

FACULTY OF PHARMACY

MEDICAL UNIVERSITY OF WARSAW

MASTER THESIS PROJECTS - PROPOSALS FOR ERASMUS+ STUDENTS

ACADEMIC YEAR 2021/22

Biosynthesis of immunoactive Selenium-containing polysaccharides in mycelial cultures of medicinal mushroom

***Lentinula edodes* (Berk.) Pegler**

Department of Drug Technology and Pharmaceutical Biotechnology

Supervisor

Jadwiga Turło, PhD, Full Professor

Short Description

The objective of the proposed project is to use biotechnological methods for biosynthesis of not described in the scientific literature macromolecular compounds – β -glucans containing atoms of selenium introduced into their structure.

Designed Se-containing polysaccharides will be isolated from the mycelial cultures of *Lentinula edodes* cultivated in media enriched with selenium compounds. Described in the scientific literature mushroom-derived polysaccharides, especially β -glucans display anticancer activity which results from their immunostimulating properties. A trace element of fundamental importance to human health, selenium (Se), has been shown to possess an analogous function with respect to the immune system. The mechanism by which selenium exerts anticancer and immunomodulating activity differs from that of *L. edodes* polysaccharide fractions, but a similar pharmacological effect suggests a possible synergism of these two agents.

The project is a continuation of the research conducted in Department of Drug Technology and Pharmaceutical Biotechnology of Medical University of Warsaw, supported by grant of the National Science Centre in Poland.

Synthesis of small-molecular peptidomimetics for drug discovery purposes

Department of Drug Technology and Pharmaceutical Biotechnology

Supervisor

Maciej Dawidowski, PhD

Short description

Peptidomimetics are chemically-derived compounds that mimic the spatial orientation of peptide side chains. This class of compounds has received much attention due to their proper pharmacokinetic and ADME profiles, which makes them potentially useful in therapy.

This project aims in synthesis of small-molecular, highly constrained peptidomimetics as protein-protein interaction (PPI) inhibitors or G-protein coupled receptor (GCPR) ligands.

The project will involve **synthetic medicinal chemistry**: design and execution of chemical pathways leading to a number of chiral scaffolds. This will be done *inter alia* by using multicomponent reactions and peptide bond formation methods. Finally, the compounds will be characterized (NMR, IR, MS) and assayed for their chemical purity (NMR, LC/MS).

New small molecular compounds as potential treatments against drug-resistant epilepsy

Department of Drug Technology and Pharmaceutical Biotechnology

Supervisor

Maciej Dawidowski, PhD

Short description

Epilepsy is a major neurological disorder affecting 65-70 mln people globally. Despite the significant improvement in efficacy and safety of pharmacotherapy of epilepsy, still an adequate seizure control can be achieved in only 70% of patients. This is a high failure rate and in view of physical, social and psychological consequences of uncontrolled seizures, the need of new agents to combat refractory epilepsy is vital.

The project aims in design and synthesis of novel small-molecular compounds with potential anticonvulsant activity. It will employ modern **synthetic medicinal chemistry** approaches and purification techniques. The synthesized compounds will be evaluated for their chemical structure and purity, using various analytical methods (NMR, IR, LC/MS).

Design and synthesis of novel compounds against Trypanosoma-related tropical diseases

Department of Drug Technology and Pharmaceutical Biotechnology

Supervisor

Maciej Dawidowski, PhD

Short description

African Sleeping Sickness and *Chagas* disease are the major neglected tropical diseases, caused by *Trypanosoma brucei* and *Trypanosoma cruzi* parasites, respectively. These diseases are lethal when not treated properly, and the current drugs are toxic and ineffective in majority of cases.

This project aims in design and synthesis of small-molecular compounds that target the parasite's *Achilles heel* – the glycosomal import of matrix proteins. This will involve design and execution of chemical pathways using *state-of-the-art* medicinal chemistry methods. The synthesized compounds will also be characterized (NMR, IR, MS) and assayed for their chemical purity (NMR, LC/MS).

