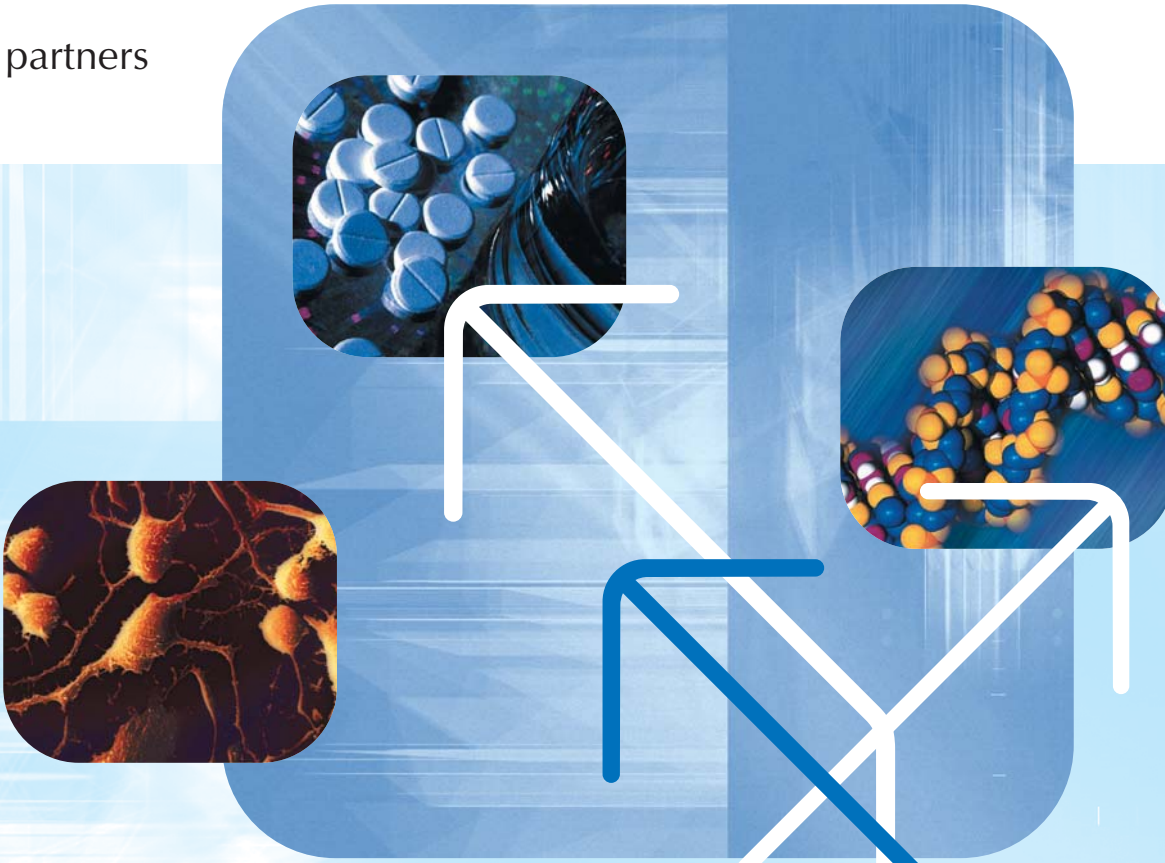
Biotechnology in the Czech Republic

Undiscovered Opportunities

TECHNOLOGY CENTRE AS CR

- List of technologies and products ready for commercialization
- Projects for research cooperation
- SMEs looking for partners



Why the Czech Republic?

A strong position and tradition in biotech oriented research

- Strong world-known science institutions in chemistry, biology, genetics, medicine and pharmacy
- High level of cooperation, interdisciplinary approach
- Recognized professionals and successful products
- Well-equipped labs

Do you know that these world - known products originated in the Czech Republic?

Soft contact lenses, Viread, Vistide, Hepsera, Ketazon, Prothiaden, Trimepranol

Complete biotech and pharma services for you

- Research
- Technology (product) testing and transfer
- Clinical trials
- Faculty hospitals with long experience in medical testing

Why to invest in the Czech Republic

- Many promising research results have not been commercialized because of lack of local capital interested in biotechnology (www.tc.cz)
- Biotech SMEs looking for cooperation
- Environment friendly to foreign investments (www.CzechInvest.cz)
- Skilled staff and highly educated professionals in biotech research and well-equipped labs

Who we are

Technology Centre promotes commercial utilisation of research and development, provides complex technology transfer services and stimulates creation and growth of small innovative businesses. **Technology Centre** co-ordinates strategic projects aimed at development of innovation policies and identification of national research priorities. **Technology Centre** is your gate to biotechnology research in the Czech Republic.

We are prepared to assist you in your first steps in the Czech Science and Technology. We have know-how in biotech R&D and extensive links to biotech SMEs throughout the whole Czech Republic and we will help you to find the right cooperation partner for you. We will provide the necessary analyses and feasibility studies. For additional information visit our web site: www.tc.cz.

List of biotechnology innovations for commercial use

This overview of biotechnology opportunities in the Czech Republic was prepared by the Technology Centre AS CR. For further information and contact details to the authors of individual contributions, please contact us:

Technology Centre
Academy of Sciences of the Czech Republic
c/o Dr. Jiří Vaněček
Address: Rozvojová 135, 165 02 Prague 6, Czech Republic
Phone: +420 220 390 700
Fax: +420 220 922 698 or + 420 220 921 217
E-mail: vanecek@tc.cas.cz
WWW: http://www.tc.cz

1. 0. 0. Pharmacy and Medicine

2. 0. 0. Agriculture

3. 0. 0. Environmental technology

4. 0. 0. Biotechnology SMEs in the Czech Republic for international cooperation

NEW POTENT ANTIVIRAL AND CYTOSTATIC DRUGS.

RNDr. A. Holý, DrSc., Institute of Organic Chemistry and Biochemistry AS CR

Laboratory of Dr. Holý discovered the new class of antiviral therapeutics based on modified nucleotides. Viread (Tenofovir) used for treatment of HIV/AIDS blocks the viral replication *via* the inhibition of reverse transcriptase. Vistide (Cidofovir) is used for treatment of CMV retinitis and Hepsera (Adefovir) for therapy of hepatitis B. These products are produced and marketed by the US pharmaceutical company GILEAD. The group of Dr. Holý has recently finished laboratory development of two new drugs.

1. O-Phosphonomethylcholine and its alkyl esters

Summary
Novel compounds which are O-phosphonomethylcholine and its alkyl esters, are new cytostatic or potential antiparasitic drugs. Phosphocholine hexyl ester (miltefosin, Miltex) is approved for use as a topical anticancer drug applicable particularly in skin cancer and breast cancer. Oral miltefosin also exhibits significant therapeutic effect on intestinal form of *leishmaniasis*, the disease caused by *Leishmania donovani* parasite which is transmitted by *Phlebotomus* fly (kala-azar fever afflicts 3 million patients a year in India, with mortality reaching 98% in untreated cases).

Innovation Principle
The present novel class of compounds comprises phosphate-modified compounds derived from choline phosphonylmethyl ether. This modification makes them non-degradable by enzymatic dephosphorylation. The hexadecyl ester of O-phosphonomethylcholine has a similar activity as its phosphate counterpart in the transplantable leukaemia model in rats. Therefore, it is quite plausible that this compound or its alkyl ester analogues could also exhibit antiparasitic activity.

