FACULTY OF PHARMACY WITH LABORATORY MEDICINE DIVISION

MASTER PROJECTS PROPOSALS FOR ERASMUS+ STUDENTS

ACADEMIC YEAR 2019/2020

Title

Synthesis of small-molecular peptidomimetics for drug discovery purposes.

Chair and 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).

Title

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

Chair and 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).

Title

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

Chair and 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 crusi* 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).

Title

An exploration of the drug polymorphism using periodic DFT calculations

Department/Laboratory

Department of Physical Chemistry

Supervisor

Łukasz Szeleszczuk, PhD, Assoc. Professor, Maciej Pisklak, PhD, Assoc. Professor

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.

Title

Molecularly imprinted materials to pharmaceutical analysis – synthesis and properties examination

Department/Laboratory

Department of Organic Chemistry

Supervisor: dr hab. Piotr Luliński and dr Monika Sobiech

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.

Title

Theoretical analysis of ADMET parameters for potential drug molecules. Molecular dynamics in analysis of intermolecular interactions drug-target macromolecule.

Department/Laboratory

Department of Organic Chemistry

Supervisor

dr Teresa Żołek and prof. dr hab. Dorota Maciejewska

Short Description

The research for new pharmaceuticals *via* computer modeling is one of the key challenges in modern medicine. In this work, we propose a simulation strategy for the prediction of pharmacokinetics of drug candidates by using currently available software ADMET Predictor™ version

8.0 of Simulations Plus which is very effective tool for calculation of absorption, distribution, metabolism, excretion and toxicity (ADMET). During the master's degree course student will learn also about the theoretical methods used in modeling of drug-target molecule interactions.

Title

Searching for new biologically active derivatives of hydroxycoumarins.

Department/Laboratory

Department of Organic Chemistry

Supervisor

dr Kinga Ostrowska, 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.

Title

Synthesis and biological evaluation of bisamidines

Department/Laboratory

Department of Organic Chemistry

Supervisor

dr Jerzy Żabiński

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) 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.

Title

1) Evaluation of the anti-inflammatory activity of chosen plant materials used in urinary tracts diseases using T24 cell model.

2) Examination of the chemical composition and anti-inflammatory activity of pharmacopoeial plant materials belonging to *Polygonum* species.

3) Isolation and structure elucidation of gut microbiota metabolites obtained from extracts prepared from chosen plant materials.

Department/Laboratory

Department of Pharmacognosy and Molecular Basis of Phytotherapy

Supervisors

Sebastian Granica, Ph.D., Assoc. Professor

Title

1. Effects of Fok-I polymorphism in vitamin D receptor gene on serum 25-hydroxyvitamin D in obese adults.

2. Combination of a high intake of snack foods with night eating and depressive symptoms among obese.

Department/Laboratory

Department of Biochemistry and Pharmacogenomics, and Centre for Preclinical Research and Technology (CePT)

Supervisor

Małgorzata Wrzosek, Ph.D., Assoc. Professor

Title

Biosynthesis of immunoactive Selenium-containing polysaccharides in mycelial cultures of medicinal mushroom *Lentinula edodes* (Berk.) Pegler

Department/Laboratory

Department of Drug Technology and Pharmaceutical Biotechnology

Supervisors

Eliza Malinowska, PhD

Short Description

The objective of the proposed project is to use biotechnological methods for biosynthesis of not described in the scientific literature macromolecular compounds – □-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 □-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.