Synthesis, characterization and application opportunities of the innovative thermosensitive liquid suppositories composed of a biodegradable micro- or nanocarrier system for hypertension therapy

Department of Biomaterials Chemistry

Supervisor

Ewa Oledzka, PhD Eng., Assoc. Professor

Short Description

An interesting group of macromolecules applied in the production of materials for medicine and pharmacy are biodegradable polymers, used in controlled drug release, tissue engineering, etc. From the medical point of view of particular importance are polymers used in so-called therapeutic systems, dosing or releasing drugs with a programmed rate.

Therefore, the objective of the proposed project is the studies under development of innovative formulation of β -blocker in the form of thermosensitive liquid suppositories composed of a biodegradable micro- or nanocarrier system for hypertension therapy. This

dosage form may be suitable for non-cooperating and unconscious patients or patients with esophageal problems, but also for patients with digestive problems as well as people with mental or metabolic disorders. The novelty of these findings relies on using new and branched biodegradable matrices with different microstructure as an efficient solution for the modification of antihypertensive drug-release properties. The developed thermosensitive liquid suppositories composed of micro- and nanocarriers with a well-defined microstructure, can be practically applied as “long-”, “medium-”, or “short-term” controlled delivery systems.

Synthesis and physicochemical analysis of mesopores silica (SBA-16) /hydroxyapatite composite - a potential new drug delivery system

Department of Analytical Chemistry

Supervisor

Łukasz Pajchel, PhD

Short Description

- synthesis of mesopores silica (SBA-16);
- synthesis of SBA-16 /hydroxyapatite composite;
- analysis of the structure, chemical composition and physicochemical properties of the composite ((PXR, FT-IR spectroscopy, Raman, ssNMR, and TEM microscopy);
- loading the two model drugs substance into the obtained composite;
- Investigation of the kinetics of the drugs release from the obtained composite;

Synthesis, structural characterization and pharmaceutical studies of new forms of selected anticancer drugs

Department of Biomaterials Chemistry

Supervisors

Edyta Pindelska, PhD, DSc, Medical University of Warsaw / Prof. Izabela Madura PhD, DSc, Eng., Warsaw University of Technology

Short Description

The aim of this project is to test the possibility of creating pharmaceutical cocrystals of selected sparingly soluble pharmaceutically active substances (APIs), drugs: psychoactive or anticancer, as well as their structural, physicochemical and pharmaceutical characteristics. Each of these classes of compounds is part of the most current research area around the world, and selected test compounds have not been systematically tested for cocrystal formation. Preparation of co-crystals may allow obtaining a new form of the drug with improved physicochemical and pharmaceutical properties compared to the pure compound

NMR and HPLC for the Profiling Extracts of Natural Product

Department of Physical Chemistry

Supervisors

Katarzyna Paradowska, PhD, Assoc. Professor / Agnieszka Zielińska, PhD / Paweł Siudem, PhD

Short Description

Nuclear magnetic resonance (NMR) spectroscopy and high-pressure liquid spectrometry (HPLC) are the methods commonly used in metabolomics study. In metabolomics, NMR enjoys several key advantages. It is a non-destructive, quantitative technique, it does not require separation or derivatization, and is susceptible to compounds that are difficult to analyze by liquid chromatography (HPLC). NMR also provides information that can be used to determine the molecular structure. There are two general approaches to the application of NMR in profiling studies: a) a non-targeted approach using chemometric analysis; b) a targeted approach to quantify the known compounds in the extract.

The use of chemometric methods in combination with NMR and HPLC for the identification of compounds contributed to demonstrating the differences between e.g. blueberries, due to sugars (glucose, fructose and sucrose), organic acids (tartaric, malic, citric and succinic) and amino acids (proline, arginine, gamma-aminobutyric acid, valine, alanine, leucine and isoleucine). Extracts will be made from the samples taken and then separated into fractions that will be analyzed by the ^1H / ^{13}C NMR nuclear magnetic resonance spectroscopy and high-performance liquid chromatography (HPLC). Chemometric methods will be used to show the differences in plant extracts. Standardization of the NMR vs HPLC protocol is a useful tool for profiling extracts from natural products.

Dietary supplements containing plant extracts - composition analysis and comparison with product labelling.

