree programmes and other university programmes.

The structure and academic profile of The Royal Danish School of Pharmacy
The future structure and academic profile of the School has been the subject of extensive debate over the summer and autumn. Staff and students have been involved in the debate in a hectic round of meetings. The extent to which the School’s departmental structure is the best framework for dynamic educational and research development was questioned. This issue is central considering the weight that the School attaches to disciplinary integration. In addition, however, the discussion on structure also had the important function of fuelling debate on the School’s academic development in terms of teaching and research.

This discussion has been promising and constructive, initially pinpointing some disciplines that warrant special attention. The decision was made to continue the process of defining special focus areas that will be dealt with effectively by working groups with the aim of finding optimal solutions for integrating disciplines at Master’s level. Initial focus will be on the area comprising social pharmacy, clinical pharmacy, pharmacotherapy and pharmacology. These key disciplines have wide potential, not only in relation to the clinical area but also very much in connection with the pharmacy sector.

Teaching in physical chemistry is another area of focus. Physical chemistry is increasingly a vital component in almost all branches of pharmacy and thus a subject that involves teachers and students from all departments. Other disciplines are on the drawing board and will be made into focus areas in future.

Key role for the Study Board
Naturally, the Study Board holds a key position in discussions about the academic development of the School. The Study Board had already started a wide variety of initiatives, such as revising Degree Regulations and introducing several new courses. One new initiative I would like to mention in particular is a compulsory course in the theory of science. Many hours were devoted to drawing up a new ministerial order for the master’s degree in pharmacy and for introducing ICT-based teaching.

The work on the focus areas mentioned above will largely fall to the Study Board, but will be accomplished by the management of the School of Pharmacy. In light of the diversity of the Study Board’s tasks, an ongoing assessment will be made of the extent to which they could be handled by the Programme Administration. Insofar as implementation of new and changed programme modules will imply changes in the departmental structure of the School, the Senate (Konsistorium) will naturally be involved in decision-making.
such areas at the School. The initiative will strengthen and promote the integration of strong relevant research areas, and it is expected that these strategic focus areas together with other national and international research groups will be able to attract external research funding.

**Research training programmes**

The School gives high priority to research training. Over the years the School has graduated a large number of PhDs, both research pharmacists and graduates with a different background. When research centres were set up at the School in 1997, the Graduate School of Drug Research was established on the basis of an allocation from the then Research Academy. In the three years since then the Graduate School of Drug Research has been the framework for numerous scientific arrangements targeted at the PhD programme. The Graduate School has also established a total of 15 PhD scholarships co-financed by the School, the Research Academy and industry. Cooperation on graduate studies intensified relations between the School and other institutions tied to the centres and the drug industry. An important part of this close cooperation is the role of industrial researchers as co-supervisors for PhD students. In recognition of this activity Novo Nordisk A/S, represented by Professor Børge Diderichsen, Director of Corporate Research Affairs, granted DKK 450,000 to award the Novo Nordisk PhD Plus Prize in recognition of particularly talented PhD students or PhD graduates.

It is expected that the School’s highly active role in research training will be continued within the framework of the Drug Research Academy, a research training programme targeted at industry. Expected to be established in early 2002, the Drug Research Academy is based on co-financing from nine drug companies, the School and the Council on Research Training (FUR). The last part of the funding package is expected to be in place shortly. In close interplay with industry, the Drug Research Academy will provide the platform for training 36 PhD students over a period of about six years.

**Spotlight on The Royal Danish School of Pharmacy**

In the area of research training, the School has also earned wide recognition from its appointment as a Marie Curie Training Site, headed by Professor Sven Frøkjær. Winning this appointment from the European Commission in sharp competition with a number of other applicants will give the School a distinctive European dimension in research training through its hosting of a considerable number of European PhD research fellows.

It is gratifying for the School to find its place in the landscape of Danish and international education and research. This attention will encourage everyone at the School to do their utmost to live up to the recognition. To underpin the significance of the School’s role, Margrethe Vestager, then Minister of Education, visited the School in September and displayed in-depth knowledge and interest in the School during individual meetings with students, teachers and management. It was a memorable day.
September 1st 2000 - January 31st 2001

In retrospect

**September 2000:** Two-hundred-and-three eager new pharmacy students arrived to start their degree programme. Also new were the 2000 Degree Regulations, which introduction meant a complete restructuring of the pharmacology curriculum, a new programme module in pharmacotherapy, a theory of science course and the introduction of a bachelor’s degree – which provides no professional qualification.

The beginning of the academic year also saw the opening of the newly renovated student centre Alternativet. At the same time, plans were presented for the conversion of Vivis Minde, a facility previously used by the Department of Pharmaceutics but earmarked for student use after conversion.

The environmental chemists at the Department of Analytical and Pharmaceutical Chemistry and the Drug Delivery group at the Department of Pharmaceutics had reason to be pleased. A grant from the Apotekerfonden enabled the purchase of a mass spectrometer. ‘We’ve had Volkswagen spectrometers before, but this is a Rolls-Royce model!’ said Jette Tjørnelund from the Department of Analytical and Pharmaceutical Chemistry. The department will use the instrument to look for drug remains in the environment while the Department of Pharmaceutics will be investigating drug delivery of model prodrugs in blood, among other things.

Steen Honoré Hansen, professor, DSc (pharm.) and head of the Department of Analytical and Pharmaceutical Chemistry, celebrated 25 years of public service. He has always played an active role in the life of the School and continues to do so.

Tom Børsen Hansen, PhD student, was awarded first prize for his work *Science, general education and competence* and received DKK 40,000 from Margrethe Vestager, Minister of Education.

In *Plexus*, Elise Rinvar, pharmacy student, argued for greater specialisation within the pharmacy programme “to better prepare the School to meet competition from new emerging educations,” as she puts it.

Dr Hans Lennernäs, professor, Uppsala University, was appointed assistant professor at the Department of Pharmaceutics. The association with an international figure will strengthen the department’s pharmacokinetic research.

The month ended on a dramatic note when the area surrounding the School was closed off and special forces called in to arrest a man seen carrying a sawn-off shotgun in the DGR student council rooms facing the University campus. Six officers in bulletproof vests armed with pistols made the discovery that the man was in fact a woman, and the gun was a plastic replica bought for use at the annual initiation of new students.

**October 2000:** Wild, wilder, wildest: revelry – student revelry – reached such heights that Rector Birthe Jensen started getting requests to ban student parties at the School. “I hope everyone will do what they can to make sure this never becomes necessary,” the rector urged, suggesting that the students behave as though they were at home. “Then they might treat the School’s property in the same way.”

A survey among new students showed that they expect a high degree of IT-based teaching. After graduating, 8% expect to find jobs in a community pharmacy while 63% count on working in the pharmaceuticals industry. About 72% of new students are female.

Programme director Else Lemmich was adamant that there are no plans to specialise pharmacy education. “The programme is well attuned to the broad job market where graduates will find work.”
In connection with Lægemiddeldagene 2000, pharmaceutical theme days, Verner Andersen, community pharmacist, (lic. pharm.), was awarded The Danish Pharmaceutical Society’s gold medal in recognition of his ‘Special contribution to Danish pharmacy practice’.

Sven Erik Jørgensen from the Department of Analytical and Pharmaceutical Chemistry was appointed research professor.

Kristian Strømgaard, assistant research professor at the Department of Medicinal Chemistry, travelled to Slovenia to receive the Krka Award 2000. The prize is awarded to promising young scientists whose PhD work has made a significant contribution to chemical and pharmaceutical research. An impressive ceremony was staged for the presentation, which was transmitted by Slovenian TV.

November 2000: The natural product chemistry group at the Department of Medicinal Chemistry has attracted new young talent: Henrik Franzky, chemical engineer, and Dan Stærk, MSc and biochemist. Both in their thirties, the two men will replace pharmacists Else and John Lemmich. “Now that the pharmacy programme is so incredibly broad, we have to have specialists to teach the individual subjects. Pharmacists can’t teach everything as a matter of course. NMR spectroscopy is one example,” Dan Stærk points out.

Pharmacy student Jeppe Voss turned over chairmanship of the student council, DSR, to Rasmus Engelbrecht.

Jørn Bo Sørensen, civil engineer, took up the appointment of IT department head. “My first priority will be to get the network functioning properly,” he said.

Elections for posts on the collegiate bodies were held. DSR chairman, Rasmus Engelbrecht, commented on voter turnout: "Somewhere between an election to the church council and the American presidential election."

December 2000: On Speech Day, Rector Birthe Jensen explained that the ‘mass drain’ of pharmacists to the private sector is the reason for the School’s difficulty in attracting and retaining staff. "We should have transfer agreements like sports clubs." On the same occasion, the students’ award for ‘Teacher of the Year’ was presented to Ole Jungersen, associate professor, PhD, who at the time had already announced his intention to retire.

At the request of students, the Department of Social Pharmacy held a teaching day to discuss the communication of requirements, objectives and methods for the department’s teaching, as well as proposals to boost student motivation. "It was a very inspiring form of evaluation," Jacob Granne, pharmacy student and member of the Study Board, concluded afterwards.

Povl Krosgaard-Larsen, professor, DSc (pharm.), raised the issue of whether the School is ready to meet the challenges of the pharmacy field in the post-genomic period. His own response is that as a minimum the School must introduce new academic disciplines and carry out reforms in traditional areas.

January 2001: The Royal Danish School of Pharmacy and Pharmakon offered a new Specialisation in Community Pharmacy programme. Nineteen community pharmacists are enrolled in the new programme, which should be viewed as an upgrade and further development of the professional qualifications of community pharmacists.

The School’s associate and assistant professors met to discuss recruitment and the problems of retaining present staff members. The School’s academic staff pointed out that increasing administrative burdens and vacancies means less time for research. "We’ve reached the limit of what is acceptable," was the general opinion.

Bjarke Ebert, one staff member who decided after several years to leave the School for a job in the pharmaceutical industry, said the problem was not that staff decide to leave their positions at the School. "That’s simply a fact of today’s world. The real problem is the School’s inability to hire qualified people to fill these vacancies when they arise."

Chairman of the PhD committee since 1993, Henning Gjelstrup Kristensen, professor, DSc (pharm.), presided for the last time over the proceedings at the annual Research Day and handed over the reins to Erik Wind Hansen, associate professor, PhD. Research Day is the day on which the School’s PhD students present the results of their research.

Jens Dencker Christensen, associate professor, PhD, retired from the position of deputy rector, two years before the expiry of the term. In consequence, the Senate (Konsistorium) decided to abandon its former practice of electing a rector and deputy rector for staggered terms, a decision originally made to ensure continuity in the management of the School.
After the final deadline for nominations to the post of rector of the School, it became clear that Povl Krogsgaard-Larsen, professor, DSc (pharm.), would succeed Birthe Jensen, assistant professor, DSc (pharm.), who has held the position since 1988.

An era of 40 years at the Royal Danish School of Pharmacy finally came to an end: Alex Mehlsen Sørensen, assistant professor, DSc (pharm.), retired. Programme director, head of department and department board member are but a few of the many offices he held over the years.

February 2001: "We must eliminate the issue of the School’s future status as an independent institution from the political agenda by offering dynamic, multi-faceted teaching, research and research programmes," pronounced Povl Krogsgaard-Larsen, professor, DSc (pharm.), who had a couple of months yet to wait before taking up the office of rector. "And we must market the School far more actively."

It was clear that the School’s two multidisciplinary centres, NeuroScience PharmaBiotec and the Centre for Drug Design and Transport, would be closed at the end of the year. Despite positive evaluations and warm recommendations by the Research Council, a political decision was made to close down the centres owing to lack of funding.

Poul Kruse, assistant professor, DSc, and Niels Møller, community pharmacist, PhD, published the seventh volume of the work on the history of Danish pharmacies, De Danske Apotekers Historie. A separate volume on a similar subject, Apotekervæsenets historie i Danmark, was published. "I’ve never been able to refer to any comprehensive works on pharmacy and its many different perspectives. This book has made that possible!" said Poul Kruse.

A new minisite on the School’s website was launched for prospective students, who can find out all about the pharmacy programme and the main fields of pharmaceutical activity at www.dfh.dk/farmaceut.

March 2001: Should the School offer educational opportunities for postgraduates in subjects other than pharmacy? What should a Bachelor’s programme contain? Do the School’s research scientists have a duty to promote awareness of pharmacists and their role in society? Do the two new programmes at Århus and Odense pose a threat to the pharmacy programme? Should the School be renamed The Pharmaceutical University of Denmark? These were just some of the compelling topics discussed at the student politics weekend retreat.

Academic staff are not the only group tackling the problem of recruiting and retaining personnel. Laboratory technicians face the same dilemma. They are hoping a new pay agreement will help attract suitable candidates to fill vacant positions.

Only about 130 people felt it worth their while to attend the School’s open house event, 30% fewer than the previous year, when a similar decrease on the year before had also been noted. "The figures are very discouraging," said Ilse Fjalland, head of the Study Division.

Mikael Ankersen, MSc, defended his doctoral dissertation entitled Discovery of Peptidomimetic Growth Hormone Secretagogues.

April 2001: For the very last time, colleagues Birthe Jensen, rector, and Jens Dencker Kristensen, deputy rector, chaired a Senate meeting in these roles.

After four terms of election, it was time for Birthe Jensen, assistant professor, DSc, to step down. She made this comment about giving praise: "We’re not very good at showing our appreciation of each other. I urge everyone to try and make this a more important part of our everyday lives." And about the job of rector: "Challenging and exciting of course – and occasionally frustrating. But never boring!"

None of the School’s research teams featured on the list of those under consideration for funds granted by Større Tværgående Forskerggrupper to major multidisciplinary research teams. "There were no projects with a pharmaceutical objective among the selected teams. This unfortunately reflects the fact that pharmaceutical activities are only making a limited impact on the state-based research system," was the disappointed comment from Povl Krogsgaard-Larsen, professor, DSc.

For the second time, the School decided to advertise itself. A full-page ad appeared in the youth magazine Chili, encouraging readers to get ‘high’ on pharmacy – a comment on an article a month earlier in the same magazine under the headline: Get stoned at the pharmacy – it’s legal.

A survey about the services of the School’s pharmaceutical library showed general satisfaction among students, whereas researchers and PhD students did not feel the library met...
their information needs. However, researchers were very satisfied with other aspects of the library service.

**May 2001:** Bjarne Fjalland, associate professor, PhD, replaced his title as head of department with that of deputy rector.

At the official reception held to mark Povl Krogsgaard-Larsen’s appointment as rector, Børge Diderichsen, Director of Corporate Research Affairs, Novo Nordisk, presented a gift of DKK 250,000 to the School’s PhD students.

Villy Dahl Jensen was appointed to head up the School’s Budgeting and Accounting Division and gave the reassurance that the School did not appear to be on the verge of bankruptcy.

**June 2001:** The Senate (Konsistorium) discussed the proposed departmental structure. With a political question mark hanging over the future of the School, Povl Krogsgaard-Larsen, rector, believes it is crucial for the School to signal to the outside world that it is an institution that moves with the times. Not all departments, however, are equally enthusiastic about the new proposals, which include combining some departments. “Explain the advantages of the new structure first!” students demanded.

The School’s IT action plan was adopted. It proposed intensive efforts in selected focus areas, which have been granted DKK 500,000 in initial support.

The Teaching Committee assigned Merete Hende, MSc (engineering), the job of mapping the type and extent of IT teaching offered at the Royal Danish School of Pharmacy. The project was expected to be completed by the end of the year.

Henning Gjelstrup Kristensen, professor, DSc (pharm.), took over as chairman of The European Pharmacopoeia, which contains the quality requirements with which all drugs distributed in Europe must comply.

**July 2001:** The Danish Association of Pharmacists, Section D for pharmacy students, changed its name to Studenternetværket [The Student Network]. “We hope the new name will conjure up an organization with a purpose,” explained board member Jacob Granne. “And a common purpose and identity are more important today than ever before,” he pointed out.

Like all other state institutions, the Royal Danish School of Pharmacy now has to pay rent for the government-owned buildings it occupies. The School is therefore granted an appropriation to finance the rent based on the value-added concept, meaning the number of exams passed by students. The intention is that institutions will economise on space when they have to pay the cost of using it.

The front cover of the July issue of *American Journal of Physiology, Gastrointestinal and Liver Physiology* featured a picture created by Birger Brodin and Carsten Uhd Nielsen from the Department of Pharmaceutics using their confocal laser-scanning microscope. The accompanying article described new aspects of how peptide transport can be regulated.

**August 2001:** The School’s new webmaster set himself the task of making the School’s website more user friendly, dynamic and up to date.

Ole J. Bjerrum was made the School’s fourth professor of pharmacology since the first appointment in the late 1960s. He comes from a position as research advisor at Novo Nordisk.

At the graduation ceremony, the School noted that the past academic year had produced 165 graduates, the largest number ever in the School’s history. Women made up 70%.

After enrolling 194 new students, the School acknowledged that for the first time it had been unable to fill its admission quota of 200 places with new pharmacy students.

**September 2001:** The School was visited by a very well-prepared Margrethe Vestager, Minister of Education. During her visit she heard about student satisfaction with the programmes and the School, while academic staff told her about the School’s vulnerable position when staff leave for jobs in the pharmaceutical industry, and management described the School’s close research ties with industry. “Some people strike the right psychological chord with me. It’s far easier to help people who enjoy their work than people who’re forever whining,” said the minister to the enthusiastic representatives of the School.

On the occasion of the publication of the book *Eksamen – eller hvad?* [Exams – or what?], Arne Jacobsen, one of its authors, gave examples from the School of how students can pass an exam without understanding the material. One of his main points was that the examination form can be an obstacle to understanding.

The daily media highlighted plans put forward by Sonja Mikkelsen, Social Democratic member of the Folketing, Danish parliament, to set up pharmaceutical programmes in...
Odense and Århus. Both university cities were open to the proposal.

The Royal Danish School of Pharmacy was appointed a Marie Curie Training Site. "We are very pleased and proud," said Sven Frøkjær, professor, PhD, "because the nomination is based on the high requirements expected of research institutions." The Marie Curie Training Sites are part of an EU framework programme whose objective is to provide financial support to enable PhD students to complete a study period at selected research institutions in other EU countries as part of their education.

The Research Centre for Quality in Medicine Use celebrated its second birthday. "Although we aren't a centre in the DKK 50 million class, there's plenty going on at the centre," assured the centre’s day-to-day manager, Professor Ebba Holme Hansen.

October 2001: The School’s politically active students staged a variety of activities aimed at generating greater student interest in working on the collegiate bodies. "We need more students to get involved in discussions and work for a better School," said Rasmus Engelbrecht, chairman of the DSR student council.

Surveys held among the School’s new students showed that the prospect of employment in the public sector does not hold wide appeal. Not one single student specifically intends to find work in the public sector after graduation. The outlook is slightly better for community pharmacies, where 7% aim to pursue their career. Top favourite is the pharmaceuticals industry, where 65% of the young students hope to find jobs. At the same time, the survey showed that more prospective students are using electronic rather than print media to seek information about pharmacy education and thus get an idea of the School and what it has to offer.

November 2001: The debate about modifying the departmental structure was put on hold while the discussion about focus areas in teaching and strategically important research fields took pride of place. The disciplines of social pharmacy, clinical pharmacy, pharmacotherapy and pharmacology were pinpointed initially.

A new initiative teamed the Royal Danish School of Pharmacy with the Royal Veterinary and Agricultural University to hold an information day on the natural sciences for careers advisors from Danish upper secondary schools. "It’s always nice to get inside information that’s not available anywhere else," one careers advisor noted in the evaluation questionnaire.

The student body on the Study Board discussed ways of getting the most out of an in-training period at a pharmacy. The intention is not to accord lower priority to the professional aspects of a pharmacist’s job but rather to put the time available to better use.

Pharmacy student Anne Zimmermann replaced Rasmus Engelbrecht as the DSR student council chairman.

December 2001: DSR’s prestigious teaching prize, Teacher of the Year, went to Dan Stærk, assistant professor, Department of Medicinal Chemistry. The DSR jury’s reason: ‘His well-structured, well-prepared approach.’

On Speech Day, Rector Povl Krogsgaard-Larsen said that the goal of The Royal Danish School of Pharmacy was to meet the need to produce an adequate number of qualified pharmacists at graduate and PhD level. Povl Krogsgaard-Larsen rejected the idea of setting up new pharmaceutical programmes purely to solve the problem of the lack of pharmacists.

Pharmacy student Anne Zimmermann expressed the students’ regret at the change of government. “We had just convinced Margrethe Vestager [former Minister of Education] of the way universities should be run.”

Anders A. Jensen, assistant research professor at the Department of Medicinal Chemistry, received the Danish Academy of Natural Sciences PhD award for his dissertation Molecular Pharmacology of Family C G-protein Coupled Receptors.

Hans P. Merkle, professor of Galenical Pharmacy, Institute of Pharmaceutical Sciences, Swiss Federal Institute of Technology Zurich, was appointed assigned professor at the Department of Pharmaceutics.

The new student building was inaugurated with the anticipated festivity.

Mikael Begtrup, professor in organic chemistry, is the first to receive the newly founded Carlsberg Prize for Research. His commitment to teaching and maintaining young people’s interest in chemistry, together with his own great interest in passing on his knowledge, were some of the factors that led to the award committee’s nomination of Mikael Begtrup.

The School’s new website was launched.
The School’s research journal, Lægemiddelforskning, was published as usual, the only difference being that for the first time it was issued without the annual report. Instead of following the academic year, it was decided to publish the annual report for a calendar year in keeping with the financial statement. The change means that the present report covers the period from 1 September 2000 to 31 December 2001.

**BITS AND PIECES**

At the beginning of December 2001, the School’s website underwent changes in both appearance and structure. The facelift was a direct result of the School’s appointment of a webmaster. The visual change represents only the first stage of a longer process intended to expand and optimise the School’s Internet-related activities and bring them up to date.

Webmaster Henrik Korzen is responsible for the daily running of the School’s website at www.dfh.dk and Intranet. He will be ably assisted by Jesper Munck, information officer, as well as the various departments of the School.

Since his appointment in August 2001, the webmaster’s primary tasks have included increasing the body of information on site as well as modernising the layout and making it more uniform.

December 2001 saw the launch of the new technologically enhanced site, complete with new structure, new layout and more information. One particularly welcome feature is the opportunity to publicise more of the School’s many ongoing activities.

Other initiatives to improve information levels and introduce new services in the course of 2002 are already being planned and prepared. These include electronic teacher-student communication options, better electronic support for students such as e-learning web pages and discussion fora.

The site structure will be made increasingly dynamic as a basis for more flexible content and to facilitate the job of maintaining and updating existing pages. The website will also be better integrated with the School’s intranet.

One of our aims is to provide easier access to relevant information, for instance, by making as much information as possible available in electronic form for School and external users alike.

The process is already underway and in the years to come, the appearance and structure of the School’s website will gradually be modified in step with the need for an up-to-date site that continually develops new services.

**New look for the School’s website**
The Study Board  
covering the autumn term of 2000 and all of 2001

Jette Jacobsen, Programme Director, Associate Professor, MSc (pharm.)

The Study Board is responsible for the administration and development of the curriculum for the Master of Science degree in pharmacy. Within the framework accepted by countries of the European Union, the Board adapts and develops pharmaceutical studies to match employment opportunities in the pharmaceutical sector.

In the period under review, the Study Board has had three programme directors. Else Lemmich, associate professor at the Department of Medical Chemistry, was programme director in autumn 2000, followed by Peter Thygesen, associate professor, Department of Pharmacology in spring 2001. The undersigned, Jette Jacobsen, associate professor, has been the programme director of the Study Board since autumn 2001.

2000 DEGREE REGULATIONS

The first three terms governed by the 2000 Degree Regulations were held for the first time in the period under review. Teaching in the other terms in the period was carried out under the framework of the 1997 Degree Regulations.

Under the 2000 Degree Regulations, the theory of science module was held in the third term for the first time. The physical chemistry module was also carried out in a different form for the first time. The module was previously taught over two terms, but under the 2000 Degree Regulations is now taught in its entirety in the third term. The head of the course and participating students have evaluated the course on theory of science and the Study Board is awaiting the results. The Study Board wants related elements of the history of science, theory of science and scientific methods to be incorporated into the subjects taught in terms 4-8 under the 2000 Degree Regulations, and for an elective course on the subject to be offered as well. These course offerings supplemented by the teaching already provided in the basic pharmacy course will ensure a vertical core of teaching in the theory of science.

The Study Board has set up a Course Committee for the theory of science module. The committee will be responsible for ensuring that the course is held, evaluated and developed.

SUBJECT INTEGRATION

To increase subject integration and coordination between individual subjects and programme modules as well as to optimise the study plan for the 2000 Degree Regulations and develop the individual subjects, working groups either have been or are still set up in the following subjects: pharmacognosy, laboratory safety, toxicology, working environment and statistics. In addition at the request of the Senate at the end of the period under review, working groups were established with management participation in physical chemistry and pharmacotherapy, clinical pharmacy, pharmacology and social pharmacy. The working group in pharmacognosy concluded its work at the beginning of 2001 with suggestions for teaching changes and new textbooks, which will be implemented in the autumn term 2002. The working group in laboratory safety drew up a compendium on laboratory safety at the start of the autumn term 2001 for use in all laboratory training courses in the first three terms. In autumn 2001 the working group continued working on material concerning biological safety in the laboratory. This material will be incorporated in the compendium on laboratory safety, so that the combined compendium can be used for all laboratory training courses offered. The working group in toxicology and working environment prepared a proposal for a subject description of working environment. The subject description remains to be finalised and further work is being done on proposals to coordinate both major and minor elements of toxicology and the working environment.

WEIGHT ON EVALUATION

In order to ensure the quality and development of the pharmacy curriculum, the Study Board places great weight on evaluation. Both single and repeated evaluations are carried out and finalised in various ways. With regard to the 2000
Degree Regulations, the Study Board has decided to evaluate the following: new study modules, study modules subject to radical changes and study modules that have been allocated another place in the programme. Up to and including the period under review the evaluation was undertaken by the heads of the courses and participating students either in writing or orally. During the period under review, the Study Board drew up a questionnaire for use in subsequent evaluations in order to standardise the process.

Continuous and systematic evaluations are made at end-of-term meetings held four times a year. Teachers, student representatives, heads of department, representatives from the Study Board and representatives from Student Counselling attend these meetings. The individual study modules are discussed in terms of teaching, teaching materials, placement in the overall programme and coordination with other modules in the same term.

NEW REQUIREMENTS

After repeated requests from several sides, including students, the Senate finally adopted an Information and Communications Technology (ICT) action plan in 2001. The Teaching Committee under the Study Board works to ensure development in teaching methods and to provide a basis for such development. For example a teaching day is held every year for all teachers at the School. In the period under review the topic for the day was ICT in teaching. The committee has held several mini-meetings for teachers about new ways to teach and evaluate results. The Teaching Committee works with the ICT Committee in order to introduce ICT in teaching in the short term and thus the opportunity to change the entire evaluation process in the longer term.

In 2001 the Study Board adopted requirements for reporting laboratory training in pharmaceutical formulation and production, the project in pharmaceutical production, trainee periods at the pharmacy, alternative traineeships and elective study modules. The background for the requirement is the experience of the Study Board that many students apparently manage to complete large segments of their course of study – meaning that they carry out most or all of their laboratory training – without having taken the theoretical part of the module. When signing up for the study modules listed above, students must have passed a specified number of obligatory courses concluded by written examinations. The requirement has been introduced to raise the level of what students get out of the teaching and to ensure that the School expends its resources on students with the right prerequisites.

Every year the Study Board ensures that there is a wide and interesting selection of elective courses. This provides the opportunity to quickly establish new courses in order to meet current preferences both inside and outside the School. The Study Board approves students’ applications for credit transfer of electives from other institutions of higher education both in Denmark and aboard. The Study Board registers and draws up a list of all approved credit transfers so that other students can consult it for inspiration.

THOUGHTS AND IDEAS WILL BE CONTINUED

At the end of 2001, cooperation with six other institutions of further or higher education concerning DCN, Dansk Center for Naturvidenskabsdidaktik (the Danish centre for didactics and the natural sciences), was concluded, although the thoughts and ideas behind it will be continued in order to develop and improve teaching. One of the projects supported by DCN and entitled “Testing examination forms directed at understanding” is still ongoing. The aim of the project is to study whether current teaching, particularly in conjunction with laboratory training, is sufficiently directed at understanding, as well as to study whether existing examination forms adequately test the academic understanding of students within pharmacy subjects. If the results are negative, there are proposals for changes in both teaching and types of examinations.

In 2001 the students on the Study Board initiated a visionary debate that the new Study Board will continue in 2002. In order to maintain the high number of pharmacy students who graduate, we must continue to develop curriculum quality.
Pharmacotherapy – a new subject

Professor Helmer Ring Larsen
and Associate Professor Mette Rasmussen

The compulsory course in Pharmacotherapy is a joint venture between the Department of Pharmacology and the Department of Pharmaceutics. The course is an innovation as the teaching is practically entirely clinical-problem based. It was introduced in the fall term of 2000.

The aim of the course is to impact knowledge and insight to the students in etiology, symptoms and clinical signs as well as current therapy in the most important diseases with respect to incidence and prevalence. However, the emphasis is laid upon the rational use of drugs in general and in the particular.

The course consists of introductory lectures, clinical case presentations and workshops. During the course the students are presented with ten clinical cases in different disease categories in internal medicine, neurology and psychiatry. The treatment options and all aspects of therapy related to the clinical case presentation is worked on by the students in study groups of 3 to 6 during a one to two weeks period. The cases are then discussed in a two hours workshop with active participation of ca. 50 students at each session headed by one external and one internal teacher. In the workshop there is ample time to evaluate the pharmacotherapy and to come up with suggestions for treatment plans.

The course is finalized by a four hours written examination consisting of four clinical cases of which the students have to choose and answer three.

The clinical problem-based teaching is executed by 4 internal teachers and 12 – 16 external lecturers, mainly specialized physicians from the Copenhagen University Hospital.
Case

History:
The patient is a 57 years old man with a previously heavy alcohol consumption and cigarette smoking for many years. He has developed cirrhosis and chronic obstructive lung disease. He is admitted because of fatigue, dizziness and tar-coloured stools for two days. Because of previous bleeding from esophageal varices, ascites and edema he is currently treated with a non-selective beta-blocker and diuretics. He has been sleeping during most of the day, while on the other hand he has had difficulty sleeping at night because of nightmares. He is complaining of cold fingers and toes as well as headache and back pain. For his pain he receives paracetamol with limited effect.

Examination:
On admission the patient is in a poor general and nutritional condition, conscious but slow cerebrated. He has clinical signs of cirrhosis, ascites and edema. Arterial blood pressure is 90/60 mm Hg, pulse 52 and temperature 37°. Following transfusion of four units of blood, the patient appears to be in a stable condition. Gastroscopy reveals a large ulcer in the duodenal bulb, covered with fibrin and without sign of actual bleeding. Only small varices without signs of bleeding may be seen.

Current treatment:
Tbl. Propranolol retard 160 mg q.d.
Tbl. Furosemide 40 mg b.i.d.
Tbl. Thiamine 300 mg q.d.
Tbl. Paracetamol 1 g t.i.d
Tbl. Ferro-duretter 1 b.i.d.

Lab. Analyses:
hemoglobin 4.1 (8.0 – 11.0 mmol/l), WBC 6.4 (3.0 – 9.0 billion/l), platelets 75 (150 – 400 billions/l), coagulation factors II,VI,IX, X 0.65 (> 0.70), serum-albumin 31 (36.6 – 84.2 g/l), ALAT 95 (<150 u/l), serum-bilirubin 45 (4 – 22 µmol/l), serum creatinine 0.145 (0.060 – 0.130 mmol/l), serum sodium 128 (136 – 146 mmol/l), serum potassium 2.5 (3.2 – 4.7 mmol/l), serum ferritin 400 (12 – 300 µmol/l).

Problems to be solved:
1. Explain how you are going to treat the patient’s duodenal ulcer.
2. Discuss if a biopsy should be taken from this ulcer.
3. Indicate the cause of the tar-coloured stools (melaena).
4. Explain how you are going to optimise the diuretic therapy and correct electrolytes.
5. Discuss if there is any medication, which ought to be discontinued.
The School is managed in accordance with the Danish University Law which came into force on 1.1.93. This law provides a framework within which more detailed regulations are given by a statute – the present statute being passed in 1994. The School is run by a rector in collaboration with the Senate (Konsistorium) and Study Board. Assisted by the deputy rector, the rector is the School’s figurehead and responsible for day-to-day management. For the period covered by this report, the rectorate consisted of:

Rector, Professor, DSc (pharm.), Dr honoris causa Povl Krogsgaard-Larsen
Deputy rector, Associate Professor, PhD (pharm.) Bjarne Fjalland

The rector’s and the deputy rector’s period of office expires 30.4.2005. The rector and deputy rector are appointed for 4 years.

The Senate is the School’s leading organ. It is responsible for the School’s interests as an education and research institution and sets guidelines for long-term activities and development. Proposals regarding alterations to the School statute have to be approved first by the Senate and then by the Ministry of Research. In addition, the Senate has to approve the School budget. The Senate consists of the rector, who serves as chairperson, and 14 members, 2 of whom are external and appointed by Danmarks Forskningsråd (The Danish Research Council), Forskningsrådnes Formandskollegium (The Chairmen of the Research Councils) and Uddannelsesrådenes Formandskollegium (The Chairmen of the Education Councils).

ON 1. 2. 2002 THE SENATE CONSISTED OF THE FOLLOWING:

Chairperson:
Rector, Professor, DSc (pharm.), Dr honoris causa Povl Krogsgaard-Larsen

External members:
Vice President, Anders Buur
Pharmacist, PhD (pharm.) Peter Lund Nielsen

Management representatives:
Deputy rector, Associate Professor, PhD (pharm.) Bjarne Fjalland
Head of Study, Associate Professor, PhD (pharm.) Tommy Nørskov Johansen
Head of Department, Associate Professor, PhD (pharm.) Erik Wind Hansen
Head of Department, Associate Professor, PhD (pharm.) Margrethe Rømer Rassing
Head of Department, Professor, PhD. (scient.) Jerzy Jaroszewski

Scientific staff representatives:
Associate Professor, PhD (pharm.) Bente Gammelgaard
Associate Professor, PhD (pharm.) Lona Christrup

Technical-administrative staff representatives:
Head of Secretariat, MSc (econ.) Henning Bo Nicolajsen
Chief Laboratory technician Ulla Geneser

Student representatives:
Thomas Hagh Jensen
Helle Poulsen
Behzad Ghorbani
A series of committees have been established under the Senate: The Library Committee, Information Committee, PhD Committee, Stipendium Committee and Election Committee.

**THE STUDY BOARD**

The Study Board is responsible for the administration and development of the curriculum for the Master of Science degree in pharmacy. The Study Board consists of 50% scientific staff and 50% Master of Science students. On 1. 2. 2002, the Study Board consisted of:

**Scientific staff representatives:**
- Associate Professor, PhD (pharm.) Tommy Nørskov Johansen (Programme Director)
- Associate Professor, PhD (pharm.) Erik Bechgaard
- Associate Professor, PhD (pharm.) Ole Jans
- Associate Professor, PhD (pharm.) Søren Troels Christensen
- Associate Professor, PhD (pharm.) Uffe Kristiansen

**Student representatives:**
- Tove Kristiansen
- Anne Estrup

**Observers:**
- Administrator, MA Judith Christiansen
- Head of Library Services Alice Nørhede
- Head of Department, Associate Professor, MSc (pharm.) Ebba Holme Hansen
- Head of department, Prof., DSc. (pharm.) Steen Honoré Hansen

Behzad Ghorbani
Eva L. Schmidt
Rasmus Engelbrecht

**Observers:**
- Study Manager, MSc (pharm.) Ilse Fjalland.

**SCHOOL ORGANISATION**

The School’s five departments provide the framework for research, teaching and related activities. Each department is led by a head of department and a departmental board. The departments comprise:

- The Department of Analytical and Pharmaceutical Chemistry
- The Department of Pharmacology
- The Department of Pharmaceutics
- The Department of Medicinal Chemistry
- The Department of Social Pharmacy

A principal co-operation committee and safety committee have been established for the entire School. Local co-operation committees have been elected in four of the departments and in the Administration Department. The School’s Administration Department is run by the Administrator, whose areas of work and responsibility are defined by the Rector. The administration is divided into the secretariat, course administration and guidance, finance department, higher education administration system (VUE), IT department, technical services and building administration.
The complete 2001 financial statement for The Royal Danish School of Pharmacy is available in Danish only. For copies please contact the finance department at The Royal Danish School of Pharmacy or our website www.dfh.dk

**STAFF**

The Royal Danish School of Pharmacy employs staff to undertake teaching and research, run the library and handle the operation of buildings, administration and other tasks. In 2001 the number of full-time scientific staff was 190.6 - several of whom are PhD students and scientific staff hired on a temporary basis - a slight reduction compared to 2000, when the number was 194.3. The reduction is largely due to temporary vacancies in permanent positions.

<table>
<thead>
<tr>
<th>Staff employees (full-time)</th>
<th>2000</th>
<th>2001</th>
<th>2002 Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Scient. staff</td>
<td>Part-time and adm. staff</td>
<td>Technical staff</td>
</tr>
<tr>
<td>Teaching</td>
<td>47.7</td>
<td>11.5</td>
<td>79.3</td>
</tr>
<tr>
<td>Research</td>
<td>145.6</td>
<td>0.6</td>
<td>37.5</td>
</tr>
<tr>
<td>Fundamental (state)</td>
<td>81.1</td>
<td>0.3</td>
<td>13.9</td>
</tr>
<tr>
<td>State/priv. Subsidies</td>
<td>53.6</td>
<td>7.6</td>
<td>61.2</td>
</tr>
<tr>
<td>PhD education</td>
<td>0.6</td>
<td>0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Contact work</td>
<td>10.3</td>
<td>0.3</td>
<td>15.6</td>
</tr>
<tr>
<td>Library</td>
<td>7.3</td>
<td>7.3</td>
<td>7.7</td>
</tr>
<tr>
<td>Buildings</td>
<td>11.4</td>
<td>11.4</td>
<td>8.0</td>
</tr>
<tr>
<td>Administration</td>
<td>1.0</td>
<td>17.2</td>
<td>18.2</td>
</tr>
<tr>
<td>Others</td>
<td>1.0</td>
<td>1.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Other building expenditure</td>
<td>0.0</td>
<td>3.9</td>
<td>3.9</td>
</tr>
<tr>
<td>Total</td>
<td>194.3</td>
<td>12.1</td>
<td>153.7</td>
</tr>
</tbody>
</table>

The scientific staff includes professors, associate professors, assistant professors, PhD students etc.
The part-time staff includes external associate professors, teaching assistants etc.
The technical and administrative staff includes laboratory workers, office workers, technicians etc.

The diagram shows The Royal Danish School of Pharmacy gives high priority to educating PhD students. The aim is to fulfil the industrial need for good scientists and The Royal Danish School of Pharmacy’s need for a new generation of scientists to replace the scientific employees who plan to retire over the next 5-10 years.
Total expenditure rose from DKK 178.4 million to DKK 214.3 million, primarily due to the new practice of paying rent for our buildings. The rental costs of DKK 30.5 million are cancelled out by rental income of DKK 31.5 million.

Research costs fell by DKK 3.9 million to DKK 85.8 million. The reduction is in the grant-funded area, which had extraordinarily high expenses in 2000 due to a change in accounting principles. Thus the reduction in costs does not represent a reduction in research activities.

Research income derives from several financial sources. The table "Revenues for research work" shows that the bulk of income derives from the state appropriation for basic research. Research revenues have risen from DKK 82.6 million to DKK 98.0 million, or an increase of DKK 15.4 million. Again the increase is tied to the change in accounting principles adopted in 2000, which resulted in extraordinarily low revenues for that year. The increase in the basic government appropriation for research is connected to a multi-year agreement with the Ministry of Science, Technology and Innovation, as well as the incorporation of the Royal Danish School of Pharmacy’s "Centre for Drug Design and Transport".