Achieved Stage
Finished project, the results are ready for application.

Application Area
Pharmaceutical industry. **Offer:** Know-how of the synthesis of the parent compound and its alkyl esters, their use as new cytostatics or potential antiparasitic drugs. Samples for biological evaluation are available.

2. Novel 6-phenylpurine 9-β-D-ribonucleosides with antineoplastic activity

Summary
Among the antineoplastic drugs there are numerous modified nucleoside antimetabolites. The main clinically used purine derivatives are adenosine analogs (adenine arabinoside, deoxycoformycin, cladribine and fludarabine). The cytostatic activity of substituted 6-phenylpurine 9-β-D-ribonucleosides is unexpected; it is characteristic for specific combinations of substituents at the phenyl residue.

Innovation Principle
Compounds of this structure can be prepared by general procedure (Suzuki reaction), consisting of a treatment of sugar-protected 6-chloropurine 9-β-D-ribonucleoside with substituted phenylboronic acid in the presence of tetrakis(triphenylphosphine)palladium and a subsequent removal of protecting groups at the sugar residue of the resulting intermediate. The cytostatic activity was assayed in vitro in transformed cell lines.

Achieved Stage
Finished project, the results are ready for application.

Application Area
Pharmaceutical industry. **Offer:** Know-how of the synthesis, biological data, samples of biologically active drug candidates.

NEW ANTITUMOUR MEDICAMENTS INHIBITING THE CELL CYCLE *VIA* THE CYCLIN-DEPENDENT KINASES.

Prof. Ing. M. Strnad, CSc., Institute of Experimental Botany AS CR

Summary
The laboratory has prepared new antitumour substances of purine type derived from the fytohormones. Striking specificity of the cytokinin derivative olomoucine, 2- (2-hydroxyethylamino)-6-benzylamino-9-purine towards the cyclin-dependent kinases (cdc2, cdk2, cdk5, ERK1) pointed to the possibility to inhibit important phases of the cell cycle (transitions G1/S and G2/M). Discovery of olomoucine as the first active inhibitor of cyclin-dependent kinases (CDK) led to the development of new generation of antitumour substances (with antimitotic activity), e.g. roscovitin and purvalanol. Our aims are:

1. to prepare more active CDK inhibitors
2. to study relationship between structure and activity in different kinase tests
3. to develop new generations of CDK inhibitors structurally different from trisubstituted purines
4. to use proteomic approach to study effects of these substances at the cell level
5. to test their cytotoxic and apoptotic effects in both animal and plant cells
6. to study pharmacokinetics and *in vitro* and *in vivo* metabolism
7. to study antitumour activity of the new substances
8. to evaluate activity, stability and metabolism of newly synthesized substances. Then, the selected most active substances can be used in pre-clinical and clinical experiments.

Innovation Principle
New classes of substances of plant origin inhibiting the cell cycle and thus also the tumour growth.

Achieved Stage
Company Cyclacel has brought roscovitin to the 2nd phase of clinical testing. Bohemin, another substance of this type, is being tested in the Czech Republic and is ready for clinical testing. Substances with much higher activities are available, which are prepared for pre-clinical tests.

Cooperating Partners
Cyclacel, Scotland; Optima Biotech, Germany; Pliva-Lachema, Czech Republic.

Application Area
Pharmaceutical and cosmetic industry, agriculture. **Offer:** We have very active substances available for potential partners.

TARGETED MACROMOLECULAR CHEMOTHERAPEUTICS FOR CANCER TREATMENT.

Prof. B. Říhová, MSc., DSc., Institute of Microbiology AS CR

Summary
Targeted macromolecular therapeutics based on N-(2-hydroxypropyl) methacrylamide (HPMA) is the subject of a joint Czech-English patent. The patent is based on binding cytostatics (our experience is mainly with adriamycin, daunomycin, farmorubicin, photoactivable chlorine e6, mytomycin C, methotrexate and 5-fluorouracil) to a soluble polymeric HPMA carrier. This so-called polymeric prodrug based on HPMA reaches its maximum efficiency when targeted (e.g. by monoclonal or polyclonal antibody, growth hormone, transferrin or its antibody, lectin, carbohydrate). However, even untargeted polymeric conjugates are far more efficient than the free drugs. The drug is bound to the polymeric carrier using an oligopeptidic spacer (mainly GlyPheLeuGly) which ensures stability and lack of activity of the conjugate during transport through the blood stream and also its intracellular degradability and pharmacological activity. The oligopeptidic spacer is deliberately selected so as to ensure that the covalent bond of the drug to this spacer is controllably degradable by lysosomal enzymes, namely D, H and L cathepsins.

Innovation Principle
The advantages of these macromolecular therapeutics comprise: a) increased efficiency, b) dramatically increased maximum tolerated dose, c) significantly reduced non-specific toxicity to healthy organs and tissues, especially to bone marrow, d) targetability, e) the ability to partially overcome the multiple drug resistance (MDR), f) increased solubility, g) increased accumulation in solid tumors (EPR effect) and h) protection or even mobilization of the immune system.

Achieved Stage
Two patients with generalized carcinoma of breast are currently (since November 2000) being treated in the Adults Oncology Department of the University Hospital in Motol by the HPMA conjugate containing doxorubicin and human IgG with very good results. Together with Léčiva Inc. we are looking into the possibilities of regular clinical tests in the Czech Republic with conjugates that have not been tested by the Charles University and with new-generation conjugates.

Cooperating Partners
Institute of Macromolecular Chemistry AS CR, Czech Republic.

Application Area
Health care, pharmaceutical industry.

NEW TYPES OF VACCINES AGAINST VIRUSES AND TUMOURS.

P. Šebo MSc., PhD., Institute of Microbiology AS CR

Summary
The search for effective ways of inducting cell immunity responses of so-called subsidiary and cytotoxic T lymphocytes ($CD4^+$, respectively $CD8^+$) that belong to the main defensive mechanisms against many infections and tumours is an important immunological problem. Induction of these lymphocytes requires the serum antigens to be processed by professional antigen-presenting cells (APC) and presented in a complex with MHC I and II class molecules, which can then stimulate the T-lymphocytes. Detoxified adenylate cyclase toxin (ACT) is capable of specific binding to the professional APC cells and delivering into them the incorporated foreign serum antigens. Our previous results show that ACT carrying epitope from the LCMV and HIV viruses and tumour antigens is capable of inducing specific immune responses that protect inoculated mice e.g. from otherwise lethal LCMV virus infection or from growth of transplanted experimental tumours. As a sequel to this project, new ACT derivatives carrying a number of antigens will be constructed and tested as a new, widely applicable approach to the preparation of preventative and therapeutic vaccines against viral diseases, tuberculosis and some tumours.

Innovation Principle
A completely original type of unreplicative protein antigen carrier with unique affinity for antigen-presenting cells.

Achieved Stage
The work is in the phase of basic research and pre-clinical testing of applied research.

Cooperating Partners
Institute Pasteur, Paris, France; Chiron Vaccines Pharmaceutical Company, Siena, Italy; Ludwig Institute of Cancer Research, Brussels, Belgium.

Application Area
Vaccines for protection against viral infections and selected tumours.