Department of Physical Chemistry

Supervisors

Agnieszka Zielińska, PhD / Katarzyna Paradowska, PhD, Assoc. Professor

Short Description

The subject of research - dietary supplements - is becoming increasingly popular among researchers and nutritionists, due to their common use by consumers in the prevention of various diseases. Products registered as drugs are analyzed in accordance with the requirements of the relevant Pharmacopoeia. However, dietary supplements which are more easily accessible to consumers do not require such external quality tests. Many studies showed that most of the preparations had a different content of herb extracts, vitamins etc. than declared by the manufacturer, thus their biological availability can be highly diversified.

The aim of the project is the quantitative and qualitative analysis of selected group of dietary supplements. The contents of the active compounds will be determined by the nuclear magnetic resonance (NMR) spectroscopy and high-pressure liquid spectrometry (HPLC). The student will learn the techniques of extract preparation, as well as analytical (NMR and DAD/RI – HPLC) and statistical methods.

An exploration of the drug polymorphism using periodic DFT calculations

Department of Physical Chemistry

Supervisor

Łukasz Szeleszczuk, PhD

Short description

Density functional theory (DFT) calculations for periodic crystalline solids were found to be a powerful tool in the pharmaceutical research. When applied properly they can be used to credibly predict various properties of the drugs, including dissolution parameters and stability.

The main object of the study will focus on the application of the periodic DFT calculations (CASTEP) in the exploration of the polymorphism. The goal will be to create the phase diagram for solid API in order to predict possible polymorphs and the conditions needed to obtain them. During the master's degree course student will learn how to properly set up periodic DFT calculations, including molecular dynamics simulations. Importantly, there is no need for the student to possess any knowledge in the molecular modeling methods nor in the informatics, yet such previous experience would be a benefit. This project is for open-minded students willing to try something new or to improve the molecular modeling skills. The results of the project will be published in the scientific journal with student as a co-author.

Molecular dynamics simulation of the self diffusion process.

Department of Physical Chemistry

Supervisor

Dariusz Pisklak, PhD

Short description

Self-diffusion is a stochastic process related to the thermal movement of molecules in a chemical system without a chemical potential gradient. This process is characterized by the diffusion coefficient parameter and depends on the temperature and the structure of the molecular system. One of the in silico approaches to describing this process is the molecular dynamics method. The aim of the master's thesis will be to use molecular dynamics simulation to analyze the self diffusion process. The research will analyze the influence of molecular topology and intermolecular hydrogen bonds on the estimated diffusion coefficient parameter.

Synthesis and physicochemical characterization of paracetamol-cyclodextrin complexes

Department of Physical Chemistry

Supervisor

Tomasz Gubica, PhD

Short description

Cyclodextrins (CDs) are cyclic oligosaccharides built from glucose units. Their molecules resemble a truncated cone with a centrally situated cage. This unique property enables CDs to form inclusion complexes with a number of organic compounds. CD complexes with Active Pharmaceutical Ingredients (APIs) benefit from better solubility, dissolution rate, stability, and bioavailability. Therefore, CDs are widely used in pharmaceutical formulation. The aim of the proposed MSc thesis will be synthesis of CD complexes with paracetamol and analytical characterization of obtained products. The analysis will include: powder X-ray diffraction (PXRD), differential scanning calorimetry (DSC), Fourier transform infrared (FTIR) and Raman spectroscopy.

Application of Artificial Neural Networks to predict the toxicity of xenoestrogens in zebrafish embryos model.

Department of Physical Chemistry

Supervisors

Katerina Makarova, PhD / Katarzyna Zawada, PhD

Short description:

Zebrafish embryos are a very popular *in vivo* model for toxicity studies. However, very often uncomplete data are published, for example data only for 24 hours post fertilization or only 96 hours post fertilization. Thus, a researcher has to repeat previous experiments before proceeding with new ones to fill the gap. Thus, there is a need for a tool to fill in the missing data and help researcher to plan future experiments and determine the range of concentrations for the new compounds.

The work will be based on development, training and testing of various types of ANN (Artificial Neural Networks) to predict mortality of the zebrafish embryos at 24, 48, 72, 96 and 120 hours postfertilization. The binding affinity, logP and concentration of selected xenoestrogens will be used as input parameters for ANN. The results of ANN prediction will be verified by a number of *in vivo* experiments with zebrafish embryos.