The Royal Danish School of Pharmacy’s financial performance for 2001 is shown in the table "Financial results 2001". An operating surplus of DKK 5.6 million accrues to a total of DKK 27 million to be transferred and used to implement strategic objectives in the years ahead. However, it has not yet been decided whether we will be allowed to keep it all. Special approval from the Ministry of Finance is required.
Since 1994 the number of students enrolled annually has increased to about 200. Figure 1 shows how many students were enrolled at the School during the period 1991-2001. The number indicates how many new students were enrolled as of 1 October in the year of enrolment. The average age of students enrolled as of 1 September 2001 was 21.9.

For the first time in many years the School has been unable to fill its admission quota. Thus as of 1 October 2001 only 186 students were enrolled. The reduction in enrolments is due to a 35% decline in the number of applicants to pharmaceutical studies over the past three years. Thus since spring 2001 the School has significantly heightened its focus on recruitment, including promoting the School's image to its primary target group of potential applicants, which is graduates of upper secondary school interested in chemistry and biology.

The majority of the students are admitted 0-2 years after graduation. This is seen as highly satisfactory and appropriate for educations based on the natural sciences.

As a result of the increase in enrolments since 1994, the School’s total student population has also risen significantly from 925 students in 1991 to 1102 students in 2001. The student population is counted on 1 October and figure 2 shows the population for the period 1991-2001.

The School’s production of MSc pharmacy graduates is shown in figure 3. The production of graduate pharmacists...
has increased in step with the increased admission of new students. In future we expect an average production of 150-160 MSc graduates annually, corresponding to a completion rate of 75-80%. This is considered highly satisfactory in comparison with other types of university studies. In the academic year 2000/2001 the School produced 165 graduates, the largest number of MSc pharmacy graduates in the history of the School. The pharmaceutical job market desperately needs MSc and PhD graduates in pharmacy, and thus offers excellent job prospects for both groups.

The average age of MSc pharmacy graduates in 2000/01 was 26.8, which also indicates that the average study period continues to be low: 5.9 years. 76% of graduates earned their MSc degree in six years or less, which is considered highly satisfactory.

**SINGLE COURSE STUDENTS**

The School offers students wishing to take single courses two enrolment options, either as “merit students” (from other institutions of higher education), or under the “open education scheme” with partial user payment. The School has required partial payment since the autumn term of 1995. The School’s selection of single courses covers all subjects – both compulsory and elective – under the Master of Science in pharmacy programme.

The table shows the development in number of single course students enrolled in the period 1991/92 - 2000/01. The considerable reduction in number of merit students in 2000/2001 relative to previous years is due to a special agreement with the University of Copenhagen that ran from 1996/1997 to 1999/2000. The special agreement allowed physical education students from the University to enrol in our basic course on statistics. If we disregard the effect of the special agreement, there has been no significant difference in the number of single course students in recent years.
About half of the single course students are enrolled in accordance with cooperation agreements with the Faculty of Science of the University of Copenhagen and the Royal Veterinary and Agricultural University concerning the two-year MSc course in environmental chemistry. The other single course students follow a very wide spectrum of our compulsory and elective subjects.

INTERNATIONAL STUDENT EXCHANGE

There are wide variations in European health care systems, which also differ from the American and Australia systems, for example. Similarly, pharmacy education also varies from country to country. Ongoing discussions focus on the opportunities to promote greater uniformity in education, particularly within Europe, and we are looking at how pharmacists are put to use in other countries, and what we can learn from that. Student exchanges are one of the ways we can contribute to constructive and well-founded discussion on the subject. The School is an eager participant in debate and supports student exchange.

One of the areas that reflect the School’s commitment to student exchange is funding. The School spent a total of DKK 250,000 in financing foreign travel, corresponding to approx. DKK 10,000 per student. Other sources of foreign travel financing are the EU Commission’s Socrates/Erasmus programme in the amount of approx. DKK 40,000 and the Scandinavian Nordplus in the amount of approx. DKK 20,000. These funds are returned if students do not utilise the exchange agreements.

In 2001 student exchanges took place in the following parts of the world:

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of students abroad</th>
<th>Number of visiting students</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>USA</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Australia</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

During the exchange the majority of students, both those studying abroad and visiting students, work on their theses, which are often based on projects carried out in laboratories.

At present the School offers only one course in English, International Health Care. We have many enquiries from foreign students about taking courses here, but the language barrier often rules out the opportunity for students to visit for the purpose of taking classes. Students writing theses, however, can often manage with English, which is spoken by advisors and most people in the laboratories.

Students whose travel has been subsidised by the School are required to fill in a questionnaire at the end of their stay abroad. Without exception, they always highly recommend foreign study to their fellow students. Any other advice they might have on the basis of their experiences abroad is passed on to the international office of the School and thus to other students. A corresponding questionnaire for students visiting us is being prepared.
Research Centres at The Royal Danish School of Pharmacy

NEUROSCIENCE PHARMABIOTEC CENTRE
The Neuroscience PharmaBiotec Centre comprises three sub-centres, two of which are coordinated by project managers from H. Lundbeck A/S and NeuroSearch A/S. The third sub-centre consists exclusively of academic research groups and is coordinated by the School of Pharmacy. The Centre is managed overall by the School of Pharmacy.

The aim of the research projects is to produce results that the pharmaceutical industry may transform into drug development projects. The academic research teams do not, however, target their efforts towards development projects or problems specific to the industry. Their aim is high level international research. Results considered to have special potential are patented and subsequently published. It is increasingly acknowledged that only results of high scientific caliber push the boundaries of modern science and provide value in this context. Both academia and the pharmaceutical industry are aware that there is no special benefit in university scientists setting out to solve specific developmental problems.

Research scientists from academic institutions and the pharmaceutical industry share the job of supervising PhD students, most of whom spend an internship period of varying length in industrial laboratories. The next generation of research scientists will, as far as possible, be trained to make a solid contribution to innovative pharmaceutical research in partnership with other academic groups.

Although the Neuroscience PharmaBiotec Centre was positively evaluated by an international panel of experts the Centre was terminated by political decision at the end of 2001.

CENTRE FOR DRUG DESIGN AND TRANSPORT
The "Centre for Drug Design and Transport" is an extramural research centre established in November 1997 as a four-year programme and therefore terminated in October 2001. The centre is based on seven Danish research groups and funded by the Danish Medical Research Council, several Danish pharmaceutical companies and the participating academic institutions. Professor Sven Frøkjær is the head of the centre.

The Royal Danish School of Pharmacy was granted additional funding due to a positive evaluation by international referees. In theory the additional funds will allow the most promising activities of the centre to be continued for up to another four-year period.

The overall objective of the "Centre for Drug Design and Transport" has been to study new principles for the design and transport of drug substances. The goal is pursued by a highly integrated collaboration between scientists specialised in different disciplines related to drug research and development. The centre covers the follow areas: organic chemistry, medicinal chemistry, membrane biophysics, drug delivery pharmacology and clinical research. The participating partners are The Royal Danish School of Pharmacy, Technical
University of Denmark, PET Centre, Aarhus University Hospital, Centre for Imaging Diagnostics and Medico-technique, State University Hospital, Department of Dermatology, University Hospital, Gentofte, and Aalborg A/S, H.Lundbeck A/S, Leo Pharmaceutical Products A/S, NeuroSearch A/S, Novo Nordisk A/S and Nycomed Pharma A/S.

The education and training of pharmaceutical scientists in a thoroughly interdisciplinary manner is a major activity of the centre and involves scientists from both academia and industry.

FKL – THE RESEARCH CENTRE FOR QUALITY IN MEDICINE USE

The Research Centre for Quality in Medicine Use (FKL – Forskningscenter for Kvalitetsfællesskabet Lægemiddeludstillingsvæsen) was established in 1999. The overall objectives of the projects are to provide scientific evidence to optimise the profession’s pharmacotherapy and the population’s medicine use. Hereby, the research contributes to improved public health and quality of life as well as improved economy of the individual and the society.

To achieve the Centre’s objectives, the approach has to be multidisciplinary, inter-professional and trans-institutional. The researchers involved in the Centre’s activities represent several disciplines including clinical pharmacy, epidemiology, general practice, health economics, health policy, public health, social pharmacy and sociology. Groups from the following academic and public institutions participate in the Centre: Pharmakon, the Danish College of Pharmacy Practice, the County of Vestsjaelland, the County of Funen, Copenhagen County, the National Institute of Public Health, Copenhagen University, the University of South Denmark, Aalborg University, the University Hospitals Centre for Nursing and Care Research (UCSF), the Institute of Rational Pharmacotherapy and NEPI – the Swedish Network for Pharmacoepidemiology. The Centre is managed by the School of Pharmacy and directed by Professor Ebba Holme Hansen of the Department of Social Pharmacy.

The Centre for Quality in Medicine Use embraces a range of projects. The major share of the Centre’s resources has been allocated to projects about pharmacy practice. The Pharmacy-University Study has broken new grounds by establishing an action research triangle which unites community pharmacists, pharmacy students and researchers in an effort to uncover medicine related problems and information needs of patients suffering from angina pectoris, asthma and diabetes. Another pharmacy practice project is focusing on self-care and self-medication. After piloting, this project has reached the intervention phase.

Another group of Centre studies analyses the Danish population’s medicine use through data obtained from questionnaire based surveys of large representative samples of adolescents and adults.

Macroperspectives on medicine supply is a thematic area looking into e.g., deregulation of the pharmacy sector and the views of different interested parties. The new medicine consumer is an innovative substudy analysing the users’ perspectives in relation to global consumer trends.

Further centre projects deal with the user’s perspective on medicine use. Under this umbrella a Danish team is coordinating a strong international multidisciplinary research group. Much interest in Danish health care is devoted to the quality of physicians’ prescribing.

The FKL-centre carries out qualitative and quantitative analyses to establish a research foundation for interventions into GPs’ prescribing.

The 1991 Pharmacy Foundation has been the major external sponsor of the Centre’s activities, but funding is also provided by the Foundation for Financing Research in General Practice and in the Health Service (The Research Foundation), the Health Insurance Fund, the Danish Medical Research Council’s Regional Fund for Eastern Denmark and various private funds.
The Danish PhD degree is a three-year programme comprising a research project, courses at PhD level, teaching and communication activities, an independent PhD thesis and subsequent defence. It is customary for PhD students to integrate a three to six month study visit to a research institute outside The Royal Danish School of Pharmacy during the course of the degree programme, preferably abroad.

As of 1 October 2001, a total of 131 students were enrolled at the school. The distribution by gender was relatively constant in 2000/2001, 1999/2000 and 1998/1999, i.e. 49% women and 51% men. We find this gender distribution satisfactory.

The age of PhD students at the time of enrolment varies slightly. In 2000/2001, the average age at the time of enrolment was 29.2 years; 27.6 years for the PhD students employed at the School. Among the enrolled PhD students, pharmacists account for about 60%, chemists and biologists 23% and engineers 8%. About 8% of the PhD students hold a MSc degree from abroad.

The School provides financial support to 56 of the 131 PhD students, in part through its own scholarships and in part through co-financed scholarships. The majority of the PhD students are fully or partly funded by external co-operators. There is a great need for PhDs in industry and thus also for external funding.
The 131 PhD students are enrolled as follows:

21 (16%) at the Department of Analytical and Pharmaceutical Chemistry
23 (18%) at the Department of Pharmacology
35 (27%) at the Department of Pharmaceutics
43 (33%) at the Department of Medicinal Chemistry
9 (7%) at the Department of Social Pharmacy.

PhD degrees conferred

From 1 October 2000 to 30 September 2001, PhD degrees were conferred on 29 PhD students. In addition, one person registered in 2000/2001 for assessment without matriculation. The students were enrolled for 3 years and 11 months on average, a decrease compared to 1998/99 and 1999/00. This development is satisfactory as the enrolment period is counted from the first day of enrolment to the day the PhD degree is conferred. The average duration of enrolment is affected by maternity leave, for one, but other unknown factors may contribute as well.

The majority of the PhD graduates from the School are employed by the pharmaceutical industry, many even before their PhD degree is conferred.

PHD COURSES

From 1 September 2000 to 31 December 2001 the school taught 18 courses specifically intended for PhD students.

Participants were primarily PhD students from the School and other Danish universities and young scientists from the pharmaceutical industry. Efforts are made to increase the international participation in the PhD courses, as well as the Danish participation in PhD courses taught by partners in the international ULLA collaboration.

ULLA SUMMER SCHOOL

The fifth ULLA Summer School was held in London in August 2001. The summer school is organised every other year by the ULLA collaboration consisting of the Faculty of Pharmacy (University of Uppsala), the School of Pharmacy (University of London), Leiden/Amsterdam Centre for Drug Research (University of Leiden and Vrije Universiteit Amsterdam), the Faculty of Pharmacy (University of Paris South), and The Royal Danish School of Pharmacy.

A total of 124 PhD students and young scientists from industry participated in the summer school in London, 26 of them PhD students from the School. Teachers from ULLA institutions also participated, nine of them from Copenhagen. The ten-day summer school offered 32 courses, each lasting from one to two days. Posters by participants were accessible throughout the Summer School.

A symposium was organised on "Non-Viral Gene Delivery".

RESEARCH DAY

Every year the PhD Study Board organises a Research Day in order to give PhD students the opportunity to make an oral presentation or present a poster about their research project. Research Day was held on 12 January in 2001. Professor David Ganderton from the University of Bath was the guest speaker.

NEW MINISTERIAL ORDER ON THE PHD DEGREE

In 1999 the PhD programme in Denmark was evaluated by the Danish Research Council. The final evaluation report was discussed by the PhD Study Board, which found recommendations made in the evaluation well in keeping with the School’s current policies. The report has given rise to a discussion about the strategic goals of the pharmaceutical PhD programme, in particular with regard to the international dimension.

In June 2001 the PhD Study Board discussed the draft of a new ministerial order on the PhD programme and the PhD degree. We are waiting for the new ministerial order from the Ministry.
Graduate School of Drug Research

The research training school, Graduate School of Drug Research, was established in September 1998 on the basis of a 5-year grant from the Danish Research Academy. The aim of the Graduate School is to train the next generation of drug researchers. Emphasis is placed on integrated research training with the aim of performing innovative drug research in an interdisciplinary and highly integrated research environment. The industrial perspective of drug research is essential to the study program. The Graduate School was at the establishment primarily based on the activities of two research centres, The Neuroscience Centre (1997-2001) and The Centre for Drug Design and Transport (1997-2001), although participation is open to all PhD students who meet the school’s requirements.

From December 1998 to August 2001, The Graduate School initiated 17 PhD studentships co-financed by the Royal Danish School of Pharmacy, The Danish Research Academy and the pharmaceutical industry. The Graduate School grants financial support to PhD courses at the School of Pharmacy to ensure the participation of leading international scientists as lecturers.

The Graduate School has been involved in the organization and hosting of a series of mini-symposia, often in collaboration with the above-mentioned research centres or scientific associations. During the period January-December 2001 the Graduate School of Drug Research organized 7 mini-symposia. All of these symposium arrangements were widely announced and were attended not only by PhD students who enrolled at the Graduate School but also by a number of other PhD students and scientists from both academia and the drug industry. One of these mini-symposia was organized as a two-day arrangement at Sore Storkro with Dr. Wolfgang Froestl, Novartis Pharma AG, Basel as the keynote speaker. All of the mini-symposia organized at the Royal Danish School of Pharmacy were also very well attended, and in agreement with the overall goal of the Graduate School, these arrangements are increasingly attracting junior scientists from Northern Germany and from the other Scandinavian countries. This international interest probably reflects that most of the speakers at the symposia are international recognized scientists. Titles of the mini-symposia organized at the Royal Danish School of Pharmacy were “Applied Heterocyclic Chemistry”, “Receptor Structure and Function”, “ADME in Drug Research”, “Drug Design Copenhagen 2001”, “Reactive Drug Metabolites - their formation, reactions, and the toxicological conse-

PHD DEGREES FROM 1 SEPTEMBER 2000 TO 30 SEPTEMBER 2001

Jens Buchardt
Supervisors: Associate Professor Per Vedesa, Department of Medicinal Chemistry, Professor Morten Meldal, Carlsberg Laboratory and Dr Niels Tækker Foged, Carlsberg Laboratory
Enrolled at Department of Medicinal Chemistry.

Karin Löwenstein Christensen
Supervisors: Professor Henning Gjølstrof Kristansen, Department of Pharmaceutics and PhD Gitte Pommergaard Pedersen, Leo Pharmaceutical Products
Enrolled at Department of Medicinal Chemistry.

Gerda Marie Friedrichsen
Supervisors: Professor Mikael Begtrup, Department of Medicinal Chemistry, Associate Professor Per Vedesa, Department of Medicinal Chemistry, Associate Professor Bente Steffansen, Department of Pharmaceutics and MSc Palé Jakobsen, Novo Nordisk A/S
Enrolled at Department of Medicinal Chemistry.

Patrick Garibay
Supervisors: Associate Professor Per Vedesa, Department of Medicinal Chemistry, Professor Mikael Begtrup, Department of Medicinal Chemistry and Chemist Thomas Haeg-Jensen, Novo Nordisk A/S
Enrolled at Department of Medicinal Chemistry.

Thomas Groth
Supervisors: Associate Professor Per Vedesa, Department of Medicinal Chemistry and Professor Morten Meldal, Carlsberg Laboratory
Enrolled at Department of Medicinal Chemistry.

Steen Gyldenærne
Supervisors: Associate Professor Sven Erk Jørgensen, Department of Analytical and Pharmaceutical Chemistry, Associate Professor Bent Halling-Sørensen, Department of Analytical and Pharmaceutical Chemistry and Research Manager Jørgen Jacobsen, The Danish Institute of Agricultural Sciences
Enrolled at Department of Analytical and Pharmaceutical Chemistry.
quences" and "From Receptor to Prescription in Clinical Neuropsychiatry".

Dr. Sonata Krikstolaityte, Kaunus University, Latvia spent a 6-month period at the Graduate School working on a project focusing on the conversion of wasp polyamine toxins into pharmacological tools and potential drugs. During this research stay Professor Algirdas Sackus, Kaunus University, Latvia visited the Graduate School as a guest scientist a number of times. Dr Mogens Nielsen was associated with the Graduate School for a number of months. Mogens Nielsen played a key role in the organization of one of the PhD courses "In Vivo Neuropharmacology" and was involved in the planning of the PhD course "Cellular Pharmacology and Toxicology". In addition, he organized and carried through a very well attended study circle on fluorescence technologies in pharmacological and biomedical research.

A number of internationally recognized scientists visited the Graduate School as guest lecturers, notably Professor Leo Hösi, University of Basel and Vice President, Dr Claus Braestrup, H. Lundbeck A/S.

Based on two major grants to the Graduate School of Drug Research from Novo Nordisk A/S, the Graduate School was in a position to grant 3 PhD’s, who had completed very successful PhD projects, Novo Nordisk PhD Plus Prizes. One of the prize recipients also received the PhD Prize of the Danish Academy of Natural Sciences.

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### PhD Training

#### Tina Weinkauf Hahn

**PhD Thesis:** Acetaminophen (paracetamol). – Pharmacokinetics and Analgesic Effect in Postoperative Patients.

**Supervisors:** Associate Professor Mette Rasmussen, Department of Pharmaceutics, Associate Professor Janne Rømsing, Department of Pharmaceutics and Dr.med. Steen W. Henneberg, Rigshospitalet and Research scientist Helle Angelo, Bispebjerg Hospital Enrolled at Department of Pharmaceutics.

#### Henrik Hegnbo Hansen

**PhD Thesis:** The Impact of Brain Injury: Involvement of the System of Endocannabinoid Ligands and Receptors.

**Supervisors:** Associate Professor Harald S. Hansen, Department of Pharmacology and Professor Steen Honoré Hansen, Department of Analytical and Pharmaceutical Chemistry

Enrolled at Department of Pharmacology.

#### Birgit Sehested Hansen


**Supervisors:** None.

Enrolled as an independent student.

#### Anders Asbjørn Jensen

**PhD Thesis:** Molecular Pharmacology of Family C G-Protein Coupled Receptors.

**Supervisors:** Professor Povl Krogsgaard-Larsen, Department of Medicinal Chemistry, Research Scientist Hans Brüuner-Osborne, Department of Medicinal Chemistry and Head of department Christian Thomsen, H. Lundbeck A/S

Enrolled at Department of Medicinal Chemistry.

#### Anette Gemal Jensen

**PhD Thesis:** Quality Assessment of Herbal Remedies. Focus on Phytopharmaceuticals Containing Hypericum perforatum L. and Ginkgo biloba L.

**Supervisors:** Professor Steen Honoré Hansen, Department of Analytical and Pharmaceutical Chemistry, Associate Professor Lene Gudiksen, Department of Medicinal Chemistry, and Head of Department Elsebet Østergaard Nielsen, NeuroSearch A/S

Enrolled at Department of Analytical and Pharmaceutical Chemistry.

#### Henrik Hegnbo Hansen

**PhD Thesis:** The Impact of Brain Injury: Involvement of the System of Endocannabinoid Ligands and Receptors.

**Supervisors:** Associate Professor Harald S. Hansen, Department of Pharmacology and Professor Steen Honoré Hansen, Department of Analytical and Pharmaceutical Chemistry

Enrolled at Department of Pharmacology.

#### Mads Skak Jensen

**PhD Thesis:** Cyanide Toxicology – Insights into Mechanisms of Action and Antidotal Strategies.

**Supervisors:** Associate Professor Erling Sonnich Thomsen, Department of Analytical and Pharmaceutical Chemistry and Professor Niels C.B. Nyborg, Novo Nordisk A/S

Enrolled at Department of Analytical and Pharmaceutical Chemistry.
Simon Bjerregaard Jensen  
Supervisor: Professor Sven Frøkjær, Department of Pharmaceutics, Associate Professor Charlotte Vermehren, Department of Pharmaceutics and Dr Ingrid Söderberg, Leeds University  
Enrolled at Department of Pharmaceutics.

Pia Knudsen  
Supervisors: Professor Ebba Holme Hansen, Department of Social Pharmacy and Associate Professor Janine Morgall, Department of Social Pharmacy  
Enrolled at Department of Social Pharmacy.

Hasse Kromann  
Supervisors: Professor Povl Krogsgaard-Larsen, Department of Medicinal Chemistry, PhD Frank A. Skak, NeuroSearch A/S and Associate Professor Tommy N. Johansen, Department of Medicinal Chemistry  
Enrolled at Department of Medicinal Chemistry.

Iben Larsson  
Supervisors: Professor Henning Qvistrup Kristensen, Department of Pharmaceutics and Associate Professor Jam Møller-Sørensgaard  
Enrolled at Department of Pharmaceutics.

Karsten Lindhardt  
Supervisors: Associate Professor Erik Bechgaard, Department of Pharmaceutics, Professor Sveinbjörn Gisarson, Iceland University, Head of Department Hanne Wulff Nielsen, Nycomed Pharma A/S and Head of Department Erik Däänksen, Leo Pharmaceutical Products  
Enrolled at Department of Pharmaceutics.

Hans-Christian Holten Lützhøft  
Supervisors: Associate Professor Sven Erik Jørgensen, Department of Analytical and Pharmaceutical Chemistry and Associate Professor Bent Halling-Sørensen, Department of Analytical and Pharmaceutical Chemistry  
Enrolled at Department of Analytical and Pharmaceutical Chemistry.

Rasmus Worm Mortensen  
Supervisors: Professor Steen Honoré Hansen, Department of Analytical and Pharmaceutical Chemistry, Associate Professor Jette Tjønelund, Department of Analytical and Pharmaceutical Chemistry, Associate Professor Claus Comett, Department of Analytical and Pharmaceutical Chemistry and PhD Ulla Grove Sidholm, Novo Nordisk A/S  
Enrolled at Department of Analytical and Pharmaceutical Chemistry.

Addmore Ndekha  
Supervisors: Professor Ebba Holme Hansen, Department of Social Pharmacy, Dr. Godfrey Woelk, University of Zimbabwe, Associate Professor Per Mølgaard, Department of Medicinal Chemistry and Senior Advisor Peter Furu, Danish Bilharziasis Laboratory  
Enrolled at Department of Social Pharmacy.

Annette Sams Nielsen  
Supervisors: Associate Professor Inger Janssen-Olesen, Department of Pharmacology and Professor Jan Engberg, Department of Pharmacology  
Enrolled at Department of Pharmacology.

Carsten Uhd Nielsen  
Supervisors: Associate Professor Bente Steffansen, Department of Pharmaceutics, Professor Sven Frøkjær, Department of Pharmaceutics, Research Associate Professor Birger Brodin Larsen, Department of Pharmaceutics and Chemist Mitchell E. Taub, Novo Nordisk A/S  
Enrolled at Department of Pharmaceutics.

Pernille Bondeskov Nielsen  
Supervisors: Professor Henning Gjelstrup Kristensen, Department of Pharmaceutics, Associate Professor Anette Müllertz, Department of Pharmaceutics and Thomas Norling, Dumex-Alpharma  
Enrolled at Department of Pharmaceutics.

Peter Aadal Nielsen  
Supervisors: Professor Tommy Liljefors, Department of Medicinal Chemistry, Professor Jerzy Jaroszewski, Department of Medicinal Chemistry, Associate Professor Per-Ola Norrby, Department of Medicinal Chemistry and Head of Department Klaus Gundertofte, H. Lundbeck A/S  
Enrolled at Department of Medicinal Chemistry.

Torben Rasmussen  
Supervisors: Associate Professor Per-Ola Norrby, Department of Medicinal Chemistry, and Professor Mikael Begtrup, Department of Medicinal Chemistry  
Enrolled at Department of Medicinal Chemistry.

Anette Graven Sams  
Supervisors: Professor Povl Krogsgaard-Larsen, Department of Medicinal Chemistry and Professor Morten Meldal, Carlsberg Laboratory  
Enrolled at Department of Medicinal Chemistry.

Majid Sheyhkzade  
Supervisors: Professor Niels C. Berg Nyborg, Novo Nordisk A/S  
Enrolled at Department of Pharmacology.

Ulrik Sidenius  
Supervisors: Associate Professor Bente Gammelgaard, Department of Analytical and Pharmaceutical Chemistry, Associate Professor Ole Jøns, Department of Analytical and Pharmaceutical Chemistry and Professor Ole Farver, Department of Analytical and Pharmaceutical Chemistry  
Enrolled at Department of Analytical and Pharmaceutical Chemistry.

Evaluation of the oral presentations at the Research Day 2001. Former PhD study Administrator Eva Horn Møller, the new Chairman of the PhD Committee Erik Wind Hansen and the former Chairman Henning Gjelstrup Kristensen. Both Erik Wind Hansen and Henning Gjelstrup Kristensen have been members of the PhD Committee since 1993.

Gitte Elgaard Terp  
Supervisors: Associate Professor Flemming Steen Jørgensen, Department of Medicinal Chemistry and Chemist Inge Theger Christensen, Novo Nordisk A/S  
Enrolled at Department of Medicinal Chemistry.

Marianne Willert  
Supervisors: Professor Povl Krogsgaard-Larsen, Department of Medicinal Chemistry and Professor Morten Meldal, Carlsberg Laboratory  
Enrolled at Department of Medicinal Chemistry.

Niels Hønberg Zangenberg  
Supervisors: Professor Henning Gjelstrup Kristensen, Department of Pharmaceutics, Associate Professor Anette Müllertz, Department of Pharmaceutics and Managing Director Lars Hovgaard, Galenica Aps  
Enrolled at Department of Pharmaceutics.

Daniel Brunicardi Timmermann  
Supervisors: Professor Arne Schousboe, Department of Pharmacology, Associate Professor Uffe Kristensen, Department of Pharmacology  
Enrolled at Department of Pharmacology.
Specialisation in Community Pharmacy

Head of the Study Board for Specialisation in Community Pharmacy, Associate Professor, Poul R. Kruse, DSc (pharm)

The educational scope of The Royal Danish School of Pharmacy is not restricted to the curriculum for the MSc degree in Pharmacy and PhD programmes. The School also sees it as its duty to provide further and continuing education programmes for pharmacists, including those working in community pharmacies. The School has therefore been actively involved in developing systematic continuing education for community pharmacists ever since programmes were introduced in 1966. Similarly, the School is represented on the Advisory Committee on Pharmaceutical Training, EU, one of whose aims is further education for community pharmacists. The School is keen to help promote the use of pharmaceutical knowledge throughout the health care sector.

Recent years’ recommendations by EU and WHO advisory committees on pharmaceutical training have prompted discussions along these lines between the School and professional authorities and organisations, including Pharmakon a/s, which runs the established pharmaceutical continuing education programme. In this connection, the question of the need for specialisation in community pharmacy was raised. As a result of these talks, representatives from the Department of Social Pharmacy and Pharmakon a/s prepared a proposal for regulations for a specialised programme that complies with the recommendations of the EU’s advisory committee. The professional authorities and organisations expressed their support for the proposal during subsequent discussions.

It was against this background that the Senate of The Royal Danish School of Pharmacy decided in April 2000 to introduce a specialised programme in community pharmacy at the School, in cooperation with Pharmakon a/s and to appoint a study board for the new programme with representatives from all sectors of the pharmaceutical profession. In June 2000, Apotekerfonden af 1991 provided a grant to develop the specialised programme and establish a secretariat, making it possible to launch the programme on 1 January 2001.

The specialised programme is intended for community pharmacists with at least two years’ working experience. Based on the pharmacist’s professional knowledge and practical experience, the programme aims to supplement pharmacists’ pharmacological, managerial and personal qualifications. On completion of the programme, the School issues a certificate documenting the qualifications gained. The programme is therefore an opportunity for community pharmacists to develop and gain accreditation for specialist skills acquired throughout their career, regardless of whether their goal is to be a pharmacy manager with responsibility for the professional development of others or a community pharmacist.

The specialised programme in community pharmacy consists of the following main subjects:

1. Pharmacotherapy and symptom assessment, including anatomy, physiology, pharmacology, pharmacokinetics, symptomatology and pathology.
2. Pharmacy practice: Performance and development of the pharmacy’s professional services based on WHO’s Guidelines on Good Pharmacy Practice (GPP), including:
   - Prescription medications for individuals: distribution, information to patients and ensuring results (pharmaceutical care)
• Personal care and symptom assessment
• Disease prevention and health promotion
• Rational medication consumption.

3. Social pharmacy: Disease-, medication- and health-related behaviour, healthcare economy, pharmacoepidemiology and management of medication consumption.

4. Healthcare advice and information, including methods for advising individuals, informing target groups, and general instruction.

5. Documentation and information, including quality development, evaluation and surveys of pharmacy practice; use of pharmaceutical information systems and information technology.

6. Pharmacy operations, including management, skills development, organisation, operations and economy.

The specialised programme has a standard duration of one working year, corresponding to 60 European Credit Transfer System points (ECTS points). Pharmacists attend the programme, which runs over a minimum of two and a maximum of six years, alongside their regular community pharmacy job.

The programme consists of the following elements:

• Compulsory courses (12 points)
• Elective courses (minimum 12 points)
• Literature study (maximum 5 points)
• Study trip (maximum 5 points)
• Dissertation (minimum 15 points).

The compulsory courses comprise an introduction and four subject courses. The four subjects are:

1. Healthcare theory, including the pharmacy profession, community health, the consumer’s perspective and medication consumption.

2. Documentation in pharmacy practice, including planning, performing and evaluating surveys, framework conditions, theories and methods.

3. Pharmacy practice management, including management and organisation, Human Resource Management, business development and pharmacy operations.

4. Professional advice and information, understanding consumers’ perspectives and expectations, framework conditions and methods.

A secretariat has been set up at the School for the specialised programme in community pharmacy. As well as providing study guidance, the secretariat will assist during the programme’s introductory phases and ensure that it develops satisfactorily in terms of practical running and academic content. An administrator has been appointed to be in charge of secretariat services, and a formal co-operation has been set up between the secretariat and the School’s new specialised programme in hospital pharmacy.

Nineteen pharmacists applied in the first admission round for the specialised programme in community pharmacy starting on 1 January 2001. An introductory course was held for them in April 2001, and the first subject course, Healthcare theory, was held in August and November 2001. Ten pharmacists applied for the second admission round for the programme starting on 1 January 2002.

The Study Board for Specialisation in Community Pharmacy has prepared a final proposal for the programme’s regulations and planned the entire programme course, as described in The Study Guide to the Specialist Programme in Community Pharmacy. The study board submitted the programme regulations to the Senate, which approved them in November 2001. At the same time, in accordance with The Development
Contract 2000-2003 between the School and the Ministry of Education, the Senate adopted a motion for the School to initiate negotiations with the Ministry as soon as possible to approve the specialised programme in community pharmacy for inclusion in a relevant module of the further and continuing education system for adults.

The introduction of the specialised programme in community pharmacy has attracted broad interest and backing from all interested parties, as evidenced by several references to the programme in pharmacy journals in 2000 and 2001. It has been particularly satisfying for the School to note that all the pharmacy profession’s authorities and organisations have nominated representatives to the study board.

The members of The Study Board for Specialisation in Community Pharmacy:

- **Poul R. Kruse**, Associate Professor, DSc (pharm), Department of Social Pharmacy, nominated by The Royal Danish School of Pharmacy (chairman)*
- **Bente Steffansen**, Associate Professor, PhD (from 1 September 2001 Associate Professor Janne Ramsing, PhD), Department of Pharmaceutics, nominated by The Royal Danish School of Pharmacy*
- **Peter Thygesen**, Associate Professor, PhD (from 1 February 2001 Helmer Ring, Professor and Consultant, Doctor of Medicine), Department of Pharmacology, nominated by The Royal Danish School of Pharmacy*
- **Kurt Fonnesbaek Rasmussen**, Director, MSc (pharm), nominated by Pharmakon a/s*
- **Kirsten Pultz**, project coordinator, MSc (pharm), nominated by Pharmakon a/s*
- **Susanne Track-Nielsen**, proprietor pharmacist, nominated by the Danish Pharmaceutical Association
- **Majken Juul Jensen**, pharmacist, nominated by the Danish Association of Pharmacists, of which she is chairman
- **Bodil Strah**, proprietor pharmacist, nominated by The Danish Pharmaceutical Society
- **Lars Arboe Harild**, examiner (from 1 September 2001, Anne-Marie Vangsted, Head of Division, MSc [pharm]), nominated by the Danish Medicines Agency
- **Mikala Vasehus Holck**, pharmacist, nominated by participants in the specialised programme for community pharmacists

* Indicates members of the executive committee of the study board

Head of Secretariat: Trine Hopp, MSc (pharm), (from 1 June 2001, Thomas Clemens Jensen, MSc (pharm)), Department of Social Pharmacy, The Royal Danish School of Pharmacy.
Research at the Department of Analytical and Pharmaceutical Chemistry covers the following main areas: analytical chemistry (involving environmental and bioinorganic chemistry as well as chemical toxicology (aimed at accidents with hazardous chemicals)) and pharmaceutical chemistry (applied physical chemistry).

RESEARCH

ANALYTICAL CHEMISTRY

Basic research in separation science
The research in analytical chemistry is devoted to basic research in separation science as well as to research in drug metabolism involving the development of new analytical methods. The development of new analytical methods is based in part on basic research. The research in separation science focuses on separation mechanisms in high-performance liquid chromatography (HPLC) and capillary electrophoreses (CE). This research is currently being expanded to cover hyphenated techniques like HPLC-mass spectrometry (HPLC-MS), CE-(MS), HPLC-nuclear magnetic resonance (HPLC-NMR) and eventually CE-NMR.

Spectrometry - especially NMR - is an important part of the research area, and the potential of using NMR in bioanalytical chemistry is explored.

A major area of application is drug metabolism, where a number of drugs are under investigation. The interaction of reactive metabolites (e.g. glucuronides) with biopolymers is also studied and structure activity relationships investigated. Part of the research is conducted in collaboration with other research groups at the School, at hospital laboratories and in the pharmaceutical industry.

Research in analytical chemistry also covers determination of trace elements and their biotransformations. The main interest here is developing new methods of speciation analysis. The analytical techniques are ion chromatography with chemiluminescence detection, graphite furnace atomic absorption spectrometry and ICP-MS in combination with HPLC and CE.

Supervisors:
Steen Honoré Hansen, professor, Dsc (pharm)
Inga Bjarnsdottir, associate professor, PhD (until September 2000)
Claus Cornett, associate professor, PhD
Bente Gammelgaard, associate professor, PhD
Ole Jøns, associate professor, PhD
Alex Mehtsen Sørensen, associate professor, PhD (until January 2001)
Jette Tjørnelund, associate professor, PhD (until September 2001)
BIOINORGANIC CHEMISTRY

The importance of inorganic chemistry in biology, especially metal ion coordination chemistry, has gained considerable appreciation during the last decade. The discovery of the roles of metal ions and metalloproteins in health and disease through genetic and biochemical studies has drawn the attention of molecular and cell biologists in increasing numbers. Indeed, there are few areas of modern biology where inorganic chemistry is not destined to make its mark. Thus, inorganic chemistry combined with molecular biology and protein chemistry in studies of metal protein interactions will influence the thinking and research activities of chemists and biologists in the future. A little appreciated fact is that the brain is a specialised organ that concentrates metal ions. So, combining inorganic chemistry with molecular biology and protein chemistry in order to study abnormal metal protein interactions will undoubtedly lead to a better understanding of the molecular origin of major neurological diseases.

The overall purpose of our research is to continue and further develop studies of the relationship between metal ions and macromolecules experimentally as well as theoretically, a field entitled bioinorganic chemistry on the border between inorganic chemistry and biology. Our collaboration with leading research groups in other countries, including powerful biotechnological centres, ensures a continuous integration with international frontline research in bioinorganic chemistry.

Supervisor:
Ole Farver, professor, DSc

ENVIRONMENTAL CHEMISTRY

Chemical environmental research focuses on the emission of elements and compounds to the internal or external environment, and on their processing and effects on these environments. Environmental chemistry integrates environmental risk assessment, toxicology, chemistry and applied analytical chemistry. Current research projects deal with the modelling of effects of emissions on aquatic ecosystems, effect and speciation of heavy metals, risk and effect analysis of medicine, and the relationship between environment and health and endocrine disruption by xenobiotics, incl. drugs.

Supervisors:
Sven Erik Jørgensen, associate professor, Dsc (Eng)
Bent Halling-Sørensen, associate professor, PhD
Søren Nors Nielsen, external associate professor, PhD
(until June 2001)

ENVIRONMENTAL RISK ASSESSMENT OF PHARMACEUTICALS

Antibiotics are used widely across Europe to treat farm animals. Once released into the environment, the pharmaceuticals and their metabolites may persist and have the potential to runoff to surface waters or leach to groundwater where they can impact human and environmental health. Unlike other classes of substances (e.g. pesticides, metals and nutrients), the environmental fate of veterinary pharmaceuticals is poorly...
understood. A three-year project is therefore being conducted involving modelling, laboratory, semi-field and field studies. The aim of the study is to identify those factors and processes affecting the fate of veterinary pharmaceuticals in order to adapt existing risk assessment models or develop new models. Laboratory studies will investigate sorption, degradability and ecotoxicity of a range of veterinary pharmaceuticals. A range of new analytical methods, LC-MS-MS in particular, will have to be developed for the purpose.

The results of these studies will be used to assess the models currently available and, where appropriate, the models will be adapted to cope with pharmaceuticals. A range of scenarios will be developed to assess the risk of veterinary pharmaceuticals.

**Supervisors:**
Flemming Ingerslev, Anne Marie Jacobsen, Ann-Louise Steinicke-Larsen, Anne Lykkeberg, Jette Tjørnelund and Bent Halling-Sørensen together with several international research groups

**Hormonally active agents in the environment**
Over the past ten years, it has appeared that a number of environmental contaminants are able to provoke adverse changes in endocrine systems in humans and in the environment. The research within this area has primarily focused on the development of a test aimed at screening the endocrine effects of chemicals on the crustacean *Acartia Tonsa*. At present an assay for testing endocrine effects on breast-cancer cells, the E-screen method, is under development.