AMINOSUGARS AS LIGANDS OF ACTIVATING RECEPTOR OF NATURAL KILLER CELLS: A STRATEGY FROM LIGAND OPTIMIZATION TO DEVELOPMENT OF GLYCODRUG FOR *IN VIVO* APPLICATION.

Doc. Ing. V. Křen, DrSc., Institute of Microbiology AS CR

Summary
Aminosugars have a good affinity for the NKR-P1A protein, the major activating receptor at the surface of rat natural killer cells. We have systematically investigated the structural requirements of the recombinant soluble dimeric form of the receptor for its optimal carbohydrate ligands. While N-acetyl-D-mannosamine was the best neutral monosaccharide ligand, its participation in the context of an extended oligosaccharide sequence was equally important. The IC_{50} value for the GalNAcβ1→4ManNAc disaccharide was nearly 10^{-10} M with a further possible increase depending on the type of the glycosidic linkage and the aglycon nature. Based on these results multivalent glycodendrimers were designed and synthesized and they proved to be very effective in the treatment of experimental tumours (colon, melanoma). Fluorescence labelling of these compounds enabled us to follow a distribution of these activators in organism and we demonstrated the targets of these glycodrugs are true NK cells. Neoglycoconjugates based on the chitooligomers were prepared and they were tested also for the interaction with the NK cells. The best conjugates bound have IC_{50} values up to 10^{-15} M.

Innovation Principle
New activating ligands for natural killer cells and possible new method of cancer treatment.

Achieved Stage
Finished laboratory study.

Application Area
Pharmaceutical industry. **Know-how offer:** Production of high-affinity ligands based on the *N*-acetylmannosamine and other hexosamines (partly covered by the Czech patents). Synthesis of novel polyvalent hexosamine-based glycomimetics for the NK cell activation (mostly unpublished results). Expertise for the production and testing *(in vitro, ex vivo* and *in vivo)* of new NK cell activators.

GENE THERAPY OF CANCER.

Prof. MUDr. V. Vonka, DrSc., Institute of Haematology and Blood Transfusion, Prague

Summary

Since the mid 90´ the group working at the Department of Experimental Virology has been involved in the development of genetic anti-cancer vaccines. The experimental system employed is represented by rodent cells transformed by human *papillomavirus* type 16 (HPV 16), the major etiological agent in cervical cancer. Our research has been proceeding along three lines, i.e. development of cell-based vaccines, recombinant viruses and DNA vaccines.

(i) Cell-based vaccines. Syrian-hamster and C57/B6 cells transformed by HPV 16 are being used. For gene modification suicide gene (herpes simplex type 1 thymidine kinase, HSV TK) and genes for various immunostimulatory factors are being employed. The most important results indicate that the tumours induced by the HSV TK-expressing cells are curable by ganciclovir (GCV) and that this treatment results in development of anti-tumour immunity in Syrian hamsters but not in the syngeneic mouse cells. Cells expressing cytokines (IL2, GM-CSF) lost their oncogenicity but were capable of inducing solid immunity against the challenge with the parental unmodified cells. Tumours induced by cells expressing HSV TK which were not curable by GCV alone were cured by specific chemo immunotherapy using both GCV and the cytokine-expressing cells.

(ii) Recombinant viruses. Recombinant *vaccinia* viruses (both replicating and non-replicating) expressing E7 protein of HPV 16 (wild or modified) and various cytokines are being employed both for direct immunization and construction of dendritic cell-based vaccines. The most important results obtained thus far indicated that the recombinant viruses were capable of inducing immunity against challenge with the parental HPV 16- transformed cells, more so when using the modified than the unmodified E7 gene. The simultaneous expression of some cytokines enhanced the immunizing potency of the non-replicating but not of the replicating recombinant *vaccinia* viruses.

(iii) DNA vaccines. DNA vaccines containing the E7 gene (wild or modified) are being examined. In agreement with the findings from other laboratories, the DNA vaccines were found to be effective both as preventive and therapeutic vaccines. Other results indicated the superiority of intradermal over intraperitoneal immunization. The modification of E7 gene and the simultaneous administration of genes encoding some but not other immunostimulatory factors resulted in enhancing the immunization effect. The single most important result was the demonstration that it was possible to modify the E7 oncogene in such a way as to get rid of its oncogeneticity without losing its immunization potency.

Various modifications of the above mentioned approaches are being tested to define optimal conditions for prime/boost strategy in the present system. Recently another project has been started at DEV aimed at developing experimental therapeutic vaccines for chronic myeloid leukaemia. The studies are carried out in a mouse model and the strategies used are similar to those described for the HPV-induced tumours.

Innovation Principle
New therapeutic method.

Achieved Stage
Laboratory experiments are running.

Application Area
Human medicine.

SEMI-SYNTHETIC PREPARATION OF ANTICANCER DRUG TAXOL AND ITS ANALOGUES.

RNDr. T. Vaněk, CSc., Institute of Organic Chemistry and Biochemistry AS CR

1. Semi-synthetic preparation of anticancer drug taxol.

Summary
The method for semi-synthetic preparation of taxol in semi-industry scale was developed.

Innovation Principle
New synthetic approach was utilized.

Achieved Stage
Finished, results ready for application.

Application Area
Pharmaceutical industry.

2. Preparation of taxol analogues.

Summary
The method for preparation of taxol analogues was developed.

Innovation Principle
New type of taxol analogues with better efficiency.

Achieved Stage
In progress, some compounds exhibit IC_{50} comparable with taxol.

Application Area
Pharmaceutical industry.

DETECTION OF PROTEOLYTIC ACTIVITY OF ASPARTIC PROTEASES SECRETED BY PATHOGENIC *CANDIDA SPP.* FOR CLINICAL DIAGNOSIS.

Ing. I. Pichová, CSc., Institute of Organic Chemistry and Biochemistry AS CR

Summary
The yeasts of the genus *Candida* are opportunistic pathogens associated with the increasing incidence of life-threatening infections in immunologically debilitated individuals. Secretion of aspartic proteinases has been determined as one of the virulence factors of the pathogenic *Candida* species. To analyze the secreted proteolytic activity of a large number of *Candida* clinical isolates, we have developed a screening system based on a solid medium containing haemoglobin as a sole nitrogen source. The cleavage of haemoglobin results in zones of clearance. The visibility of these zones can be enhanced by addition of acid-base indicator. Furthermore, some of the *Candida* strains display morphological changes on this medium.

Innovation Principle
The new method for detection of activity of proteases secreted by pathogenic *Candida spp.* was developed.

Achieved Stage
The method has been successfully tested in the clinical laboratory.

Partner Cooperation
Institute of Microbiology AS CR, Czech Republic; Faculty of Medicine, Palacký University, Olomouc, Czech Republic.

Application Area
The method can be used for the determination of the extracellular proteolytic activity of the *Candida* isolates and for rapid testing of aspartic proteinase inhibitors which can provide a basis for the development ofantimycotic drugs targeted to secreted proteinases.

SCREENING FOR PATIENTS SUFFERING FROM CELIAC DISEASE AND DEVELOPMENT OF A KIT FOR GLUTEN DETECTION IN FOOD.