Antiradical properties of cosmetic formulations with extracts from *Aronia melanocarpa*

Department of Physical Chemistry

Supervisor

Katarzyna Zawada, PhD

Short Description

There is a constant search for new sources of antioxidant compounds for anti-ageing cosmetics. One of the mechanisms of action of antioxidants is an antiradical activity. *Aronia melanocarpa* fruit are known for their antioxidant and anti-inflammatory properties. The aim of the research will be the determination of antiradical properties of cosmetic formulations with extracts from fruits of *Aronia melanocarpa*, with use of electron paramagnetic resonance spectroscopy (EPR). The extracts will be prepared from berries in different stages of development. Additionally, the stability of these formulations will be assessed

Molecularly imprinted materials to pharmaceutical analysis – synthesis and properties examination

Department of Organic Chemistry

Supervisors

Piotr Luliński PhD, Assoc. Professor / Monika Sobiech, PhD

Short description

Advanced materials of prearranged properties are required to fulfill the demands of modern biomedical analysis. For such purpose novel and sophisticated polymers based on imprinting technology can be applied. Molecularly imprinted polymers (MIPs) are fabricated using different methods in the template-tailored synthesis which allows obtaining three-dimensional cavities in the polymer network after polymerization and template removal steps. Those materials have found application in the separation techniques mainly as highly selective sorbents in solid phase extraction of biomolecules. During the master's degree course student will be allowed to possess the knowledge and the laboratory practice in the field of synthesis of MIPs, their physico-chemical characterization (also using theoretical molecular simulations) as well as their application in the separation of biomolecules important from biomedical point of view. Our team possesses years of experience in the synthesis and analysis of MIPs as well as our laboratory is fully equipped in the necessary tools for preparation and analytical evaluation of MIPs.

Searching for new biologically active derivatives of hydroxycoumarins

Department of Organic Chemistry

Supervisor

Kinga Ostrowska, PhD Assoc. Professor

Short Description

The students will carry out the synthetic modifications of coumarin scaffold. The identification of new compounds will be defined by NMR and FTIR spectroscopic analyses and their purity will be confirmed by MS method. The obtained novel coumarin derivatives will be assayed for anticancer and antimicrobial activity as well as for 5-HT receptors' affinity. Structure activity-relationship (SAR) will be discussed.

Synthesis and biological evaluation of bisamidines

Department of Organic Chemistry

Supervisor

Jerzy Żabiński, PhD

Short Description

Immunocompromised humans and other mammals are potential targets for opportunistic infections. For example, widespread use of immunosuppressive medications plays a crucial role in the development of PCP in patients with autoimmune diseases (rheumatoid arthritis, Crohn's disease, AIDS) and following transplantations. Despite current searches for the next generation of anti-PCP therapy, no compound has passed all of the phases of clinical trials.

Bisamidines are potent lead structures, and their synthesis and *in vitro* evaluations can be very interesting scientific goal.

Development of a liquid chromatography/mass spectrometry screening methods for the identification and determination of active pharmaceutical ingredients in counterfeit medicinal products

Department of Bioanalysis and Drug Analysis

Supervisors

Prof. Zbigniew Fijałek / Joanna Giebułtowicz Ph.D., Assoc. Professor

Short description

Counterfeit medicines, imitations and substandard medicines are a growing problem worldwide. The problem is situated both in developing countries as in industrialized regions. In the developing countries the problem concerns the whole medicine supply chain, especially essential medicines like antibiotics, anti-malaria products. This is often due to the lack of effective enforcement agencies and the high prices of genuine medicines in these countries. In the industrialized world the problem concerns essentially life style drugs like the PDE-5 inhibitors, anabolic hormones and slimming products, although sometimes counterfeited antibiotics or insulin are intercepted by the customs. The growing threat of these products is mainly due to the extension of the internet, where about 50% of the medicines sold through internet sites disclosing their identity is estimated to be counterfeit.

To effectively fight against the counterfeiting of medicines appropriate analytical methods are needed.

Developing of fiber carriers containing culture system for paclitaxel production in *Taxus* x media transformed root cultures

Department of Pharmaceutical Biology and Medicinal Plant Biotechnology

Supervisor

Katarzyna Sykłowska-Baranek, Ph.D.