The analytical chemical aspects have been put more in focus in a recently started project. Methods to preconcentrate surface water are being developed, and analytical methods (HPLC-MS-MS) and the previously mentioned bioassays are used in the search for an overall picture of the oestrogen potential of surface waters.

**Supervisors:**
Henrik Rasmus Andersen, Søren Nors Nielsen, Flemming Ingerslev and Bent Halling-Sørensen together with the Technical University of Denmark

**CHEMICAL TOXICOLOGY**

Based on the simultaneous use of toxicology and chemistry, information on hazardous substances and accidents involving such substances has been made available to public authorities, the medical community and others. Several of these inquiries have resulted in toxicological investigations. Two main research branches have appeared: inhalation toxicology (pulmonary edema, toxic smoke from fires, criteria for evacuation, etc.) and clinical toxicology (hospital reception and treatment of patients suffering from the effects of chemical accidents, antidote preparedness, etc.). Thus the Department functions as a centre of knowledge on the use of hazardous substances and accidents involving such substances.

**Supervisor:**
E. Sonnich Thomsen, associate professor, PhD

**PHARMACEUTICAL CHEMISTRY**

The pharmaceutical chemistry research programme relates to optimisation of drug formulation involving prodrug design and salt formation. Aspects of drug delivery under investigation encompass factors influencing bioavailability and duration of drug action. Current research may be divided into four areas that are more or less interrelated (i) “Manipulation of drug solubility through prodrug design and salt formation” including both aqueous and lipid solubility, (ii) “Parenteral depot formulations” with the focus on oil solutions and crystal suspensions, (iii) “Prodrugs - identification of transport groups exhibiting a biological functionality” where we have initiated a search to identify suitable chemical compounds with significant affinity to blood components, and (iii) “Facilitation of biomembrane drug transport by prodrug design. Furthermore, the pharmaceutical chemistry group is engaged in pharmaceutical chemical profiling of drug substances including assessment of drug stability. Our research is partly conducted in collaboration with both internal and external groups.

**Supervisors:**
Claus Selch Larsen, professor, PhD DSc (pharm)
Helle Brandsted, associate professor, PhD
Gitte Juel Friis, associate professor, PhD (until December 2000)
Karim Fredholt, associate professor, PhD (until October 2000)
Flemming Madsen, associate professor, PhD (until September 2000)
Søren Nors Nielsen, associate professor, PhD (from June 2001)
Kirsten Eberth, associate professor, PhD

**DONATIONS AND GRANTS**

Ole Farver gratefully acknowledges support from the Danish Natural Science Research Council; the Danish Medical Research Council; the Lundbeck Foundation and the Novo-Nordisk Foundation.

Bent Halling-Sørensen has together with senior researcher, PhD Lars Bøg Jensen, SVS received each DKK 375,000 per year for a two year period (2001-02) from SJVF (Statens Jordbrugsvidenskabelige Forskningsråd) to the project:
“Assessment of the fate and resistance development of selected antibiotic metabolites in soil” grant no. 53-00-0279.

Bent Halling-Sørensen and Jette Tjørnelund have received DKK 4.0 mio from The EU 5th frame programme (project period 2000-03): Environmental risk assessment of veterinary medicines in sludge (ERAVSMIS). Project no. EESD-ENV-99-1, EVK1-1999-00034P, for a three year project

Claus Selch Larsen and Helle Brandsted have received DKK 680.000 from Centre for Drug Design and Transport.

Bent Halling-Sørensen has from the Danish Environmental Agency received DKK 500.000 for the project “Drugs and the environment” projects no. 00-650-24.

Steen Honoré Hansen received DKK 300.000 from the Danish Medical Research Council for partly financing of a micro HPLC equipment.

Svend Erik Jørgensens current supported projects are: Enreca Project with Dar es Salaam University prolonged to August/September 2003 – DKK 4.3 million and EU-supported project, coordinator Sovan Lek, Toulouse University, EURO 118.000.

GUESTS

PhD Dina Tawfik Mohammed El-Sherbiny from Mansoura (Egypt), September-December 2000.
Dr Stig Pedersen from University of Oslo, Norway, October 2000.
Dr. Michael G. Rowan from University of Bath, UK, June-August 2001.
Dr. Paul Blackwell from Cranfied University, England, visited the environmental chemistry group in February 2001 in order to work on the development of an analytical method to be used in a common research project financed by the EU. PhD student Jianhua Wang, Technical University of Denmark (1.10-30.11.00)
Hu Weiping from Nanjing Institute of Limnology and Geography, Chinese Academy of Science. Year 2000 Fall.
Sixtus Kayombo from Dar es Salaam University, August-November 2001.

ARRANGEMENTS

The Environmental chemistry group arranged (30.7.–10.8. 2001) the course “Environmental risk assessment of pharmaceuticals and chemicals” as part of “The Øresund Summer University 2001”. 25 students from 12 different countries participated in the course.

PRESENTATIONS


Halling-Sørensen B. Occurrence and environmental properties of antibiotics used in Denmark. Presented at the SETAC conference Organic soil contaminants 2-5 September 2001 at Eigtved Parkhus, Copenhagen Denmark.

Hansen SH. “Challenging the principles of setting limits in pharmacopoeial tests”. The Future Face of the European Pharmacopoeia Nice, 8-9 February 2001 (Invited lecturer).

Hansen SH. “Hyphenation of CE to ICP-MS and to nanospray MS for high sensitivity and selectivity in biomedical analysis”.14th International Bioanalytical Forum, 3-6 July 2001 at the University of Surrey, Guildford, UK (Invited plenary lecturer).


MEMBERSHIPS OF EXTERNAL COUNCILS AND BOARDS

Claus Selch Larsen is a member of the Danish Academy of Technological Sciences, chairman of the Biopharmaceutical Section, Danish Pharmaceutical Society, member of Fagligt Forum under The Danish Council for Scientific and Industrial
Research (until July 2001), member of the editorial board for European Journal of Pharmaceutical Sciences, and member of the scientific advisory board for the biotech company Zealand Pharmaceuticals (until June 2001).

**Bente Gammelgaard** is a member of Centre for Educational Development in University Science

**Bent Halling-Sørensen** is external censor at the Technical University of Denmark.

**Steen Honoré Hansen** Chairman of The Chromatographic Society, Scandinavian Section and President of The Separation Sciences Foundation. Member of the board of ProPharma A/S and the board of The Propolis Research Center A/S. Member of the board of The Chemical Working Party and the Working Party for Natural Products of the Pharmacopoeial Board in Denmark. Member of the Commission and of the Expert Group no.10B under the European Pharmacopoeia Commission, Strasbourg.

**Svend Erik Jørgensen** is editor in chief of Ecological Modelling and Member of ILEC's scientific committee (International Lake Environmental Committee). Since 1988 bureau member. Since 1995 President (chairman). He also spends a lot of his time as a member of the following editorial boards: Water Resource Developments, General Systems, Urban Systems, Environmental Software and Modelling, Ecological Engineering, Journal of Analytical and Environmental Chemistry, Lakes and Reservoirs, Research and Management, SAR- and QSAR in Environmental Research, Environmental Modelling, Ecological Indicator (Associate editor in chief) and Ecohydrology.


Member of an Expert Panel (5 members), focusing on Application of Models to develop ERA for chemicals (U.S. - EPA, 1999 - ). Member of a UNESCO board for Ecohydrology, 2001- present.

**PROJECTS**

**ANALYTICAL CHEMISTRY**

**Capillary electrophoresis (CE)**

New principles of performing CE with high electroosmotic flow at low pH have been achieved using a number of dynamic coatings of the internal surfaces of fused silica capillaries. The principles have been applied in bioanalyses of small as well as of larger molecules (proteins). Furthermore, this new separation technique have been hyphenated to ICP-MS as well as to sheathless MS which also will improve the applicability within bioanalyse and thus for use in studies of drug metabolism. Microemulsions have also been explored for use in drug analysis, purity testing of drug substances and in bioanalysis. (Jette Tjamelund, Jørgen Olsen, Anette Gemal Jensen, Stig Pedersen-Bjergaard, University of Oslo, Inga Bjørnsdottir, Dina Tawfik Mohammed El-Sherbiny, Charlotte Gabel Jensen and Steen Honoré Hansen)

**Drug metabolism**

The metabolism of drugs are compared in various in vivo models (liver slices, liver homogenates as well as isolated enzyme systems). For this purpose selected drug substances (e.g. naproxen, tolfenamic acid, ibuprofen, warfarin and dextrometorphan) are used as probes. Analytical chemical methods such as HPLC, HPLC-MS and HPLC-NMR have been used to study the formation of metabolites in the models tested. The reactivity of phase II metabolites towards proteins have been an important issue.

A major field is reactive drug metabolites and their possible role in idiosyncratic drug reactions. Focus has been on acylglucuronides and acyl-CoA-adducts. The formation of CoA-adducts results in the incorporation of the drug substances into a number of endogenous metabolic pathways. (Ingba Bjørnsdottir, Claus Cornett, Steen Honoré Hansen, Rasmus Worm Mortensen, Jørgen Olsen, Nina Hagen, Jette Tjamelund, Christian Skonberg, Ulrik Sidenius, Jane K. Johannessen, prof. Ian T. Wilson, AstraZeneca, UK and prof. Jeremy K. Nicholson, University of London, UK)

**Hyphenation techniques**

In order to obtain more data information faster different kinds of couplings between separation techniques with spectroscopic techniques have been studied. Of special interest are the following couplings: LC-NMR-MS/MS; CE-NMR; CE-MS/MS; CE-ICP-MS. The LC-MNR-MS/MS hyphenation have been used for the investigation of constituents and Hypericum perforatum and other plants. A system for ion pair HPLC-NMR-MS have also been developed for identification of impurities in basic drug substances. (Steen Honoré Hansen, Jette Tjamelund, Claus Cornett, Anette Gemal Jensen, Jørgen Olsen, Inga Bjørnsdottir, prof. Ian D. Wilson, AstraZeneca, UK)

**Quality control of drug substances**

A project that involves development and validation of analytical chemical methods for determination of identity and purity. The project is performed in collaboration with members of a group of experts under the European Pharmacopoeia Commission. (Alex Mehllsen Sørensen, Steen Honoré Hansen)
Mononuclear metalloproteins
Intramolecular electron transfer

Intramolecular electron transfer (ET) in bacterial proteins like the azurins has provided basis for experimental as well as theoretical studies of biological electron transport. With a copper ion attached directly to amino acids and without the presence of foreign group like e.g. heme we have the simplest possible prosthetic group, namely the copper ion itself. The protein is characteristic with its very robust β-sheet construction and since the three dimensional structure has been determined for a large group of azurins from different bacterial origin as well as for many mutated proteins it is an ideal candidate for studies of relationships between structure and reactivity. Systematic exchange of amino acids have provided important information in this respect, and we now pursue studies on intramolecular ET in azurin mutants with very large driving force. We have so far been able to determine the reorganization free energy for a β-sheet protein and determined the electronic tunneling factor.

Kinetic isotope effects have so far never been treated, neither theoretically nor experimentally, for the biologically important non-adiabatic ET processes. Not only the dynamic properties for H2O and D2O are significantly different, but also the local structures of the two solvents vary. These parameters influence the polarization correlation distance and lead to changes in solvation and cause a definite deuterium isotope effect. We have recently published our studies on thermodynamic and kinetic isotope effects on azurin.

Another interesting aspect of biological ET is the effect of polarization on the long distance electronic coupling. Professor Robert Huber’s group at the Max Planck Instute in Martinsried has produced a new type of “atomic” mutants where certain hydrogen atoms in aromatic amino acid residues have been exchanged by fluorine atoms. This substitution is practically isosteric (the x-ray structures of the proteins have been determined) while the polarity of the fluorinated side chains has been inverted. We are presently studying the electronic couplings in these mutants by determining the rates of ET.

Purple azurin
Structure and spectroscopy

The effect of axial ligand mutation on the binuclear CuA site in a recombinant azurin bas has been investigated by advanced magneto-spectroscopic techniques. The changes in the spin density in the CuA site, as manifested by the hyperfine couplings of the weakly and strongly coupled nitrogens, and of the cysteine protons, were followed using a combination of advanced EPR techniques. X-band (9 GHz) electron-spin-echo envelope modulation (ESEEM) and two-dimensional (2D) hyperfine sublevel correlation (HYSCORE) spectroscopy were employed to measure the weakly coupled N-14 nuclei, and X- and W-band (95 GHz) pulsed electron-nuclear double resonance (ENDOR) spectroscopy for probing the strongly coupled N-14 nuclei and the protons. The high field measurements were extremely useful as they allowed us to resolve the T2 and CuA signals in the g=2 region and gave H-1 ENDOR spectra free of overlapping N-14 signals. These effects were associated with an increase in the Cu-Cu distance and subtle changes in the geometry of the Cu7-S2 core which are consistent with the electronic structural model we have developed earlier.
Multicentered metalloproteins and -enzymes

During the last years we have studied intramolecular ET in multi centered macromolecules. An important issue which we want to pursue is the coupling between electron transport and coordination of the oxidizing substrate (e.g. O$_2$ and NO$_2$). Gating processes where rearrangements of nuclei often becomes rate determining has so far not been studied in sufficient detail, although we have already encountered examples of intramolecular ET which is controlled by O$_2$-coordination.

CuNiR

Denitrification is one of the most important and concomitantly one of the most complicated biological ET processes. In collaboration with a British group we study the kinetics of enzymatic nitrite reduction by the copper containing nitrite reductase from Alcaligenes bacteria in an attempt to throw light on the connection between structure, substrate binding, and reactivity. CuNiR catalyzes the one-electron reduction of nitrite to NO. We have already publishes results on the native enzyme and are presently studying different single site mutated enzymes.

CD1NiR

The heme containing nitrite reductase from Pseudomonas bacteria is another respiratory enzyme that we presently study. Like the above copper enzyme it catalyzes the one-electron reduction of nitrite to NO as well as the four-electron reduction of dioxygen to water. Cytochrome cd$_1$ nitrite reductase is a homodimer, each monomer containing one c-type and one d$_1$-type heme as prosthetic groups. The interheme distances across the dimer interface of at least 3.8 nm ensure electron transfer between monomers to be negligible, however. CD1NiR constitutes an optimal system for studies of the connection between intramolecular heme ET and intermolecular ET between substrates and enzyme. There has been considerable debate about the relevance of structural changes including ligand switching during redox cycling and the physiological implications of a possible gating mechanism. We have already established a cooperativity between the hemes and a dependence of ET rates on the reduction state of the enzyme. The first part of our studies is now in print.

Selenium metabolism in humans

Selenium is an essential element that exerts its effects via the selenoproteins and so far more than 30 selenoproteins have been identified. The biological functions of all these proteins have not been completely elucidated yet, but some of the well characterized proteins are involved in antioxidative processes in the body. In recent years the element has attracted some attention as a possible protective agent against certain forms of cancer. The cancer protective effect was observed after prolonged intake of doses exceeding the amounts necessary to keep the essential selenoproteins fully functional. Thus, the the protective effect may be due to other selenium compounds than the selenoproteins.

However, the metabolism of selenium is far from completely understood and the majority of earlier studies on selenium metabolism were performed in vitro or in animal experiments.

The main purpose of this project is to separate, identify and quantify the different selenium containing compounds in human biological samples - mainly plasma and urin - with the ultimate aim of improving the understanding of human selenium metabolism.

This involves the use of hyphenated techniques where different separation systems are coupled to the ICP-MS (Inductively Coupled Plasma Mass Spectrometry) or MS detectors. The separation techniques comprise chromatographic techniques as reversed phase, ion-exchange and ion-pairing chromatography together with capillary electrophoresis. Special interest is taken in development of interfaces between the separation systems and the ICP-MS detector in order to solve problems with incompatibility between optimum flow ranges. Furthermore, solutions for circumventing problems based on the different compatibility of the preferred sol-
vents between the separation system and the detector are examined.

As the natural concentrations of the selenium species is at the low µg/L level and some of the compounds are suspected to be unstable, different pretreatment procedures are investigated and stability studies are undertaken.

(Hejnaan Jøns, Flemming Ingerslev, Ole Farver)

Trace multielement analysis in biological material
This project involves the simultaneous analysis of trace elements with influence on human health with focus on interaction between the elements. The analytical technique is ICP-MS.

(Bente Gammelgaard, Ole Jøns)

Environmental risk assessment of pharmaceuticals
Antibiotics are used widely across Europe to treat farm animals.

Once released to the environment, the pharmaceuticals and their metabolites may persist and have the potential to runoff to surface waters or leach to groundwater where they can impact human and environmental health. Unlike other classes of substances (e.g., pesticide, metals and nutrients), the environmental fate of veterinary pharmaceuticals is poorly understood. A 3 year project is therefore being performed involving modelling, laboratory, semi-field and field studies. The aim of the study is to identify those factors and processes affecting the fate of veterinary pharmaceuticals in order to adapt existing risk assessment models or to develop new models. Laboratory studies will investigate sorption, degradability and ecotoxicity of a range of veterinary pharmaceuticals. To do so a range of new analytical methods especially on LC-MS-MS has to be developed.

The results of these studies will be used to assess currently available models and, where appropriate, the models will be adapted to cope with pharmaceuticals. A range of scenarios will be developed to assess the risk of veterinary pharmaceuticals. (Flemming Ingerslev, Anne Marie Jacobsen, Ann-Louise Steinicke-Larsen, Anne Lykkeberg, Jette Tjørnelund and Bent Halling-Sørensen)

Hormonally active agents in the environment
Over the past ten years it has appeared that a number environmental contaminants are able to provoke adverse changes in endocrine systems in humans and in the environment. The research within this area has primarily been focusing on the development of a test aimed at screening the endocrine effects of chemicals on the crustacean, Acartia Tonsa. Currently an assay for testing endocrine effects using on breast-cancer cells, the E-screen method, is under development.

The analytical chemical aspects has been put more in focus in a recently started project. In this project, methods for preconcentration of surface water is developed, analytical methods (HPLC-MS-MS) and the previous mentioned bioassays is used in the search of an overall picture of the estrogen potential of surface waters. (Henrik Rasmus Andersen, Søren Nors Nielsen, Flemming Ingerslev and Bent Halling-Sørensen together with the Technical University of Denmark)

Parabens, a group of compounds possessing estrogenic potency in in-vitro assays – what is the toxicological and ecotoxicological significance of these findings?
In the beginning of the 1990’s it was discovered that a variety of chemical compounds used in various activities such as agriculture (pesticides), industry (chemicals), food and pharmaceuticals (preservatives), as well as natural compounds derived from plants and fungi, posses estrogenic or other hormonal effects detectable in various in-vitro and in-vivo assays. These effects occurred despite their low structural similarity to the natural hormones. The toxicological and ecotoxicological significances of these findings are not always clear. Such finding often seems to provoke a heavy debate in the public media and creates an immediate public demand of banning the chemical in question. Last summer Denmark faced such a discussion when the public media disclosed that UV-screens used in e.g. sun lotion to reduce UV-radiation to the skin, possessed estrogen potency in both an in-vitro assay and for some of them also in an in-vivo assay. The newspapers and green organisations claimed an immediate ban of all sun lotions that contained these UV-screens. As a result, the population was left with the dilemma of choosing between two risks. Evolution of sun burns with potential risk to later develop skin cancer or being exposed to hormonally active chemicals.

To limit the number of such often hasty conclusions regarding the use of chemicals, risk assessment methodologies should be much more developed in the direction of a communicative management tool in today’s society. The strength of risk assessment as a management tool is that it provides a means for handling the “unknowns”. The “unknowns” that in fact exist for most chemicals are handled by using precautionary principles in such assessment. Furthermore, risk as-
The parabens are also an example of recently found “xeno-estrogens”. In the sections of environmental chemistry and toxicology at the Royal Danish School of Pharmacy we have lately studied the parabens. Current literature shows that the estrogenic potency of the parabens increases markedly with the size of the molecule as well as with the branching of the alkyl-substituents. Figure 1 shows the general structure of parabens together with the natural estrogen hormone, 17β-estradiol, and 4-alkylphenols which have been proved as xeno-estrogens. The figure shows that the parabens does not resemble 17β-estradiol at all, but that there is some similarity with alkylphenols. (Alkylphenols were identified as xeno-estrogens a decade ago based on effects in both rats and fish and their use is now regulated) Parabens are known to be unstable in different matrices due to their vulnerability towards ester hydrolysis.

Parabens are often used in the western world as preservatives for food, cosmetics, pharmaceuticals (used in e.g. solutions for injection or infusion) and health care products. The compounds are nearly always used as mixtures of several alkylparabens, and their branched isomers to broaden the spectrum of preservation. The compounds are regulated in Denmark so that a maximum of 300-mg paraben/kg is allowed for preserving food. Furthermore, cosmetics is permitted to contain up to 0.4 % of a single paraben and no more than 0.8 % of a paraben mixture. No legislation rules the use of parabens in pharmaceuticals.

We tested the estrogenic activity of a number of parabens, including both the n-forms and iso-forms (e.g. both n-butylparaben and iso-butylparaben) with the so-called E-Screen assay. In this assay, a breast cancer cell line (the MCF-7 cells) proliferates due to the presence of estrogenic active chemicals. In total twelve parabens were assessed.

Results showed as expected that the proliferation of MCF7 cells increased with the dose of all twelve parabens. The relative potencies of e.g. 2-ethylhexylparabens and ethylparaben are 5,500 times and 230,000 lower, respectively, compared to 17β-estradiol. We also found that the iso-parabens were significantly more estrogenic than the n-parabens.

The question was now whether these findings could imply that parabens would be a risk for humans or the environment. The answer is at present: It is not likely. However, results from in-vitro testing can of course not standalone. Proper risk assessment should be performed, including other relevant informations such as physico-chemical data of the chemicals, analytical measurement of paraben mixtures, covering a number of relevant exposure scenarios to both humans and the environment.

To assess the parabens we therefore investigated two relevant scenarios that especially were identified as vulnerable to humans and to the environment with regard to the identified exposure routes. In the following we give a very brief summary of the scenarios and of the calculations included.

In scenario I, we attempt to assess the exposure of parabens in pharmaceuticals, dosed as daily injections (Heparin preserved with methylparaben) to a pregnant woman from the 2nd to 35th week of pregnancy. This is the most vulnerable period of the pregnancy for the foetus to be exposed to the compounds. Other pharmaceuticals containing parabens were also assessed. It was concluded that the highest calculated risk of introducing cell deformities in the foetus induced by parabens was one out of a million, compared to similar data for DES (synthetic estrogen). This is generally considered as an acceptable risk. But still, a few questions are left. Some lotions include the iso-parabens identified as more potent ones. A similar assessment would need non-existing data for the iso-parabens or could we for instance use in vivo experiments on linear parabens to predict the risk of using the branched parabens? Furthermore, we do not know if the ester hydrolysis in e.g. the blood or sewage breaks down the branched compounds as rapid as the linear ones.

In scenario II, similarly, we tried to assess the risk for the aquatic environment using a scenario covering the sewage treatment plant. Parabens used in health care products or cosmetics are transported with sewage water from the shower or bathtub to the sewage treatment plant. In the environment parameters such as biodegradation, sorption, hydrolysis, pH and photolysis may have impact on the resulting concentration of the compounds in the treated effluent. The calculated or measured concentration is then compared to effect concentrations on relevant species (acute or chronic effects) from different trophic levels of the aquatic food chain. If the calculated
or measured concentrations in the treated sewage exceed the effect concentrations times an assessment factor, the compounds may be a risk for the environment. Different scenarios taking in to account more or less information on the fate of the parabens, all gave results indicating that the concentrations of the compounds in the sewage were at least a factor 100 – 1000 below the effect concentrations. But our study also revealed that available data on relevant chronic effect concentrations are very sparse so that more relevant data should be gathered. In other words a definitive conclusion regarding the risk of parabens in scenario II can not be given.

Our research study aim to pass a few messages. The public media is often ready to conclude that society is facing a risk connected with chemicals based on too few facts.
1. The chemicals (parabens), even though they exhibit estrogen potency in a in-vitro assay, does not impose a risk using the available informations in relevant scenarios.
2. Furthermore, the same chemicals may (in this case the parabens), because of a variety of applications, be the subject of quite different exposure scenarios.
3. The biological and chemical fate of the chemicals are important informations to include in a risk assessment and might be quit different for the same compound in different environments.

A much broader awareness of risk assessment as a management tool able to communicate risks to society is therefore urgently wanted. We should learn to communicate our conclusions not only based on documented informations but also on the "unknowns" by using precautionary principles in the assessment. This would balance the communication to society of the risk of chemicals.

As a further conclusion we might ad that the present study needed information from several other disciplines than toxicology in order to fulfil the assessments. Analytical chemistry could be used both to identify the included parabens in the formulations and analyse the treated sewage. Furthermore we needed physical chemistry to assess the stability of the parabens in different matrices such as blood and sewage. Knowledge about microbiology and biology were used to assess the biodegradation and perform the MCF7 assay. Furthermore good skills in literature survey is important in risk assessment.

(Henrik R. Andersen, Morten M. Pedersen, Mille Holst-Jørgensen, Seren Nors Nielsen, Flemming Ingerslev, Erling Sonnich Thomsen and Bent Halling-Sørensen)

CHEMICAL TOXICOLOGY

For decades this department has served as a center of knowledge on hazardous chemicals, both on handling and in case of accidents. The number of calls is about 50 per year. Several of these inquiries have resulted in further toxicological evaluations. Two main research branches have appeared: inhalation toxicology (pulmonary edema, toxic smoke from fires, criteria for evacuation, etc.) and clinical toxicology (hospital reception and treatment of patients suffering from the effects of chemical accidents, antidote preparedness, etc.).

A compulsory course on toxicology is given. An important aspect is that the students are supposed to have a good knowledge of chemical compounds and of the properties of groups of chemicals. The reason is that many of the problems from worker’s and consumer’s safety, from environmental pollution and from chemical disasters implies knowledge of chemistry and toxicology, simultaneously. Similar considerations apply to the safety course at the beginning of the study.

Projects on toxicology and chemical safety:
• Releases of toxic gases from chemical spills or from chemical fires.
• Antidotes and procedures for acute poisonings, especially if these can be used by laypersons.
• The combination of chemistry and toxicology with technical and tactical knowledge forms the basis for advising e.g. the authorities, the politicians, and the media on hazardous chemicals: the risks and the preventive and mitigative measures. Unfortunately, this activity becomes increasingly relevant as the knowledge of chemistry and toxicology decreases both for the groups mentioned and in the general public.

(Erling Sonnich Thomsen)

PHARMACEUTICAL CHEMISTRY

Prolonged release of bupivacaine after subcutaneous injection of an oil mixture formulation in the rat

For decades anaesthesiologists have sought an agent that would provide local anaesthesia lasting for days rather than hours. Such an agent would be invaluable for providing post-operative pain control and for treatment of chronic pain. Among other characteristics the ideal long acting local anaesthetic agent should affect sensory, but not motor fibers. No agent currently exists that possesses all the desired properties. Therefore, most efforts have primarily been concerned with modifying formulations of existing local anaesthetics to yield new mechanisms that will sustain ultra long duration anaesthesia. Bupivacaine is a frequently used local anaesthetic. The treatment of wound sites with administration of bupivacaine at or near the end of surgery is common practise. For clinical use the drug is formulated as an aqueous solution (Marcain®) and the duration of action is approximately 4-6 hours. The site of action of bupivacaine is the tissue surrounding the injection area, however, a significant amount of the dose enters into the blood shortly after the injection. When bupivacaine is
injected as an aqueous solution it is readily mixed with the tissue fluid and distributed to both the nerve cells and the blood. High concentrations of bupivacaine in the blood might give rise to severe cardiac toxicity and therefore have to be avoided.

A means to obtain prolonged bupivacaine release and at the same time to minimise toxic side effects, is to incorporate the drug substance into a formulation from which it is slowly released. Bupivacaine can be dissolved in vegetable oil mixtures (in the free base form). These oils are not miscible with water and after injection of such bupivacaine oil solutions the drug has to be released into the aqueous tissue fluid before it can exert its action. By variation of the composition of the oil mixture it is possible to vary the bupivacaine release rate from the oil. As a part of a PhD project bupivacaine was injected subcutaneously in rats in an aqueous and in an oil mixture. First, the rats were given Marcain® and one week later the oil formulation containing the same amount of bupivacaine was injected. After each injection blood samples were taken as a function of time and the concentration of bupivacaine in each sample was determined. As seen from Figure 2 relatively high plasma concentrations of bupivacaine is initially obtained after injection of Marcain®, and the concentration in the blood declines rather fast with time. In contrast, injection of the oil solution gives rise to a relatively constant plasma concentration of bupivacaine over an extended period of time (up to 24 hours). In addition, compared to Marcain® the oil solution initially results in much lower blood concentrations thus minimising the risk of unwanted bupivacaine side effects. The study indicates that it might be possible to design pharmaceutical formulations endowed extended duration of action.

(Claus Selch Larsen)

1. PARENTERAL DEPOTS:

1a. Pharmaceutical chemical characterisation of oil solutions

The aim of the project has been to develop and characterise an in vitro release model to be used in investigations of the rate of release of drug substances/prodrugs from oil solutions including a chemical kinetic description of the release processes. The model has been used to study the influence of various formulation factors on the control of the rate of drug release from oil formulations. Furthermore the model has been used to establish an in vitro–in vivo correlation.

(Dorrit Bjerg Larsen (PhD student), Karin Fredholt (H. Lundbeck A/S) and Claus Selch Larsen)

1b. Design of prodrugs of polar drug substances aiming at obtaining depot effect after parenteral administration

Polar drug/model drug substances under investigation include nicotinic acid, local anaesthetics and dipeptides. The focus of the project embraces: (i) development of an in vitro release model for the assessment of the rate of release of lipophilic prodrug derivatives from oil solutions, (ii) comparison of (a) potential lipase mediated degradation of clinically used oil vehicles, and (b) the rate of disappearance of such oil vehicles from the injection site after i.m. and s.c. injection in pigs, and (iii) enhance oil solubility of polar drug candidates by using the prodrug approach in combination with hydrophobic ionpairing.

(Susan Weng Larsen (PhD student), Gitte Juel Friis (Coloplast A/S), Michael Ankersen (Novo Nordisk), and Claus Selch Larsen)

1c. Design of low solubility salts of drug substances

The project aims at achieving greater insight into the effect of structural parameters on the solubility of salts and the establishment of models for the prediction of aqueous solubility of
salts. A particular focus area is the formation of low solubility salts of drug substances containing a carboxy or amino group. The project includes preparation and pharmaceutical chemical characterisation of salts, and in addition, aspects of the design of in situ crystal suspension formulations.

(Henrik Parshad (PhD student), Karla Frydenvang and Tommy Liljefors (Dept. Medicinal Chemistry), and Claus Selch Larsen)

2. PRODRUGS – IDENTIFICATION OF TRANSPORT GROUPS EXHIBITING A BIOLOGICAL FUNCTIONALITY:

2a. Optimisation of oral bioavailability of drugs by avoidance of first-pass metabolism

Many potential drug candidates are highly metabolised after oral administration due to first-pass metabolism in the liver. It is known that binding of drugs to tissue and plasma proteins are important parameters influencing the metabolism and elimination of such compounds. By using the prodrug approach the aim of this project is to investigate the feasibility of incorporation of a biological functionality in the transport group in order to circumvent or minimise liver first-pass metabolism. As a start efforts will be devoted to identify chemical structures (fatty acid-like structures) as transport groups possessing optimal affinity to human serum albumin.

(Jesper Østergaard (PhD student), Helle Brandsted, Lars Dalgaard (H. Lundbeck A/S), and Claus Selch Larsen)

3. FACILITATION OF BIOMEMBRANE DRUG TRANSPORT BY PRODRUG DESIGN:

3a. Prodrugs of nucleotide bases

Oligonucleotide-based therapy might be considered as a new and highly specific tool for the treatment of diseases such as cancer and virus infections. The therapeutic use of antisense oligonucleotides is, however, hampered due to instability of the backbone. In addition, the polar character of the molecules is an impediment for their passage of biological membranes. The aim of the project is (i) to optimise passive transport of such agents over the bacterial cell wall by prodrug derivatisation, and (ii) to investigate the influence of the physicochemical properties of such derivatives on the rate of release from pharmaceutical matrices.

(Karsten Petersson (PhD student), Helle Brandsted, Karen Krogsfjeld (Statens Serum Institut), and Claus Selch Larsen)

3b. Prodrug types of isoxazole structures

An interesting class of GABA\(_A\) antagonists share an isoxazolol ring. The polar nature of this ring structure at physiological pH is less optimal as regards transport over biological membranes. Such pharmacologically active agents may therefore not be effectively delivered to their site of action: the central nervous system. The aim of the project is to identify suitable prodrug types for the isoxazolol structure which combine improved transport properties with desirable cleavage rates.

(Bente Frølund (Dept. Medicinal Chemistry) and Claus Selch Larsen)

4. MANIPULATION OF DRUG SOLUBILITY:

4a. Use of the combination of prodrug design and salt formation - a strategy to enhance aqueous solubility of drugs

By modern medicinal chemistry a great number of compounds exhibiting desired receptor profiles emerge. Unfortunately, insufficient water solubility resulting in low and variable bioavailability after oral administration prevents many pharmacologically interesting chemical entities from further development. Improvement of this basic physicochemical property might be achieved by employing the prodrug approach which involves only a transient masking of the physicochemical properties since the parent active agent is regenerated in vivo. Furthermore, it is well known that the use of different counterions can result in salts differing several orders of magnitude with respect to aqueous solubility. Thus, the aim of the project is to enhance the aqueous solubility of poorly water-soluble compounds achieved by the combined approach involving prodrug design and optimisation of salt formation.

(Anders Bach Nielsen (PhD student), Anders Buur (H. Lundbeck A/S), Karla Frydenvang and Tommy Liljefors (Dept. Medicinal Chemistry) and Claus Selch Larsen)
Department of Medicinal Chemistry

Head of Department: Ulf Madsen, Associate Professor, PhD

The Department of Medicinal Chemistry conducts teaching and research in organic chemistry, spectroscopy, medicinal chemistry, natural products chemistry, pharmacognosy and structural chemistry. All subjects are related to drug research and because virtually all drugs used in therapy today are organic compounds, detailed knowledge of organic chemistry and chemical structure is indispensable for drug experts. The teaching gives students in-depth knowledge of organic chemistry, and integrates chemistry and biology into the process of educating drug experts.

RESEARCH

The research profile of the Department is illustrated by the figure below and the general description of the research groups. More detailed descriptions of selected projects are given under Projects.
PHARMACOGNOSY

The Pharmacognosy Group works with medicinal plants in teaching and research. The research projects comprise a range of disciplines from ethnobotany and chemotaxonomy to bioassay guided fractionation of plant extracts and purification of active compounds. Plant material is obtained from the Tropics, mainly African countries (Burkina Faso, Kenya, Nigeria, and Zimbabwe), the Mascarene Islands (Reunion and Mauritius), as well as India and other Asian countries (Vietnam). Plants used in traditional medicine are studied in selected biological assays for antimicrobial, antihypertensive, anthelminthic and antimalarial activity. Most of these projects are carried out as joint venture projects with scientists from tropical countries and with colleagues from the Royal Danish School of Pharmacy and other Danish research laboratories.

NATURAL PRODUCTS

In search of new leads with novel pharmacological properties, it is of interest to test large numbers of compounds. Therefore, the use of combinatorial libraries is of particular importance to drug discovery. Nature provides an unsurpassed source of chemical diversity, and combinatorial libraries of natural products are an important supplement to synthetic combinatorial libraries. Studies of natural products and of their potential as drugs are the basic activity of the group. Research includes plant selection, pharmacological characterisation of the extracts, dereplication, structure elucidation (mainly by NMR methods), pharmacological characterisation of pure constituents, and medicinal chemistry in relation to promising structures.

STRUCTURAL CHEMISTRY

The three-dimensional structures of molecules provide important information about the properties of the molecules, and thereby a key to understanding the relationships between molecular structure and biological activity. The Structural Chemistry Group uses experimental methods like X-ray crystallography to determine the three-dimensional structure of low-molecular weight compounds, macromolecules, e.g. receptors and enzymes, and protein-ligand complexes. Computational methods like molecular mechanics and quantum mechanics are used to predict molecular properties and to calculate molecular interactions between the ligands (neurotransmitters, hormones, enzyme inhibitors etc.) and their macromolecular target molecules (receptors, enzymes etc.). By studying molecular interactions, it is possible to construct so-called 3D-QSAR’s (three-dimensional quantitative structure-activity relationships), which enable new ligands to be designed and their biological activity and selectivity predicted.

NEUROMEDICINAL CHEMISTRY

The goal of the Neuromedicinal Chemistry (NeMe) Group is to design tools and model drugs, which interact specifically with the target receptors. Bioisosteric principles (molecular mimicry) are used extensively to transform endogenous transmitter substances or naturally occurring compounds into receptor specific model drugs. Structure-based design of new ligands is performed in collaboration with the Structural Chemistry Group. This is an integral part of the projects aiming at receptors where sufficient data on the receptor proteins are available. An important aspect of all of these projects is to design and synthesise the target molecules with established stereochemistry. The enantiomers of pharmacologically active compounds are frequently obtained by optical resolution methods based on diastereomeric procedures or chiral chromatographic (HPLC) separation techniques. Normally, the absolute stereochemistry of enantiomers is established by X-ray crystallographic methods supported by circular dichroism and
HPLC parameters. Molecular pharmacology has become an integral component of modern medicinal chemistry, and the research activities of this part of the NeMe Group involve receptor cloning and pharmacological studies using mutated and chimerised receptors. The NeMe Group has extensive collaborative projects with the drug industry.

SYNTHETIC CHEMISTRY

The Synthesis Group is involved in the development of a broad range of new synthetic methods and advanced techniques including metatlation reactions, transition metal catalysed reactions, cyclisations and stereoselective processes. The target molecules are diverse but frequently compounds of biological relevance. The metatlation reactions deal with the preparation of mainly lithium, magnesium, zinc, boron, silicon and tin compounds. Transition metal chemistry is focused on palladium catalysed cross-couplings establishing C-C, C-N and C-O bonds and is used, for example, in arylation and heteroarylation reactions. Anionic cyclisation is another important subject. Special attention is paid to monoselective, regioselective and stereoselective protocols. Selectivity is achieved by the use of designed directing, activated, or superactivated groups in combination with suitable protecting groups. Target compounds range from functionalised 5-membered nitrogen heterocycles, unnatural amino acids, peptides, neurotransmitter analogs, bioisosters, prodrugs, transporter conjugates and lipids to chiral ligands and acylation catalysts for peptide synthesis. The studies include computational methods with the aim of predicting reactivity, elucidating reaction mechanisms and creating rules for rational design of reaction sequences. Computations are also used to optimise structural design. NMR-spectroscopy is used extensively for structure elucidation and to establish correlations between NMR parameters and physical and chemical properties.

TEACHING

The Department offers the following compulsory courses: Organic Chemistry • Biorganic Chemistry • Pharmacognosy • Drug Design and Development. The courses in Organic Chemistry and Pharmacognosy include laboratory training in addition to lectures and class teaching.

The following elective courses are offered: Spectroscopy • Medicinal Chemistry • Structural Chemistry • Advanced Organic Chemistry • Phytochemistry, Pharmacac and Toxins • Ethnopharmacology • Herbal Medicines • Intellectual Property Rights in Pharmaceutical Sciences. Approximately 30 PhD students are enrolled at the Department, three-quarters of them financed by external funding.

The following PhD courses (taught in English) are offered: Advanced Techniques in Synthetic Organic Chemistry • Advanced Structural Chemistry and Molecular Modelling • Receptor Structure and Function • Drug Design and Discovery • In Vivo Neuropharmacology.