Prof. H. Tlaskalová MD, DSc., Institute of Microbiology AS CR

Summary
Celiac disease or gluten enteropathy belongs to the immunologically based severe chronic diseases of the digestive tract which afflict both children and adults. In genetically predisposed individuals the disease manifests itself after ingestion of gluten-containing food. The treatment of celiac disease consists in a lifelong maintenance of a gluten-free diet. Recent research showed that the incidence of celiac disease is higher than expected - about 1:250. The disease may have atypical or even latent form, especially in older children and adults. A high incidence of lymphomas and other malignities is one of the most serious consequences of untreated or insufficiently treated celiac disease. Celiac disease is often combined with other chronic diseases - especially with autoimmune systemic diseases. The aim of the project is to screen for celiac disease in groups of risk patients suffering from autoimmune diseases or other diseases that are often combined with celiac disease or are its consequences by using serological examination of antigliadin antibodies and autoantibodies (directed against endomysium, tissue transglutaminase or calreticulin). One of the other aims of the project is to develop the immunoassay kit that could be used to determine the amount of gluten in food intended for patients on a gluten-free diet.

Innovation Principle
Detection of gluten in food for patients suffering from celiac disease presents problems. Imported foreign kits are prohibitively expensive for most of smaller food industry establishments. The development of a new kit will help to reduce the price of this important laboratory assay.

Achieved Stage
Finished project, the results are ready for application.

Cooperating Partners
Institute of Clinical Immunology, 1st Faculty of Medicine, Charles University, Czech Republic.

Application Area
Pharmaceutical industry, food industry.

THE USE OF TELOMERASE IN CANCER DIAGNOSTICS.

RNDr. J. Fajkus, CSc., Institute of Biophysics AS CR

Summary
Telomere biology can be dated since description of terminal chromosome sequences - telomeres, and consecutive characterization of the mechanism of their synthesis by "telomere terminal transferase" - telomerase - in 1985. Studies in the past decade have lead to the characterization of telomeres, telomerase and a number of telomere binding proteins in various organisms including human. Telomerase has been demonstrated to be necessary for infinite proliferation of cells (cellular immortality). It has been shown that telomerase functions as immortalizing factor also in cancer cells. Telomerase can thus be used both as tumour marker for diagnostics, and as a target for cancer therapy.

Laboratory of DNA molecular complexes of the Institute of Biophysics AS CR currently provides telomerase activity and expression measurements and analysis of telomere lengths *in situ* both for diagnostic and research purposes in collaboration with medical institutions in Brno within a frame of the research projects. However, it does not provide any commercial services; for routine use the techniques are being transferred to the medical institutions.

The use of telomerase in cancer diagnostics will be followed by introducing therapeutic approaches based on targeting telomerase in cancer cells. In parallel, controlled expression of telomerase for rejuvenating senescent cells and tissues in treatment of degenerative disorders and for transplantations will be a basis of cell and tissue engineering.

Innovation Principle
A new diagnostic tool.

Achieved Stage
Cancer diagnostics is finished project, ready for application. Use in the cancer therapy - running project.

Cooperating Partners
Medical Faculty Hospital, Brno, Czech Republic; Research Institute of Child Health, Brno, Czech Republic.

Application Area
Medicine.

NEW FERTILITY DIAGNOSTIC KITS.

J. Pěknicová, Ph.D., Institute of Molecular Genetics AS CR

Summary
Preparation of new monoclonal antibodies against human sperm proteins, *in vitro* production of monoclonal antibodies, development of diagnostic kits for human sperm pathology and assisted reproduction.

Innovation Principle
A new diagnostic tool based on new monoclonal antibodies.

Achieved Stage
Finished project.

Cooperating Partners
EXBIO Prague, Inc., Czech Republic.

Application Area
In human medicine, andrological laboratories, the laboratories of assisted reproduction.

DETECTION OF *TOXOPLASMA GONDII* IN CLINICAL MATERIAL BY PCR.

Prof. MVDr. I. Literák, CSc., University of Veterinary and Pharmaceutical Sciences, Brno

Summary
In the years of 1996 - 2000, 54 people (65 samples) were examined for the presence of *Toxoplasma gondii* agent. These people were suspected for toxoplasmosis (congenital, nodular, neural or ophthalmologic form) based on the serologic examinations. For detecting of *T. gondii* in samples, the biological experiment on the laboratory mice was used. In the year 1999, these biological experiments were supplemented with PCR with specific primers annealing to the *TGR1E* repetitive sequence (reaction conditions of type 1 and 2) and a "hemi-nested" PCR with primers annealing to the *B1* gene of *T. gondii*. DNA for PCR was isolated from parallel samples from every tissue examined. Out of 65 samples, 28 were examined by PCR only, 23 by biological experiment only and 14 by both methods. The amniotic fluids, placentas, vitreous humours, bloods, serums, cerebrospinal fluids and organs (liver, heart tissue, lung, spinal cord and spleen) were examined. The isolation experiments on mice were negative in all samples. The positive results in the single PCR with conditions 1, 2 and in the "hemi-nested" PCR were obtained in 48 % (n = 42), 76 % (n = 33) and 79 % (n = 33) of samples, respectively. So, the sequence and the reaction conditions used influenced the detection of *T. gondii* by PCR. The PCR (sequences *B1* and *TGR1E* with second type of reaction condition) is suitable method for the detection of *T. gondii* in the clinical materials in contrast to the biological experiment on laboratory mice. PCR is suitable method for quick, specific and sensitive laboratory diagnosis of toxoplasmosis in men.

Innovation Principle
New laboratory test for detection of toxoplasmosis.

Achieved Stage
Finished laboratory testing, ready for application.

Application Area
Human medicine.

VACCINE AGAINST LYME DISEASE AND LABORATORY DIAGNOSTIC METHODS OF THE DISEASE.

Prof. RNDr. L. Grubhoffer, CSc., Institute of Parasitology AS CR

Summary
The vaccine against Lyme disease used in the USA cannot be used in Central Europe, because the spectrum of causative agents is different in this region. With cooperation of the research team from the USA a vaccine against Lyme disease is being developed with respect to the species complex of its causative agent *(Borrelia burgdorferi sensu lato)* in Central Europe. The candidate antigens are recombinant molecules of the surface components of *borrelia*, OspA and OspC, or their chimeras. At the same time attention is focused on laboratory diagnostics of Lyme disease, namely in the area of immunochemical techniques and methods of molecular biology: preparation of hybridomas producing monoclonal antibodies against the surface antigens of *borrelia* and their utilization in the EIA tests; a set of PCR reactions with the panel of primers enabling the identification of species of *borrelia* in ticks and patient sera.

Innovation Principle
A completely new type of vaccine useful in Central Europe will be developed.

Cooperating Partners
State University of New York, Stony Brook, NY, USA; Brook Biotechnologies, Inc., USA

Achieved Stage
The appropriate hybridomas and monoclonal antibodies have been prepared. After the laboratory tests will be finished, preclinical tests will follow.

Application Area
Medicine.

SANDWICH ELISA FOR OSTEOARTHRITIS SCREENING AND FOR PROGNOSIS OF ITS PROGRESSION.

RNDr. V. Vilím, CSc., Institute of Rheumatology, Prague

Summary
Osteoarthritis is a common disease, causing pain and disability in a significant proportion of the adult population. It is characterized by the progressive destruction of articular cartilage and concomitant changes in subchondral bone. A great effort has been focused on developing assays for "molecular markers" namely cartilage derived macromolecules or their fragments whose release into the circulation from the joint may reflect disturbances in the joint tissue turnover. A particular need has been to develop the test to sensitively detect the initiation and to predict the progression of osteoarthritis.