Short description

Among various biotechnological approaches developed for biopharmaceuticals production, transformed root cultures are believed to be one of the most promising due to their fast growth and significant biosynthetic capacities. The *Taxus* spp. *in vitro* cultures were developed as a new source of paclitaxel, the anticancer compound used for treatment of breast and ovarian cancers. To enhance biotechnological production of paclitaxel the new system composed of fibre carriers will be investigated. Their effect on root biomass accumulation and paclitaxel yield will be investigated.

Stress factors in naphthoquinone biosynthesis in *Rindera graeca* in vitro root cultures

Department of Pharmaceutical Biology and Medicinal Plant Biotechnology

Supervisor

Katarzyna Sykłowska-Baranek, Ph.D.

Short description

- supplementation of *Rindera graeca* root cultures with various elicitors (eg. silver nitrate, arachidonic acid etc.) and/or plant growth regulators (eg. ABA, ethylene)
- investigation of media supplementation of biomass increase
- chemical analysis of resulted plant material.

Isolation and identification of monoterpenoids with caffeic acid moiety from rootstocks of *Arcuncus dioicus***Department of Pharmacognosy and Molecular Basis of Phytotherapy**

Supervisor

Sebastian Granica, Assoc. Prof.

Short description

Our previous research revealed that root of *Arcuncus dioicus* contain a series of interesting natural products belonging to the group of monoterpenoids. The student will be responsible for the preparation of extracts and isolation of chosen compounds using chromatographic techniques including column chromatography and prep HPLC. Purified compounds should be identified using NMR and X-ray techniques.

Influence of skin microbiota on the chemical composition of plant extracts used in skin diseases**Department of Pharmacognosy and Molecular Basis of Phytotherapy**

Supervisor

Sebastian Granica, Assoc. Prof.

Short description

The study will be focused on the evaluation of the influence of skin microbiota on chemical composition of extracts from plant used in skin problems. Skin microbiota will be collected from healthy volunteers and incubated in the presence or absence of the prepared extracts. Changes in the chemical composition will be monitored by HPLC-DAD-MS technique.

Evaluation of biological potential of *Tormentillae rhizome* in chosen cell models

Department of Pharmacognosy and Molecular Basis of Phytotherapy

Supervisor

Sebastian Granica, Assoc. Prof.

Short description

Tormentillae rhizome is a plant material traditionally used in the treatment and prevention of diarrhea. The student will check the influence of characterized by HPLC-MS extract on caco-2 cells using molecular biology techniques.

Isolation and permeability assays of chosen natural products present in *Tormentillae rhizoma*

Department of Pharmacognosy and Molecular Basis of Phytotherapy

Supervisor

Sebastian Granica, Assoc. Prof.

Short description

Tormentillae rhizome contain flavan-3-ol derivatives and ellagitannins. These compounds are believed to be responsible for the bioactivity of the raw plant material. The student will check the bioavailability of compounds isolated and identified from *Tormentillae rhizome* using caco-2 cell model.

Examination of gut microbiota metabolism of anthraquinone derivatives from *Hypericum perforatum*.

Department of Pharmacognosy and Molecular Basis of Phytotherapy

Supervisor

Jakub Piwowarski, Assoc. Prof.

Short description

Hypericum perforatum is a plant material traditionally used in the treatment of depression and associated diseases. However the gut microbiota metabolism of orally administered extracts from this plant material remains unknown. The student will check how gut microbiota of healthy volunteers changes the chemical composition of tincture from *Hypericum perforatum* using HPLC-DAD-MS method.

UPLC and HPTLC methods development for chemical modifications of urolithin A.

Department of Pharmacognosy and Molecular Basis of Phytotherapy

Supervisor

Jakub Piwowarski, Assoc. Prof.

Short description

Urolithin A is a bioactive compound produced by gut microbiota after oral ingestion of plant ellagitannins. The chemical modifications of Uro A can affect its biological properties. Modified compounds can have different bioavailability, which must be evaluated using analytical tools. The student will be involved in the development of analytical methods based on UPLC and HPTLC techniques for the quantification of UroA derivatives obtained via chemical modifications in cell media after evaluation of compounds in different bioassays.