SCIENTIFIC GUESTS

Prof. Marco de Amici, Universita di Milano, Italy.
Dr Karine Audouze-Taboureau, NeuroSearch A/S, Ballerup, Denmark.
Sir, Prof. Tom L. Blundell, University of Cambridge, United Kingdom.
Prof. Lars Bohlin, University of Uppsala, Sweden.
Prof. Guiseppe Campiani, Universita’ degli Studi di Siena, Italy.
Dr Paolo Conti, Universita di Milano, Italy.
Dr Caterina Fattorussro, Universita’ degli Studi di Siena, Italy.
Dr Michael H. Howard, DuPont Company, USA.
Dr Henry Hägerstrand, Åbo Akademi University, Finland.
Dr Elisabeth Marseglia, Cavendish Laboratory, Cambridge, United Kingdom.
Dr Roman Laskowski, Birkbeck College, University of London, United Kingdom.
Dr Hellen A. Oketch-Rabah, University of Nairobi, Kenya.
Prof. Algirdis Sackus, Kaunas University of Technology, Lithuania.
Dr D. Shankar, Foundation for Revitalization of Local Health Traditions, Bangalore, India.
Dr Tracy Spalding, Acadia Pharmaceuticals, San Diego, California, USA.
Prof. Ronald Stenkamp, University of Washington, Seattle, USA.
Prof. Olov Sterner, University of Lund, Sweden.
Dr Owe Wiborg, Aarhus University Hospital, Aarhus, Denmark.
Prof. Jean-Marie Wurtz, Institut de Genetique et de Biologie Moleculaire et Cellulaire, France.

GUESTS RESEARCHERS

PhD student Luca Guandalini, August-December 2001.
Dr Elin S. Olafsdottir, University of Iceland, June-August 2001.
Dr Michael G. Rowan, University of Bath, United Kingdom, July-August 2001.
ARRANGEMENTS


“Seminars in Natural Products and Pharmacognosy” are a monthly event at the Department.

MEMBERSHIP OF EXTERNAL COUNCILS AND BOARDS

Anne Adsersen
• Member of the Subcommittee on Pharmacognosy under the Danish Pharmacopoeia Commission.

Mikael Begtrup
• Member of the steering group for the Department of Physics and Chemistry, The Teaching University of Denmark.
• Member of the Evaluation Center’s board for assessment of the universities teaching in physics, mathematics and chemistry.
• Member of the steering group and the scientific committee for the 32nd Chemistry Olympiad.
• Member of the scientific committee for the European Colloquia on Heterocyclic Chemistry.
• Member of the editorial board for Chemical Communications.
• Scientific editor for ARKIVOC, an electronic journal for organic chemistry.

Hans Bräuner-Osborne
• Member of the Management Committee of the European Federation for Medicinal Chemistry.
• Member of the board for the Danish Society for Pharmacology and Toxicology.

Søren Brogger Christensen
• Chairman of “Studiefonden” of the Danish Union of Pharmacists.
• Member of a panel, which evaluated the Department of Horticulture, the Danish Institute of Agricultural Sciences, Årslev.

Karla Frydenvang
• Member of the Danish National Committee for Crystallography.

Lene Gudiksen
• Head of the Subcommittee on Pharmacognosy.
• Member of the Danish Pharmacopeia Commission.
• National Representative in ESCOP (European Cooperative for Phytotherapy) scientific committee.

Jerzy W. Jaroszewski
• Chairman of the Danish Chemical Society, Section of Organic Chemistry.

Birthe Jensen
• Rector until May 1, 2001.
• Member of the board of UNI.C.
• Member of the board of MVA (Medicon Valley Academy).
• Member of the board of the Symbion Foundation until May 1, 2001.
• Member of the board of European Association of Faculties of Pharmacy (EAFFP).
• Chairman of board of the ULLA network until December 31, 2001.
• Chairman of Evaluation Panel, Pharmacy Education of Helsinki University, December 2001.

Jette Sandholm Kastrup
• Member of the board for DANSYNC, Danish Centre for Synchrotron Based Research.

Povl Krogsgaard-Larsen
• Member of the Danish Academy of Sciences and Letters.
• Member of the Danish Academy of Technical Sciences.
• Member of the Danish Academy of Natural Sciences.
• Member of the board of directors of the Carlsberg Foundation.
• Member of the board of Carlsberg A/S.
• Chairman of the board of the Carlsberg Laboratory.
• Vice-chairman of the board of the Alfred Benzon Foundation.
• Member of the Danish Rector’s Conference.
• Member of the board of the Symbion Foundation.
• Member of the board of the Danish Research Training Council.
• European editor of Journal of Medicinal Chemistry.
• Member of the editorial boards of 7 medicinal chemistry and pharmaceutical journals.

Tommy Liljefors
• Member of the Management Committee of COST (European Co-operation in the Field of Scientific and

- Member of the editorial board for Journal of Molecular Graphics and Modelling.

Per Mølgaard
- Co-ordinating secretary for The International Tundra Experiment (ITEX).
- Danish contact for the ethnobotanical section of AETFAT (Association for the Taxonomy Study of the Flora of Tropical Africa).

Nina Ronsted
- Member of the Council for Health Studies and Education.

Ulla Wagner Smitt
- Treasurer of The International Society for Ethnopharmacology.

DONATIONS AND GRANTS

Mikael Begtrup
DKK 100,000 – Carlsberg Research Prize (Carlsberg Forskerpris).
Co-financing of a 300 MHz NMR spectrometer from the Danish Council for Natural Sciences.
Financing of 1 PhD student from Lovens Kemiske Fabrik.
Co-financing of 5 PhD students and 1 post doc from Novo Nordisk A/S.

Hans Bräuner-Osborne
DKK 300,000 from The Danish Medical Research Council for the project “Molecular pharmacology and mechanistic studies of family C G-protein coupled receptors”.
For additional research centre grants see “Research Centres Grants”.

Søren Brøgger Christensen
DKK 500,000 a year from the Danish Cancer Society (Kraeftens Bekæmpelse) for the project “Development of tissue-specific prodrugs for treatment of prostatic cancer” (1.1.02-31.12.04).
USD 70,000 from the National Cancer Institute, Maryland, USA for development of methods for large-scale isolation and prodrug preparation of Thapsigargin.

A grant together with Karen Krogfelt (Statens Seruminstitut) from the Danish Medical Research Council for the project “Anti-adhesion therapy” (1999-2002).

Rasmus Praetorius Clausen
DKK 1,140,000 from the Lundbeck Foundation in a 3-year period.

Henrik Franzyk
DKK 2,997,000 from the Danish Technical Research Council for the Talent-project “Solid-phase Synthesis of Neuroactive Polyamine Derivatives”.
DKK 150,000 from the Carlsberg Foundation to support this research.

Karla Frydenvang
DKK 465,000 from Alfred Benzon Foundation for the project “Solid state properties of pharmaceutically relevant compounds” (31.8.01-30.8.02).

Jerzy W. Jaroszewski
DKK 3,500,000 from Apotekerfondet for purchase of NMR equipment.
DKK 250,000 from the Danish Medical Council for the project “Analogue of polyamine wasp toxins”.
DKK 254,058 from the Novo Nordisk Foundation for the project “Selective antagonists at ionotropic receptors”.
DKK 25,000 from Ben-Gurion University, Israel, for studies of Balanites.

Danida ENRECA project “Ethnopharmacology of Indian medicinal plants” (expired in June 2001)

Danida ENRECA project “Medicinal plants from East Africa”.
For additional research centre grants see “Research Centres Grants”.

Christina Kasper
DKK 391,636 from the Carlsberg Foundation for the project “Studies of glutamate receptors with special reference to structure-based drug design” (1.1.01-31.12.01).

Jørgen Bonefeld Kristensen
DKK 62,712 from Novo Nordisk A/S - a one-year Novo Nordisk Scholarship.

Ingrid Kjøller Larsen
DKK 70,000 from DANSYNC, Danish Centre for Synchrotron Based Research.
DKK 250,000 from the Danish Medical Research Council for the project “Protein crystallography in drug research. Structure determination of biomacromolecules and their complexes with ligands/drugs (2001-2003)”.
DKK 80,000 from the Novo Nordisk Foundation for the project “Protein crystallography in drug research. Characterization of biomacromolecules by dynamic light scattering”.
For additional research centre grants see “Research Centres Grants”.

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Povl Krogsgaard-Larsen
DKK 1,836,000 from the “Drug Design and Transport Centre”
granted by the Danish Medical Research Council (account-
ing year 2000-2001).
ECU 177,00 together with Jerzy W. Jaroszewski from EU.
DKK 400,000 from the Alfred Benzon Foundation.
For additional research centre grants see “Research Centres
Grants”.

Per Mølgaard
DKK 150,000 from the Commission for Scientific Research
in Greenland for the project “Development of analytical
methods for secondary compounds in Arctic plants”.
DKK 180,000 together with Søren Brøgger Christensen from
Danida via a grant to Ole Skovmand, Intelligent control for
supporting an environmental project in Burkina Faso, Africa.
DKK 210,000 from the Danish Research Council for the
project “Special chemicals and pharmaceuticals from plants”.

Britt Petersson
PhD grant from DANSYNC, Danish Centre for Synchrotron

RESEARCH CENTRES GRANTS

Povl Krogsgaard-Larsen, Ingrid Kjøller Larsen and Tommy
Liljefors: DKK 6,000,000 from the Lundbeck Foundation for
the research programme “Neuro-medicinal chemistry.
Molecular design, specificity and recognition” (1999-2001).
Povl Krogsgaard-Larsen, who is the co-ordinator of this pro-
gramme received DKK 1,150,000 per year. Ingrid Kjøller
Larsen and Tommy Liljefors each received DKK 425,000 per
year.

Hans Bräuner-Osborne, Jerzy W. Jaroszewski, Ingrid Kjøller
Larsen and Tommy Liljefors
DKK 6,700,000 from the research centre NeuroScience
PharmaBiotec A Strategic Drug Research Centre” (1997-
2001). The centre is granted by Danish Medical Research
Council with totally DKK 29,700,000. Povl Krogsgaard-
Larsen is director of the centre.

Ingrid Kjøller Larsen, Tommy Liljefors, Jerzy W. Jaroszewski
and Povl Krogsgaard-Larsen: DKK 635,000 from the
PharmaBiotec funding, which from January 2000 became a
part of the annual appropriation to the Royal Danish School
of Pharmacy (until January 2000 PharmaBiotec was funded
by the State Biotechnology Programme).

PROJECTS

Special chemicals and pharmaceuticals from plants
There is a great need for medicinal plant products of a high
quality, and Danish agriculture is interested in alternative crop
plants to the traditionally grown cash crops. Our research
work comprises plant chemicals like fatty acids, caffeic acid
derivatives, alkamides and iridoids for technical and medicinal
purposes. These compounds are all plant derived, and in
most cases there is only little information of how to grow
these plants, especially under Danish conditions. To deter-
mine the quality of medicinal plants validated analytical meth-
ods are highly important, and a major part of the project is
confined to the establishment of validated analytical methods.
In connection with plant production, diurnal and seasonal
variation in plant secondary compounds may play a central role.

Echinacea purpurea, the purple coneflower, cultivated in Tåstrup for investigation of a potential
seasonal variation in the content of cichoric acid and alkamides.
The project has run over the latest five years with financial support from the Danish Research Councils. Within the project emphasis has been put on plants with content of fatty acids, plants with caffeic acid derivatives and plants with iridoids, all with potential use in the technical and pharmaceutical industry directly or after derivatization.

Caffeic acid derivatives are important antioxidants and major ingredients of many plants commonly used in herbal remedies. Main emphasis has been given to Echinacea purpurea in an attempt to give guidelines for production and use in Denmark. Evidence of the activity of the compounds in Echinacea is still lacking, and we have ongoing investigations of the biological activity of the major constituents, cichoric acid, alkamides and polysaccharides. As a first result we have verified the activity of cichoric acid as an antioxidant comparable to rosmarinic acid.

Iridoids are compounds of restricted occurrence in the plant kingdom, often confined to the same taxonomic groups as contains caffeic acid derivatives, although these are more widespread. They are very promising as starter material for the synthesis of pharmacologically active compounds to be used in the treatment of cancer or HIV. In a taxonomical study of the genus Plantago we are making use of DNA sequencing and the chemotaxonomic value of iridoids and caffeic acid derivatives characteristic for this taxon. Iridoids and caffeic acids are common in the whole order of Scrophulariales, incl. Plantaginaceae, with a number of potential medicinal plants. (Per Malgaard, Kim Itenov, Nina Ransted, Line Sandager, Søren Johnsen, Line Thygesen and Peter Christensen in collaboration with Henrik Franzyk [the Natural Products Group], Claus Cornett [Department of Analytical and Pharmaceutical Chemistry], Søren Rosendal Jensen, [Department of Organic Chemistry, the Technical University of Denmark] Poul Flengmark [Danish Agricultural Research Institute, Research Centre Flakkebjerg] and Leif Skibsted [Department of Food Chemistry, Danish Agricultural University].)

**The ENDOD project for the control of schistosomiasis transmitting snails**

This project is carried out in cooperation with a Zimbabwean counterpart and the Danish Bilharziasis Laboratory (DBL) and is dependent on financial support from Danida to DBL. The aims are to facilitate the cultivation of the Endod plant (Phytolacca dodecandra) and application of the molluscidal berries to infected water, in an integrated control of schistosomiasis (Bilharziasis), a tropical water related disease, where fresh water snails are crucial for transmission of the parasite.

Control of the intermediate host snails supports the other aspects of the general control of schistosomiasis, which affects more than 200 mio. people in the Tropics.

In the reference period a sociological study of community participation was completed by a PhD student from Zimbabwe. His study concerned introduction of the Endod-plant as an easily grown and locally applied snail control measure. This should offer a low cost - low technology self help device in combination with chemotherapy, improved water and sanitation, and health education in the control of schistosomiasis. See also: www.dfh.dk/activities/endod/index.htm.

(Per Malgaard in collaboration with Ebba Holme Hansen [Department of Social Pharmacy), Peter Furu [Danish Bilharziasis Laboratory], Addmore Ndekha [Blair Research Laboratory, Harare, Zimbabwe].)

**Ethnopharmacological studies of plants from Réunion Island**

This project investigates plants used in traditional medicine in Réunion Island and plants related to traditionally used plants. Recent studies include three endemic Melicope species (synonym Euodia), M. borbonica, M. coodeana and M. obscura selected on basis of their biological activity in preliminary screening assays. The three species showed significant in vitro antibacterial, antifungal, antimalarial and/or antioxidative activities.

From the leaves of M. borbonica, 15 constituents have been isolated and identified. The antifungal activity could be assigned to xanthoxylne and scoparone, present in very high concentrations, as well as to limettin and 1,4-epidioxy-bisabol-2,12-diene. These compounds showed inhibition of the in vitro growth of Candida albicans and Penicillium expansum. The two major methoxyflavones from the leaves inhibited the NF-κB transcription factor.

Three flavones, 5,7-dihydroxy-3,8-dimethoxy-3’,4’-methylenedioxyflavone (1), 5,7-dihydroxy-3,6,8-trimethoxy-3’,4’-methylenedioxyflavone (2) and 5,7-dihydroxy-3,6,8,3’-A’-pentamethoxy-flavone, out of five isolated from M. coodeana were new structures and the presence of the unusual methylenedioxyflavones in this species is of chemotaxonomic impor-
rance. From *M. coodeana* compounds with antimalarial and antioxidative activity have been isolated but the structures not finally elucidated.

Four compounds with antibacterial and antifungal activity have been isolated from *M. obscura.*

(Anne Adsersen, Ulla Wagner Smitt, Henrik Toft Simonsen in collaboration with Jerzy W. Jaroszewski [The Natural Products Group], Dominique Strasberg [University of Réunion]).

**Secondary plant compounds in Arctic plants**

This project is linked to ITEX - the International Tundra Experiment (http://www.systbot.gu.se/research/ITEX/itex.html), which is a circumpolar co-operation with stations at more than 20 sites in the arctic area. By observation and manipulation with selected, wide spread plant species, the aims are to anticipate the reaction of these plants and the environment they occur in to an eventual global climate change. The observations and manipulations are carried out after the same instructions at all sites.

Our contribution mainly concerns plant secondary constituents, and the effect on these compounds of a change in weather conditions in the Arctic. These compounds are of importance in relation to protection against herbivory and are probably affected by increased temperatures, which may lead to a change in relative reproductive success. The main emphasis is put on chemical compounds in *Salix arctica, Papaver radicatum, Cassiope tetragona,* and plant phenolics in general. As arctic plants have not been thoroughly investigated, we have so far been able to identify two genuine compounds new to plants.

(Per Mølgaard, Karen Christensen, Anette Lauritzen, Jakob Tjelum, in collaboration with Claus Cornett [Department of Analytical and Pharmaceutical Chemistry]).

**Optimisation of the antiplasmodial effect of the natural product licochalcone A**

The antiplasmodial and antileishmanial activities of Chinese licorice roots (*Glycyrrhiza inflata*) has been related to the content of licochalcone A. Orally administration of this compound to mice infected with malaria clears the infection efficiently but only in relatively high doses. This drawback might be related to a poor absorption of the drug from the stomach or guts.

The structure of licochalcone A enables syntheses of a large numbers of analogues and thereby facilitates medicinal chemistry studies. A positive relation between the chemical structure and biological activity has previously been proven (a QSAR model) but the model is only valid for poorly water-soluble analogues. A number of water-soluble analogues were prepared and their ability to kill malaria parasite *in vitro* were determined. A poor variation in their biological activities prevented development of a QSAR-model.

(Klaus Jensen, Søren Brøgger Christensen).

**Structure and pharmacology of natural products**

Structure elucidation and biological characterisation of natural products is a mainstream activity of the Natural Products group. The research is currently focused on antiprotozoal compounds. The group’s own biological laboratory performs drug-sensitivity assay using various strains of *Plasmodium* parasites as well as assays for cytotoxic activity using wild type and multidrug-resistant human cancer cell lines, available via collaboration with National Cancer Institute, Bethesda, USA. Studies of effects of natural products on *Plasmodium falciparum* involve investigations of their action on erythrocyte membrane, as it was recently discovered, that incorporation of various compounds into the lipid bilayer of erythrocytes, in which the malaria parasites are cultured, inhibits indirectly the parasite growth and invasion. This effect appears as a false positive result in the *in vitro* assay. Further studies of nature of the effect of erythrocyte membrane modifications on parasite growth are in progress.

Studies of phytochemical and pharmacological effects of natural products involve investigations of alkaloids from Apocynaceae, Asclepiadaceae, Periplocaeeae and Flacourtiaceae.
During the period covered by this annual report, many novel phenanthroindolizidine alkaloids, cytotoxic at the nanomolar level, have been identified. Iranian *Perovskia* species have been identified as a new source of tanshinones, clinically useful natural products originally isolated from the Chinese drug dan-shen. Several highly leishmanicidal, novel isoflavans have been isolated from *Smirnowia* species. Novel terpenoids belonging to malabaricane and aromadendrane series have been identified from *Apocynaceae* and *Flacourtiaceae*, respectively.

The core-activity of the group is NMR and a number of NMR spectroscopic studies have been carried out. These include conformational studies of alkaloids using dynamic NMR, use of $^2$H NMR in biosynthetic studies (with Nina Rønsted), use of $^{31}$P NMR to characterise influence of ischemia upon composition of brain phospholipids (with Harald Hansen, Department of Pharmacology), use of pulsed-gradient spin-echo NMR to characterise self-diffusion in pharmaceutical microemulsion delivery systems (with Mads Kreilgaard, Department of Pharmacy), and conformational analysis of polar molecules in aqueous solution (with Peter A. Nielsen and Tommy Liljefors, Structural Chemistry). An external grant will enable a deployment of state-of-the-art 600 MHz NMR facilities and HPLC-MS-NMR equipment during 2002.

(Jerzy W. Jaroszewski, Dan Stærk, Henrik Franzyk, Jette Christensen, Hanne Ziegler, Majid Sairafianpour, Thomas Hagh Jensen, Vicki Clausen, Bogdan Buchnik [University of Odense], Karim Bagherzadeh [Isfahan Research Centre of Natural Resources, Iran], Henry Hägerstrand [Åbo Akademi University], Carl Erik Olsen [Royal Veterinary and Agricultural University], Ulla Wagner Smitt, Anne Adsersen and Henrik Toft Simonsen [The Pharmacognosy Group], Partick Ekpe [University of Ghana], Lise Bolt Jørgensen [University of Copenhagen], Lars Hvid [Copenhagen University Hospital], Elin S. Olafsdottir [University of Iceland], Hellen Oketch Rabah [University of Nairobi]).

**Synthesis of analogues of polyamine wasp toxins**

Through the development of ligands with a potent and specific interaction with receptors it is possible to acquire knowledge about the structure and function of the receptors even in cases where the three-dimensional structure of the receptor is not available. This applies to many membrane-bound receptors in the central nervous system (CNS). A ligand-type which is of our particular interest is the group of polyamine spider and wasp toxins, which have been shown to be non-competitive inhibitors of ion channel coupled glutamic acid and acetylcholine receptors. In general these polyamine toxins, called philanthotoxins, are built from three different sections (depicted below as sections 1-3): a polyamine moiety, an amino acid, and an acyl moiety.
In a preliminary hypothetical model for the binding of philanthotoxins (see figure) it was suggested that these compounds block the ion channels due to an electrostatic binding to ionized carboxylic acid residues in the transmembrane portion of the receptor, and via hydrophobic interactions of the amino acid side chain and acyl chain with the outer part of the receptor. Polyamine toxins have been shown to exhibit a protective effect on nerve cells, and therefore are interesting as leads in medicinal chemistry research towards treatment of neurodegenerative diseases. It was previously shown, that the polyamine chain is essential for activity on glutamate receptors, whereas the inner amino functionalities may be omitted in compounds interacting with acetylcholin receptors.

The present research is concerned with the design and synthesis of novel conformationally restricted apolar head groups (i.e., sections 2 and 3). These are then used in parallel solid-phase synthesis of compounds with improved biological activity as compared to natural philanthotoxins. Also, novel sequential solid-phase methods for synthesis of the polyanine part are being developed. Here the main effort is to obtain polyamines, in which N-alkylated, α- or β-alkyl substituted amines have been incorporated. This requires development and optimisation of novel synthetic methods, which subsequently will allow a systematical study of structure-activity relationships in much more diverse libraries of analogues of polyamine toxins than those investigated previously. The use of computational methods to correlate the structure of the apolar head groups with the observed receptor affinity is currently under consideration for future synthetic analogues. The tests regarding receptor binding is currently performed in co-operation with University of Nottingham, United Kingdom. (Henrik Franzik, Jarzy W. Jaraszewski, Malene Ryborg Jørgensen, Christian Adam Olsen, Povl Krosggaard-Larsen [The Neuromedicinal Chemistry], Kristian Strømgaard [Columbia University, New York], Kim Andersen [Lundbeck A/S], Peter N. R. Usherwood and Ian Mellor [University of Nottingham]).

Protein modelling and ligand design by computational methods

By using a combination of computational methods the molecular events associated with many biomolecular processes can be studied. The availability of experimentally determined 3D-structures of proteins and ligand-protein complexes makes it possible to directly study the details of molecular recognition and perform so-called structure-based computer-aided ligand design. Even when the detailed structure of the receptor or enzyme is not known, it is often possible by molecular modelling to construct reliable three-dimensional models, which allows important issues like activity, selectivity and resistance to be studied. In cases where only pharmacological data for a set of ligands are available, 3D-pharmacophore models and 3D-QSAR models which describe important requirements for the interactions between the ligands and a particular receptor or enzyme may be developed.

A number of enzymes and ligand-binding domains of receptors have been studied in order to identify the molecular features responsible for affinity, selectivity and in some cases also resistance. One of the enzymes we have studied is matrix metalloproteinase (MMP). Human MMP’s have been found to be involved in many different disease states, e.g. arthritis, cancer and osteoporosis. In these diseases, an imbalance is observed between the MMP’s and their natural inhibitors, and accordingly, it is desirable to be able to selectively inhibit the different MMP’s. Key differences have been identified between several of these enzymes. New methods for selection of possible binding modes (conformations) and subsequent prediction of their relative binding strength have been developed based on multivariate statistics. These methods have been extensively evaluated on a large and structurally diverse set of
A substituted flavone fitted to a pharmacophore model for the benzodiazepine site of the GABA_A receptor. The pharmacophore model has been used for the design of the compound which displays high affinity for the receptor with a $K_i$ value of 0.9 nM. S1-S5 represent areas occupied by the receptor. H1 and H2 are hydrogen bond donating receptors sites, whereas A2 is a hydrogen bond accepting site. L2 denotes a lipophilic cavity.

ligand-macromolecule complexes. The MMP project is carried out in collaboration with Dr Inge Thøger Christensen, Novo Nordisk A/S.

Studies on ligand-protein interactions have been performed for two novel anti-cancer targets MetAP-2 (methionine aminopeptidase) och VEGF (the vascular endothelial growth factor) aiming at the design of new ligands which may be developed into anti-cancer drugs. These studies have been done in collaboration with Leo Pharmaceuticals.

On the basis of the availability of three-dimensional structures for the ligand binding domain of an ionotropic glutamate receptor (iGluR2) in complex with various ligands, a number of studies have been performed aiming at an understanding of subunit/subtype selectivity and the design of new subunit/subtype selective ligands. These studies have in particular focused on the role of water molecules in the ligand binding site for the ligand binding mode as well as for ligand affinity and selectivity. Studies along these lines have also been performed for metabotropic glutamate receptors on the basis of the experimentally determined structure of the ligand-binding part of the mGluR1 receptor. Collaborators in the glutamate receptor projects have been Professor Arne Schousboe, Department of Pharmacology, the Protein Crystallography and the Neuromedicinal Chemistry Groups at the Department of Medicinal Chemistry and Prof. Guiseppe Campiani, Siena, Italy.

3D-pharmacophore models have successfully been used for the design of novel high-affinity ligands for the GABA and benzodiazepine sites of the GABA_A receptor. Pharmacophore models for subtypes of neurokinin receptors (NK1 and NK2) have been developed and, addition, for all subtypes of the $\alpha_\text{1}$-adrenoceptor. Ligand design on the basis of these models have been initiated.

The pharmacophore model for the benzodiazepine site of the GABA_A receptor has been used for database searches and a number of new interesting lead compounds have been identified. These studies have been performed in collaboration with H. Lundbeck A/S, NeuroSearch A/S, Dr Ingrid Pettersson at Novo Nordisk A/S, Professor Olov Sterner, University of Lund and Professor Mogens Nielsen.


Pharmaceutically important physico-chemical properties

The oral bioavailability of a drug compound is an extremely complex property influenced by factors like absorption, distribution, metabolism and excretion (ADME properties). Solubility is one of the key factors determining absorption, and accordingly prediction of aqueous solubility has become a major issue in the drug development process.

New models for prediction of aqueous solubility and several other ADME properties have been developed and extensively compared with models previously reported in the literature. The purpose of these studies is to develop tools, which make
Three-dimensional model of acetyl salicylic acid coloured according to atom type. The water-accessible surface is shown as a semi-transparent cloud around the molecule.

it possible to determine the ‘drug-likeness’ of compounds prior to synthesis.

Solubility is influenced by solid phase properties, e.g. molecular structure and crystal packing, as well as by external factors like temperature, pH and ionic strength. The crystal packing is a fine balance between many weak and stronger intermolecular contacts, but unfortunately, crystal structures are generally not predictable. Projects have been undertaken in order to achieve improved understanding of the relationships between solid phase properties such as solubility and compressibility on one side and the actual crystal packing on the other side. A series of substituted benzoic acid salts have been analysed in order to achieve insight in the effect of structural parameters on the formation of low solubility salts, and a series of parabenes have been analysed for the structural effect on elasticity and compressibility. The ultimate goal is to be able to predict the solid phase properties and to design new compounds with optimal characteristics.

These projects involve collaborations with Professor Claus Selch Larsen at the Department of Analytical and Pharmaceutical Chemistry, Professor Sven Frejkjær and Professor Henning Gjelstrup Kristensen at the Department of Pharmacy and Dr Inge Thøger Christensen, Novo Nordisk A/S.

(Karla Frydenvang, Tommy Liljefors, Birthe Jensen, Jørgen Bonefeld Kristensen, Flemming Steen Jørgensen).

Structural studies of CNS proteins by X-ray crystallography
An increased knowledge on three-dimensional structures of proteins is necessary to fully understand their function at a molecular level. The protein crystallography group is mainly focusing on three types of CNS proteins: ionotropic glutamate receptors (iGluRs), neural cell adhesion molecule (NCAM), and α-synuclein. iGluRs and NCAM are membrane-
Crystallisation and evaluation of crystals are fundamental steps in the structure determination of proteins by X-ray crystallography.

bound receptors involved in a series of important processes within the central nervous system. α-synuclein is a brain protein, which plays a role in neurodegenerative diseases such as Parkinsons and Alzheimers disease.

Within the glutamate receptor project, we have so far focused on the ligand-binding domain of GluR2 in complex with different AMPA receptor agonists and antagonists. Several structures of complexes have been determined providing a wealth of information on ligand binding and receptor activation. The structures of GluR2 in complex with ligands show different binding modes for the ligands and disclose domain movements taking place upon ligand binding. Expression and purification of other receptor subunits has been initiated to address subtype selectivity.

In the NCAM project, it is our goal to stepwise build up the whole extracellular part of the receptor by structure determinations of fragments of NCAM, and to determine structures of NCAM in complex with heterophilic binding partners. This year, we determined the structure of NCAM-IgI-II-III, and the structure has allowed us to put forward reliable models for both NCAM cis and trans interactions, reflecting interactions of molecules on the same cell and on opposed cells. NCAM-IgI-II-III-IV has recently been crystallised, and co-crystals of NCAM-IgI-II and sucroseoctasulphate have been obtained to address the question whether homophilic and heparin binding can occur simultaneously.

α-Synuclein is a 14 kDa protein, which belongs to a family of natively unfolded proteins without, or with very little, secondary structure elements. Different crystallisation conditions and various additives are being investigated in order to trigger the protein, as well as two mutants thereof, to fold and crystallise. Folding is probably triggered by binding to its biological target, as well as by polymerisation (fiber formation).

In addition, the structures of three peptide nucleic acids (PNAs) have been determined. PNA analogues are potential antisense/antigene drugs. All projects are performed in collaboration with both national and international collaborators from universities and industry.


GABA_A receptor ligands and GABA uptake inhibitors
The GABAergic neurotransmitter system involves a number of synaptic processes and mechanisms, which have been studied pharmacologically and constitute potential therapeutic targets. In continuation of previous projects in this field, the design and development of ligands for the GABA_A receptor and the GABA uptake system have been of primary interest.

The project on GABA_A receptor ligands has been continued in close collaboration with Professor Tommy Liljefors and his group. According to a previously proposed pharmacophore model for GABA_A receptor agonists, a receptor cavity in the vicinity of the 4-position of the 3-isoxazolol ring in 4-PIOL, a low-efficacy partial GABA_A agonist, exists. To explore the dimensions and other properties of the receptor cavity, a number of analogues of 4-PIOL, in which the 4-position of the 3-isoxazolol ring is substituted by different groups, has been synthesised. This study has transformed 4-PIOL into the
highly potent GABA<sub>A</sub> antagonist 1. During the past year, 1 has been developed into a series of very potent GABA<sub>A</sub> antagonists including compound 2, which in functional assays is even more effective than 1.

Similar structural changes have been made for the isothiazolol analogue of 4-PIOL, thio-4-PIOL, which has been shown to possess markedly higher efficacy than 4-PIOL. Although the chemistry of 3-isothiazolols is complex, a series of thio-4-PIOL analogues has been synthesised and shown to be significantly more potent than the 3-isoxazolol analogues.

In collaboration with professor Arne Schousboe and his group at the Department of Pharmacology a number of very significant and, from a therapeutic point of view, potentially important results on the GABA uptake project have been obtained. The cyclic amino acid, nipecotic acid, was discovered by the NeMe group as a specific GABA uptake inhibitor some years ago and subsequently converted into the antiepileptic drug, tiagabine, by incorporation of the lipophilic DTB group as an N-substituent at Novo Nordisk A/S. In the NeMe group

N-Me-exo-THPO was subsequently synthesised and shown to be a glia-selective GABA uptake inhibitor. The DTB-analogue of N-Me-exo-THPO has now been fully characterised as a very potent GABA uptake inhibitor showing a unique pharmacological profile different from that of tiagabine. Due to a very complex chemistry required for the synthesis there has been no further development of this compound.

Very recently the isomeric amino acids 3 and 4 have been shown to have weak GABA uptake inhibitor effect. By introduction of lipophilic substituents, both 3 and 4 were converted into GABA uptake inhibitors showing yet another unique pharmacological profile. This effect of the analogues of 3 and 4 is now under further exploration in animal behavioural studies in order to elucidate their therapeutic potential.

The projects described are interdisciplinary collaborative projects involving other research groups at DFH and in the industry.

(Titi Akinleminu, Rasmus Praetorius Clausen, Bente Frølund, Karla Frydenvang, Povl Krogsgaard-Larsen, Christian Madsen, Lotte Olsen, Dorte Seir Petersen, Tine Bryan Stensbøl).

Excitatory amino acid receptor ligands
The central excitatory amino acid neurotransmitter, glutamic acid (Glu), operates through a large number of receptor subtypes divided into two groups, the ionotropic (iGlu) receptors and the metabotropic receptors, the latter group belonging to the superfamily of 7-TM receptors. The iGlu receptors comprise the NMDA, the AMPA (GluR1–4), and the kainic acid (GluR5–7 and KA1–2) receptors. In recent years the research has been focused on the AMPA and kainic acid subgroups of receptors.

During the past one year period a number of research projects related to bioisosteric replacement of carboxy groups have been accomplished. As part of an ongoing project using 3-isoxazolols as carboxy group bioisosteres, new analogues of AMPA containing aromatic substituents in the 5-position of the 3-isoxazolol ring, exemplified by the pyrazinyl analogue (1), have been synthesized in an effort to further map out structural requirements for AMPA receptor agonist activity. In connection with these studies, a new and versatile method for the

![Proposed bioactive conformation of 1 placed in a pharmacophore model for GABA<sub>A</sub> agonists. The tetrahedron indicate areas occupied by the receptor.](image-url)
preparation of 5-substituted 3-isoxazolols via acylated
Meldrum’s acids has been developed.

In another project 1-hydroxyazole-containing α-amino acids
have been synthesised and pharmacologically evaluated.
These studies have identified the 1-hydroxy-1,2,3-triazole (2a and
2b) and the 1-hydroxy-1,2,3-triazole (3a and 3b) analogues
as new and useful bioisosteres at iGlu receptors and at Glu
transporters. Molecular modelling studies using a published
chemical structure of the ligand binding site of GluR2 have
shown that these compounds can bind to the receptor in an
“AMPA-like mode” making the same favorable contacts as
AMPA and not entering sterically forbidden zones.

Important progress has also been achieved in projects us-
ing the 3-isothiazolol ring system as a carboxy group
bioisostere at Glu receptors. In this regard regioselective lithi-
ation and functionalisation of 3-(benzylxox)isothiazole has
been carefully investigated, and these studies has led to the
preparation of thiobotenic acid, the sulfur analogue of the
neurotoxic natural product ibotenic acid. The pharmacological
characterisation of thiobotenic acid carried out so far shows
interesting agonist activity at iGlu as well as mGlu receptors.

The 3-hydroxy-1,2,5-thiadiazole ring system, which forms
the distal acidic part of the α-amino acid TDPA, is structurally
closely related to the 3-isothiazolol ring present in thiobotenic
acid. Pharmacological studies on the enantiomers of TDPA
have revealed a complex and interesting pharmacological
profile. In addition to a moderate agonist activity at group I
mGlu receptors, (S)-TDPA selectively interacts with the Glu
transporter EAAT2, and shows agonist activity at AMPA re-
ceptors. In contrast, (R)-TDPA shows a more clear pharma-
cology, being a selective AMPA receptor agonist
with almost the same affinity as (S)-TDPA. The
transporter activity and the unusually low stereo-
selectivity at AMPA receptors observed for TDPA
makes the 3-hydroxy-1,2,5-thiadiazole a unique
carboxy group bioisostere.

ACPA and its demethyl analogue, which are ana-
logues of AMPA, have been resolved using chiral
HPLC. X-ray crystallography has been used to es-
establish the absolute configuration of the resolved
enantiomers. The configurational assignment ob-
tained from this X-ray study has been supplement-
ed by an asymmetric synthesis of (S)-ACPA and an
X-ray analysis of a derivative of (S)-ACPA.
Pharmacological studies have revealed that the po-
tent AMPA receptor agonist activity of ACPA resides
exclusively in the S-enantiomer, and that both
enantiomers of demethyl-ACPA are relatively weak
AMPA receptor agonists, (S)-demethyl-ACPA being
the most potent.

In continuation of ongoing projects, the crystal
structures of the potent GluR5 receptor agonists,

Chemical structure of selected ionotropic Glu receptor ligands.
ATPA and thio-ATPA, have been solved. Together with quantum chemical calculations these studies show, that whilst the 3-isoxazolol tautomer of ATPA predominates in all phases, the 3(2H)-isothiazolone tautomer of thio-ATPA predominates in the crystal structure and most likely in weakly acidic aqueous solution.

Furthermore, hybrid analogues of the kainic acid receptor agonists (2S,4R)-4-methyl-Glu and ATPA (exemplified by 4) have been prepared and show highly selective GluR5 receptor affinity.

Many of the mentioned projects have been performed in close collaboration with other research groups at the Royal Danish School of Pharmacy, in particular structural chemists and molecular pharmacologists and other research groups in the pharmaceutical industry. (Hans Bräuner-Osborne, Lotte Brehm, Lennart Bunch, Rasmus P. Clausen, Bente Frølund, Karla Frydenvang, Mette Guldbrandt, Mette B. Hermit, Tommy Nørskov Johansen, Povl Krogsgaard-Larsen, Ulf Madsen, Birgitte Nielsen, Frank Sleek, Tine B. Stensbøl, Ulink Svane Sørensen, Jón Valgeirsson, Stine B. Vogensen).

**Family C 7TM receptors**

Human G-protein coupled receptors are generally divided into three families (Family A, B and C) based on their resemblance in amino acid sequence. All G-protein coupled receptors span the cell membrane seven times and are thus also called 7 transmembrane (7TM) receptors. Family C, which consists of eight glutamate (mGlu1-8), two GABAA and one calcium-sensing (CaR) receptor, has traditionally been characterised by a unusually large amino-terminal ligand binding domain (see figure).

The NeMe group has developed pharmacological assay for the mGlu, GABAA and CaR receptors that enable us to study compounds synthesised in the NeMe group and by collaborators. In this way new potent ligands have been developed which display selectivity for subsets or individual receptor subtypes.

Based on mutational studies we have been able to identify amino acids in the amino terminal domain, which are directly involved in agonist binding. The recent publication of the X-ray crystal structure of the ligand binding domain of the mGlu1 receptor has led us to generate computer models of the remaining seven mGlu receptors. These models...
are being tested by mutagenesis with the aim of increasing our understanding of ligand selectivity.

Numerous studies have shown that the family C receptors are homo- or heterodimers. Based on the X-ray crystal structure it has been proposed that agonist binding leads to activation by bringing the two 7TM domains in the dimer closer together. This hypothesis has been tested by use of a technique called bioluminescence resonance energy transfer (BRET).

The NeMe group has recently cloned a new group of previously unknown family C receptors. In contrast to previous assigned family C members, this new group is characterised by a short amino terminal domain. The expression pattern and cellular localisation of the new receptors has been determined (see figure). 1000 putative ligands have been screened in a FLIPR high-throughput assay, but unfortunately no active ligands have yet been identified.