Cartilage oligomeric matrix protein/thrombospondin 5 (COMP/TSP 5) is one of the most promising serologic markers with regard to the ability to predict development of osteoarthritis. Our laboratory has developed a panel of monoclonal antibodies to human COMP. To evaluate the prognostic utility of serum COMP level measured with a new sandwich ELISA clinical study using 48 patients has been performed. The study has shown that serum COMP has the potential to be a prognostic marker of the disease progression. High COMP levels, persisting in the patients with radiographic progression over the 3-year study period, indicated differences in disease activity detectable throughout the entire follow-up interval. Serum COMP levels show strong correlation with radiographic osteoarthritis status. COMP level may aid in identifying groups of patients at risk of faster disease progression and in differentiating groups of patients during clinical studies and drug trials.

Innovation Principle
New monoclonal antibodies were prepared. The test allows identification of patients endangered of the fast disease progression.

Achieved Stage
Development in the laboratory has been finished; clinical study using 48 patients has been performed.

Application Area
Human medicine, pharmaceutical industry.

NEW MONOCLONAL ANTIBODIES FOR USE IN RESEARCH AND CLINICAL PRACTICE.

Prof. V. Hořejší, Ph.D., Institute of Molecular Genetics, AS CR

Summary
A series of anti HLA-G antibodies (utilization in oncology and molecular biology research and potentially in clinical diagnostics); antibodies against leukocyte surface molecules (CD46, CD44, CD63; utilization in haematology and oncology research); antibodies against signalling proteins (TRIM, SIT, PAG, Daxx; utilization in biology research).

Innovation Principle
A hybrid technology, new monoclonal antibodies.

Achieved Stage
Finished project, the results are ready for application.

Application Area
Medical diagnostics, research.

COMPOSITE SKIN FOR HEALING OF BURNS AND OTHER SKIN DEFECTS - CULTIVATION OF PRIMARY HUMAN KERATINOCYTES ON *XENODERMIS.*

E. Matoušková, Ph.D., Institute of Molecular Genetics AS CR

Summary
Human allogenic or autologous skin epidermal cells are cultivated together with lethally irradiated 3T3 cells (these do not divide but produce a number of growth factors) on acellular pig *xenodermis* (pig dermis). The dermis serves for transport of keratinocytes and simultaneously provides the system with biomechanical properties of normal skin (consistence, adhesiveness, haemostatic effect, easy handling). The "composite skin" is applied with keratinocytes facing the wound; the dermis forms the outer protective layer. The system displays a strong stimulatory effect on wound healing.

Innovation Principle
In contrast to the *in vitro* cultured simple epidermis, keratinocytes are cultured and applied to the wound on a delivery system with skin properties.

Achieved Stage
Finished project, the results are ready for application.

Application Area
Pharmaceutical industry, medicine.

POLYMER CARRIER FOR CULTIVATION AND SUBSEQUENT TRANSPLANTATION OF SKIN CELLS IN EXTENSIVE SKIN DEFECTS.

Ing. J. Vacík, CSc., Institute of Macromolecular Chemistry AS CR

Summary
Extensive skin defects caused by burning or long-term bedsore are a serious medical problem. They may cause death or permanent disability of the patient. Large skin injuries lead to great loss of fluids, infection risks or even total sepsis. The patient's own skin is the only permanent replacement of the injured skin. However, this source is very limited.

We have developed a new way of skin injury treatment. It is based on transfer of cultured skin cells (keratinocytes) to the defect on the surface of special polymer carriers. Fibroblasts as auxiliary cells with blocked division capability are first cultured on the surface of the polymer carrier. These cells allow adherence and initial growth of keratinocytes. After some time, the fibroblasts die off and the polymer carrier with propagated keratinocytes is applied onto the burn or bedsore so that keratinocytes are in contact with the injury. The keratinocytes leave the carrier and colonize the injury surface producing at the same time growth factors which stimulate healing. In addition, the polymer carrier covers the wound and favourably affects the microclimate in the injury area.

The selection of polymer carrier is limited by strict conditions such as good biological tolerance, practically no toxicity and irritability for tissues, sufficient adhesion of cells to its surface and, at the same time, the ability of the cell layer to be easily detached from the carrier after colonization of the injury area. After a number of studies the lightly crosslinked poly(2-hydroxyethyl methacrylate) was selected as the most suitable polymer carrier for cultivation and transplantation of keratinocytes.

Innovation Principle
The material based on poly(2-hydroxyethyl methacrylate) is advantageous for several reasons. It has been used in medicine for more than 40 years without any side effects and has served as a standard in studying biocompatibility of other polymer materials. Hydrogels, to which it belongs, are generally little adhesive and not very suitable for cell cultivations. However, we have been successful in developing an effective method for cultivation of keratinocytes on these carriers. In addition, after the application to the injury surface, the hydrogel carrier forms an optimal cover for attachment of transplanted keratinocytes. It contains nearly 40 per cent of aqueous phase (i.e. cultivation medium with antibiotics). Thus the nutrition of cells and their protection from

infection is ensured for the initial period after the application. For treatment of patients, it is possible to use either their own cultured epithelium or that from tested donors. In the former case, taking of skin sample minimally embarrasses the patient and, at the same time, his own keratinocytes are capable of creating the definite cover even on the areas that cannot heal spontaneously. In the latter case, stocks of frozen cells make the preparation of grafts less time-consuming and the donor keratinocytes stimulate spontaneous healing.

Achieved Stage
Clinical testing is being performed on a limited scale.

Cooperating Partners
The First and Third Faculties of Medicine, Charles University, Prague, Czech Republic.

Application Area
Medicine, particularly treatment of extensive skin defects.

NANOSTRUCTURAL CERAMIC MATERIAL FOR JOINT AND BONE REPLACEMENTS.

Prof. RNDr. J. Cihlář, CSc., Institute of Materials Engineering, Brno

Summary
Synthesis and properties of nanometric one- and multicomponent oxide powders and colloidal sols on the base of alumina, zirconium and titanium have been studied in our laboratory. Ceramic powders of high purity, chemical homogeneity, narrow particle size distribution and defined shape were prepared by chemical "sol-gel" methods from ionic and non-ionic precursors. Sol-gel syntheses are perspective for the development of large-scale preparation of multicomponent nanometric powders. The availability of the nanometric ceramic particles with high stage of homogeneity will stimulate the development of new methods of forming and fabrication of nanoceramics.

The nanocrystalline ceramic has superior mechanical properties, good biocompatibility, bioactivity, and no toxicity making it useful as biomaterial in human medicine. The most promising is their use in orthopaedics as artificial bone and joint replacements or in dentistry as dental implants. Artificial replacements fabricated from nanocrystalline ceramic will benefits from its superplasticity, diffusion bonding ability, and/or high fracture toughness.

Innovation principle
The new type of material for use in medicine.

Achieved Stage
Project in progress.

Application Area
Medicine: joint and bone replacements, dental implants.

NEW METHOD OF PRODUCTION OF D-ARABINOSE.

Ing. V. Jiřičný, CSc., Institute of Chemical Process Fundamentals AS CR

D-Arabinose is a monosaccharide used in pharmaceutical industry as a starting material for production of B12 vitamin, preparation of special antibiotics and cytostatics. We have developed method of D-Arabinose production which is based on degradation oxidation of salts or derivatives of D-gluconic acid without oxidizing agents or catalysts. The reaction proper is carried out electrochemically on the surface of fluidising particles.

Innovation Principle
With respect to chemical oxidation the proposed process exhibits high yield and selectivity of the oxidation where no substances are introduced into the reaction mixture and so subsequent isolation of D-Arabinose is markedly simplified resulting in low running costs. The process exhibits extremely high production capacity per unit volume resulting in lowering of investment costs. No ecological damages by side products are produced.

Achieved Stage
Pilot plant production line (production capacity 0.3 kg D-Arabinose /hour, one metric ton per year) consisting of fluidised bed electrochemical reactor and subsequent separation process has been developed and operated in Agrokombinat Slušovice (Czechoslovak manufacturer) in 1989.

Cooperating Partners
Research Institute for Pharmacy and Biochemistry; Agrokombinat Slušovice, Czech Republic.

Application Area
Pharmaceutical industry.

SYNTHESIS OF ENDOPEPTIDASE-RESISTANT ANALOGS OF INSULIN AND [8-D- ARGININE]DEAMINOVASOPRESSIN (DESMOPRESSIN, dDAVP).

RNDr. T. Barth, DrSc., Institute of Organic Chemistry and Biochemistry AS CR

1. Synthesis and purification of tri- and tetrapetides of the carboxyterminal sequence of human insulin.

Summary
The peptide hormone insulin plays an important role in the regulation of many metabolic processes in animals and humans. It is essential that the structure of the molecule is intact in order to have this effect.
The B23-B30 (especially the B23-B25 and B23-B26) sequence of the peptide chain is the most vulnerable.
A series of tri- and tetrapeptides with peptide bonds protected against degradation was prepared by solid phase synthesis. The peptides were freed from the resin, purified by HPLC and characterized by MS, CEZ and amino acid analysis.

Innovation Principle
Analogues of insulin with truncated carboxy chain (sequence B23-B25 or B26) possess a similar insulin activity as the natural insulin. The N-methylation of some bonds enhances their metabolic stability.

Achieved Stage
Finished project, the results are ready for application.

Cooperating Partners
Institute of Animal Physiology and Genetics AS CR, Czech Republic; Institute of Experimental Endocrinology SAV, Bratislava, Slovakia.

Application Area
The peptides can be used for preparing semi synthetic truncated analogues of human insulin that are more resistant to degradation. **Commercial offer:** The laboratory methods, documents, technical assistance during the preparation of the substances and their purification, inclusions in the catalogues of fine chemicals.

2. Synthetic analogues of [8-D-arginine]deaminovasopressin (Desmopressin, dDAVP).

Summary
The synthetic analogue of vasopressin, Desmopressin, is successfully used in the substitution therapy of diabetes insipidus. The regulation of water reabsorbing in the kidneys of patients with this illness is disturbed. During the 30 years that this compound has been used, various pharmaceutical forms have been developed, including injections, nasal sprays and the currently used tablets. When it is taken in the form of tablets, the peptide is more exposed to the enzymatic degradation and only about 1% of the dose applied reaches the kidney receptors. Desmopressin analogues have been prepared that are resistant to endopeptidase cleavage both at the N- terminal and the C-terminal part of the peptide chain. The analogues have some antidiuretic activity when applied subcutaneously.

Innovation Principle
A more stable molecule of the Desmopressin analogue with antidiuretic activity that could be applied orally.

Achieved Stage
Finished project, the results are ready for application.

Cooperating Partners
Institute of Medical Physiology, Copenhagen University, Copenhagen, Denmark.

Application Area
Pharmaceutical industry, medicine.

STEVIA REBAUDIANA AS A SOURCE OF NATURAL NON-ENERGETIC SWEETENER, STEVIOSIDE.

RNDr. T. Vaněk, CSc., Institute of Organic Chemistry and Biochemistry AS CR

Summary
The possibility of cultivation of *Stevia rebaudiana* in area of the Czech Republic as well as potential utilization of dry biomass and isolated stevioside was studied.

Innovation Principle
In contrast to the widely used aspartame, stevioside is thermostable. Because of its high concentration in plant (up to 11%) there is potential for direct use of dry biomass e.g. in tea mixtures.

Achieved Stage
Finished project, the results are ready for application.

Cooperating Partners
Czech Agricultural University, Czech Republic.

Application Area
Food industry.

DEVELOPMENT OF THE VACCINE AGAINST *COCCIDIOSIS* IN RABBITS.

RNDr. M. Pakandl, CSc., Institute of Parasitology AS CR

Summary
Coccidiosis is one of the most important diseases in domestic rabbits. The most used method of its prevention is still the use of anticoccidics; however, this brings many disadvantages, above all the rise of resistance. A living, attenuated vaccine produced by BIOPHARM has been successfully used in chickens. Vaccination is also a promising possibility in rabbits. In France (INRA, Tours) attenuated lines of four species have been prepared so far. However the attenuated line of the most pathogenic species *Eimeria flavescens* has not yet been obtained in any laboratory in the world. The acquisition of the attenuated line of this species is crucial for future development of a living attenuated vaccine.

The aim of the project is to obtain a pure strain of *E. flavescens,* to derive an attenuated line of it and to compare its basic characters (prepatent period, duration of sporulation, oocyst morphology and endogenous development) with those of the original strain and then construct a vaccine against *coccidiosis* and bring it in the distribution. The partner will participate in the development of the vaccine and it is also a potential user of the vaccine - the producer and the distributor. We assume that the vaccine will be used by the breeders of rabbits, according to the tradition mainly in small breeds, but also in large-scale breeds.

Innovation Principle
New vaccine.

Achieved Stage
A pure strain of *E. flavescens* was obtained and its endogenous cycle was studied (finished). Further research is being done on its attenuation with two different methods; the results are expected to be obtained in 2002. At the same time a pure strain of *E. piriformis* which was obtained from the French laboratory (INRA - PAP, Tours) is being attenuated. There are also some successful preliminary results of vaccination of animals with attenuated lines of *E. magna* and *E. media.*

Cooperating Partners
BIOPHARM, Research Institute of Biopharmacy and Veterinary Drugs, Czech Republic.

Application Area
Agriculture, veterinary medicine.

POLYMER CONJUGATES OF LECIRELIN AND CLOPROSTENOL WITH PROTRACTED EFFECT FOR USE IN VETERINARY MEDICINE.

Doc. Ing. K. Ulbrich, DrSc., Institute of Macromolecular Chemistry AS CR

Summary
The preparations that have been used so far in order to influence the reproductive cycle and to treat pathological states of reproductive organs in farm animals are mostly low-molecular-weight peptides or hormones (i.e. natural neurohormone GnRH or its synthetic analogue lecirelin and natural prostaglandin cloprostenol or its synthetic derivatives). A serious drawback of these hormones is their rapid elimination from blood circulation by glomerular filtration or by enzymatic degradation. Therefore the hormones have only short time of action resulting in relatively low efficacy of oestrus induction and a low birth rate of farm animals. By conjugation of lecirelin and cloprostenol with polymer carrier (hydrophilic synthetic copolymers of N-(2-hydroxypropyl)methacrylamide, high-molecular-weight water-soluble preparations were obtained exhibiting not only higher stability after administration but also higher specificity of the effect and markedly prolonged action. Thus the active hormone is much more effectively utilized after the administration as the conjugate in comparison to the administration of the hormone alone. Consequently, induction of breeding may be much improved.