(Hans Bräuner-Osborne, Anders A. Jensen, Mette B. Hermit, Petrine Wellendorph).

New synthetic methodologies

The synthesis group has been working on several new synthetic methods of importance in medicinal chemistry. Regio-selective introduction of functional substituents and cross-couplings have been performed with complete control in all positions in 1-hydroxypyrazole and pyrazole. The reactions have been combined with new anionic cyclisation reactions which have provided several new ring systems and ring systems of significant interest in medicinal chemistry. Similar reactions have been performed in the imidazole and thiophene series.

Effective methods for the preparation of 2-substituted phenylboronic esters have been developed. These compounds serve as synths and have a enormous potential in synthesis and medicinal chemistry allowing connection of two functional aryl groups and construction of rings by anionic cyclisation.

Cross-coupling reactions have also been employed by the construction of tamoxifen analogues with improved properties. Subsequent anionic cyclisation have given a highly active analogue with constricted conformation.

A broafly applicable synthon for preparation of phenylglycines and heterocyclic analogues has been developed and its versatility demonstrated by preparation of a series of new or difficult accessible amino acids. A protocol for preparation of heterocyclic phenyl analogues has also been established. Several of the new compounds are under biological testing.

New drug substances have been coupled to peptide carriers in order to improve the transport of the drug through the intestinal barrier. New methods for construction of libraries of privileged structures using solid phase chemistry have been initiated.

New methods for isotop labeling of drug metabolites and positron emitting drug tracers are under development.

Development of methods for preparation of lipid conjugates for drug targeting is in progress.

(Mikael Begtrup, Patrizia Cali, Peter Elm, Jørgen Eskildsen, Jesper Kristensen, Uffe Larsen, Jan Pawlas, Rune Severinsen, Martin Wenckens, Niels Østergaard og Per Vedsø).
SPHERE OF INTEREST

The Department of Pharmaceutics deals with the formulation, processing and quality assurance of drug products, i.e. the objectives involved in bringing a drug substance into an effective and safe dosage form. Further, the activities include how to administer the drug product safely and optimise the effect for the individual patient. The scientific and teaching objectives are therefore dosage form design, processing of dosage forms, quality assurance, clinical pharmacy and pharmacotherapy.

The formulation design of drug products takes its starting point in the chemical, physico-chemical, pharmacokinetic and pharmacodynamic properties of the drug substance, the route of administration and the manufacturing method. The stability of the substance as such and in formulation, the choice of excipients and different approaches to overcome the transport across restrictive biological barriers are objects of interest. Chemical, physical and pharmaceutical-technical methods for evaluation of drug formulations are necessary tools.

The Department participates in an extramural research centre, the Centre for Drug Design and Transport. Professor Sven Frøkjær is the head of the centre, established as a four-year programme to be terminated on 1 November 2001.

Professor Henning G. Kristensen is chairman of the European Pharmacopoeia Commission, which is important to the functioning and development of the Department.

RESEARCH

The four main areas of research at the Department of Pharmaceutics are:

Pharmaceutical formulation: Formulation of drug products taking into consideration the physical, chemical and pharmacokinetic and pharmacodynamic properties of the drug substance, the route of administration, the processing method and clinical use of the product

Civil servants from The Ministry of Education and The Ministry of Research visited the department in November 2000.
**Drug delivery:** Design of drug delivery systems actively controlling and optimising the absorption of drug substance and/or its transport in the living organism to the site of action.

**Processing technology:** Unit operations applied in the processing of drug products and the influence of the method selected on formulation design.

**Clinical pharmacy:** Optimisation of the therapeutic result of a medication taking into consideration the biopharmaceutical profile of the drug product and its pharmacokinetic and pharmacodynamic properties.

The character of the research is interdisciplinary and integrated. Projects are typically carried out in research groups of scientists from various research groups established at the Department of Pharmaceutics and from other university departments, university hospitals and hospital pharmacies and the pharmaceutical industry.

The number of PhD students at the Department has grown steadily in recent years. In 2001 approximately 35 PhD students were supervised by staff members of the Department of Pharmaceutics in collaboration with supervisors from the pharmaceutical industry. The involvement of adjunct professors is very important in this context. At present adjunct professors are managing director Ole Wörs, Glatt Norden, Dr. Vagn Handlos, head of the State University Hospital Pharmacy, Professor Dr. Gert Storm from the University of Utrecht in the Netherlands and Professor, Dr. Hans Lennernäs, Uppsala University, Sweden. Professor, Dr. Hans Peter Merkle, ETH Zurich, Switzerland, has been appointed adjunct professor in 2001.

The bulk of PhD scholarships are based on external funding, in particular from the Danish pharmaceutical industry in keeping with contracts established on drug formulation training and the Centre for Drug Design and Transport. The agreed industrial funding is, however, running out. The number of PhD students will therefore decline dramatically during the next two years unless we are able to attract new funding.

The strategy of the Department of Pharmaceutics is to strengthen international relations by exchanging PhD students and staff members with university departments abroad. Consequently nearly all PhD students visit university departments abroad as part of their PhD programme. The Department also attaches great importance to hosting foreign PhD students and scientists to establish collaborative research.

**PHARMACEUTICAL FORMULATION**

The formulation of low soluble drug substances intended for oral delivery has been subject to intensive research in recent years. Current projects focus on the effects of luminal liquids on the dissolution/solubilisation of drug substances, lymphatic transport of lipophilic substances and formulation of lipid-based drug delivery systems. The research is conducted in collaboration with the Danish pharmaceutical companies, Dumex Alpharma A/S, Leo Pharmaceuticals A/S and H. Lundbeck A/S, as well as with scientists at universities abroad. A new research consortium within the Øresund region was established in 2001. The Department participates in a project on *in vivo in vitro* correlations of lipid-based formulations. External partners are Lund University, Sweden, Camurus, Sweden, AstraZeneca R&D Lund, Sweden and Nycomed Pharma, Denmark.

*In vitro* methods suitable for the screening of drug substances and their formulations have been established on the basis of aqueous media simulating the compositions of the gastro-intestinal liquids in fasted and fed states. Further, a lipolysis model for dissolution testing and evaluation of effects of fat-enriched diet on oral absorption has been established. The model is subject to evaluation in collaboration with Aventis Pharma, Frankfurt. An increasing number of new drug substances are highly lipophilic and thus prone to lymphatic...
transport. Animal models (rats, dogs) for studies of lymphatic transport have been established and applied in investigations on the role of triglycerides in systemic absorption.

Investigations on lipid-based formulations, which were concluded in 2001, concern the development of dry emulsions and SEDDS for oral delivery of low soluble drugs and the use of tocopherols as a vehicle for low soluble drugs.

Lipid-based formulations for parenteral use are also subject to research. The projects concern the role of structured lipids in parenteral drug delivery and emulsion technology. The aim is to investigate the possibilities of incorporating hydrophilic as well as lipophilic drug substances into the lipid-based vehicles.

Particulate drug delivery systems are the subject of two projects carried out in collaboration with Cheminova and Pharmexa.

**DRUG DELIVERY**

The research within the area of Drug Delivery is focused on drug transport across biological membranes and studies on lipid-based drug delivery systems.

Macromolecules such as peptides, proteins, and oligonucleotides present a unique pharmaceutical formulation challenge. The therapeutic application of these groups of compounds is limited by several problems, such as lack of physical and chemical stability and the lack of optimal physico-chemical properties for adequate transport across biomembranes. Thus, the pharmaceutical sciences face the challenge of gaining a more basic understanding of transport problems and developing strategies to solve them.

Access to well-characterized in vitro models to study drug transport across biological membranes is of the utmost importance. Various models based on tissue as well as cell culture models are established in the Department, i.e. intestinal, buccal, and nasal membranes, cornea, and skin, the human colon cell line, Caco-2, and the human buccal cell line, TR 146. These in vitro models are important tools for obtaining a more fundamental understanding of the molecular and pharmaceutical parameters, which are of significance for drug transport across biological membranes. However, in some situations the findings from in vitro studies have to be confirmed in vivo in order to establish biological relevance. These studies are usually conducted on mice, rats, or rabbits.

To obtain effective drug therapy, the drug substance must be able to reach the site of action in a therapeutically active concentration. Various approaches are taken to optimise the drug delivery properties of drugs to improve membrane transport and release characteristics. Combining bioreversible derivation with carrier-mediated transportation has developed the classic prodrug approach further. Within this area, the Department is focusing on the potential use of the di-/tripep-

tid carrier as a transporter for drugs with poor membrane transport characteristics. This research is being conducted in collaboration with the Department of Medicinal Chemistry.

The development of particulate drug delivery systems based on liposome technology is also a focus area. These activities are carried out in collaboration with Professor O. G. Mouritsen, the MEMPHYS-group, Department of Physics, University of Southern Denmark.

As more therapeutic proteins are made available, it is essential to formulate these drugs into safe, stable and efficacious delivery systems. Our research goal in this area is to obtain a basic understanding of parameters controlling the physical stability of proteins in pharmaceutical systems, primarily by investigating the effect of excipients and studying protein-interface interactions. A Protein Formulation Network has recently been established in collaboration with a number of Danish pharmaceutical companies.

In the area of oligonucleotide/DNA drug delivery, the aim is to develop polymeric and lipid-based drug delivery systems that can effectively deliver oligonucleotides or plasmid DNA to the target site. The therapeutic focus within this area is gene and antisense therapy as well as DNA vaccination.

**PROCESSING TECHNOLOGY**

The research within processing technology focuses on the formulation and processing of solid dosage forms intended for oral administration. Central themes are particle technology, unit operations and pharmaceutical preformulation. Particle agglomeration has long been a major research field. The research group is well equipped with various types of mixer-granulators. Current research concerns melt granulation and melt pelletisation in high shear mixers, in particular the role of binder viscosity for the formation and growth of agglomerates.

Other projects deal with the use of melt agglomeration for developing matrix pellets with predictable dissolution properties, e.g. the use of solid dispersion technique to increase the dissolution rate of low soluble drugs. This research is conducted in collaboration with Danish pharmaceutical companies, in particular H. Lundbeck A/S.

Pelletization in rotor-fluidised beds is studied to develop rapidly disintegrating pellets. The project is conducted in collaboration with Glatt Norden and Professor P. Kleinebudde, University of Halle, Germany.

Compaction of particulate solids into tablets has been the subject of studies on mathematical modelling. This experimental work is based on the use of a compaction simulator.

Finally, the research group has established research on the atomisation of aqueous solutions with a view to coating fine particles and the preparation of inhalable particles. The use of effervescent atomisation in combination with spray drying is being investigated with a view to the design of the atomizer.
At a later stage the research will be re-directed towards the coating of fine particles. Investigations on the preparation of inhalable particles are being made in collaboration with AstraZeneca Lund R&D and the University of Lund, Sweden.

**CLINICAL PHARMACY**

Clinical pharmacy deals with rational pharmacotherapy and optimising the clinical use of drugs. The main research areas for the Clinical Pharmacy group concern indicators to evaluate the drug dosing-response relationship, and drug monitoring by clinical pharmacokinetic service. Pain management is one of the main areas of interests for the group. Opioids are studied in patients with chronic pain of malignant as well as non-malignant origin. Paracetamol and other non-steroid anti-inflammatory drugs (NSAIDs) are studied in patients with acute pain, children as well as adults. The pharmacokinetics of prednisolone in the acute phase of the treatment of children diagnosed with acute lymphoblastic leukemia is another research area of great interest. The group is often involved in projects concerning the influence of drug formulation and devices on patient compliance and acceptance.

**CENTRE FOR DRUG DESIGN AND TRANSPORT**

The “Centre for Drug Design and Transport” is an extramural research centre established in November 1997 as a four-year programme and therefore terminated in October 2001.

The centre is based on seven Danish research groups and funded by the Danish Medical Research Council, several Danish pharmaceutical companies and the participating academic institutions. Professor Sven Frøkjær is the head of the centre. See page 26 Research Centres at The Royal Danish School of Pharmacy.

**TEACHING**

During the summer of 2001, a major renovation of the Department was finalised and the amount of square meters increased to provide better teaching and research facilities. The new conditions are very much appreciated by staff and students alike.

In the academic year 2000/2001, the Department taught the introduction to the study of pharmacy, compulsory and optional courses in pharmacy, supervised students doing their master’s theses and held PhD courses.

The introduction to the study deals with lectures and tutorials in drug formulation and manufacturing and knowledge of the European Pharmacopoeia. Further, demonstrations in how to prepare e.g. tablets and parenteralia are given.

Students are trained to master drug formulation, drug production and evaluation as well as quality assurance. The compulsory courses combine lectures, tutorials, laboratory work, written exercises and oral presentations. During the fourth year of the programme, students carry out a project within drug formulation and one within drug manufacturing. The content of the course in drug formulation was revised in 2001, and a different textbook used (Physicochemical Principles of Pharmacy). A project entitled “Test of an examination form for better evaluation of the students’ understanding and ability to solve more complex pharmaceutical problems” has been planned and will be carried out in the spring 2002.

Furthermore, the Department of Pharmacy together with the Department of Pharmacology held a compulsory course in pharmacotherapy.

The Department also offered elective courses in advanced drug formulation, industrial production and quality assurance of pharmaceuticals, validation in the manufacture of pharmaceuticals, controlled release, clinical pharmacy, statistical design of experiments, registration of drugs and seminars and clinical practice in clinical pharmacy.

The two PhD courses dealt with drug delivery and clinical evaluation of drug products, respectively. Furthermore, the
Department made contributions to other PhD courses, e.g. biological membranes, permeation barriers and drug targeting.

The Department of Pharmaceutics supervised 77 students earning their master's theses. About half of these students worked on their theses at national or international pharmaceutical production sites or institutes. A number of foreign students prepared their theses at the Department.

During the past three years, 18 students received their PhD degree from the Department. Fifteen of the projects in the field of drug formulation were funded by Danish pharmaceutical companies, the Danish Research Academy and the Danish Medical Research Council through the Centre for Drug Design and Transport. This programme has now been terminated and unfortunately the number of PhD students at the Department is decreasing. However, 34 people were registered for the PhD degree programme on 1 January 2002.

**SPECIALISATION IN HOSPITAL PHARMACY**

The need for specialised training in Hospital Pharmacy has been acknowledged for several years. To improve the clinical and scientific skills of hospital pharmacists, the Danish Society of Hospital Pharmacy Managers in co-operation with the Royal Danish School of Pharmacy are preparing a new postgraduate programme. The new programme will focus on clinical pharmacy – the optimal use of drugs for the benefit of each patient and society. The curriculum will be equivalent to one year of courses, although it will be taught over a longer period of time.

Janne Ramsing, Department of Pharmaceutics, is head of the Study Board for "Specialisation in Hospital Pharmacy".

**GUESTS AND EVENTS:**

Professor Hans P. Merkle, Galenische Pharmazie ETH, Zürich, has been attached to the department as assigned professor.

Professor Gert Storm, Department of Pharmaceutics, Utrecht University, The Netherlands.

Professor Hans Lennernäs, Department of Pharmaceutics, University of Uppsala, Sweden.

Dr. Thomas Abberger, University of Innsbruck, Austria, joined the agglomeration research group from August 13 to September 7, 2001.

David Ilardia, PhD student at the university in Vittoria, Spain, joined the GISOL research group from January to July 2001.

Regina Westmeyer, pharmacy student at the university in Kiel, Germany, joined the research on particulate DNA-formulations for a 6 months period from September 2001.

Christina Jimenez, MSc, Barcelona, has joined the GISOL-group since October 1, 2001.


Member of the Scientific Programme Committee: Henning G. Kristensen, Sven Frøkjær

Benzon Symposium - Drug Metabolism: Regulation and Importance, September 16-20, 2001, Copenhagen.

Member of the organizing committee: Sven Frøkjær

**MEMBERSHIP OF EXTERNAL COUNCILS AND BOARDS**

Henning Gjelstrup Kristensen is a member of the Academy for Technical Sciences (ATV), chairman of the Danish Pharmacopoeia Commission and chairman for its sub-committee on Pharmacy. In 2001 he was elected chairman of the European Pharmacopoeia Commission for a period of three years. He is chairman of the Group of Experts No. 12 (Drug Dosage Forms) and has the chair for a number of Working
Design of oral formulations by pelletization techniques

High shear mixers and a conventional as well as a rotary fluidised bed are applied for pelleting of powders. Hydrophilic and hydrophobic meltable binders and aqueous binder solutions are applied as binder liquids. The effects of the physical and physicochemical properties of raw materials and binders and the effects of process variables on the properties of the final pellets, e.g., porosity, disintegration and disintegration times, are studied.

Jette Jacobsen has received DKK 10,000 from

Generalkonsul Ludvig Tegner og Hustrus Mindelegat for analytical equipment.

Hanne Marck Nielsen has received a grant from the Alfred Benzon Foundation for a post doctoral stay at ETH Zürich, Switzerland.
solution, are investigated. These studies are the basis of the design of pellets with a modified drug release including prolonged release formulations, gastro-resistant formulations, and colon specific delivery systems as well as pellets containing solid dispersions.

(Torben Schaefer, Helle Eliasen, Anita Johansen, Jakob Kristensen, Anette Seo, Ole Warts, Henning Gjelstrup Kristensen, Per Holm, H. Lundbeck A/S, and Peter Kleinebudde, University of Halle).

**Absorption enhancing solid dosage forms**
Different formulation principles and production techniques that might be applicable for enhancing the oral absorption of low soluble drugs have been screened. At the present time, the preparation of dry emulsions by means of spray drying is investigated. Different drug substances will be included in the formulations, and the physical stability and the oral bioavailability of the formulations will be tested.

(Tue Hansen, Per Holm, Kirsten Schultz, H. Lundbeck A/S, and Torben Schaefer).

**Microencapsulation by atomization techniques**
The aim of the project is the encapsulation of solid particles with polymers in order to modify and control the dissolution rate of the solid. The project has, so far, dealt with the atomization of polymer solutions using an effervescent atomizer. The design of the atomizer has been optimized for spray drying processes. The studies show that effervescent atomization has some advantages compared to other atomization methods: Reduced air consumption, atomization of viscous liquids and the possibility to produce small droplets.

(Frederik Pedersen, Torben Schæfer, Ole Warts, Henning Gjelstrup Kristensen)

**Inhalable particles**
The use of spray drying technology for the preparation of inhalable particles is investigated in a project performed in a collaboration with Lunds University and AstraZeneca R&D Lund. The purpose of the project is to investigate and optimise the physical stability of spray dried powders with particle sizes in the range below 5 μm. Based on an investigation on a series of carbohydrates it has been demonstrated that the glass transitions temperature of the amorphous carbohydrate affects the crystallinity of the spray dried products. The current studies focuses upon the possibilities to control the crystallinity of spray dried particles.

(Kristina Ståhl, Anders Axelsson, Lunds University, Kjell Bäckström, AstraZeneca R&D Lund, Torben Schaefer and Henning G. Kristensen)

**Formulation of nebuliser liquids**
The aim of the project is to formulate solutions of antibiotics, which are deliverable to the airways and lungs for the treatment of infections by fungi. So far, the project has been concerned about the development of an in vitro model to simulate the deposition of the antibiotic in the airways. Various nebulisers are investigated. The model will be used to evaluate formulated solutions and suspensions.

(Kenneth Manby Pedersen, Vagn Handlos and Lars Heslet, State University Hospital)

**Evaluation of the compression and compaction characteristics of powders**
The project includes a critical evaluation of the Heckel and Walker equations and their ability to describe the compressibility of powders. A model for description of compactibility (the ability of a powder to cohere into or to form a compact) and the lamination tendency is investigated through combination of the elastic properties under pressure and the Walker coefficients of plastic deformation. The statistical distribution of crushing strength of tablets has been investigated and confirmed the hypothesis that the data followed a standard normal distribution rather than the general accepted Weibull distribution.

(Jørn Møller-Sonnergaard, Henning Gjelstrup Kristensen)

**Critical compaction characteristics of pellets and excipients with impact on the physical stability of polymer membranes.**
The release of drug from Modified-release tablets formulated with filmcoated pellets (polydepot) are controlled by the polymer membrane. By compaction of the pellets the membrane will be damaged or distorted with an uncontrolled effect on the dissolution rate of the tablet. The aim of the project is to investigate the combination of pellet manufacturing method, type of polymer film and tablet excipients that minimizes the negative effect on the dissolution rate.

(Casper Crilles Larsen, Per Holm, H. Lundbeck A/S, Jørn Møller-Sonnergaard)

**Gastrointestinal solubility of low soluble drugs (GISOL)**
The GISOL-projects focus upon the in vivo and in vitro dissolution of low soluble drugs belonging to Class II in the Biopharmaceutics Classification System. The research group has established predicative dissolution methods based on media simulating the composition of the gastrointestinal fluids in fasted and fed states. Further, an in vitro lipolysis model has been developed for studies of the dissolution of hydrophobic drug substances, e.g. danazol and probucol. The use of the model is being investigated by studies on a range of drug substances characterised by log P values in the...
range of 3 – 10; these studies are performed in collaboration with H. Lundbeck A/S, Denmark, and Aventis Pharma, Germany.

The possibility for establishing in vivo in vitro correlations by the use of the simulated media for dissolution testing is investigated in a study on the absorption of danazol. The effects of meals and fluid intake are subject for a clinical study, which in a later stage will be compared with dissolution data in order to elucidate for example effects of the in vivo hydrodynamics.

In 2001 a new project on in vivo in vitro correlations of lipid-based oral formulations, e.g. microemulsions and SEDDS, has been established in the Øresund region. External partners participating in the project are Lunds University, AstraZeneca Lund, Cumurus, Lund, Nycomed Pharma, Denmark, DTC Denmark and Scantox Denmark.

Other ongoing research projects concern the transport of solubilised drug substances across Caco2 cell monolayers and the evaluation of the micellar properties of dissolution media simulating the jejunal fluids.

(Liis Hanberg Zangenberg, David Ilardia, Vikeke Hovgaard Sunesen, Flemming Seir Nielsen, Anette Müllertz, Lars Hovgaard and Henning G. Kristensen)

Lipid-based formulations for oral delivery of low soluble drugs

Lipid-based formulations for oral delivery utilise the degradation pathways of triglycerides and other lipids to improve the dissolution and absorption of hydrophobic drug substances. A project on the use of tocopherols as a vehicle for low soluble drugs has been concluded in 2001. The influence of lipids upon the lymphatic transport of drug substances has been the object for studies in the past three years, partly in collaboration with Professor W.N. Charman, Australia. Animal models (rats, dogs) has been established for investigating the effects of various triglycerides on the lymphatic transport and systemic absorption of haloperidone. In the continuation of the project attention is paid to the pharmacokinetics and pharmaceutically transported drug substances. Another project concerns formulation and evaluation microemulsions for oral delivery of drugs. This project is performed in a collaboration with H. Lundbeck A/S Denmark.

(René Holm, Janne Orskov Christensen, Pernille Bondeskov Nielsen, Ditte Maria Karf, Tomas Norling, Duex-Alpharma, Kirsten Schultz and Birgitte Malgaard, H. Lundbeck A/S, Betty Lomstein Pedersen, Nycomed Pharma, Anette Müllertz and Henning G. Kristensen).

Solid lipid nanospheres

The potential use of SLN technology to reduce of the aquatic toxicity of pesticides is investigated in a project performed in a collaboration with Cheminova A/S. The physical stability of SLN based on two types of lipophilic carriers is affected by the formulation, in particular by the compatibility of the active substance and the lipid and by the choice of surfactant. A stable SLN system has been developed and submitted to various tests on insects and fish.

(Henrik F. Frederiksen, Morten Pedersen, Anita Wengel and Henning G. Kristensen)

Particulate formulation of DNA-vaccines or protein-based vaccines

Pharmaceutical formulation of nanopheres based on lipids to be loaded with DNA is the subject for a collaborative research with the State University Hospital, Copenhagen, and States Serum Institute. The research aims at a formulation intended for mucosal application. In another project performed in collaboration with Pharmexa, Denmark, the aim is to develop a particulate vaccine formulation based on a polymeric carrier.

(Annette Vinthner Heydenreich, Anne Mette Beyer, Regina Westmeyer, Lars Hovgaard, Henning G. Kristensen, Annan Gautam, Pharmexa, Hans Skovgaard, the State University Hospital)

PHARMACEUTICAL FORMULATION/DRUG DELIVERY

Parenteral depot formulations

Until now, the most successful principle to control drug release from oily depot formulations have been by modifying the partition coefficient of the drug substance, e.g. by using prodrugs. There have been less interest in developing more general formulation principles. In the present project, water-in-oil emulsions are studied as potential depot formulations for water-soluble drug substances including proteins.

(Simon Bjerregaard Jensen, Lene Jørgensen, Charlotte Vermehren and Sven Frakjaer)

Pharmaceutical characterisation of chalcones

A number of chalcones have been shown to be effective as antiparasitic compounds. However, this class of compounds possesses physico-chemical properties which make the pharmaceutical formulation challenging. Based on results from preformulation studies, various lipid based formulations are developed in order to optimise the therapeutic effect of selected chalcones.

(Sven Frakjaer, Bente Steffansen, Agnete Dyssgaard and Soren Bregger Christensen, Department of Medicinal Chemistry and Arsalan Kharazmi, Department of Clinical Microbiology, The State University Hospital/Lica Pharmaceutical A/S).

Protein stability

Denaturation, aggregation, and precipitation of proteins are major problems in the formulation of protein based drugs. A
more basic understanding of the molecular mechanisms for protein fibrillation and the factors, which have an influence on the fibrillation, may serve as a model for other globular proteins and, thereby, improve the rational for developing protein-based drug in general. The kinetic of insulin fibrillation and the effects of excipients on conformation and conformational changes on the stability of therapeutically relevant proteins is studied. Other aspects of protein stability, which are investigated, relates to the understanding of interfacial effects on the physical stability of proteins in pharmaceutical systems.

(Liza Nielsen, Susanne Sønderkær, Susanne Møllmann, Marco van de Weert, Sven Frekjær, Ejvind Jensen and Peter Langballe, Novo Nordisk A/S, Lars Lindgaard Hansen, Pharmexa A/S, Jens Brange, Brange Consult, Ulla Elofsson, Swedish Institut of Surface Chemistry, and John Carpenter, University of Colorado).

Transdermal patches

The objective of project is to study the release kinetics of enhancers and drug substances from transdermal patches and to study how the enhancer effect on various drug substances is dependent on the release kinetics of the enhancer. The influence of enhancer on characteristics of importance for the application of patches, e.g. adhesive properties, is also studied. This project is completed by December 2001.

(Michael H. Qvist, Sven Frekjær, Flemming Madsen, Coloplast A/S, Bo Kreilgård, Leo Pharmaceutical Products A/S and Ulla Hоеck, Pharmacia & Upjohn)

Carrier mediated transport

Many different factors may influence on drug/prodrug absorption after oral administration. One of the main barriers for oral drug absorption may be that many compounds display poor permeability across biological membranes. Factors such as the physico-chemical property of the compound, its in vitro metabolism as well as efflux and influx transport mechanism(s) may influence on its netto transepithelial transport.
A confocal laser scanning image of Caco-2 cells. The caco-2 cell line is a commonly used cell model of the small intestinal epithelium, and express the peptide transporter hPepT1 at the apical membrane. Image details: Nuclei are labelled with propidium iodide (red) and the actin skeleton of the cells is labelled with Alexa-488 phalloidin (green). The image was generated on a Zeiss LSM 510 by Birgitte Eltong/Susanne N Sørensen.

Partition coefficient of the drug substance, e.g. by using prodrugs. There have been less interest in developing more general formulation principles. In the present project, water-in-oil emulsions are studied as potential depot formulations for water soluble drug substances including peptides and proteins. (Lene Jørgensen, Charlotte Vermehren, Sven Frokjaer and Simon B. Jensen, Novo Nordisk A/S).

Liposomes as drug delivery system against inflammation

The project focuses on development of a specific delivery system which carries the drug to inflammatory tissue. Transport and release of drug may potentially be controlled by utilizing the local conditions of the target organ, e.g. specific enzyme activities. The phospholipid degrading enzyme, phospholipase A2, exists in increased concentration in inflammatory tissue.

The degradation of long-circulating, surface modified liposomes by phospholipase A2 is faster compared to conventional phospholipid liposomes. Studies of the fate of surface modified liposomes in infected tissue in rats in vivo are included in the project as well.

The project includes studies of activity of inflammatory exudate containing liposome degrading factors, e.g. phospholipase A2 and macrophages, toward surface modified liposomes. (Charlotte Vermehren, Sven Frokjaer, Jesper Davidsen in collaboration with Kent Jørgensen, Liplasome A/S and professor Gert Storm, Department of Pharmaceutical Sciences, Utrecht, The Netherlands).

Surface properties of lipid membranes and the association of small acylated peptides

Acylated peptides and proteins can bind to surfaces of lipid membranes by electrostatic and hydrophobic forces. Acylated peptides and proteins display an increased circulation time in the blood stream – which from a drug delivery perspective make them interesting. The aim of the project is on the one hand to investigate how the membrane association of acylated peptides affects the lipid membrane behavior and on the other hand how the membrane association affects the secondary structure of the peptide. (Tina Bjeldskov Pedersen, Sven Frokjaer, Kent Jørgensen and Ole G. Mouritsen in collaboration with The MemPhys group, Department of Chemistry, Danish University of Technology).

Activity of membrane associated enzymes in relation to surface modified liposomes

Incorporation of different amounts of lipopolymers into liposomes increases the in vitro and in vivo stability. This is manifested as a significant prolongation of the intravascular circulation time. The project involves studies of the activity of liposome degrading enzymes such as phospholipase A2 and C
towards surface modified liposomes. Such results are of importance for a deeper understanding of the mechanisms involved in the extravascular stabilization and release of incapsulated material from the liposomes. (Jesper Davidsen, Charlotte Vermehren, Sven Frøkjær, in collaboration with Kent Jørgensen, Liplasome A/S and Ole G. Mouritsen, The MemPhys group, Department of Chemistry, Danish University of Technology).

**NAPE-containing liposomes**

Incorporation of the phospholipids N-acyl-phosphatidylethanolamines (NAPE) into liposomes stabilizes the liposomes in the presence of human serum. The stabilization of NAPE-containing liposomes in serum may be attributed to different factors such as changes in fluidity and vesicle surface. The project focuses on the in vivo behaviour of liposomes containing different amounts of NAPE as well as the destabilization of these liposomes by enzymatic degradation and lipid exchange. (Charlotte Vermehren, Sven Frøkjær in collaboration with Harald S. Hansen and Gitte Petersen, Department of Pharmacology).

**Transport across biomembranes**

The objective of this project is to obtain a more basic understanding of key parameters of importance for passive diffusion of drug substances across biological membranes. This may contribute to the development of in vitro characterisation programs with a greater predictive power than the methods used to day. Presently, peptides and peptide analogs are used as model compounds. This makes it possible to study the importance of molecular parameters such as conformation, molecular weight, lipid-water partitioning water accessible surface, and surface polarity. The influence of absorption enhancers on membrane transport of drug molecules is also studied in various models. (Lene Kranup, Jan Hest, Lars Hovgaard, Sven Frøkjær in collaboration with Flemming Steen Jørgensen, Department of Medicinal Chemistry and Inge Thøger Christensen, Novo Nordisk A/S)

**Intranasal application of drugs e.g. peptides**

The research is primarily concentrated on studying the potential of intranasal administration. The focus is especially on drugs used in acute situations and delivery of peptide drugs. The various projects include the study of in vitro/vivo permeation, degradation of drugs and estimation of low irritating potential absorption enhancers. The absorption and distribution into the brain after nasal application is also an issue. (Erik Bechgaard, Morten Bagger, Karsten Lindhardt in collaboration with Sveinbjörn Gizurarson, University of Iceland)

**Solubilisation of low solubility drugs for intranasal application**

The maximum volume for nasal application is normally 50-100 μl per nostril. Therefore, it is often necessary to use cosolvents in nasal formulations to be able to dissolve a clinical dose. Cosolvents, however, may give rise to local mucosal irritation, why it is important to identify substances and concentrations, which are effective and at the same time acceptable in relation to the indication. Various formulation aspects are evaluated for low solubility drugs and the bioavailability from formulations is studied in rabbits and sheep, providing the possibility of correlating the two animal models. (Erik Bechgaard, Karsten Lindhardt in collaboration with Sveinbjörn Gizurarson, University of Iceland)
Intracerebral microdialysis: Probe implantation procedure performed on an anaesthetised rat

Olfactory absorption
Distribution of drugs to the brain following nasal administration
Intracerebral microdialysis in the rat has been implemented as a model for studies of olfactory absorption of drugs. The model has been characterised in terms of blood-brain barrier integrity following probe implantation. The model has been found to be suitable for determinations of unbound concentrations of drugs in vivo in the extracellular fluid of blood and brain, based on dialysate concentrations. Specifically, pharmacokinetic studies of drug absorption and distribution to blood and brain following unilateral nasal administration to rats, has been carried out using lidocaine, fluorescein and morphine-6-glucuronide as model substances.

Experiments with morphine-6-glucuronide were performed as a pilot study. With lidocaine, which easily passes the blood-brain barrier, no signs of olfactory absorption were found, neither as higher extracellular concentrations in the brain nor as higher absorption rates following nasal administration. With fluorescein, which has a low blood-brain barrier permeability, the study showed higher absorption rates and lower Tmax values in the right side of the brain following unilateral nasal administration indicating limited olfactory absorption in the rat.

(Erik Bechgaard and Morten Bagger)

In vitro models for buccal mucosa
In vitro models for buccal mucosa have been employed to study buccal permeability and toxicity of drugs, including peptides, and pharmaceutical adjuvants.

One model is based on the cell line TR146 originating from a human buccal carcinoma. Filter-grown TR146 cells form a multilayered epithelium and studies of morphology, permeability and profile of keratins have demonstrated a differentiation pattern of TR146 cells similar to normal human buccal epithelium. Another model is based on porcine and human buccal mucosa mounted in the Ussing chamber. Characteristics of the in vitro models have been evaluated, e.g. comparison of enzyme activities and the influence of molecular size and lipophilicity on the permeability of drugs as well as the effect of bile salt enhancers. The effect of pH on the permeability of drugs, e.g. nicotine, has been investigated.

(Hanne Mørck Nielsen, Margrethe Rømer Rassing)

Toxicity assessment in the TR146 cell culture model – development, optimization and comparison of assays
Different toxicity assays has been optimized for dividing TR146 cells and for TR146 epithelium for three different permeability enhancers in order to investigate the mechanisms of action.

(Heidi Ugelstad Eirheim, Hanne Mørck Nielsen)

Iontophoresis as a technique to enhance in vitro buccal drug delivery
Iontophoresis as non-invasive physical enhancer in buccal drug delivery has been studied. The results demonstrated the feasibility of the iontophoretic approach to enhance and control the rate of buccal drug delivery. A new three-chamber iontophoretic diffusion cell has been developed to reflect the in vivo iontophoretic drug delivery more closely.

(Jette Jacobsen, Margrethe Rømer Rassing)

Epidermal growth factor (EGF): in vitro and in vivo studies and clinical testing of treatment of oral mucositis induced by radiotherapy
The overall objective of the project is the introduction of a new medical therapy with topical application of EGF in cancer patients to relieve oral mucositis induced by radiotherapy. The project includes studies on EGF on the cell line TR146, development of a pharmaceutical formulation with EGF, studies of the healing effect of EGF on oral mucositis and clinical testing of the pharmaceutical formulation. Initial studies have been carried out.

(Hanne Marck Nielsen, Margrethe Rømer Rassing in collaboration with Helle Birgitte Dahl Olin, Maria Elisabeth Christensen, State University Hospital)
Intercellular matrix in the TR146 cell culture model and in vivo/in vitro correlation to human buccal epithelium.
The objective of the project is to characterize the lipid content of the intercellular matrix in the TR146 cell culture model and to examine the influence of different enhancers on the lipid structure. Furthermore, to correlate the permeability of drug substances across the TR146 cell culture model to the permeability across human buccal mucosa in situ. For the in vivo studies a custom-designed chamber has been developed. Nicotine has been chosen as a first model substance.
(Charlotte Adrian, Margrethe Rømer Rassing in collaboration with Helle Birgitte Dahl Olin, State University Hospital)

CLINICAL PHARMACY

Development and maintenance of a quality assurance system for the medication procedures in a critical care unit.
The aim of the project is to reduce the number of medication errors and to improve drug therapy.
(Lona Christrup, Mette Rasmussen in collaboration with Intensive Care Unit, Herlev University Hospital).

Long-term treatment of chronic pain patients with morphine
The aim of the study is to gain knowledge of the connection between dose/administration route, plasma concentration of morphine/morphine metabolites and side-effects and analgesia, in order to improve the treatment of patients suffering from chronic pain.
(Lona Christrup, Steen Honoré Hansen, Department of Analytical and Pharmaceutical Chemistry, in collaboration with the Multidisciplinary Pain Centre, Herlev University Hospital).

Local ocular pain treatment with opioids
The aim of the project is to evaluate if opioids applied locally in the eye can exert analgesia if it is mediated by peripheral opioid receptors. The transport of opioids across the cornea and the distribution in the eye are investigated in vitro and in vivo in rabbits. Additionally, the analgesia following administration of opioids in the eye in a clinical set up is investigated.
(Lona Christrup, Bente Steffansen in collaboration with Department of Pharmacology, The Royal Veterinary and Agricultural University, The Pain Clinic, Aalborg University Hospital, and the Multidisciplinary Pain Centre, Herlev University Hospital).

LAAM - potential use as an opioid analgesic
LAAM is an opioid drug, and when used in the maintenance treatment of drug addicts to suppress abstinence syndroms, it has a duration of action of 3-4 days. The purpose of the study is to evaluate if LAAM has a future as an analgesic drug substance. The binding of LAAM and its two metabolites nor- and dinor-LAAM to the opioid and NMDA receptors is investigated in vitro. The analgesic effect of all three substances is evaluated after administration in mice. The duration of action with respect to analgesia as well as the equipotential doses to methadone is investigated in patients suffering from chronic pain. Finally, a HPLC method for quantification of LAAM and its metabolites is being set up.
(Lona Christrup, in collaboration with H:S Multidisciplinary Pain Centre, Copenhagen University Hospital and Department of Clinical Biochemistry, Bispebjerg University Hospital).

Pharmacokinetics and -dynamics of paracetamol
The pharmacokinetic and -dynamic parameters of paracetamol are investigated in adult postoperative patients in order to optimize pain management with paracetamol.
The pharmacokinetics of paracetamol are also investigated in the postoperative phase in children.
Oral, intravenous and rectal administration is used.
(Mette Rasmussen and Janne Ramsing in collaboration with physicians at hospitals in Copenhagen, and Tina Hahn, Coloplast A/S).

Non-opioid analgesics
To improve postoperative pain management in ambulatory surgery patients, several projects are carried out evaluating the analgesic effect of non-opioid analgesics. The research focuses on mechanism of action, pharmacokinetics and -dynamics, and side effects of the drugs. The use of a multimodal approach as well as the influence of different formulations of the drugs on analgesia are investigated.
(Janne Ramsing, Tina Hoff Duedahl in collaboration with physicians at Herlev and Gentofte University Hospitals and at the State University Hospital).

Pharmacokinetics of prednisolone.
The prognosis for children with acute lymphoblastic leukemia depends on the amount of residual disease after four weeks of treatment. In this project, a possible correlation between the plasma concentration of prednisolone and the amount of residual disease is evaluated. Further, the kinetics of prednisone is examined and the bioavailability is evaluated in relation to the gastro-intestinal function. Oral and intravenous administration is used.
(Kamilla B. Petersen and Mette Rasmussen in collaboration with physicians at The National University Hospital, Rigshospitalet).
Department of Pharmacology

The Department of Pharmacology conducts research and teaching within a broad biological field including biochemistry, microbiology, physiology, pharmacology, pharmacotherapy and molecular biology focusing on effects and side effects of drugs and their importance in connection with pathological conditions.