Innovation Principle
New veterinary drugs with protracted effect were developed which enable to influence the reproductive cycle and oestrus induction as well as the induction of delivery of farm animals, particularly cows, sheep, and goats. The drugs are effective in the treatment of pathological states of reproductive organs of the above animals as well.

Achieved Stage
The efficiency of these conjugates was tested on sufficiently large groups of farm animals. Laboratory synthesis and, subsequently, also production technology of the preparations were managed in amounts sufficient for use in few hundreds of animals.

Cooperating Partners
Research Institute of Biopharmacy and Veterinary Drugs Co. Pohoří-Chotouň, Jílové u Prahy (Biopharm Co.), Czech Republic. The project was funded by the Léčiva Co., Prague, Czech Republic.

Application Area
Veterinary medicine.

NOVEL INSECTICIDAL COMPOUNDS AGAINST THE TERMITES BASED ON JUVENOGENS.

RNDr. B. Bennettová, CSc., Institute of Entomology AS CR

Summary
Search for new compounds of high activity on a broad spectrum of insect pests. Selection of the most promising compounds in laboratory assays and their testing in the field.

Innovation Principle
New method of termite control.

Achieved Stage
Laboratory tests are finished; preparation of a larger amount for the field tests has been initiated.

Cooperating Partners
Institute of Organic Chemistry and Biochemistry AS CR, Czech Republic; CSIRO, Australia. Selected juvenogen will eventually be produced commercially by the company Chemispol, Kutná Hora, Czech Republic.

Application Area
Protection of wooden buildings against termites, possibly also use in plant protection.

IMMUNOCHEMICAL DETECTION OF FUNGI PATHOGENS *PHYTOPHTHORA FRAGARIAE* AND *COLLETOTRICHUM ACUTATUM* IN STRAWBERRY.

RNDr. J.Krátká, Dr.Sc., Research Institute of Crop Production, Prague

Summary

Phytophthora fragariae and *Colletotrichum acutatum* are quarantine fungi pathogens of strawberry. According to EPPO they occur in Central Europe, namely in Germany and Austria, but the pathogens have the potential of spreading to all neighbouring countries where strawberry is cultivated. Although both pathogens are currently absent in the Czech Republic, they are included in the List of Quarantine Pests to prevent their introduction. To detect the pathogens in a host, EPPO recently recommended biological, immunochemical and molecular methods. For their detection in the latent stage, it is very important to use rapid and sensitive methods.

Two polyclonal and two monoclonal species-specific antibodies were prepared to detect *Phytophthora fragariae*. Laboratory rabbits and mice were immunized using purified and non-purified protein extracts from the mycelial mass of the pathogen. The antibodies did not cross-react with other important fungi pathogens of strawberry, such as *Botritis cinerea, Colletotrichum acutatum, Fusarium* sp. and *Verticillium albo-atrum*. PTA-ELISA was used to test the antibodies. Monoclonal antibodies are now being prepared in large scale and tested in collaboration with EXBIO Corporation in order to prepare the diagnostic kits. *P. fragariae* was detected in artificially infected strawberries (cultivars Elsanta, Vanda, Kama) using PTA-ELISA, immunoprinting and dot blot. Detection of the pathogen was optimal in undamaged roots or roots with necrotic tips only. At the later stage of infection, when whole roots are necrotic, the crown was more suitable for successful detection.

Four polyclonal and two monoclonal antibodies to detect *Colletotrichum acutatum* were prepared and tested. Purified antigens (protein extracts) were used for immunization of laboratory rabbits and mice. Antibodies did not cross-react with several other fungal pathogens of strawberry *(Phytophthora fragariae, P. cactorum, Botrytis cinerea, Verticillium albo-atrum, Pythium ultimum)*. PTA-ELISA, dot blot, immunoprinting and immunofluorescent microscopy were used to test the specificity and sensitivity of the antibodies. After artificial infections of strawberry (cultivars Elsanta, Vanda, Kama), *Colletotrichum acutatum* was detected by PTA-ELISA and immunoprinting in roots, crowns, petioles and fruits in the latent stage of the disease.

To detect both pathogens at the early stages of infection, at least two of the immunotechniques described above should be used.

Innovation Principle
New mono- and polyclonal antibodies.

Achieved Stage
The antibodies have been prepared and tested. The kit is being developed.

Cooperating Partners
EXBIO Corporation, Prague, Czech Republic.

Application Area
Agriculture.

DETECTION OF HERBICIDE RESIDUES IN SOIL AND WATER USING PHOTOSYNTHETIC BIOSENSORS.

J. Masojídek, MSc., PhD., Institute of Microbiology AS CR

Summary
Herbicide residues present in soil cause many problems to the environment and to humans. Some slowly degradable chemicals can accumulate in the soil and consequently in plant products. Movement through the soil layers and penetration to the groundwater is an environmentally important characteristic of the herbicide residues. The photosynthetic biosensor is based on an isolated photosystem 2 complex immobilized on a printed Pt/Ag-AgCl mini-electrode placed in a flow-through vessel. The aim of the project is to adapt the present laboratory biosensor for measurement of herbicide residues in soil extracts and liquid samples.

Innovation Principle
Compared to physical-chemical methods of herbicide assay the biosensor measurement provides information on the actual biological effect of herbicides. Detection using electrochemical biosensors based on photosystem 2 offers faster and cheaper preliminary test for herbicides (compared to the classical chemical analyses) with the possibility of field use.

Achieved Stage
The device should be tested in agricultural practice.

Cooperating Partners
Institute of Agriculture Ltd., Kroměříž, Czech Republic; Palackého University, Olomouc, Czech Republic.

Application Area
Agriculture, fishing, nature protection.

PHYTOREMEDATION, THE NEW APPROACH TO ENVIRONMENT REMEDIATION.

RNDr. T. Vaněk, CSc., Institute of Organic Chemistry and Biochemistry AS CR

Summary
Selected plants are utilized for removal of xenobiotics (organic compounds, toxic metals, radionuclides) from contaminated soil and water.

Innovation Principle
In comparison with chemical and/or physical methods, phytoremediation is less harmful to the environment and generally less expensive. Its public acceptance is considerably higher than that of "traditional" methods.

Achieved Stage
In progress, in some aspects ready for application.

Cooperating Partners
Agritec, University of Pardubice, Czech Republic; Institute of Experimental Botany AS CR, Czech Republic; European cooperation in the frame of COST 837 Action.

Application Area
Environment remediation, cleaning of polluted soils and waste-waters.

DEVELOPMENT OF A NEW SORBENT FOR REMOVAL OF AMMONIA FROM AIR.

RNDr. M. Kočiřík, CSc., J. Heyrovský Institute of Physical Chemistry AS CR

Summary
World emissions of ammonia are estimated to 25 to 35 mil ton/year. Its presence in the environment is considered to be harmful and ammonia emissions are liable to regulations. For this reason, new types of sorbents for ammonia abatement have been developed, based on the natural zeolite Clinoptilolite impregnated with different inorganic acids. The sorbents are designed for fixed bed adsorbers to remove ammonia from waste air. No thermal activation is required before application and the spent sorbents can be likely used as soil conditioners and fertilizers.

Innovation Principle
Use of the natural Clinoptitolite which after impregnation gives ammonia sorbents with a sorption capacity comparable to that of special active carbons developed for ammonia removal.

Achieved Stage
Registered utility model No. PUV 2001-1238 has been awarded. We are now testing the compatibility of the spent sorbent with plants.

Cooperating Partners
Institute of Chemical Technology, Prague, Czech Republic.

Application Area
Environmental protection, agriculture.

NEW MATERIALS FOR CATALYTIC AND SORPTION PROCESSES: DEVELOPMENT OF ADSORBENTS FOR REMOVAL OF MALODOROUS COMPOUNDS.

Ing. A. Zukal, CSc., J. Heyrovský Institute of Physical Chemistry AS CR

Summary
Development of new adsorbents based on chemically and structurally modified silica gels which exhibit an excellent performance in adsorption/blocking of malodorous compounds.

Innovation Principle
A general method was invented enabling to obtain adsorbents based on inorganic oxides such as silica gel, which yield either enhanced selectivity towards one or several groups of target molecules according to the requirements of application (such as organic acids, organic bases, organic heterocompounds), or a very high general activity towards a broad range of organic compounds (universal adsorbent). The new adsorbents have performance characteristics substantially surpassing those of known standard materials such as active carbon, zeolites and active inorganic oxides. In addition, the developed materials are inexpensive, non-toxic and friendly to the environment and their industrial production does not require substantial investments.

Achieved Stage
Finished project, the results are ready for application. The invention is protected by the following European patent application: J. Rathouský, A. Zukal et al: Doped adsorbent materials with enhanced activity, European Patent Office, Application No. 01119181.4-2104.

Cooperating Partners
Procter & Gamble Co., USA.

Application Area
Environmental protection.

BIODEGRADATION TECHNOLOGIES FOR DECONTAMINATION OF SOIL AND WATER FROM OIL AND OIL PRODUCTS AND OTHER POLLUTANTS.

M. Sobotka, MSc., Institute of Microbiology AS CR

Summary
Technologies based on monocultures or mixed bacterial cultures are optimized in the composition of the medium, C-sources, cultivation conditions, composition and concentration of pollutants. Technologies of preparation of active lyophilizates are being designed. The technologies are applicable in the on-site and in-situ regimes. Biofilters with cells bound on carriers are designed for gas pollutants. New technologies with mixed bacterial population with proleolytic, amylolytic and lipolytic activity are utilized in the cleansing of wastes from fats, organic compounds and in the process of waste liquefaction in pits.

Innovation Principle
New biodegradation technologies.

Achieved Stage
Finished project. The results are used in many polluted localities in the Czech Republic (oil industry, coke industry, heavy engineering, etc.).

Cooperating Partners
Bioasan Prague Ltd.; Envisan GEM Prague Ltd.; Dekonta Kladno Inc.; G - Service Prague Ltd.; BIO-GEO-EKO Brno Ltd.; SCHB Prague Ltd.; Eveco Prague Ltd., Czech Republic.

Application Area
Cleaning of polluted soils and water.

PHOTO(ELECTRO)CATALYTIC DECONTAMINATION OF WATER USING SOLAR ENERGY.

RNDr. J. Ludvík, CSc., J. Heyrovský Institute of Physical Chemistry AS CR

Summary
Electrochemical, photocatalytic, photoelectrocatalytic and sonoelectrochemical oxidative degradation of the phenylurea herbicide Diuron has been studied and mutually compared. It has been found that its photoelectrochemical oxidation on illuminated TiO_2 layers polarized by external potential in aqueous media and homogeneous photocatalysis on quantum-size Q-TiO_2 particles leads to the consecutive oxidative demethylation at the side-chain, whereas photochemical and photoelectrochemical treatment in aprotic solution results in oxidation of the benzene ring and dechloration. A detailed kinetic scheme was suggested and proved. On the other hand, the (sono)electrochemical oxidation causes dimer formation.

Innovation Principle
The fate of phenylurea herbicides in the soil as well as in the water was investigated only from the analytical point of view, in order to monitor the presence of these xenobiotics. Our project is the active approach to the environmental protection - how to decontaminate the water using cheap and environmentally friendly photocatalysts and renewable energy.

Achieved Stage
The research in small scale (i.e. under laboratory conditions - illumination by UV lamps) is finished in the case of the herbicide Diuron. Now, it would be useful to continue in large scale using the solar energy.

Cooperating Partners
Department of Inorganic Technology, Institute of Chemical Technology, Prague, Czech Republic.

Application Area
Purification of drinking water, detoxification of surface waters in agriculture.

AMARANTH - www.medis.cz/ateko

Research and development, projection and commercial use of technologies for amaranth processing. Production of amaranth mixtures, extrudates, flour (gluten-free), bakery and fractions (fibre and oil with squalene).

BAXTER - www.baxter.cz

Biopharmaceuticals for blood coagulation, haemodialysis, and infusion sets, vaccinations, immunoglobulin.

BIOPHARM - www.biopharm.cz/

Distribution of veterinary and human drugs.

BIOVENDOR - www.biovendor.cz

Development and distribution of RIA and ELISA kits, mono and polyclonal antibodies, diagnostics for microbiology.

CLONESTAR - www.clonestar.cz

Peptide synthesis and modification, hybridomas, mono and polyclonal antibodies.

DIAGENES s.r.o. - www.diagenes.cz/

Development and distribution of diagnostic kits for human medicine, bio products for research laboratory.

ENVISAN-GEM - www.envisan.cz

Biological decontamination of soil and water, remediation *ex situ* and *in situ*

EXBIO Praha a.s. - www.exbio.cz

Development, production and distribution (bulk quantities, OEM-based supply) of monoclonal antibodies for immunology, cell biology and virology.

GENEAGE technologies - www.geneagetech.com/

Recombinant protein production, services for molecular biology and genomics, DNA arrays and DNA sequencing.

IMMUNOTECH a.s. - www.immunotech.cz/

Biggest producer of immunodiagnostics in the Czech Republic with its own research and development unit. Development and distribution of RIA and ELISA kits, production of monoclonal antibodies.

IVAX Opava - www.ivax-cr.com/

The second largest pharmaceutical company in the Czech Republic (formerly known as Galena) who develops and produces drugs for human medicine (Final Dosage Forms and Active Pharmaceutical Ingredients). The company recently received the approval by FDA for production of Active Pharmaceutical Ingredients and Non-sterile Final Dosage Forms for the U.S. market.

LONZA - www.lonzabiotec.cz/

Biotransformation and distribution of L-carnitin.

MEGA - www.mega.cz/

Biodegradation of pollutants, decontamination of water and soil. Manufacturing and application of encapsulated microbial and plant cells (patented technology), cell particles and immobilized enzymes.

TOP-BIO - www.top-bio.cz

Production and distribution of reagents for molecular PCR, DNA amplification and RNA isolation.

VIDIA s.r.o. - www.vidia.cz/

Research, development and production of immunological preparations. Diagnostics for human medicine: Immunodiagnostics, kits for detection of herpes viruses, ELISA kits.

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Technology Centre AS CR

Address: Rozvojová 135, 165 02 Prague 6, Czech Republic
Phone: +420 220 390 700
Fax: +420 220 922 698 or + 420 220 921 217
E-mail: vanecek@tc.cas.cz
WWW: http://www.tc.cz