A detailed broad spectrum of knowledge about drug effects and the methods used to investigate them at cellular levels, in isolated tissues, in the whole animal and in patients, is of fundamental importance and an indispensable basis for drug experts. The teaching gives pharmacists in-depth knowledge about biochemistry and microbiology, including molecular biology and integrated pharmacological knowledge in which anatomy, physiology, pharmacology and biological standardization are integrated. This knowledge will enable pharmacists...
to function as drug experts. The research at the Department forms the scientific basis for the education.

RESEARCH

Research at the Department of Pharmacology covers a wide range of activities directed at drugs, their effects and side effects, their importance in connection with pathological conditions, as well as their effects on the immunological system.

Research includes biochemical, pharmacological, pharmacokinetic and molecular biological studies related to characterisation and development of specific drugs. It is based on studies in cell cultures, isolated tissues and smaller animals and includes, among other things, characterisation of receptors, transport systems in cell membranes, mechanisms for regulation of biosynthesis and for release of peptides, studies of second messengers, intracellular mechanisms and various gene techniques. Primary research fields are pharmacology (including neuro-, molecular- and vascular pharmacology), molecular biology and pharmaceutical microbiology.

Pharmacological research aims to improve the clinical use of drugs. Current research in the vascular pharmacological area focuses on the transduction mechanisms for peptides and classical neurotransmitters in cerebral, ocular and coronal vascular tissues from animal and human in relation to diseases like migraine, ischaemia and diabetes. Neuropathic pain is a new research field at the Department. A set of rat models for neuropathic pain is under establishment for testing with new and well-known antagonists and agonists for the involved receptor systems. The goal of the project is to improve the treatment of neuropathic pain.

The molecular- and neuropharmacological research seeks to improve understanding of the effects of neuro-active amino acids, an important part of the efforts to develop new drugs to treat neurodegenerative diseases. The research is interdisciplinary in its combination of molecular, cellular and pharmacological aspects of neurotransmitters. Current research focuses on GABA as a neurotransmitter, on glutamate- and GABA-mediated neurotransmission, on the formation of endocannabinoids and on opioid- and NMDA-receptors using cell cultures, isolated tissues and electrophysiological techniques. The molecular and cellular role of different mediators e.g. cytokines and nitrogen oxide in neurotoxic and neuroprotective effects in the brain is another issue in neuropharmacological research. Communication between the neuroendocrine and the immune system in the neurohypophysis is another area of study. Other research objects are the biological function of essential fatty acids and phospholipases in the cell membrane, receptor mediated regulation of intercellular enzymes and the formation of second messengers.

The molecular biology group uses genetic engineering to generate novel antibodies and peptides relevant to the diagnosis and treatment of immunological diseases. Current research focuses on generating recombinant antibodies with antigen-specific MHC restricted specificity of T cells used as reagents for basic and clinical investigations and immunotherapy. The detailed involvement of selected viral surface proteins in viral infection cycle is another area of investigation.

Pharmaceutical microbiological research focuses on the development of new methods to evaluate pharmaceuticals. Current research concerns in vitro pyrogen testing based on the use of cell lines.

TEACHING

The Department teaches compulsory theoretical courses in biochemistry, physiology and biological standardisation, microbiology, anatomy, pharmacology and pharmacotherapy together with laboratory courses in microbiology and pharmacology. In the period under review, the Department taught elective courses in pharmacokinetics and pharmacodynamics, basic methods in molecular biology, experimental pharmacology in-vitro, biochemical laboratory technique, microbiological and immunological methods of drug control.

The work to make a radical change in teaching in order to focus on pharmacology continues. The new curriculum will come into force starting next term, which means that courses in anatomy, physiology and biological standardisation and pharmacology will be integrated into two courses: basic pharmacology and organ-related pharmacology. The Department of Pharmacology together with the Department of Pharmacy
also held a compulsory course in pharmacotherapy. Finally, an introductory course in cell biology was introduced.

About 40 students have completed their master’s theses in connection with the Department; half of these students received their practical training in foreign research laboratories (pharmaceutical industry and abroad).

Some staff members were involved in PhD courses both at the School and at other universities again this year.

**MEMBERSHIP OF EXTERNAL COUNCILS AND BOARDS**

*Klaus Bahl Andersen* is censor of Aarhus University, December 2001.


**Jan Engberg** is member of the reviewing boards of: Immuno-technology, Biochim. Biophys. Acta, Journal of Immunological Methods, Nucl. Acids Res, Trends of Biochemical Sciences, Biotechnology, FEBS-letters and Proceedings of the National Academy of Science (USA). He is member of the advisory boards of the National Research Councils for medical sciences in Holland, Sweden and Australia and member of evaluation committees at the faculties of Medical and Natural Sciences in Copenhagen, Aarhus, Odense and Roskilde.


**Aase Frandsen** is President of the Danish Society for Neuroscience and member of the council for The National Association for Treatment of Brain Disease. She is member of the council for The Federation of European Neuroscience Societies (FENS) and member of the governing council for International Brain Research Organisation (IBRO). Organizer of meeting of EU consortium ERDYS. Editor of Journal of Neurochemistry. Referee for Journal of Neurochemistry; Neurochemistry International, Brain Research, Neuropharmacology, Journal of Cerebral Blood Flow and Metabolism, European Journal of Biochemistry, Journal of Clinical Anatomy, and Journal of Neuroscience Research. Officially appointed examiner at the University of Copenhagen.


**Harald S. Hansen** is censor at DTU and KVL and has been international reviewer for a grant application to Science Foundation Ireland. He has been member of the assessment committees for PhD-theses at DFH, at Biocentrum-DTU and at Syddansk University Odense and been chairman for the assessment committee for a professorship at DFH. He is member of the Board of directors for The Danish Nutrition Society, for International Society for the Study of Fatty Acids and Lipids (ISSFAL), is alternate member of The Danish Committees on Scientific Dishonesty, the Danish State Nutrition Council, is member of 2 consulting groups affiliated to the Danish State Nutrition Council concerned with “Dietary fat, children and atherosclerosis” and “Dietary prevention of obesity”, and chairman for the National Council of Nutritional Science at the Royal Danish Academy of Sciences and Letters.

**Inger Jansen Olesen** is member of the Danish Pharmacological and Toxicological Society, the International Headache Society, The International Society of Cerebral Blood Flow and Metabolism. She is a member of the reviewing board of Br. J. Pharmacol., Stroke and Cephalalgia.

He is registered in the ISI-Thomson list “Highly Cited Researchers” of the 100 most frequently cited researchers in the field Neuroscience (www.isihighlycited.com).

**DONATIONS AND GRANTS**

**Tue Banke** has received a post-doc scholarship from The Alfred Benzon Foundation for a stay of one year at Dept. Pharmacol., Emery Univ., Atlanta, Ge, USA and has received a 3-year post-doc scholarship from The Danish Medical Research Council (2002-2004).

Ole Jannik Bjerrum has received DKK 15.000 from Novo Nordic, DKK 350.000 from EU Accompanying Measures: EUFEPs 2002: New Safe Medicine Faster. An integrated Congress.

Jan Engberg has received the following funding (for projects) DKK 150.000 from The Danish Cancer Society “Generation of recombinant antibodytoxins directed against tumor associated peptide/HLA complexes with T cell receptor-like specificity”, DKK 312.715 from The Novo Nordic Foundation “Generation of recombinant antibodies specific for MHC/peptide complexes of relevance for the pathogenesis of multiple sclerosis”, DKK 89.660 from The Danish Research Council for Medical Sciences. Identification of hippocampus specific corticosteroid-specific genes using DNA micro arrays and DKK 300.000 from Apotekerfoundation “Generation of recombinant antibodies specific for MHC/peptide complexes of relevance for the pathogenesis of multiple sclerosis”.

**Bjarni Fjalland** has received DKK 200.000 from The Lundbeck Foundation and DKK 100.000 from Ib Henriksen Foundation in support of the project “CGRP - an important partner in painperception”.

Aase Frandsen has received DKK 60.000 from SSVF Start Program (22-01-0054).

Georgi Gegelashvili continued to administer research grants received DKK 600.000 per year, for the period 1998-2002 from The Danish Medical Research Council, DKK 40.000 from The Novo Nordic Foundation. He has obtained further funding DKK 88.350 from The Novo Nordisk Foundation for the period 2001-2002, and DKK 260.000 from The Danish Medical Research Council for year 2002. He has received a senior visiting fellowship and a research grant from The Alfred Benzon Foundation DKK 150.000 for a project carried out in the USA 2000-2001. He has been awarded a Boje Benzon Stipendium DKK 520.000 per year.

**Harald S. Hansen** has received DKK 750.000 from SSVF, DKK 280.000 from Carlsberg Foundation, DKK 400.000 from Lundbeck Foundation, DKK 300.000 from Augustinus Foundation, DKK 50.000 from Director Ib Henriksens Foundation, DKK 100.000 from Eva & Henry Krænkels Memorial Foundation, DKK 90.000 from Novo Nordic Foundation.

Arne Schousboe had a 3-year grant from The Lundbeck Foundation (DKK 400.000 per year (1999-2001)). He has received a 3-year grant from The Danish Medical Research Council (2001-2004; DKK 500.000 per year).

**Helle S. Waagepetersen** has a 3½-year (2000-2003) post-doc grant (DKK 600.000 per year) from The Danish Medical Research Council.

**STAFF**

In the past year Ole Jannik Bjerrum was appointed professor of pharmacology and the position of associate professor in pharmacology was reappointed. At the moment two positions as associate professors in pharmacology are vacant due to resignation. One position has been upgraded to a full professorship in pharmacokinetics and drug metabolism. It is hoped that the position will be filled soon. The Department is staffed by five professors (one vacancy), 16 associate professors (one vacancy), one assistant professor, three external associate professors, three senior clerks, 13 laboratory technicians, In the year passed Ole Jannik Bjerrum has been appointed as professor in pharmacology.
one temporary laboratory technician, one trainee, three laboratory porters, one assistant and four cleaners. At present 17 PhD students are employed at the Department. In addition several research assistants and technicians are employed on grants from external funds. Several staff members (both scientific and technical-administrative staff) have left their positions for jobs primarily in the pharmaceutical industry.

PROJECTS

NEUROPHARMACOLOGY

GABA as transmitter
The project deals with secretion from the intermediate- and posterior hypophysis. The existence of numerous neuropeptides and neurotransmitters as well as receptors for different neuroactive substances has been shown in the hypophysis. In different in vitro systems the pharmacological significance of neuroactive substances for secretion of hormones is investigated. In the year passed the GABA-receptors in the hypophysis have been in focus. The influence of different neurosteroids on the GABA-receptors in the hypophysis has been investigated by means of electrophysiological techniques in slices from rat hypophysis (patch clamp) and on isolated organs. It has been shown, that there are several binding sites for neurosteroids at the GABA-receptors and that there are difference in the sensitivity of the receptors in the intermediate- and posterior hypophysis.

The connection between the pharmacology of GABA$_A$-receptors and there subunit composition is examined by a combination of patch-clamp electrophysiology and RT-PCR analysis of mRNA at single nerve cells. By use of cell cultures and slices from different part of the brain the regional variation of the characteristics of the GABA-receptors is examined (cooperation with F.F. Johansen, Neuropathological laboratory, University of Copenhagen).

The pharmacology and mechanism of receptoractivation for partial GABA$_A$-agonists are examined by patch-clamp electrophysiology in cultures of nerve cells. The effect of substances with modulating effect at GABA$_A$-receptors (benzodiazepines, barbiturates, neurosteroids and metalions) is also examined as well as new substances synthesised at the Department of Medicinal Chemistry (Cooperation with J.D.C. Lambert, Department of Physiology, University of Århus and researchers at Department of Medicinal Chemistry, Royal Danish School of Pharmacy).

(Uffe Kristiansen, Bjørn Fjalland, Bjarke Ebert, Suzanne Hansen, Henrik Vestergaard, Gunilla Steven)

Communication between the immune and the neuroendocrine system
The research is dealing with the communication between the immune and the neuroendocrine system at the neurohypophysial level. In previous experiments we have shown the ability of interleukin-1$\beta$ to stimulate the release, both in-vivo and in-vitro, of oxytocin and vasopressin. At the present we are investigating the pattern of cytokines release from cultured glia cells from the neurohypophysis (pituicytes) and the mechanisms which control this release. The main objective is to elucidate whether a paracrine communication between the pituicytes and the axonal terminals in the neurohypophysis exists.

(Jens Juul Dencker Christensen, Erik Wind Hansen, Lise Moesby, Tine Klawes, Janne Magelhøj Colding, Helle Dyhrfield, Betina Schøler)

MOLECULAR PHARMACOLOGY

In collaboration with the neuromedicinalchemical group at the Department of Medicinal Chemistry the pharmacological characterisation of new substances at glutamate- and GABA-receptors is undertaken. The binding profile of new radioactive glutamate and GABA-ligands is investigated by means of binding studies in homogenates and receptorautoradiographic methods.

In collaboration with the neuromedicinalchemical group and the research institute at Merck, Sharp & Domes in England the connection between the subunit composition of humane GABA-receptors and the pharmacological profile of a series of agonists, partial agonists and antagonists is examined.

With the purpose of development of new strategies to treat neuropathic pain a series of strong analgesics is investigated in receptorbinding models, isolated organs and electrophysiologically with respect to effect on the NMDA-receptors.

(Bjarke Ebert, Martin Mortensen, Bjørn Fjalland, Durita Poulsen)
Pathophysiologica investigation of neuropathic pain through pharmacological intervention

Pain of nerve injury (neuropathic pain) is difficult to treat. Preclinical and clinical experiments with analgetica have shown discrepancy which probably reflecting individual patient variation in the activation of the pain provoking mechanisms of sensing, transmission and transduction. The goal of the project is through better knowledge of the pathophysiological mechanisms to improve the individual treatment regimen. A set of rat models for neuropathic pain is under establishment for testing with new and well-known antagonists and agonists for the involved receptor systems. (Ole J. Bjerrum and Majid Sheykhzade)

Neurotoxic and neuroprotective effects of nitrogen oxide

Nitrogen oxide (NO) is involved in both neurotoxicity and neuroprotection depending on where, when, why, how and how much NO is formed. Thus, NO formed from eNOS under ischemia is neuroprotective whereas NO from nNOS and iNOS under this take is neurotoxic.

Using primary cultures of cortical neurons and cerebellar neurons we are studying the formation of NO under different neurotoxic stress stimuli and trying to correlate the amount or character of NO formed with cell death or survival. To further elucidate the mechanism of action we are studying the intracellular targets for NO with special emphasis on mitochondria as we have found that NO inhibits respiration in neurons. (Trine Meldgaard Lund, Gunilla Steven, Marianne Michaely, Arne Schousboe in collaboration with John Garthwaite, UCL, UK)

Glutaric aciduria type 1 – a metabolic disease with neurodegenerative symptoms

Patients with glutaric aciduria type 1 have mutations in the gene coding for the glutaryl-CoA dehydrogenase enzyme. This enzyme is essential in the catabolism of lysine, hydroxylysine and tryptophan, thus an accumulation of the metabolites 3-hydroxy-glutaric acid, glutaric acid and glutaconic acid is seen in these patients. The objective of this study is to elucidate whether these metabolites are responsible for the neuropathological findings in these patients. Using cultures of cortical neuronse we are studying the viability of the cells after treatment with the metabolites and have found that they are neurotoxic. We are now in the process of finding the target for these neurotoxic compounds, this probably being the NMDA subtype of glutamate receptors, having ruled out any effect on the other glutamate receptor subtypes and glutamate uptake. (Trine Meldgaard Lund, Arne Schousboe, Darryl Pickering, Anders S. Kristensen in collaboration with Allan Meldgaard Lund and Ernst Christensen, Department of Clinical Genetics, Copenhagen University Hospital)

Characterization of glutamate receptors

In order to investigate the role of the various AMPA receptors (AMPA-R) in the normal functioning of the brain (e.g. memory formation), as well as their role in pathological conditions (e.g. stroke, epilepsy, Alzheimer’s disease), it would be highly advantageous to have subtype-selective agonists and antagonists. The latter could have potential applications as therapeutics.

Using the cloned, recombinant wild-type and mutant rat AMPA-R (GluR1–4) we have made significant progress in the last year towards an understanding, at the molecular level, of the properties of both the receptor proteins and of the agonist chemical structures that can lead to subtype selectivity and increased affinity and potency. Site-directed mutagenesis of GluR1 and GluR3 have revealed amino acid residues within the vicinity of the agonist binding site that are responsible for controlling both agonist affinity and desensitisation kinetics. Using this experimentally gained information, we have employed computer homology modelling of GluR1-4 to predict new structures of compounds that should have increased potency, affinity and selectivity. In the future, we hope to be able to increase our current selectivity factor of 125-fold to > 1,000-fold. (Darryl Pickering, Anders S. Kristensen, Tue G. Banke and Arne Schousboe in collaboration with Ulf Madsen, Jeremy Greenwood and Tommy Liiefors, Dept. Med. Chem.)

Characterization of GABA<sub>j</sub> receptors

Using Sf9 cells as an expression system the assembly process for GABA<sub>j</sub> receptors has been investigated. In receptors formed from α1, β2 and γ2 subunits it was found that muscimol (GABA agonist) binding appears prior to binding of flunitrazepam (modulator) or TBPS (channel blocker). Thus, binding of the agonist may not require a fully formed operational receptor complex of a pentameric configuration. It was additionally shown that the γ2 subunit plays a key role in the receptor assembly process. The chimeric subunits α1/γ2 and γ2/α1 representing the extracellular N-terminal domain of α1 and γ2 subunits, respectively have been used in combination with β2 and β2γ2 to elucidate the significance of these domains for desensitization. The α1/γ2 chimera did not exhibit desensitization after GABA stimulation independent of the combination with β2 or β2γ2. This suggests that the C-terminal segment of the α1 subunit may be important for the desensitization properties. More detailed investigations of site directed mutagenic receptors may allow identification of the molecular site involved in the desensitization mechanism. (Lisbeth Elster, Claus F. Poulsen, Darryl Pickering, Ulfie Kristiansen and Arne Schousboe in collaboration with Dr. R.W. Olsen, Dept. Mol. Med. Pharmacol., UCLA, Los Angeles, CA, USA)
Characterization of GABA transporters

GABA transporters cloned from mouse (GAT1-4) and transiently expressed in HEK cells have been used to study the subtype selectivity with regard to inhibition of GABA transport by a number of lipophilic derivatives of exo-THPO. All analogues inhibit GABA transport mediated by GAT1 and a small number of these also exhibited inhibitory activity for GAT2. The anticonvulsant activities of exo-THPO has been compared with that of its N-methyl and N-ethyl derivatives previously identified as inhibitors of neuronal and astrocytic GABA uptake with differential potency. It was found that the potency as anticonvulsants in mice prone for audiogenic seizures correlates with the potency of these compounds as inhibitors of astroglial GABA uptake but not to that as inhibitors of neuronal GABA uptake. The GABA transporters specificity of a new series of GABA-analogues, amino-cyclohexane carboxylic acid derivatives with lipophilic side chains, are now under investigation. These compounds exhibit a novel pharmacological profile with regard to inhibition of subtypes of GABA transporters.

(Orla M. Larsson, Alan Sarup, Darryl Pickering, Lone Petersen, Helle Dyhrfjeld and Arne Schousboe in collaboration with Dr. U. Sonnewald, Univ. of Trondheim, Norway and Dr. N.C. Danbolt, Univ. of Oslo, Norway and Dr. Jens Zimmer, Univ. Odense)

Heterogeneity of astrocytic mitochondrial metabolism

Using 13C-labeled lactate or glucose and subsequent NMR and GC/MS analysis of samples from astrocytes and their incubation media it has been demonstrated that these two substrates are differentially metabolized by these cells. Moreover, it was shown that astrocytic mitochondria are heterogeneous since different populations are involved in biosynthesis of releasable citrate and glutamine. A model of four different types of mitochondria with TCA cycle associated with metabolism of acetyl CoA derived from exogenously supplied or endogenously produced lactate has been proposed. Further experimentation is needed to shed light on the functional importance of such heterogeneity.

(Helle S. Waagepetersen, Orla M. Larsson, Kirsten Thuesen and Arne Schousboe in collaboration with Dr. U. Sonnewald, Univ. of Trondheim, Norway.)

The cytoprotective role of ER-stress proteins.

The Endoplasmatic reticulum (ER) plays a central role in the cellular stress response as the structure where protein modification, processing and quality control are exerted. In addition, the ER is the intracellular reservoir for Ca2+, an ion involved in many signalling reactions, including those mediating the stress response. A protein in the lumen of the ER called GRP78 (Glucose Regulated Protein or BIP (immunoglobulin Heavy Chain Binding Protein) is homologous to the cytosolic chaperone and stress protein HSP70. GRP78 is a member of a family of stress proteins (including e.g. GRP94, GRP75, GRP58, GRP170) that all functions as stress proteins. While the cytoprotective role of the GRP-family, especially GRP78, is well documented within the fields of cancer biology and immunology very little evidence has been obtained from neurobiological research. GRP78 obtains a key positions as a chaperone protein in connection with the synthesis of ER-associated ribosomes and protein translocation into the lumen of ER. GRP78 is upregulated significantly on the levels of mRNA and protein in vivo as well as in vivo models of ischemia. This emphasizes the possible cytoprotective role of GRP78 in ischemia and other conditions involving glutamate toxicity.

Recently we have observed that a 16 hours pre-treatment with low, non toxic doses of the EAA NMDA significantly reduces the cytotoxic potential of subsequent exposure to toxic doses of NMDA (the phenomenon of tolerance). This phe-
nomen is accompanied by a significant (up to 80%) upregulation of GRP78. We are currently working on characterization of the pharmacological basis for the establishment of the tolerance. Furthermore, it is investigated whether or not there is a causal relation between GRP78 and the NMDA mediated tolerance against glutamate toxicity. Likewise the influence of GRP78 on EAA mediated Ca\(^{2+}\) signals is investigated.

(Aase Frandsen, Pia Birch Nielsen, Paulo Girao, Arne Schousboe).

(GRP expression in collaboration with Professor Wulf Pachen, Dept of Exp neurology, Max-Planck Institute of Experimental Neurology, Cologne)

The role of cytokines in neurodegeneration and neuroprotection

New results indicate a common area of function between the stress activated signalling from the ER and signalling through TNF p55- receptors (TNFR1). This area arises through an activation of the transcription factor NF-κB through an internal stress stimulus to the ER (EOR, ER overload response). An externally released NF-κB activation is seen e.g. when TNF binds to TNFR1. This binding recruits the transduction molecules FADD/MORT1 (FAS associated death domain protein) and RIP (receptor interacting protein). FADD/MORT1 mediates the proapoptotic effect of TNF whereas the RIP activates the antiapoptotic effect of NF-κB. In primary cultures from TNFR1-deficient mice we are currently investigating if changes in NF-κB (and other pro- and antiapoptotic factors) specifically can be ascribed to the lack of the TNFR1-receptor or changes in the EOR.

(Aase Frandsen in collaboration with Prof. Bente Finsen and coworkers, University of Odense)

The role of IFNγ in toxicity induced in CNS induced by ischemia or inflammation

The sensitivity of nerve cells towards ischemic damage is increased by IFNγ. Even though IFNγ not normally are found in association with ischemia in the brain, this finding allows the possibility that IFNγ alone or in combination with e.g. EAAs and TNF in a fundamental manner may change the susceptibility of the CNS not only to ischemic conditions but also in connection with leucocyte infiltration in the brain seen in patients with disseminated sclerosis. Recently, we have demonstrated that IFNγ is potentiating the toxic effect of NMDA and AMPA in cultured neurons from IFNγ deficient mice, and we are currently investigating the pharmacology of this response.

(Aase Frandsen in collaboration with Prof Bente Finsen and coworkers, University of Odense)

CUSTOM MADE ANTIBODIES

Generation of recombinant antibodies recognizing MHC/peptide complexes of relevance for the pathogenesis of multiple sclerosis

The purpose of the project is to generate antibodies recognizing specific MHC/peptide complexes of relevance for the pathogenesis of multiple sclerosis. The strategy is that such reagents will be useful in modulating the autoimmune T cell response. To generate such antibodies we use the so-called page display technology where the total antibody repertoire of immunized animals are cloned and expressed in bacterial cells. The antibody libraries are generated by a PCR (Polymerase Chain Reaction) based method and allows for isolation of the wanted specificity through positive selection.

Generation of antibodies that recognize specific MHC/peptide complexes of relevance for the pathogenesis of specific melanoma cancers

Studies of melanoma patients have revealed the identity of activated T cells specific for defined MHC/peptide complexes. These peptides are derived from tumour associated antigens. Thus, these MHC/peptide complexes become cell surface markers for these malignancies. We want to use the technology described above to generate antibodies specific for these MHC/peptide complexes since we have shown previously that such antibodies can be conjugated with cytotoxic reagents with the effect of killing cells in a MHC/peptide-specific manner.
Studies of the effect of glyceryl trinitrate infusion in rat on nitric oxide synthase in dura and cerebral blood vessels

NO is a powerful vasodilator of general importance for the arterial diameter. It was recently shown that NO is of main importance in the migraine pathogenesis. A 20 minute intravenous infusion of glyceryl trinitrate (GTN) induce a migraine attack fulfilling the criteria for migraine without aura, in migraine patients at an average time of 5.5 hrs after the infusion. Furthermore, L-NMMA, an inhibitor of NOS is effective in the treatment of an acute migraine attack. The long time lag of 5.5 hrs from GTN infusion to maximum migraine pain intensity could indicate that NO initiate a slowly progressing pathological reaction, that eventually will lead to a migraine attack.

We have found that after infusion of GTN the synthesis of inducible NOS is upregulated in dura from rat. The maximal amount of NOS is found 4-6 hrs after the GTN-infusion is terminated, i.e. at the time when the migraine patients develop the delayed headache (migraine attack). In the following studies we intend to illuminate changes in the expression also of endothelial and neuronal nitric oxide synthase (NOS) in dura and all the three NOS enzymes in cerebral blood vessels after the infusion of GTN. Furthermore, we will investigate how infusions of GTN involve changes in the sensitivity of cerebral blood vessels to perivascular transmitters.

The results from the project will lead to an increased knowledge about which of the three different NOS enzymes that is upregulated and their localization. Furthermore, it will give us an increased understanding of the mechanisms underlying an eventual hyper- or hyporeactivity of cerebral blood vessels after mental stress.

(Inger Jansen Olesen, Tina Zinck, Majid Sheykhzade, Trine Meldgaard Lund, Kirsten Busk)

Clinical and experimental micro array investigations of mRNA expression during migraine

We have in a human model of migraine found a number of substances that 5-7 hrs after an intravenous infusion trigger a migraine attack. The key to the understanding of the outbreak of the migraine attack lie in the mechanisms activated during the infusion and that hour’s later lead to the migraine pain. If several substances with different mechanisms of action initiate a migraine attack, they must share a mechanism that is of vital importance for the development of the migraine attack.

We have in a previous study shown that infusion of glyceryl trinitrate (GTN) in the rat results in an increased expression of...
crease in \([\text{Ca}^{2+}]_{i}\) by inhibiting the \(\text{Ca}^{2+}\) influx through membrane hyperpolarization mediated partly by activation of the large conductance \(\text{Ca}^{2+}\)-activated potassium channels, (2) a decrease in \([\text{Ca}^{2+}]_{i}\) presumably by sequestrating cytosolic \(\text{Ca}^{2+}\) into thapsigargin-sensitive \(\text{Ca}^{2+}\) storage sites and (3) a decrease in the \(\text{Ca}^{2+}\)-sensitivity of the contractile apparatus. In resting coronary arteries, however, there seems to be an interplay between different types of \(K^{+}\) channels.

(Majid Sheykzhade in collaboration with Niels C. Berg Nyborg, Novo Nordisk A/S)

**MICROBIOLOGY**

**Microbiological control of pharmaceutical products**

Pharmaceutical products for parenteral administration must be free of pyrogens. Pharmaceutical preparations are tested for pyrogens by the “Test for pyrogens” (rabbit pyrogen test) or “Test for bacterial endotoxins” (LAL test). Both pyrogen tests have limitations. Therefore we work towards alternative in-vitro assays. The monocytic cell line Mono Mac 6 is being evaluated for its use in detection of pyrogens in pharmaceutical preparation. In vivo monocytes play a key role in the fever pathogenesis. When exposed to pyrogens they release cytokines that mediate fever.

Like the rabbit pyrogen test, we have found that the Mono Mac 6 cells are able to detect a broad spectrum of pyrogenic microorganisms. The cell culture assay is being optimized to achieve a higher sensitivity to pyrogens.

Spores and vegetative bacteria of the gram-positive *Bacillus subtilis* and the cell wall component lipotheicoic acid are able to induce IL-6 in Mono Mac 6 cells. This makes the Mono Mac 6 assay a useful tool to study the thermostability of these microorganisms and cell wall components.

The Mono Mac 6 assay is a valuable tool to test pharmaceutical products for pyrogenic contamination.

(Jens Juul Dencker Christensen, Erik Wind Hansen, Lise Moesby, Janne Magelhaj Colding, Helle Dyhrfjeld, Betina Schøler)

**Retroviral membrane fusion**

The fusion protein of Moloney murine retrovirus is investigated. The fusion protein is a transmembrane protein. During virus maturation a 16 amino acid peptide (the R peptide) is cleaved of the cytoplasmic tail in order for the fusion protein to gain activity. The R peptide has the sequence VLTQQY-

**Studies of the effect of feverfew and parthenolide on nitric oxide synthase activity in cerebral arteries and dura of guinea pig**

*Tanacetum parthenium*(L) commonly known as feverfew is a popular herbal remedy advocated for fever, arthritis and migraine. The anti-migraine effect is mainly attributed to sesquiterpen lactones present in the plant. Parthenolide, the predominant sesquiterpen lactone in feverfew is regarded as the most important of the biologically active substances isolated from the plant. The exact mechanism by which feverfew and parthenolide act in order to exhibit prophylactic anti-migraine effect is still unknown. A number of recent studies indicate that NO is a crucial molecule for the induction of migraine, the present study is therefore designed to study the effect of feverfew and parthenolide on enzymes catalyzing the formation of NO in cerebral arteries and dura.

(Inger Jansen Olesen, Per Mølgaard, Anne Adsersen, Trine Meldgaard Lund, Majid Sheykzhade, Kirsten Aagaard Busk)

**Signalling pathway for CGRP in isolated resistance coronary arteries of rat**

The intramyocardial resistance arteries regulate the coronary perfusion. These arteries are densely innervated by sensory nerve endings containing calcitonin gene-related peptide (CGRP) and substance P. CGRP is a potent and powerful vasodilator, which is released during cardiac ischemia, and low pH levels indicating an important role for CGRP in regulation of coronary blood flow under ischemic conditions. The purpose of our study was to investigate the mechanism of action behind CGRP-induced relaxation in isolated rat intramural coronary arteries.

Our results clearly demonstrate that CGRP relaxes precontracted rat coronary arteries via three mechanisms: (1) a decrease in \([\text{Ca}^{2+}]_{i}\) by inhibiting the \(\text{Ca}^{2+}\) influx through membrane hyperpolarization mediated partly by activation of the

**DEPARTMENT OF PHARMACOLOGY**
served whereas the last amino acids varies largely and can be deleted without serious consequences for the viral life cycle.

We have changed the lysine group (K) to T or R as it is a candidate for the palmitoylation (amide binding). No biological affects was observed, which either shows that the palmitoyl group is not located here, or that the palmitoylation does not have biological effects.

Deletions in the well-conserved region were made (TQQY-HQLK deletion, TQQY deletion, QYH deletion and HQLK deletion). By transfection in cells these all give biological effects:

The TQQYHQLK deletion gives a premature fusion, does not produce virus particles and is lethal for the cells. The smaller deletions all give slight premature fusion, produce virus particles, which though have a poor replication.

Analysis of protein cleavage is currently being investigated. (Anne Zedeler, Randi Jensen, Klaus B. Andersen)

### BIOACTIVE LIPIDS

Phospholipids are building blocks of the cell membranes, but phospholipids are also precursors for extracellular and intracellular signaling molecules that function as local hormones (autocoids) and as second messengers, respectively. Some of these bioactive lipids are formed from arachidonic acid, which again is formed from the essential fatty acid linoleic acid. Fish oils contains long-chain n-3 fatty acids, which can affect the arachidonic acid metabolism, and the dietary content of n-3 fatty acids can thus affect different biological parameters. Furthermore, dietary n-3 fatty acids are essential for the development of the brain. Other bioactive lipids comprises diacylglycerol, phosphatidic acid, platelet activating factor, lyso phosphaticid acid, ceramide, sphingosine-1-phosphate, phosphatidylinositol 3,4,5-trisphosphate, 2-arachidonoyl-glycerol, anandamide, and N-acyl-ethanolamines. We are currently focusing on understanding the functions of N-acyl-ethanolamine phospholipids (NAPE) and of N-acyl-ethanolamines (NAE) in the brain.

**Biochemical characterization of the NAPE/NAE system**

We are characterizing the enzymes involved in the formation of NAPE (N-acyl-transferase) and in the formation of NAE (NAPE-hydrolysing phospholipase D). Furthermore, we are studying the formation of these lipids in cultured neurons and brain slices, and quantifying NAPE in tissue extracts by negative ionisation electrospray mass spectrometer.

NAPE and NAE can be formed in cultured neurons exposed to excitotoxic concentrations of glutamate or other compounds that can induce cell injury. NAPE is believed to have a membrane stabilizing effect, and NAPE is formed as a stress response in cultured neurons and in rat brain in vivo. Some molecular species of NAE, e.g. N-arachidonoyl-ethanolamine (also called anandamide) and N-palmitoyl-ethanolamine are ligands for different cannabinoid receptors, and these two species of NAE have different biological effects. N-Arachidonoyl-ethanolamine has the same biological effects as Δ⁹-tetrahydrocannabinol and N-palmitoyl-ethanolamine has antinociceptive and antiinflammatory effects. 2-Arachidonoyl-glycerol, that can be formed during inositol phospholipid turnover, is also a ligand for the cannabinoid receptors. 2-Arachidonoyl-glycerol, anandamide and N-palmitoyl-ethanolamine are considered as endocannabinoids. Thus NAPE may be a neuronal stress lipid and it is precursor for different endocannabinoids.

(Harald S. Hansen, Birthe Moesgaard, Henrik Hansen, Gitte Petersen, Grete Sørensen, Jytte Palmgreen in collaboration with Steen Honøré Hansen (Royal Danish School of Pharmacy), J.J. Fernández-Ruiz (Complutense University, Spain), C.I. Konomidou (Humboldt University, Tyskland), and H.H.O. Schmid (University of Minnesota, USA))

**NAPE and NAE in human brain tumors**

We are quantifying in human brain tumours the activity of N-acyltransferase, NAPE-hydrolysing phospholipase D, and Fatty-Acid-Amide-Hydrolase, three enzymes that take part in the turnover of anandamide. Furthermore, we are also quantifying different NAE molecular species. Anandamide and congeners may have a function in regulating the growth rate of brain tumours.

(Harald S. Hansen, Birthe Moesgaard, Gitte Petersen, Jytte Palmgren, Grete Sørensen in collaboration with M. Kosteljanets and Helle Broholm (Danish State hospital), and H.H.O. Schmid and P.C. Schmid (University of Minnesota, USA))

**Dietary n-3 fatty acids and human brain development**

Harald S. Hansen is engaged in a project on the importance of dietary n-3 fatty acids for human brain development.

(In collaboration with L. Lauritzen and K.F. Michaelsen Research Institute for Human Nutrition, Royal Danish Agricultural and Veterinary University)
The Department of Social Pharmacy conducts research and teaching within Social Pharmacy. The Department is also responsible for interdisciplinary teaching activities, including the compulsory course on occupational health, the pharmacy internship and the new postgraduate specialisation programme in community pharmacy.

Social Pharmacy may be defined as the discipline dealing with the role of medicines at the level of the individual, group/organisation and society. Social Pharmacy also embraces the activities of the pharmaceutical profession. Hence, Social Pharmacy spans a variety of themes from the experiences and perceptions of the medicine user to national and international drug policy.

Within Social Pharmacy theories and methods from the humanities, the social sciences and natural sciences are applied in a cross-disciplinary manner.

The majority of the Department’s research is conducted in interdisciplinary and inter-institutional project groups. Staff members also participate in or co-ordinate international research projects.

The Department’s research on ‘Medicine Use’ aims at improving the rationality of medicine management and use among professionals and among users. The goal of the research in ‘Pharmacy practice’ is to support the development of the pharmacists’ professional role and to evaluate pharmacy activities in health care.

The teaching of the Department includes the following compulsory courses:

- Introductory Course (1st term) taught in collaboration with other departments of The Royal Danish School of Pharmacy
- Dissemination and Methodology in Social Pharmacy (3rd term)
- Occupational Health (4th term)
- Social Pharmacy including Management & Organisation (5th - 6th term)
- Pharmacoeconomics (6th term)
- Drug Dispensing and Customer Communication (7th term)
- Pharmacy Internship (8th term).

Within the period under review the Department taught the following elective courses:

- Communication and Information
- Pharmacoeconomics
- Research Methods in Social Pharmacy
- Models for Technology Assessment in Health Care
- International Health Care.

The Department offers two PhD courses with international participation and with English as the course language: ‘Methodological Perspectives in Health Services Research’ and ‘Quantitative approaches to the evaluation of health care inputs’. These courses were not taught in the period covered by the report.
Specialisation in Community Pharmacy
The Department is heavily involved in the co-operation between The Royal Danish School of Pharmacy and Pharmakon a/s on the new specialisation programme in community pharmacy. A fuller description of the new postgraduate programme is given in a separate chapter, Specialisation in Community Pharmacy, in the present report. The Specialisation in Community Pharmacy programme is underway, and the first Introductory Course was held on 5-9 April 2001 (Ellen Westh Sørensen and Trine Hopp) and the Course in Health Care Theory was held on 20-24 August and 20 November 2001 (Ellen Westh Sørensen and Thomas Clemens Jensen).

FKL – THE RESEARCH CENTRE FOR QUALITY IN MEDICINE USE
The Research Centre for Quality in Medicine Use (FKL – Forskningscenter for Kvalitetssikret Lægemiddelanvendelse) was established in 1999. The overall objectives of the centre’s projects are to provide scientific evidence to optimise the professionals’ pharmacotherapy and the population’s medicine use. In this way the research contributes to improved public health and quality of life as well as improved economy of the individual and society. The majority of the Department’s scientific staff are involved in one or more centre projects. The Centre is directed by Professor Ebba Holme Hansen of the Department.

The Centre’s approach is multidisciplinary, inter-professional and inter-institutional. The researchers involved in the Centre’s activities represent several disciplines and institutions, including Pharmakon, the Danish College of Pharmacy Practice, the County of Vestsjælland, the County of Funen, the National Institute of Public Health, Copenhagen University, the University of South Denmark, Aalborg University, the University Hospitals Centre for Nursing and Care Research (UCSF) and the Institute of Rational Pharmacotherapy. The 1991 Pharmacy Foundation has been the major external sponsor of the Centre’s activities.

The Department’s involvement in FKL-projects is described under ‘Projects’.

ARRANGEMENTS AND GUESTS AT THE DEPARTMENT
From 20 September until 24 December 2000, Master’s thesis students Christian Huyghe and Karen Hoebeke, Vrije Universiteit Brussels, worked on their Master’s thesis ‘Qualitative and quantitative analysis of the asthma therapeu-
tic outcomes monitoring (TOM) projects’ (advisor: Ellen Westh Sørensen).

The Department arranged the yearly 2-day course for the internship pharmacies January 15 to 16, 2001. Approximately sixty supervisors from community pharmacies and hospital pharmacies participated.

Professor Th F J Tromp, Groningen Universitet, visited the Department 27 November 2000.

Dr. Ines Krass, University of Sydney, visited the Department 23 January 2001.

Charlie Benrimoj, Dean, Faculty of Pharmacy and Professor of Pharmacy Practice, The University of Sydney, visited the Department 29 January 2001

B.Pharm. (Hons) Mike Rouse from Zimbabwe, visited the Department 16 May 2001.

Alison Roberts, Honour Thesis student, Faculty of Pharmacy, The University of Sydney, Australia, studied at the Department from 1 July until 21 December 2001

Ellen Westh Sørensen and Trine Hopp arranged a research seminar: ‘Strategies for Dissemination of Pharmaceutical Care Services’ 7-10 June 2001 at the Department of Social Pharmacy. Participants in the meeting and presenters: Charlie Benrimoj, University of Sydney, Alison Roberts, University of Sydney, Parisa Aslani, University of Sydney, Hanne Herborg, Division of Research and Development, Pharmakon, Miguel Angel Gastelurruti, University of Granada, Ellen Westh Sørensen and Trine Hopp.

Dr. Hans-Rüdiger Elster, Martin-Luther-University, Halle, visited the Department to discuss student exchange and mutual research interests on 28 September 2001

Parisa Aslani, BPPharm (Hons), MSc PhD, MPS, MRPharmS, The University of Sydney, visited the Department for a one day meeting on 15 October 2001. Parisa Aslani made a presentation entitled ‘Consumer Opinions on Medicines Information and Factors Affecting Use’. Trine Hopp and Alison Roberts made a presentation entitled ‘Development of Pharmacy Practice with special focus on implementation-processes. Project status and theory thoughts’.

The Medicine Consultants Aase Nissen and Helle Neel Jakobsen as well as Clinical Pharmacist Lisbeth Bregnhøj, from Copenhagen County, presented their ongoing projects at a departmental seminar on 17 December 2001.

The Department has hosted several meetings of the FKL – Research Centre for Quality in Medicine Use throughout the period of the report.

MEMBERSHIP OF EXTERNAL BOARDS AND COMMITTEES

EXTERNAL PROFESSIONAL POSITIONS:

Ebba Holme Hansen
• President of the Danish Pharmaceutical Society (until March 2001)
• Director of the Research Centre for Quality in Medicine Use (FKL)
• Member of the Council of EUFEPS – European Federation for the Pharmaceutical Sciences (until March 2001)
• Member of STAC – Scientific and Technical Advisory Committee of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Disease
• Member of the International Task Force, American Society of Consultant Pharmacists
• Member of the Project Co-ordinator Network ENRECA – Enhancement of Research Capacity in Developing Countries
• External evaluator of NEPI, The Swedish National Network for Pharmacoepidemiology (with Professor PMK Lunde, Norway)
• Member of the evaluation panel for a professorship in social pharmacy at the University of Oslo
• Member of the evaluation panel for a professorship in social pharmacy/pharmaco-economics at the University of Tromsø
• Member of the Advisory Committee to the Ministry of Foreign Affairs on children’s and adolescents’ conditions in developing countries
• Peer reviewer: Pharmacy World and Science, European Journal of General Practice
• Member of the Editorial Board of Journal of Social and Administrative Pharmacy
• Member of the Editorial Board of International Journal of Pharmacy Education.

Trine Hopp
• Board Member of the Section for Social Pharmacy under the Danish Pharmaceutical Society
• Member of the group ‘Quo Vadis 2000’, Astra-Zeneca postgraduate training
• Member of Task Force Groups of The Association of Danish Pharmacists.

Pia Knudsen
• Board Member of The Danish Society of Pharmacoepidemiology.
Laila Launsø
• Member of the National Board of Health’s Council on Alternative Treatment
• Member of the Steering Committee of the Disease and Society - International Network
• Member of the Board of The Danish Knowledge and Research Centre of Alternative Treatment
• Chairperson of the Research and Knowledge Centre for Unconventional Cancer Treatment
• Chairperson of the Centre for Bridgebuilding in Health Care
• Research Consultant for European Council for Classical Homeopathy (ECCH)
• Member of the Treatment Board in the Danish Association of Sclerosis
• Chairperson of a working group on developing a team of conventional and unconventional therapists in relation to treating patients having sclerosis, The Danish Association of Sclerosis
• Member of the Board for Evaluation of a Homeopathic Education for Health Professionals, Helsedepartementet, Oslo.

Ellen Westh Sørensen
• External Examiner, Tromsø University, Institute of Pharmacy
• Member of the Course Committee of the Specialisation in Community Pharmacy
• Member of the Scientific Committee for the 12th International Social Pharmacy Workshop 2002
• Member of the Supervision Group for the project The Consultative Pharmacy, carried out by the Research and Development Department at Pharmakon a/s
• Member of the Editorial Board of the International Journal of Pharmacy Practice
• Member of the Committee for Postgraduate Training of Pharmacists (PUF-A)
• Member of the board ‘Interdisciplinary Communication Course, Copenhagen’
• Member of the Organising Committee for the Forum of Health Care Research meeting October 2001.

Janine Morgall Traulsen
• Officially appointed external examiner for Engineering and Social Studies
• Member of the Advisory Board: The Danish National Institute for Medical Technology Assessment, Ministry of Health
• Adjunct Professor – Mercer University Southern School of Pharmacy.

GRANTS

Ebba Holme Hansen has received:
DKK 2,347 million (2000) and DKK 903,000 (2001) from The Danish Ministry of Foreign Affairs towards the continued implementation of a research education programme to develop primary health care research in Nepal. In collaboration with Department of Social Pharmacy; Department of Psychology and Department of Public Health, University of Copenhagen; DSI • Danish Institute for Health Services Research and Development; Department of Epidemiology and Social Medicine, University of Aarhus; and Tribhuvan University, Kathmandu.

On behalf of FKL – Research Centre for Quality in Medicine Use, Ebba Holme Hansen received a grant of DKK 2.5 million from The 1991 Pharmacy Foundation for co-ordination and administration and the following projects: The Pharmacy-University Study, co-ordinated by Ellen Westh Sørensen and Lotte Stig Haugbølle, and Improved Self-medication and Self-care co-ordinated by MSc (pharm) Hanne Herborg (Pharmakon).

Erik Knudsen, Vestsjællands Amt, in collaboration with Ebba Holme Hansen, has received DKK 200,000 (2000) and DKK 338,500 (2001) from the Danish Medical Research Council’s Regional Fund for Eastern Denmark for the FKL project: The research foundation for intervention strategies towards medicine prescribing and use. (The grant is administered by Vestsjællands Amt).

Ebba Holme Hansen is member of the project group ‘Clinical pharmacist in primary health care’ co-ordinated by Bente Kirkeby that has received a donation of DKK 700,000 from The 1991 Pharmacy Foundation. (The grant is administered by Frederiksborg Amt).

Claus Møldrup has received DKK 1,111 million from the Centre for Evaluation and Health Technology Assessment, The National Board of Health in support of a post-doc study on pharmacogenomics.

Ellen Westh Sørensen received DKK 100,000 from The Hørslev Foundation for the FKL project Pharmacy-University Study for the period 2001-2002.

PROJECTS

MEDICINE USE

Intentions, Values, Rationales and Strategies in GPs’ Prescribing
The knowledge assembled in the literature about GPs’ intentions, values, rationales and strategies when prescribing drugs is sparse. An understanding of the GPs’ perspective is
Prescribing of Antibiotics in Iceland
This project explores general practitioners’ views, reflections and strategies when dealing with infections and prescribing antibiotics. The project springs from a former PhD study at the Department.
(Ebba Holme Hansen in collaboration with Ingunn Björnssdóttir, CEO, PhD (pharm), and Almar Grímsson, MSc (pharm), Iceland).

Behaviour of Rural Mothers in Response to Diarrhoea in Children
Diarrhoea is one of the most common causes of child mortality in developing countries. Plenty of interventions have aimed at disseminating and improving the use of ORS (Oral Rehydration Salt) in relation to diarrhoea, however, without sufficient success. This project aims at studying the user side of the issue by exploring the mothers’ perceptions and views re symptoms and treatment of diarrhoea in children. The project springs from a Master’s of Social Pharmacy thesis.
(Ebba Holme Hansen in collaboration with Farai Chinyanganya, MSc, PhD, United Kingdom).

Popular Attitudes to Medicines and Medicine Supply
The literature in the social sciences is scarce on how different segments of the population view the benefit of medicines and the medicine supply system. This project analysis the Danish population’s perceptions of what constitutes a medicine and attitudes and behaviours re the benefit of medicines and herbal remedies, where they should be available, information during the purchase situation, etc. The data were collected as part of the Danish Health & Illness Survey year 2000 and covers large representative national samples of Danes. The survey provides the opportunity to relate data on the attitudes to a number of population characteristics including illness, medicine use, health care utilisation, and life style. The results of the project will contribute to the user perspective on quality management in the health care. Furthermore, there will be a contribution to the development of policy in the drug arena.
The project is affiliated with FKL – Research Centre for Quality in Medicine Use.
(Ebba Holme Hansen in collaboration with Niels Kr. Rasmussen, National Institute of Public Health).

Medicine Use among Children and Adolescents
Medicine use is one of the domains studied in the WHO project, Health Behaviour in School-Aged Children (HBSC). The study comprises a series of cross-sectional school surveys of national representative samples of girls and boys aged 11, 13 and 15. The project started in 1987. Twenty-eight countries and more than 120,000 respondents participated in the 1998 survey. The study analyses the use of medicine in relation to sex, age and country over time. Analyses include associations between medicine use and symptoms, social status, psychosocial conditions and social network.
The project is affiliated with FKL - Research Centre for Quality in Medicine Use.
(Ebba Holme Hansen in co-operation with the national co-ordinators for the HBSC project: Bjørn Holstein and Pernille Due, Institute of Public Health, Copenhagen University, and the international HBSC Co-ordinator Candace Currie, University of Edinburgh).

TUPP – The User Perspective on Psychotropic Drugs
TUPP was initiated by the European Drug Utilisation Research Group, formulating the need for qualitative pan-European research on medicine use. The overall objective of the project is to explore the social meanings attached to the use of psychotropic medicines at different locations in Europe. The core project is based on qualitative in-depth interviews with at least 20 informants in each country. As the consumption of SSRIs is increasing rapidly all over Europe, the study of these medicines is mandatory for each research group. A multidisciplinary project group with participants from 11 countries and 13 research groups has been established.
The Danish sub-studies are affiliated with The Research Centre for Quality in Medicine Use.
(Ebba Holme Hansen, Project Co-ordinator, Søren Troels Christensen, Kristin Eskildsen, Stig Helweg-Jørgensen and Pia Knudsen in co-operation with approximately 25 researchers from European countries and WHO EURO, Pharmaceuticals Programme).

Danish sub-studies:

Psychotropic Drug Dependency in a User Perspective
This project explores the users’ experiences, reflections and strategies in relation to long-term use and being dependent on psychotropic drugs. The analyses are based on 50 in-
depth, semi-structured interviews with people with a self-diagnosed dependence on benzodiazepines, primarily. (Ebba Holme Hansen and Stig Helweg-Jørgensen).

Young Women’s Use of SSRIs
The objective of this PhD study is to contribute to an understanding of the use of SSRIs among younger women by addressing the users’ subjective experiences. The empirical foundation of the project consists of Danish women aged 18 to 34 with SSRI prescriptions. The women were identified through pharmacies located in the Copenhagen area. A total of twelve in-depth interviews including six re-interviews were conducted.

It can be concluded that the users of SSRIs relate the use of the medicine not so much to clinical conditions as to social meanings. It can further be concluded that the use of SSRIs is related to ambivalent feelings. The medicine is experienced as a helper that enables the users to regain their social functioning, and at the same time as a labelling agent. This study showed that the use of SSRIs has more implications than just controlling the illness. The use of SSRIs has social meanings. It stigmatises the users, and it has an effect on the users’ self-concept.

The study is linked to TUPP - The User Perspective on Psychotropic Drugs and to FKL - Research Centre for Quality in Medicine Use. (Pia Knudsen supervised by Ebba Holme Hansen (main supervisor) and Janine Morgall Traulsen).

Enhancement of Research Capacity in Nepal: A Primary Health Care Project
The background for this Danida sponsored project is partly the Nepalese research system’s lack of competence and capacity in terms of primary health care, including drug use, and partly the widespread problems that characterise Nepalese health care in relation to an overwhelming morbidity level and an extremely poorly functioning health care. The project therefore has two main goals.

- To strengthen the research competence at university level in Nepal through the accomplishment of research courses and education up to PhD level.
- To focus PhD projects towards primary health care in Nepal, and to use the results directly as a part of the Nepalese health policy and in health care practice.

The objective of the project is to integrate two parallel processes of development namely a researcher training programme and an inter-disciplinary research programme, that has primary health care as its research agenda.

The PhD studies carried out with the Department deal with the projects: Quality Assessment of a Health Care Information System: A Case Study from Nepal (Sharad Onta), Assessing the Quality of the Provision of Antibacterials in the Nepalese Health Care System (Shiba Karkee), and A User Perspective on Tuberculosis Treatment (Pranaya Mishra). (Ebba Holme Hansen (Project Co-ordinator), Ib Bygbjerg, Institute of Public Health, University of Copenhagen, Rolf Kuschel, Department of Psychology, University of Copenhagen, and Svend Sabroe, Department of Epidemiology and Social Medicine, University of Aarhus. The Nepalese counterparts are the following professors from the Tribhuvan University, Kathmandu: Mathura P Shrestha, Kumud K Kafle, Rishikesh R Regmi, and Ayan B Shrestha. The project is associated to the Danish ENRECA programme (Enhancement of Research Capacity in Developing Countries)).

Health Interview Surveys in Europe (EuroHIS); Medicine Use
EuroHIS is a WHO co-ordinated European project aiming at the development of standardised questionnaires to be used in national and cross-national health surveys. In this sub-study nationally used questionnaires dealing with medicine use are collected and reviewed. Based on the findings, a battery of questions are developed and validated to form the basis for future national and international surveys. Researchers from five countries and the WHO participate in the medicine use project. The collaborative work is funded by a BIOMED grant from the EU. (Ebba Holme Hansen in co-operation with researchers from Finland, Greece, Israel and WHO EURO).
CEEMedicines
This project aims at mapping and analysing the medicine markets in Eastern European countries. Data on registered medicines on the market in each country are collected. The project is financially supported by the EU and co-ordinated by Dr. Pietro Folino-Gallo, Università Cattolica del Sacro Cuore, Rome.
(Ebba Holme Hansen in co-operation with researchers and medicine regulators from ten countries and WHO EURO, Pharmaceuticals Programme).

Social Determinants of Medicine Use in the Danish Population
The aim of this study is to characterise the medicine use of the Danish population with special focus on social inequality. The analyses use data from The Danish Health and Illness Survey 2000 conducted by the National Institute of Public Health. This interview survey of the population contains social and demographic background information as well as information on health and illness behaviour and self-reported use of medicine. The analyses will include multivariate analyses and different therapeutic groups of medicine.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use.
(Merete W. Nielsen, PhD student, is supervised by Ebba Holme Hansen (main supervisor) and Niels Kristian Rasmussen, National Institute of Public Health).

The Practices of Dispensing and Non-Dispensing Doctors
The number of dispensing doctors has increased world-wide in recent years. What are the implications of this trend, what are the consequences for the quality of medicine therapy? This PhD project aims at evaluating and comparing the prescribing practices of dispensing and non-dispensing doctors and to assess the quality of dispensing doctors’ pharmacy practices. Data have been collected.
(Birna Trap, PhD student, MSc (pharm), BCom, under the supervision of Ebba Holme Hansen (main supervisor), Hans Hogerzeil, WHO HQ/Geneva, and Charles Todd, University of Zimbabwe).

A User-evaluation of Treatment with Conventional Drug Therapy and Classic Homeopathic Treatment Concerning Allergy and Asthma
(Laila Launso and Charlotte Grum, MSc, Psychologist; Henriette Brendler, BA, Centre of Bridgebuilding in Health Care, Copenhagen; Anne Hvengaard, MSc, Project Manager, DSI, Institute for Health Care, Copenhagen, Cooperation with Vinjar Fanneba, MD, Professor and Director of Research Centre in Alternative Medicine, University of Tromsø, Norway)

The Development of Drug Therapy in Denmark
The project is a historical analysis of the factors, including religious, philosophical, scientific, technological and legal aspects, which have determined the development of drug therapy in Denmark since the introduction of the concept of authorized drugs in the 17th century.
(Poul R. Kruse).

Cancer Patients’ Use and Assessment of Herbal Medicine
A survey study on 395 cancer patients’ patterns of usage of herbal medicine is conducted. The primary aim of the project is to establish a database to which cancer patients and therapists have access.
(Laila Launso and The Research and Knowledge Centre for Unconventional Cancer Treatment: Helle Andersen, MSc; Louise Rannov, BA; Henrik Langgaard MD)

Social, Ethical and Legal Aspects of Pharmacogenomics
This research project focuses on pharmacogenetics and pharmacogenomics as a research strategy for future drug research and development. The aim of the project is to investigate the pros and cons of pharmacogenomics in a post-marketing perspective with focus on the social, ethical and legal dimension.
(Claus Møldrup)

Evaluation of a New Drug Distribution Legislation in Iceland – a European Laboratory
A new drug distribution law took effect in Iceland in 1996. The main thrust in this legislation is the right of all registered pharmacists to open one pharmacy each and the abolishment of the drug price regulation by the government and abatement of the strict rules governing drug advertising to the public. A multi-study evaluation of the effects of the change in legislation was initiated in 1995. Various research methods were employed, including focus group interviews with users of pharmacy services, interrupted time series analyses of economic and drug utilisation data, and focus group and one-on-one interviews with pharmacists. Data collection and analysis was completed in 1999. In 2000 and 2001 the results of this evaluation were prepared in the form of articles.
(Janine Morgall Traulsen, Anna Bima Almarsdóttir, Iceland, Almar Grímsson, Iceland, and Ingunn Bjömsdóttir, Iceland)

The New Medicine Consumer
The goal of this project is to investigate social and economic trends, which are currently affecting medicine users – attitudes, knowledge and action. The project focuses on theory development as well as data collection. A literature review began at the end of 2001. The empirical part of the study is being
planned and will include individual interviews and focus group interviews. Janine Traulsen received a "research stipend" from DFH beginning September 2001 to develop this project. From 1st October 2001 a PhD student, Bertel Rüdinger, joined the project.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use. (Janine Morgall Traulsen).

Popular Beliefs about Medicine

Eight focus group interviews were carried out in urban and rural Iceland to answer the research question – What are the hopes and fears of the lay public in Iceland with regard to pharmaceutical R & D including issues pertaining to the Health Care Database? Iceland was chosen to study this phenomenon in the wake of the public debate about the Icelandic Health Care Database (the aim is to code medical, genealogical and genotypical information on the entire population). The project consists of a literature review, theory building and focus group interviews followed by individual interviews. Data collection took place in 2001 and analysis and report writing will take place in the first half of 2002.

(Responsibility for carrying out the project lies with a project group: Janine Morgall Traulsen, Ingunn Björnsdóttir (principal investigator), Iceland, and Anna Bima Almarsdóttir, Iceland).

PHARMACY PRACTICE

The Distribution of Medicine in Denmark
– in the Light of Deregulation

On 30 May 2001 the members of the Danish Parliament agreed to deregulate the distribution of medicine to the public. The main change is that a wide range of OTC-medicine (e.g. painkillers and laxatives) can be sold outside pharmacies beginning 1 October 2001. In the future OTC-medicine will become part of the normal sale of convenience goods. The deregulation is a climax of many years of ongoing discussions concerning how to regulate the distribution of medicine in Denmark. Having in mind the general advance of market orientated health reforms in western societies one could wonder: Why has the Danish pharmacy sector not been subject to deregulation before? And why only deregulate the sale of OTC-medicine? The PhD project will contribute with knowledge of the mechanisms that influence policy processes in this area.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use. (Jakob Bjerg Larsen supervised by Janine Morgall (main supervisor), Poul R. Kruse and Assistant Professor, MSc (pol sci), PhD Karsten Vrangbæk, Department of Political Science and Institute of Public Health, University of Copenhagen).

Pharmaceutical Care in Denmark

In Denmark and internationally, the structure of medicine supply has been discussed during the past 30 years. The role of the community pharmacist has been a focal point of this discussion. Pharmaceutical Care has been one of the strategies used to ensure a professional role for the pharmacist in the future. The aim of this PhD project is to analyse the foundation for and implementation of Pharmaceutical Care in Danish community pharmacies. Empirical data have been collected by a postal questionnaire involving all Danish pharmacies.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use. (Charlotte Rossing supervised by Ebba Holme Hansen (main supervisor) and Janine Morgall Traulsen).

Professional Development of Pharmacy Practice
– with special focus on implementation processes

There are different traditions for carrying out intervention research in the various professional groups. Descriptive and effectiveness studies dominate. The overall purpose of this PhD project is to describe and understand the relationships that influence the implementation process of professional interventions within pharmacy practice in Denmark. The study is carried out from an organisational perspective. This perspective is necessary in order to follow and analyse the intervention process and in order to understand possible reasons for problems in relation to implementation.

The PhD project is part of a bigger international project with the overall aim ‘Development of strategies for dissemination of pharmaceutical care services’. Through collaboration with PhD student Alison Roberts, University of Sydney, the descriptions and understandings of the relationships that influence the implementation process will be achieved through quantitative studies as well as qualitative studies.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use. (Trine Hopp under the supervision of Ellen Westh Sørensen (main supervisor), MSc (pharm) Hanne Herborg, Pharmakon, and Dr. PH Lis Wagner, UCSF. The international project group includes from the University of Sydney, Australia: PhD student Alison Roberts under the supervision of Professor Shalom (Charlie) Benrimoj (main supervisor), Parisa Aslani, Lecturer; Tim Chen, Lecturer; and Kylie Williams, Lecturer).

The Pharmacy-University Study - an action research project involving the pharmacy, pharmacy students and researchers in pharmacy practice

The project is carried out in cooperation between researchers from the Department of Social Pharmacy, researchers from Pharmakon, supervisors in the pharmacies and pharmacy students during their internship in the pharmacies. The project was initiated in 1998 has run for a three-
year period, first year involving the angina pectoris patients, second year type 2-diabetes patients, third year asthma patients. The overall purpose of the project is to contribute to quality development of pharmacy practice and pharmacy practice research in the area of pharmaceutical care. The aims of the project are threefold:

- to form the basis of an improvement of the pharmacy’s advice to patient groups, based on the user perspective, and to contribute to a basis for decisions for the individual pharmacy’s policy concerning the patient group
- to develop and test participatory action research as a way of developing pharmacy practice
- to support the pharmacy students during their internship in pharmacy work with pharmaceutical care, achieve a good understanding of the user perspective and get experience in pharmacy practice research.

During 1999, 2000 and 2001, data have been collected in the form of interviews with the following patient groups: angina pectoris patients (123), type 2 diabetes patients (176) and asthma patients (80). At the same time, through questionnaires, the pharmacy staff has brought out their knowledge and desire for information concerning the same patient groups. In 1999, 2000 and 2001, results from the patient interviews and the staff questionnaires were presented to the staff of the participating pharmacies (1999: 40 pharmacies, 2000: 50 pharmacies, 2001: 28 pharmacies), and the current activities of the pharmacies were recorded. The activities in the pharmacies, from all the three years, will be evaluated.

Internship students have been responsible for the interviews and the organization of tasks on the premises of the participating pharmacies. The materials of the project can be found on the internet www.dfh.dk/dfh-apotek/.

Part two (2001-)

The results from the three patient groups uncovered a great quantity of drug related problems. Therefore, the project group has decided to carry out a new phase of the project (second phase). The objective of the second phase is dissemination of the results, in an easily accessible form, to the interested parties in the health sector (patient associations, pharmacies, MDs, outpatients’ clinics, the counties pharmaceutical consultants) as a contribution to work with improved medicine use to these selected patient groups.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use.

ARTFARM. Nordic Database for Studies and Projects within Pharmacy Practice

The objective is to procure relevant Nordic scientific studies for practitioners and students of pharmacy practice. The main goal is to be an incentive to research on pharmacy practice. The project is affiliated with FKL - Research Centre for Quality in Medicine Use.

\[ \text{Project Manager: Hanne Herborg, Pharmakon. Other members of the project group: Ellen Westh Sørensen; Steffen Jarlov, GP; Bertil Marklund, Med.Dr. Project Co-ordinators: Birthe Sandegaard, Bente Frökjaer, Dor-the Tomsen and Dorte Glintborg Nielsen.} \]

Improved Self-medication and Self-care

The objectives of the project are: 1) To develop and implement service for systematic counselling on self-care and self-medication in community pharmacies aimed at empowering users to make decisions and solve problems in order to obtain better quality of life. 2) To develop a model for a controlled study aimed at documenting the outcomes of the service and testing the instruments for data collection.

The pilot study was completed in 2001, and the main study has started. The project is part of an international research co-operation, Pharmaceutical Care Network Europe (PCNE). In Denmark, a preliminary study is carried out where the intervention is developed and tested.

The project is affiliated with FKL - Research Centre for Quality in Medicine Use.

\[ \text{(Project Manager: Hanne Herborg, Pharmakon. Other members of the project group: Ellen Westh Sørensen; Steffen Jarlov, GP; Bertil Marklund, Med.Dr. Project Co-ordinators: Birthe Sandegaard, Bente Frökjaer, Dor-the Tomsen and Dorte Glintborg Nielsen.} \]

Intervention in Pharmacy

- a Case Study about the Implementation of Pharmaceutical Care at Brønshøj Apotek

The development and implementation of pharmaceutical care in a community pharmacy has been followed over a period of 2-3 years. The proprietor, the staff and a research consultant have developed ‘tools’ for the implementation of pharmaceutical care in community pharmacy. The development- and implementation process has been followed. The theoretical basis is organisation theory. The design is participatory action research and formative evaluation. Data collection methods
were interviews of staff and research consultant and documents from the pharmacy. The change strategy and the barriers and facilitators for the development and implementation of the new practice is described.

( Ellen Westh Sørensen in co-operation with Research Consultant Liselotte Winther, Pharmakon, and Pharmacy Proprietor Inge Børsting and staff at Brønshøj Apotek).

OTHER PROJECTS

A User-evaluation of Medicine, TCM Acupuncture and Nutrition Therapy concerning Patients having Bronchial Infections/Symptoms

(Laila Launso and Eva Brendstrup, MSc, Centre of Bridgebuilding in Health Care, Copenhagen).

Bridgebuilding in Health Care

A concept for bridgebuilding in health care between pharmacists, physicians and alternative therapists has been developed including research projects. The focus has been on conceptualising the practitioners’ treatment models consisting of four components: disease/health theories; diagnostic systems; treatment methods and expected and experienced outcomes. The results are used in relation to seminars focusing on building dialogues and co-working between conventional health care groups and alternative therapists.

(Laila Launso and therapists and researchers from Centre for Bridgebuilding in Health Care and from The Research and Knowledge Centre for Unconventional Cancer Treatment and senior students from University of Roskilde, University of Copenhagen and Department of Social Pharmacy, The Royal Danish School of Pharmacy).

Physicians and Pharmacists Practising Unconventional Treatment

A study has been conducted on 20 physicians’ and pharmacists’ motives for education and practice in unconventional treatments, their experiences from practising both conventional and unconventional treatments and their experience with reactions from professional colleagues.

(Laila Launso).

A User-evaluation of Unconventional and Conventional Cancer Treatment

(Laila Launso and Henrik Langgaard, MD, Charlotte Kira Kimby, MSc; Louise Rønnov, BA, The Research and Knowledge Centre for Unconventional Cancer Treatment; Inge Henningsen, MSc, Associate Professor, Department of Statistics, University of Copenhagen).

Evaluation of Community Involvement in Schistosomiasis Control

More than 200 million people worldwide are affected with Schistosomiasis, a debilitating long lasting tropical disease. In Zimbabwe, a community participation project has utilised the dried berries from a locally grown plant as molluscicide. The plant is Phytolacca dodecandra - locally called Gopo. The present PhD project has evaluated the above community participation project by analysing attitudes, behaviours and knowledge as well as learning, gender and power issues.

(Addmore Ndeka, PhD, MA (Sociol). Supervisors: Ebba Holme Hansen (main supervisor), Per Mølgaard, Department of Medicinal Chemistry, Peter Furu, Danish Bilharziasis Laboratory, and Dr. Godfrey Woelk, University of Zimbabwe).
The Danish Pharmaceutical Library

Head of Library Services: Alice Nørhede

THE LIBRARY

The aim of the Library is to support research and education at the Royal Danish School of Pharmacy and serve the needs of the School’s staff and students. Part of the national network of research libraries, it is open to the public and invites all interested users to benefit from its traditional and electronic collections.

The Library provides training and guidance in the use of its services and how to seek information in the school’s networked databases and on the Internet.

The Information Officer is attached to the library’s administration.

ACTIVITIES AND PROJECTS

The library board and library staff have thoroughly discussed and evaluated the library’s service profiles and strategies through 2001.

During the period September 2000 - December 2001, the library has improved its range of services and information about the services. Transformation to the electronic library is actively underway e.g. downloading full-text articles from the library’s range of electronic journals reached 21,000 articles, an increase of 100% from December 2000 to December 2001. Students and researchers have the benefit of direct reservation and request of copies or books through the library’s OPAC. Interlibrary loan requests are received by e-mail or the facilities in bibliotek.dk.

Many tests of electronic databases and reference works are facilitated through the home page of the library: Internet edition of the Combined Chemical Dictionary, Nature full-text edition, Pharma-Transfer, Landolt-Börnstein, Encyclopaedia Britannica - just to mention a few.

The library’s home page was expanded and improved through autumn 2001. It now provides access to an automatically generated list of new books; LIST-FARM - a holding list of printed journals in the library; an automatically generated alphabetical list with links to the electronic journals the library subscribes to; an annotated web-guide; help-sheets to accessible databases and much more.

The user survey made it clear that an increase in opening hours was necessary. The library extended the opening hours by 4 hours every week starting September 2001.

The merging of the Dictionary of Organic Compounds, Dictionary of Natural Products and other electronic dictionaries made the library upgrade its access to the networked edition called the Combined Chemical Dictionary November 2000. The upgrade ensures direct access to information from laboratories and classrooms.

In December 2000 the library took out an Internet subscription to the citation database Web of Science and from January 2001 access was opened to Science Direct, ensuring access to approx. 1200 electronic journal titles from Elsevier.

The library system ALEPH was upgraded September 2000, which gave rise to a good deal of trouble for both library staff and library users.

Also in 2001 the Danish Pharmaceutical Library participated actively in several projects concerning "Denmark’s Electronic Research Library" (DEF), e.g. the library is still part of the project to convert the old card catalogues to electronic media.

From August 2000 Alice Nørhede headed a DEF project including four other libraries to develop a user survey based on the international accepted model for European Customer Satisfaction Index (ECSI). In February 2001 the questionnaire was distributed to the users of the five libraries and in summer 2001 the results were presented to the board of DEF.

The project generated interest as well as appreciation from the library society. A report is available on:
http://www.dfh.dk/bibliotek/brugertilfredshed_rapport.php3e
Facilities of DADS (Denmark Article Database Service) - a gateway to electronic journals used intensively by in-house researchers and students - was much improved in the beginning of 2001. Unfortunately, the library had to terminate access in December 2001 due to a 100% increase of the subscription price to the system. Termination started a flood of protests from researchers and students at the Royal Danish School of Pharmacy, but there does not appear to be a solution at this time.

Approx. 35,000 visits were paid to the library from January 2001 to December 2001.

**TEACHING AND GUIDANCE**

**Study Start programme:** Since the start of a new structure for the Study Start programme in 1998, the library has participated in introduction courses for new students. In September 2000 and 2001 the library offered all new students a lecture on how to use electronic services in the Danish library system, a hands-on lecture on using the Internet for information retrieval and a tour of the library – presented in 2001 in the guise of a treasure hunt. Students then carried out compulsory exercises. Both students and library staff evaluate this training every year and every evaluation results in further adjustment and updating of the programme presented.

The library participates in teaching the compulsory course in "Organic Synthesis" during the second term and presents the printed versions of Chemical Abstract and Beilstein and the electronic version Crossfire/Beilstein.

In autumn and spring optional courses are run for staff and students in the use of MEDLINE, IPA, and Analytical Abstracts. Approximately 30 participants attend these courses every term. As many services are now offered through FARM-base - the Library’s OPAC – an introduction to FARM is arranged for the staff every term.

A new initiative in September 2001 was participation in the compulsory course "Social Pharmacy including Management & Organisation" (5th term). It was arranged as a classroom demonstration encouraging students to use electronic services available on the school’s Intranet and on the Internet.

**Continuing and postgraduate education:** In January 2001, the Department of Social Pharmacy arranged a postgraduate course for student pharmacy advisors. The library contributed a course entitled: Searching for information in the physical and electronic library.

In connection with Danmarks Farmaceutiske Selskabs Sektion for Klinisk Farmacie (The Danish Pharmaceutical Society – Section for Clinical Pharmacy) course in spring 2001, the research librarian taught techniques for seeking information on the Internet.

In summer 2001 the library participated in a course for students entitled "Specialist Education of Pharmacy Practice".

Every January and October the library offers a course to PhD students: *Bibliographic Software. Hands-on Use of the Reference Manager.* The course attracts about 10 participants every time.

Alice Nørhede lectured at the Royal School of Librarianship and Information Sciences for fourth-term students as well as at two continuing education courses in autumn 2000 and summer 2001. She also made a presentation to the members of the Danish Librarians’ Group for Medical Information in March 2001. All presentations focused on the theme: "Finding pharmaceutical information on the Internet".

**EVENTS, VISITS AND MEETINGS**

November 2000 12 library students visited the Danish Pharmaceutical Library. They attended a lecture held by Alice Nørhede, presenting the library and its activities in the context of the organisational, educational and economic conditions. Later this winter, two library students visited the library and interviewed the research librarian about the reference services.

Spring 2001 two colleagues from the library of Kann Rasmussen (Velux) visited our library.

December 2001 two senior scientists from the Institute of Pharmacology in Oslo visited the library to study the historical collection of the library.
January 2001 Alice Nørhede was twice a member on a panel debating “The practical project” – part of the librarian degree offered by The Royal School of Librarianship and Information Science.

Alice Nørhede gave a lecture about the results of the library’s user survey DEF project called: “User satisfaction in the electronic library” at the Nordic Summer School, The Royal School of Librarianship and Information Sciences, July 2001.

Alice Nørhede made a presentation of the same project at the official opening of the “DEF portal”, September 2001.

MEMBERSHIP OF EXTERNAL ORGANISATIONS AND COMMITTEES

Alice Nørhede

• Chairman of De Små Chefers Forum - an organisation of approx. 200 smaller Danish research and special libraries until August 2001. She is still a member of the Board.
• Appointed member of Biblioteksrådet (Library Council) an advisory body for the Danish National Library Authority, until August 2001.
• Second vice-president on the EAHIL Board (European Association for Health Information and Libraries), until January 2001.
• Member of The Danish Librarians’ Group for Medical Information.
• Member of a working group autumn 2000 at the Royal School of Library and Information Services planning the end of the Librarian degree programme as a practical project analysing a concrete library-related issue.
• Appointed member to a committee by the Danish National Authority until August 2001 dealing with superstructure and information supply of the council libraries.
• Member from December 2001 of a working group dealing with research library statistics.

Martin Weile

• Appointed member of the Danish Bibliographic Centre Netpunkt working group 2001.

GRANTS

In the summer of 2001, the Library received a donation from Apoteker J.B. Mikkelsens og hustru Kgl. translaticie Gudrun Mikkelsens Farmaceutiske Fond. The donation was used to buy software and books.

In the summer of 2001, the Library received a donation from Apotekervonden af 1991. The grant was used to buy books for students taking the Specialist Education of Pharmacy Practice.

See the Internet for more information about the library and its activities.

The website of the Danish Pharmaceutical Library www.dfh.dk/bibliotek
FARM (The Library’s OPAC) http://dfb.dnlb.dk:8020/ALEPH
Danmarks Elektroniske Forskningsbibliotek www.deff.dk/

THE INFORMATION OFFICER

Jesper Munck, the information officer, is the editor of Plexus – the official magazine issued by The Royal Danish School of Pharmacy. Plexus was published in its current form for the first time in 1999/2000 and is intended for employees and students, as well as the pharmaceutical world outside the School to some extent. Since its relaunch in 1999, both the size and circulation of the publication have increased 20%. In 2000 Plexus began cooperating with De Danske Studieblade, which handles advertising sales for seven Danish magazines representing university institutions.

The information officer is a member of the editorial committee of Lægemiddelforsknings [Drug Research], a popular scientific journal that publishes the results of the research conducted by the Royal Danish School of Pharmacy and associated research centres.

The magazine is extremely popular with its target group, upper secondary chemistry and biology teachers, who receive the magazine free of charge every year.

A new recruitment website (www.dfh.dk/farmaceut) targeted at potential students was launched in February 2001. The site is a team effort by the information officer along with MSc Henrik Fylking Nielsen (Novo Nordisk) and Lærke Vester-Andersen, study guide officer from the Course Administration.

In August 2001 a new webmaster, Henrik Korzen, joined the School staff. He works together with the information officer to present the news and services, general content and graphics for the School’s website.

Together with the registrar, study supervisors, PhD administration and information committee, the information officer was responsible for PR activities in conjunction with the School’s Open House Day. The same team also put together the enrolment materials – The pharmacist is the drug expert – and a series of presentations focusing on the pharmacy degree programme and its potential, and requirements for enrolment.

The information officer is the official contact person for the press and other external bodies and he answers - or organises responses to enquiries to the School.

MEMBERSHIP OF EXTERNAL ORGANISATIONS AND COMMITTEES

Jesper Munck is a:

• Member of EUPRIO (European Universities Public Relations and Information Officers Association)
Well aware of the increased competition for potential students, the Royal Danish School of Pharmacy advertised in Danish media twice during 2001. In March the School released a poster, The pharmacist is the drug expert, and followed up a month later with an advertisement in the magazine Chili, headlined: Get high on pharmacy – it’s legal. In both layout and content, the advertisement was a response to an article run the previous month by the same magazine entitled: Get stoned at the pharmacy – it’s legal. The School’s advertisement was edited slightly to become the flyer for the School’s annual Open House Day. The flyer was also handed out to upper secondary schools in the autumn of 2001 at study orientation meetings called STORM meetings.
Publications

DEPARTMENT OF ANALYTICAL AND PHARMACEUTICAL CHEMISTRY


Halling-Sørensen B. Inhibition of aerobic growth and nitrification of bacteria in sewage sludge by antibacterial agents Arch Environ Contam Toxicol 2001;40:451-460.

Halling-Sørensen B, Jensen T, Tjørnelund J, Montfors MHMM. Worst-case estimations of predicted environmental soil concentrations (PEC) of selected veterinary antibiotics and residues in Danish Agriculture. Pharmaceuticals in the environment - Sources, fate, effects and risks 2001;143-156.

Halling-Sørensen B, Sengelov G, Tjørnelund J. Toxicity of Tetracyclines and Tetracycline degradation products to environmental relevant bacteria including selected Tetracycline resistant bacteria. Arch Environ Contam Toxicol (in press).


Jørgensen SE. Application of exergy and specific exergy as ecological indicators of coastal areas. Aquatic Ecosystem Health and Management 2000;3:419-430.


Jørgensen SE. Toward a Consistent Pattern of Ecosystem Theories. The Scientific World 2001;1:71-75.


Jørgensen SE. Exergy of an isolated living system may increase. Advances in Energy Studies 2001;573:580.


Loke ML, Tjernelund J, Halling-Sørensen B. Determination of the distribution coefficient (log kd) of oxytetracycline, tetracylin, olapinoxid and metronidazole in manure. Chemosphere (accepted).


PHD THESES


Lützhøft HH-CH. Environmental Risk Assessment of Antimicrobials. Royal Danish School of Pharmacy, Department of Analytical and Pharmaceutical Chemistry, The Royal Danish School of Pharmacy, 2000.

Kayombo S. Development of a Holistic Model for the design of Faculative Waste Stabilisation Ponds in Tropical Climate. Section of Environmental Chemistry, Department of Analytical and Pharmaceutical Chemistry, Royal Danish School of Pharmacy, 2001.


OTHER PUBLICATIONS


DEPARTMENT OF MEDICINAL CHEMISTRY


The importance of the Ala 116-Pro 136 region in the calcium-sensing receptor.


The role of Arg 78 in the metabotropic glutamate receptor mGlur1.


The role of Arg 78 in the metabotropic glutamate receptor.

Resolution, configurational assignment, and enantiopharmacology at glutamate receptors of 2-amino-3-(3-carboxy-5-methyl-4-isoxazolopyridinionic acid (ACPA) and demethyl-ACPA. Chirality 13:523-532.


Terp GE, Johansen BN, Christensen IT, Jørgensen FS. A new concept for multidimensional selection of ligand conformations (Multiselect) and multidimensional scoring (Multiscore) of protein – ligand binding affinities. J Med Chem 44;2001:2217-2221.


PHD THESIS

Buchardt J. A solid phase combinatorial approach to phosphinic peptide inhibitors of matrix metalloproteinases. Carlsberg Laboratory and Royal Danish School of Pharmacy, 2000.


Garibay P. The combinatorial synthesis of possible insulin mimetics. Royal Danish School of Pharmacy, 2000.

Jakobsen CM. Design, synthesis, and pharmacological evaluation of Thapsigargin analogues and prodrugs for targeting apoptosis to prostatic cancer cells. Royal Danish School of Pharmacy, 2001.


Nielsen PA. Strongly polar molecules in aqueous solution studied by NMR and computational chemistry. Royal Danish School of Pharmacy, 2000.

Pawlas JI. Construction and functionalization of annelated 1-hydroxypyrrolezoles. II Nickel-catalyzed hydroamination of 1,3-dienes using alkylamines. Royal Danish School of Pharmacy, 2001.


Sams AG. Solid phase aldol and Diels-Alder reactions in the formation of novel peptide isosteres as putative protease inhibitors. Royal Danish School of Pharmacy, 2000.

Sandager L. Genes and enzymes involved in the biosynthesis of tricylglycerol in plants and yeast. Swedish University of Agricultural Sciences, Alnarp and Royal Danish School of Pharmacy, 2001.


Terp GE, Johansen BN, Christensen IT, Jørgensen FS. A new concept for multidimensional selection of ligand conformations (Multiselect) and multidimensional scoring (Multiscore) of protein – ligand binding affinities. J Med Chem 44;2001:2333-2343.


OTHER PUBLICATIONS


Jensen AA, Brüauer-Osborne H. Øget forståelse af vigtig receptor i hjerne [Increased understanding of important receptor in the brain]. Lægeidemødelærling 2000;28-29.


Nielsen CU, Amstrup J, Steffansen B, Frokjaer S, and Brodin, B. Epidermal growth factor inhibits glycylsarcosine transport and hPepT1 expression in a human intestinal cell line, Am J Physiol Gastrointest Liver Physiol 2001;281:G191-G199.


Nielsen CU, Amstrup J, Steffansen B, Frokjaer S, Brodin B. Epidermal growth factor (EGF) inhibits glycylsarcosine (Gly-Sar) transport and hPepT1 expression in human intestinal cell line. Am J Physiol Gastrointest Liver Physiol 2001;281:G191-G199.


PHD THESES


Bjerregaard S. Parenteral water-in-oil emulsions as sustained release systems for hydrophobic compounds. 2001.


Wilberg-Larsson BI. Commnination of particulate solids in a Micros Ring Mill. 2001.


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Bagger MA, Beckgaard E. Genvej til hjerne via nessen. [Short cut to the brain via the nose] Lægemiddelforsknin 2001;24-25.


Høst J, Jørgensen FS, Christensen IT, Hovgaard L, Frøkjaer S. Molecular determinants of desensitization and assembly of the chimeric GABA_A receptor subunits (α_1/γ_2) and (γ_3/α_4) in combination with β_2 and γ_2. Neurochem Int 2001;38:581-592.


DEPARTMENT OF PHARMACOLOGY


Waagepetersen HS, Sonnewald U, Larsson OM, Schousboe A. Multiple compartments with different metabolic characteristics are involved in biosynthesis of intracellular and released glutamate and citrate in astrocytes. Glia 2001;35:246-252.


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Hansen H.H. The impact of brain injury: Involvement of the system of endocannabinoids ligands and receptors.

Sams-Nielsen A. Characterization of CGRP induced effects in human and guinea pig cerebral arteries.

Sheykhzade M. Characterization of calcitonin gene-related peptide receptor subtype and function in rat coronary arteries.

Timmermann D. Subcellular localization and pharmacological characterization of voltage-gated calcium channels in cultured neocortical neurones.

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OTHER PUBLICATIONS


Knudsen P, Hansen EH, Morgall J. Fra iden til asken med antidepressiv medicin. [From the fire into the frying pan with antidepressant medicine]. *Lægemiddelforskning* 2000;34-5.


Launso L. Døre der åbner sig: Om grænseoverskridende læger og farmaceu-ter i det danske sundhedsvesen. [Doors opening: About physicians and pharmacists as boundary walkers in the Danish health care system]. Højbjerg, Forlaget Hovedland 2001 (196 pp).

Larsen JB. Kend spillets regler. [Know the rules of the game]. *Farmaceuten* 2001;13(16):4-5.


Mølerguson C. Vil doping være forbøjligt idrætsudøvere i fremtiden? [Will doping only be a part of sports in the future?]. Fremtidorientering 2001;3:8-11.


Munck J. Danmarks Farmaceutiske Højskole er udnævnt til Marie Curie Training Site. [Royal Danish School of Pharmacy appointed a Marie Curie Training Site.] *Plexus* 2001;33(5):21.

Munck J. FKL. Levedygtigt center har passeret de første to år. [Viable centre survives first two years.] *Plexus* 2001;33(5):32.


Munck J. Vester-Andersen L. DFHs informationsaktiviteter over for potentielle studere. [Royal Danish School of Pharmacy’s information initiatives for potential students.] *Plexus* 2001;33(6):37.


Nørhede A. Gratisk adgang til patentdatabasen Derwent Innovations Index, DI. [Free access to patents. Derwent Innovations Index, DI is open.] *Plexus* 2001;33(1):22.


Nørhede A. Derfor mangler Danmarks Farmaceutiske Bibliotek penge... [That’s why the Danish Pharmaceutical Library is short of money...] *Plexus* 2001;33(4):24,26.


Nørhede A. Mere biblioteksservice til stud.pharm’.rne. [More library service for students at the Royal Danish School of Pharmacy.] *Plexus* 2001;33(6):37.


Nørhede A. Steffensen R, Byralsen L, Dahlstrom-Nielsen P. Brugertilfredshed i de elektroniske biblioteker [User satisfaction in electronic libraries].
DEPARTMENT OF ANALYTICAL AND PHARMACEUTICAL CHEMISTRY


Caroline Marie Hasted. Carbonate esters possessing fatty acid like structures as model prodrug derivatives of phenol. Supervisors: Jesper Østergaard and Claus Selch Larsen.


Caroline Marie Hasted. Carbonate esters possessing fatty acid like structures as model prodrug derivatives of phenol. Supervisors: Jesper Østergaard and Claus Selch Larsen.


DEPARTMENT OF MEDICINAL CHEMISTRY


Birgitte Søndergård Hertz. Syntese af glycin analoge ud fra 1- hydroxypyrazol. [Synthesis of glycin analogues from 1-hydroxypyrazole]. Supervisor: Mikael Begtrup.

PAGE 120
Søren Johnsen. Sæsonvariation af cichoriersyre og alkylamider i Echinacea purpurea. [Seasonal variation in the content of cichoric acid and alkamides from Echinacea purpurea]. Supervisors: Per Mølgaard.


Anne Kruse Lykkeberg. Sæsonvariation af cichoriesyre og alkylamider i kantlyng, Cynanchum vincetoxicum. [Seasonal variation in the content of cichoric acid, and alkamides from the medicinal plant Cynanchum vincetoxicum]. Supervisors: Per Mølgaard, Anne Adsersen.

Alma Mustafic, Dea Marie Melskens. Syntese af potentielle GABA_A receptor ligander. [Synthesis of GABA_A receptor ligands]. Supervisor: Bente Frulad.


Keld Agerbæk Siiger. Fremstilling af (R/S)-2-amino-3-(1-hydroxypyrazol-5-yl) propan syre. [Synthesis of (R/S)-2-amino-3-(1-hydroxypyrazol-5-yl) propan acid]. Supervisor: Mikael Begtrup.

Brian Skole. Isolering og strukturoklaring af potentielle malarialaktive indholdsstoffer i Landolphia dulcis. [Isolation and structure elucidation of potential antimalarial constituents from Landolphia dulcis]. Supervisors: Jerzy W. Jaroszewski, Dan Stærk.


DEPARTMENT OF PHARMACEUTICS


Peter Baade. Evaluation of the efficiency of different fluidisation coating equipment at various humidities. Supervisors: Jørn Møller-Sonnergaard, Per Holm, H. Lundbeck A/S.


Anders Christensen. Metabolism of Oxycodeone in female Sprague Dawley and Female Dark Agouti rat liver microsomes. Supervisors: Andrew Somogyi, University of Adelaide and Lona Christrup.


Tue Hansen: Estimation of segregation in the manufacture of tablets by direct compression. Supervisors: Per Holm, H. Lundbeck and H. G. Kristensen.


Susanne Hostrup: Liposomes as drug delivery system for acylated peptides. Supervisors: Sven Frøkjær, Simon Bjerggaard Hansen, Novo Nordisk A/S.


Lone Friis Jensen, Mikala Holt-Pedersen: Investigation of peptide transporter activity in buccal TR146 and intestinal Caco-2 cell culture models using glycyllsarcosine and valacyclovir as substrates. Supervisors: Bente Steffansen, Carsten Udh Nielsen and Hanne Marck Nielsen.

Louise Moe Jönsson: The process of reformulating the Pentasa suppository 1 g. Supervisors: Birgitte Nissen, Ferring Pharmaceuticals, Australia and Lona Christrup.


Jakob Gjøstrup Kristensen: Strategic considerations on implementation of quality-assurance relevant to development of new drugs to a global market. Supervisors: Jørn Møller-Sonnergaard, Eva De Bang, Morten Juul Sørensen Novo Nordisk A/S.


Kristine Juul Nilsson, Louise Vendelbo Jacobsen: Medicine taking behaviours in Type 2 diabetics at Walton Diabetes Centre. Supervisors: Dave Thornton, University Hospital Aintree, Liverpool, UK and Mette Rasmussen.

Tanna Friis Nønnecke, Susanne Kristensen: Evaluation of Mini Mental State Examinations (MMSE’s) as a Screening Tool for Cognitive Dysfunction in Patients with Chronic Non-Malignant Pain. Supervisors: Jette Højsted, H:S Rigshospitalet and Lona Christrup.


Mikala Holt-Pedersen, Lone Friis Jensen: Investigation of peptide transporter activity in buccal TR146 and intestinal Caco-2 cell culture models. Supervisors: Hanne Marck Nielsen, Carsten Udh Nielsen and Bente Steffansen.


Martin See Rasmussen: Matrix tablets based on low viscous HP/PMC. Supervisors: Lone Nørgaard, Alpharma Ltd. and H. G. Kristensen.

Baljit Singh: Formulation of cationic dendrimer labelled gold particles for adsorption and delivery of plasmid DNA. Supervisors: Lise Lund and Birger Brodin.
Anne Hagsten Sørensen: Comparison of valaciclovir and Glu(acv)-Sar prodrugs with affinity for hPepT1; stability, affinity and transport. Supervisors: Anne Engbrecht Thomsen and Bente Steffansen.

Mette Thorvaldsen: Aminoglycoside Therapy at Intensive Care Units at Danish Hospitals. Supervisors: Jan Bonde, Amtssygehuset in Herlev and Lona Christrup.


Huong Tran, Maja Neddekkær: Formulation and characterization of a nanoemulsion. Supervisor: Hanne Mærck Nielsen.

Signe Walmar, Mette Wulff: Aquous ethyl cellulose coating of granulate for manufacturing of Penalata tablets with a specified dissolution profile. Supervisors: Jann Møller-Sørensgaard and Birgitle Nissen, Ferring A/S.


DEPARTMENT OF PHARMACOLOGY


Mette Fryland: Immunologisk status ved depression og under antidepressiv behandling. [Immunological status in Major depression and during antidepressant treatment]. Supervisor: Bjarke Ebert.


Fida Issa: Cellulær lokaliseringsst STUD of glukagon-injinerne pep-1 receptor. [Cellular localization of glucagon-like peptide-1 receptors]. Supervisor: Peter Thygesen.

Mikkel Rostgaard Jensen, Allan Astrup Kah: Kvantificering af Fos-positive neuroner som udtryk for nociception hos grise efter intramuskulære injection af viscoleo, sesamolie og fre fectsyr. [Quantification of Fos-positive neurons as a marker of nociception in pigs after intramuscular injection of Viscoleo, sesam oil and fatty acids]. Supervisor: Bjarne Fjalland.

Lars Ketliasson: Salbumatol initieret IL-6 udskillelse i pituicytter. [Salbumatol induced IL-6 release from pituicytes]. Supervisor: Lise Moesby.


Rikke Marie Lund: Screening for adjuvant effekt af diphthhalater i murin injektionsmodel. [Screening for adjuvant effect of diphthhalates in a murine injection model]. Supervisor: Peter Thygesen.


Annemette Due Pedersen: LPS-induceret nitrogenoxid produktion i dyrkede cellekulturer fra murine neurohypophys. [LPS-induced release of nitrogenoxide by cultured cells from the murine neurohypophysis]. Supervisor: Erik Wind Hansen.

Mikkel Pind: Identifikation af protein-protein interaktioner mellem GABA_A receptor alpha_2-subunit intracellulær domæne og et eller flere intracellulære proteiner ved brug af gærcrete-2-hibridsystemet. [Finding protein-protein interactions between the alpha_2-subunit intracellular loop of the GABA_A receptor and one or several intracellular proteins affecting the alpha_2-subunit, using the yeast two-hybrid system]. Supervisor: Arne Schousboe.


Alan Sarup: Differential regulation of the expression of the glutamate transporters GLT-1 and GLAST by soluble factors in cultures of astrocytes and organotypic hippocampal slice cultures. Supervisor: Arne Schousboe.

Anja Hvid Simonsen: Biokemiske markerer i præklinisk forskning. udvikling af et enzym linked immunosorbent assay til måling af type IV collagen i urin. [Biotechnical markers in preclinical research development of an enzyme linked immunosorbent assay measuring type IV collagen fragments in urine]. Supervisor: Erik Wind Hansen.


DEPARTMENT OF SOCIAL PHARMACY

Janne Hjorth Henriksen: Danskernes brug af naturlægemidler – og relationer til helbred, sundheds- og sygdomsadfærd, uddannelse og indkomst. [Use of herbal medicine within the Danish population – and relations to health, health and illness behaviour, education and income]. Supervisor: Ebba Holme Hansen.

Karen Hoebek, Christian Huyghe (Belgian SOCRATES students): Qualitative and quantitative analysis of the asthma therapeutic outcomes monitoring (TOM) projects held in Belgium and Denmark. Danish supervisor: Ellen Weth Sørensen. Belgian supervisor: Prof. Dr. Apr. Sophie Sarre (Vrije Universiteit Brussel).


Majken Nørskov Petersen: Udbredelsen af “rational farmakoterapi” på danske apoteker med hensyn til håndkøbslægemidler. [Diffusion of “rational pharmacotherapy” on Danish community pharmacies in regard to non-prescription drugs]. Supervisor: Lotte Stig Haugbølle.

Bertel Rüdinger: Fra elfenbenstårn til økonomisk faktor – De danske universiteter under globaliseringen. [From the ivory tower to an economic factor – Danish universities in the light of globalisation]. Supervisor: Janine Morgall Traulsen.
### Staff

**THE ROYAL DANISH SCHOOL OF PHARMACY**

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E-mail: dfh@dfh.dk

(E-mail: initials followed by @dfh.dk)

<table>
<thead>
<tr>
<th>HEADS OF SCHOOL</th>
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<tr>
<td><strong>Rector</strong></td>
<td>Povl Krogsgaard-Larsen (rektor)</td>
<td>Professor, DSc (pharm.) professor, dr.pharm.</td>
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<tr>
<td><strong>Deputy Rector</strong></td>
<td>Bjarne Fjalland (bf)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<th>MANAGEMENT</th>
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<tr>
<td><strong>Administrator</strong></td>
<td>Judith Christiansen (jc)</td>
<td>MA cand.mag.</td>
</tr>
<tr>
<td><strong>Head of Personnel Division</strong></td>
<td>Elisabeth Ris (elri)</td>
<td>MA (law) cand.jur.</td>
</tr>
<tr>
<td><strong>Head of Study Division</strong></td>
<td>Ilse Fjalland (if)</td>
<td>MSc (pharm.) cand.pharm.</td>
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<tr>
<td><strong>Head of the Study Board</strong></td>
<td>Jette Jacobsen (jeja)</td>
<td>Associate Professor, MSc (pharm.) lektor, cand.pharm.</td>
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<tr>
<td><strong>Head of the Budgeting and Accounting Division</strong></td>
<td>Villy Dahl Jensen (vdj)</td>
<td>MA cand.scient.pol.</td>
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<tr>
<td><strong>Head of the Information Office</strong></td>
<td>Jesper Munck (jemu)</td>
<td>MA cand.mag.</td>
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<tr>
<td><strong>Head of Library Services</strong></td>
<td>Alice Narhede (alin)</td>
<td>Librarian DB1 bibliotekar DB1</td>
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### Departmental Board 2001

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<tr>
<th>Position</th>
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<tr>
<td>Head of Department</td>
<td>Professor Steen Honoré Hansen</td>
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<tr>
<td>Deputy Head of Department</td>
<td>Associate Professor Bent Haling-Sørensen</td>
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<td>Professor</td>
<td>Claus Selch Larsen</td>
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<td>Laboratory Porter Court</td>
<td>Associate Professor Bente Gammelgaard</td>
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<tr>
<td>Associate Professor</td>
<td>Claus Cornett</td>
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<tr>
<td>PhD student</td>
<td>Anne K. Lykkeberg (observer)</td>
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<tr>
<td>Student</td>
<td>Jesper R. Bojsen</td>
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### Departmental Board 2002

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<th>Position</th>
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<tr>
<td>Head of Department</td>
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<tr>
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<td>Associate Professor Bent Haling-Sørensen</td>
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<tr>
<td>Associate Professor</td>
<td>Bente Gammelgaard</td>
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<tr>
<td>Senior Laboratory Technician</td>
<td>Tove Eckhardt</td>
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<tr>
<td>PhD student</td>
<td>Anne K. Lykkeberg (observer)</td>
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<td>Student</td>
<td>Rune Gildsig</td>
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### Secretariat

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<tr>
<td>Helle Sigetty Boje</td>
<td>+45 35 30 62 61</td>
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<tr>
<td>Inge Miller</td>
<td>+45 35 30 62 75</td>
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<tr>
<td>Søren Kragh</td>
<td>+45 35 30 64 62</td>
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<td>Fax:</td>
<td>+45 35 30 60 10</td>
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### Scientific Staff

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<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Andersen, Henrik Rasmus (hra)</td>
<td>PhD student, MSc, ph.d-studerende, cand.scient.</td>
</tr>
<tr>
<td>Bendahl, Lars (labe)</td>
<td>PhD student, MSc, ph.d-studerende, cand.scient.</td>
</tr>
<tr>
<td>Brix, Rikke (rbr)</td>
<td>PhD student, MSc, ph.d-studerende, cand.scient.</td>
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<tr>
<td>Brandssted, Helle (hb)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<tr>
<td>Cornett, Claus (cc)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<tr>
<td>Eberth, Kirsten (ke)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<tr>
<td>Farver, Ole (of)</td>
<td>Professor, DSc, professor, dr.scient.</td>
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<tr>
<td>Gammelgaard, Bente (bg)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<tr>
<td>Hagen, Nina (nh)</td>
<td>PhD student, MSc (pharm.) ph.d-studerende, cand.pharm.</td>
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<td>Haling-Sørensen, Bent (bhs)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<tr>
<td>Hansen, Steen Honoré (shh)</td>
<td>Professor, DSc (pharm.) professor, dr.pharm.</td>
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<tr>
<td>Ingerslev, Flemming (fl)</td>
<td>Assistant Professor, MSc (pharm.) adjunkt, ph.d., cand.polyt.</td>
</tr>
<tr>
<td>Jacobsen, Anne-Marie (arnja)</td>
<td>Research Assistant forskningsassistent</td>
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<tr>
<td>Jensen, Bent Packert (bp)</td>
<td>PhD student, MSc (pharm.) ph.d-studerende, cand.pharm.</td>
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<tr>
<td>Johannessen, Jane K. (jkg)</td>
<td>Assistant Professor, MSc (pharm.) adjunkt, cand.pharm.</td>
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<td>Jens, Ole (oj)</td>
<td>Associate Professor, PhD (pharm.) lektor, ph.d. (pharm.)</td>
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<td>Kristensen, Mads Gjelstrup (mgk)</td>
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<td>Larsen, Claus Stelch (csl)</td>
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<td>Steinicke, Ann-Louise (alsl)</td>
<td>Research Assistant forskningsassistent</td>
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Thomsen, Erling Sonnich (est)  
Associate Professor, PhD (pharm.)  
lektor, ph.d. (pharm.)

Zhang, Jingjie (jz)  
PhD student, MSc (pharm.)  
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Østergaard, Jesper (joe)  
PhD student, MSc (pharm.)  
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Teaching Assistants

Gerd Askaa, Hans Bjerge, Jens Corfitzen, Frank Hansen, Poul Einer Hansen, Henning Brandt Jensen, Inger Spangsberg Jensen, Niels Rhod Larsen, Mette Sandby Holkenfeldt, Kirsten Rald, Jeanette Reschka

Administrative and technical staff

<table>
<thead>
<tr>
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<tr>
<td>Andersen, Kirsten (ka)</td>
<td>Senior Laboratory Technician laboratorieoverassistent</td>
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<td>Bech, Lioubov (lib)</td>
<td>Trainee, Laboratory Technician laborantpraktikant</td>
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<td>Boje, Helle Sigetty (hbs)</td>
<td>Head of Section kontorfuldmægtig, cand.negot.</td>
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<td>Eckhardt, Tove (te)</td>
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<td>Hansen, Karen Margrethe (km)</td>
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<td>Joehnson, Lars Halldor (lth)</td>
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<td>Kongsbach, Anette Due (adk)</td>
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<td>Cleaner rengøringsassistent</td>
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<td>Lunow, Elzbieta (elu)</td>
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<tr>
<td>Miller, Inge (im)</td>
<td>Senior Clerk overassistent, ED</td>
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<td>Milosevic, Melita</td>
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<td>Schwerkdeger, Court (csc)</td>
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<td>Vejlemand, Nina Stober (nsv)</td>
<td>Laboratory Engineer laboratorieteknikker</td>
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DEPARTMENT OF MEDICINAL CHEMISTRY

Departmental Board 2001

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Associate Professor Per Malgaard
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Larsen, Uffe (ul) PhD student, MSc ph.d.-studerende, cand.scient.
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<td>Scholarstudent</td>
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<td>Ljøfors, Tommy (tl)</td>
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<td>Sorensen, Lisæ Baadsgaard (lbs)</td>
<td>Senior Laboratory Engineer</td>
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**DEPARTMENT OF PHARMACEUTICS**

**Departmental Board 2001**

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<tr>
<td>Head of Department:</td>
<td>Associate Professor Margrethe Rømer Rassing</td>
<td>Deputy Head of Department:</td>
<td>Associate Professor Bente Steffansen</td>
</tr>
<tr>
<td>Deputy Head of Department:</td>
<td>Associate Professor Bente Steffansen</td>
<td>Associate Professor Jørn Møller-Sonnergaard</td>
<td>Assistant Engineer Arne Steinicke Jensen</td>
</tr>
<tr>
<td>Associate Professor</td>
<td>Jørn Møller-Sonnergaard</td>
<td>Assistant Engineer</td>
<td>Arne Steinicke Jensen</td>
</tr>
<tr>
<td>Student Erik Thiøgesen</td>
<td>PhD student Camilla Foged (observer)</td>
<td>Student Jacob Granne</td>
<td></td>
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</tbody>
</table>

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<table>
<thead>
<tr>
<th>Name</th>
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<tr>
<td>Adrian, Charlotte (ca)</td>
<td>PhD student, MSc (pharm.)</td>
<td>ph.d.-studerende, cand.pharm.</td>
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<td>Bagger, Morten (moba)</td>
<td>PhD student, MSc (pharm.)</td>
<td>ph.d.-studerende, cand.pharm.</td>
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<tr>
<td>Bechgaard, Erik (eb)</td>
<td>Associate Professor, PhD, MSc (pharm.)</td>
<td>lektor, ph.d. (pharm.)</td>
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<td>Beier, Anne Mette (aho)</td>
<td>PhD student, MSc (pharm.)</td>
<td>ph.d.-studerende, cand.pharm.</td>
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<tr>
<td>Biodin, Birger (bbr)</td>
<td>Associate Research Professor, PhD</td>
<td>forskningslektor, (lic.scient.)</td>
</tr>
<tr>
<td>Christensen, Janne Ørskov (jach)</td>
<td>PhD student, MSc (pharm.)</td>
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<td>Christrup, Lona Louring (lc)</td>
<td>Associate Professor, PhD, MSc (pharm.)</td>
<td>lektor, ph.d. (pharm.)</td>
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<td>Davidsen, Jesper (jeda)</td>
<td>PhD student, MSc (pharm.)</td>
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<td>Eriksson, André Huss (ahe)</td>
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<td>Foged, Camilla (cfo)</td>
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<td>Frokjær, Sven (sdf)</td>
<td>Professor, PhD, MSc</td>
<td>professor, ph.d. (pharm.)</td>
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### Administrative and technical staff

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<td>Christensen, Malene</td>
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<td>Zhao, Ya Hong</td>
<td>Cleaner</td>
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</tbody>
</table>

**Secretariat**

- Ruth Jensen: +45 35 30 63 21
- Eva Nielsen: +45 35 30 63 29
- Fax: +45 35 30 60 20

**Scientific Staff**

- Andersen, Klaus Bahl (kba): Associate Professor, PhD lektor, ph.d. (lic.scient.)
- Christensen, Jens Dencker (jdc): Associate Professor, PhD lektor, ph.d. (lic.pharm.)
- Christensen, Lars Harder (lhc): Scholarship Student (pharm.) stud.pharm. student
- Clausen, Rikke (ricl): PhD student, MSc ph.d.-studerende, cand.scient.
- Dalsgaard, Grethe Tang (gtd): Research Assistant, MSc (pharm.) forskningsassistent, cand.pharm.
- Engberg, Jan (fax: 35 30 60 22) (je): Professor, DSc professor, dr.scient.
- Erichsen, Helle Kirstein: PhD student, MSc (pharm.) ph.d.-studerende, cand.pharm.
- Fjaland, Bjarne (bf): Associate Professor, PhD lektor, ph.d. (lic.pharm.)
- Frandsen, Aase (aaf): Associate Professor, DSc lektor, dr.scient.
- Fuglsang, Anders (anfu): PhD student, MSc (pharm.) ph.d.-studerende, cand.pharm.
- Gegelashvili, Georgi (gege): Associate Professor, PhD lektor, ph.d.
- Hansen, Erik Wind (ewh): Associate Professor, PhD lektor, ph.d. (lic.pharm.)
- Hansen, Harald S. (hsh): Assistant Professor, DSc docent, dr.scient.
- Hansen, Henrik: Assistant Research Professor, MSc (pharm.) forskningsadjunkt, cand.pharm.
- Hermansen, Keld: Veterinary Advisor veterinær tilsyn
- Jensen, Liselotte Brix (ibj): PhD student, MSc ph.d.-studerende, cand.scient.
- Jensen, Marianne Lerbech: PhD student, MSc ph.d.-studerende, cand.scient.
- Johansen, Thue: PhD student MSc (med.) ph.d.-studerende, cand.med.
- Klavsen, Tine (tkl): PhD student, MSc (pharm.) ph.d.-studerende, cand.pharm.
- Kristiansen, Uffe (uk): Associate Professor, PhD lektor, ph.d. (pharm.)
- Kristensen, Anders Skov (ask): PhD student, MSc ph.d.-studerende cand.scient.
- Kyhl, Lars Erik Broksæve (kek): PhD student, MSc (pharm.) ph.d.-studerende, cand.pharm.
- Larsen, Søren Thor: PhD student, MSc (pharm.) ph.d.-studerende, cand.pharm.
- Larsson, Orla Miller (orr): Associate Professor, PhD lektor, ph.d. (lic.scient.)
- Lund, Trine Meldgaard (tml): Associate Professor, PhD lektor, ph.d. (lic.pharm.)
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### Teaching Assistants

Jesper Drøgemüller

### Administrative and technical staff

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<td>Bonnichsen, Michael (mibo)</td>
<td>Laboratory Porter/keeper</td>
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<td>Busk, Kirsten Aagaard (kab)</td>
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### DEPARTMENT OF SOCIAL PHARMACY

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<tr>
<td>Hopp, Trine</td>
<td>PhD student, MSc (pharm.)</td>
</tr>
<tr>
<td>Jensen, Thomas Clemens</td>
<td>University Instructor, MSc (pharm.)</td>
</tr>
<tr>
<td>Karke, Shiba</td>
<td>PhD student, MSc (clin. pharmacol.)</td>
</tr>
<tr>
<td>Knudsen, Pia</td>
<td>Assistant Professor PhD (pharm.)</td>
</tr>
<tr>
<td>Kruse, Poul R.</td>
<td>Associate Professor, DSc (pharm.)</td>
</tr>
<tr>
<td>Larsen, Jakob Bjerg</td>
<td>PhD student, MSc (pharm.)</td>
</tr>
<tr>
<td>Launso, Laila</td>
<td>Associate Professor, DSc (sociology)</td>
</tr>
<tr>
<td>Mishra, Pranaya</td>
<td>PhD student, MSc (clin.pharmacol.)</td>
</tr>
<tr>
<td>Møldrup, Claus</td>
<td>Assistant Research Professor, PhD (pharm.)</td>
</tr>
<tr>
<td>Nielsen, Merete W.</td>
<td>PhD student, MSc (pharm.)</td>
</tr>
<tr>
<td>Rossing, Charlotte</td>
<td>PhD student, MSc (pharm.)</td>
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<tr>
<td>Rüdinger, Bertel</td>
<td>PhD student, MSc (pharm.)</td>
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<tr>
<td>Sørensen, Ellen Westh</td>
<td>Associate Professor, MSc (pharm.)</td>
</tr>
<tr>
<td>Trap, Birna</td>
<td>PhD student, MSc (pharm.), BCom</td>
</tr>
<tr>
<td>Traulsen, Janine M. Morgall</td>
<td>Associate Professor, PhD (sociology)</td>
</tr>
<tr>
<td></td>
<td>Administrative and technical staff</td>
</tr>
<tr>
<td>Andersen, Gunhild (ga)</td>
<td>Clerk, Cleaner</td>
</tr>
<tr>
<td>Jensen, Anne Blem (abu)</td>
<td>Senior Clerk, Language Secretary</td>
</tr>
<tr>
<td>Nørgaard, Jette (jen)</td>
<td>Senior Clerk, Language Secretary</td>
</tr>
<tr>
<td>Sørensen, Jytte (js)</td>
<td>Managing Clerk, BCom</td>
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</table>
THE DANISH PHARMACEUTICAL LIBRARY

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Fax: + 45 35 30 60 60

Opening Hours:
Monday – Thursday: 9 - 16; Friday 10 - 15.30
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Information desk + 45 35 30 64 60

E-mail: dfhlib@dfh.dk

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Annemette Møller Hansen, The Library
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Orla Miller Larsson, Department of Pharmacology
Margrethe Rømer Rassing, Department of Pharmacy
Erling Sonnich Thomsen, Department of Analytical and Pharmaceutical Chemistry
Ellen Westh Sørensen, Department of Social Pharmacy
Henrik Parshad, PhD Department of Pharmacy
Marianne Hald Larsen, student
Anne Zimmermann, student

Staff
E-mail: Initials followed by @dfh.dk

Bladt, Birgitte Ruste (brb) Clerk assistant
Hald, Niels Peter Krogh Student Assistant studentemedhjælp
Hansen, Annemette Møller (amh) Research Librarian, MSc (pharm.) forskningsbibliotekar, cand.pharm.
Keller, Marianne (mk) Librarian bibliotekar
Kaad, Lene (leka) Librarian bibliotekar
Munck, Jesper (jemu) Information Officer, MA informationsmedarbejder, cand.mag.
Nørhede, Alice (aln) Head of Library Service biblioteksleder
Overgaard, Ole (oko) Library Porter biblioteksbeljænt
Petersen, Filip Hetmar Cleaner rengøringsassistent
Thiesen, Lis (lt) Senior Clerk overassistent
Weile, Martin (mw) Librarian bibliotekar
# Administration Department

**Opening hours:**
Monday – Thursday 8.30 - 16; Friday 8.30 - 15.30

**Phone:** +45 35 30 60 00
**Fax:** +45 35 30 60 01

**E-mail:** Initials followed by @dfh.dk

## Heads of School

**Rector:**
Povl Krogsgaard-Larsen (rektor)  
Professor, DSc (pharm.)  
professor, dr.pharm.

**Deputy Rector:**
Bjarne Fjalland (bf)  
Associate Professor, PhD (pharm.)  
lektor, ph.d. (pharm.)

**Administrator**
Judith Christiansen (jc)  
MA  
cand.mag.

**Security officer**
Johansen, Jørgen Stage (jsj)  
Laboratory Engineer  
laboratorietykørier

## Personnel Department

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Qualification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almegaard, Tine (ta)</td>
<td>Administrative Officer, LLB</td>
<td>fuldmægtig, cand.jur.</td>
</tr>
<tr>
<td>Grindeberg, Marianne (magi)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Hansen, Tina Senn (tsh)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Jensen, Anni Kølner (akj)</td>
<td>Senior Clerk, Receptionist</td>
<td>overassistent, receptionen</td>
</tr>
<tr>
<td>Knudsen, Tage Ø. (tk)</td>
<td>Head Porter</td>
<td>betjentformand</td>
</tr>
<tr>
<td>Langhoff, Birgit (bila)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Pedersen, Susanne (ap)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Riis, Elisabeth (eli)</td>
<td>Head of Secretariat, LLB</td>
<td>sekretariatschef, cand.jur.</td>
</tr>
<tr>
<td>Sørensen, Anne (ans)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Tribe, Louise (ltr)</td>
<td>Administrative Officer, LLB</td>
<td>fuldmægtig, cand.jur.</td>
</tr>
</tbody>
</table>

## Course Administration

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Qualification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fjalland, Ilse (fi)</td>
<td>Registrar, MSc (pharm.)</td>
<td>studiechef, cand.pharm.</td>
</tr>
<tr>
<td>Flarup, Malene (mfl)</td>
<td>Office Trainee</td>
<td>kontorelev</td>
</tr>
<tr>
<td>Jørgensen, Marianne W. (mw)</td>
<td>Administrative Officer, BcomInt</td>
<td>fuldmægtig, cand.merc.int.</td>
</tr>
<tr>
<td>Laursen, Inge Debois (id)</td>
<td>Administrative Officer, MSc (pharm.)</td>
<td>fuldmægtig, cand.pharm.</td>
</tr>
<tr>
<td>Ottosen, Susanne (sus)</td>
<td>Managing Clerk</td>
<td>kontorfører</td>
</tr>
<tr>
<td>Sjelle, Pia (pia)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Uliksen, Gitte Metz (gmu)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
</tr>
<tr>
<td>Vester-Andersen, Lærke (iva)</td>
<td>Administrative Officer, MSc (pharm.)</td>
<td>fuldmægtig, cand.pharm.</td>
</tr>
<tr>
<td>Wiese, Lone (lw)</td>
<td>Senior Clerk</td>
<td>overassistent</td>
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## Course Guidance

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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</tr>
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<tbody>
<tr>
<td>Dahl, Christoffer (cdl)</td>
<td>Student Counsellor, pharmacy student</td>
<td>studievejleder, stud.pharm.</td>
</tr>
<tr>
<td>Kendra, Jimmy (jjk)</td>
<td>Student Counsellor, pharmacy student</td>
<td>studievejleder, stud.pharm.</td>
</tr>
<tr>
<td>Koch, Bettina (beko)</td>
<td>Student Counsellor, pharmacy student</td>
<td>studievejleder, stud.pharm.</td>
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### Finance department

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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</thead>
<tbody>
<tr>
<td>Andersen, Dorthe (doan)</td>
<td>Senior Clerk overassistent</td>
</tr>
<tr>
<td>Bernhard, Rikke (rbj)</td>
<td>Senior Clerk overassistent</td>
</tr>
<tr>
<td>Christiansen, Anja (ac)</td>
<td>Office Trainee</td>
</tr>
<tr>
<td>Freidal, Manon (mf)</td>
<td>Senior Clerk overassistent</td>
</tr>
<tr>
<td>Haugan, Brita (bh)</td>
<td>Managing Clerk kontorfuldmægtig</td>
</tr>
<tr>
<td>Jensen, Ann-Mari Østergaard (am)</td>
<td>Senior Clerk overassistent</td>
</tr>
<tr>
<td>Jensen, Villy Dahl (vdj)</td>
<td>Finance Manager, BSc (econ.) okonomichef, cand.scient.pol.</td>
</tr>
<tr>
<td>Jørgensen, Tina Lund (tlj)</td>
<td>Clerk assistant (+ DSR)</td>
</tr>
<tr>
<td>Knudsen, Flemming Siggaard (fsk)</td>
<td>Managing Clerk fuldmægtig</td>
</tr>
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</table>

### Higher education administration system (STADS)

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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</thead>
<tbody>
<tr>
<td>Borgholm, Birthe (bb)</td>
<td>Electronic Data Consultant, MSc edbkontulent, cand.scient.</td>
</tr>
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### Web

<table>
<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Korzen, Henrik (heko)</td>
<td>Webmaster</td>
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### IT department

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Andersen, Jesper Stemann (jsa)</td>
<td>Student Assistant studentermedhjælp</td>
</tr>
<tr>
<td>Aunfelt, Karsten (kau)</td>
<td>System Administrator systemadministrator</td>
</tr>
<tr>
<td>Hossein, Ehsani (hoeh)</td>
<td>Electronic Data Assistant, Engineer edb-tekniker, ingeniør</td>
</tr>
<tr>
<td>Szymanski, Thomas (tsz)</td>
<td>Student Assistant studentermedhjælp</td>
</tr>
<tr>
<td>Sørensen, Jørn Bo (bos)</td>
<td>Head of IT IT-leder</td>
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### Technical services

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Christensen, Tom</td>
<td>Mechanic maskinarbejder</td>
</tr>
<tr>
<td>Olsen, Allan (alol)</td>
<td>Mechanic maskinarbejder</td>
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<tr>
<td>Olsen, Freddy</td>
<td>Technical Assistant specialarbejder</td>
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<tr>
<td>Petersen, John (jop)</td>
<td>Engineer maskinnæstter</td>
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### Building administration

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Bender, Allan</td>
<td>Porter betjent</td>
</tr>
<tr>
<td>Harder, Ronald (roha)</td>
<td>Porter betjent</td>
</tr>
<tr>
<td>Knudsen, Tage O. (tk)</td>
<td>Head Porter betjentformand, portner</td>
</tr>
<tr>
<td>Rasmussen, Kjeld (kjr)</td>
<td>Building Administrator bygningsforvalter</td>
</tr>
</tbody>
</table>