Title

Antioxidant and UV- protective properties of hydrogels with extracts from Aronia melanocarpa

Department/Laboratory

Department of Physical Chemistry

Supervisors

Katarzyna Zawada, PhD/Agnieszka Zielińska, PhD

Short Description

Hydrogels are a group of polymeric materials, the hydrophilic structure of which make them capable of holding large amounts of water in their cross-linked polymeric network. Hydrogels have received considerable attention in the last years, due to their wide range of applications, for example in pharmaceutical and cosmetic formulations. Aronia melanocarpa fruits are mainly known for its use as an antioxidant, and also for anti-inflammatory and antimutagenic properties. The aim of the research will be the determination of UV- protective and antioxidant properties of hydrogels with extracts from fruits of Aronia melanocarpa, with use of spectroscopic techniques, including electron paramagnetic resonance spectroscopy (EPR). The extracts will be prepared from fruits in different ripening stages, thus contain different composition of constituents.
Additionally, the stability of these formulations and the pharmaceutical (transdermal) availability of the extracts components will be assessed

Title

Application of hybrid docking/3D QSAR approach in predict activity of pharmacologicaly active compounds.

Department/Laboratory

Department of Physical Chemistry

Supervisors

Dariusz Pisklak, PhD; Jakub Harwacki, MSc.

Short Descritpion

In silico approach is one of the modern methodologies in drug design. There are two main approaches which are used . One of them is based on docking of potential drugs into active site of protein, this methodology allows to determine the bioactive conformation of a ligand , but is poor in prediction of protein affinity. Alternative approach is based on the 3D QSAR model (COMFA, COMSIA) where the prediction of potential activity is more reliable but the knowledge of the bioactive conformation is essential.
Aim of the study is to exploit the docking approach to obtain binding mode of the molecules , and by superimposing those conformation obtain a reliable 3D QSAR model for predicting the pharmacological activity. The molecular targets would be β adrenergic receptors which crystal structures are deposited in PDB database.

Title

Toll-like receptors expression in Graves-Basedow orbitopathy

Department/Laboratory

Department of Biochemistry and Pharmacogenomics, and Centre for Preclinical Research and Technology (CePT)

Supervisors

Prof. Grażyna Nowicka, PhD, DSc.

Short Description

Background: Toll-like receptors (TLR) expressed on inflammatory cells play a key role in host defense against pathogens, benefiting the host. TLR are also expressed on other cells, including tumor cells, epithelial cells, endothelial cells, adipocytes or necrotic cells. Triggering of TLR induces inflammatory process.
Graves' disease, also known as toxic diffuse goiter, is an autoimmune disease that affects the thyroid. One of the symptoms of Grave's disease may include eye bulging, a condition caused by Grave's orbitopathy, and 30-80% of people with that condition develop eye problems.
The aim: of the study is to evaluate the expression and function of Toll-like receptors and other innate-immunity receptors in orbital adipose tissue and adipocyte cell line.
Material and methods:
Material: established human adipocyte cell lines and orbital adipocyte tissue obtained from patients underwent endoscopic orbital decompression due to Grave's disease.
Methods: in vitro cultures, qPCR, immunohistochemistry, flow cytometry, signaling.

Title

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

Department/Laboratory

Department of Bioanalysis and Drug Analysis

Supervisors

Prof. Zbigniew Fijałek

Short Descritpion

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.

Title

Synthesis, characterization and application opportunities of the biodegradable, macromolecular drug conjugates

Department/Laboratory

Department of Biomaterials Chemistry

Supervisors

Ewa Oledzka PhD Eng.

Short Description

An interesting group of macromolecules applied in the production of materials for medicine and pharmacy are biodegradable polymers, used in endoprosthetics, 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 this study is the synthesis, characterization (structural, physicochemical and biological) and application opportunities of the biodegradable, macromolecular drug-conjugates. The polymeric matrices will be synthesized from the heterocyclic monomers in the presence of natural initiators, whereas the macromolecular conjugates will be obtained by a covalent conjugation of the drug to the synthesized polymeric carriers. The influence of the topology of the obtained polymeric matrices, the microstructure of polymer chains on the biological properties as well as kinetics of hydrolytic and enzymatic degradation and the drug release profiles will be defined.

Title

Kinetic properties of Nav1.1 ion channel bearing mutations identified in Dravet Syndrome

Department/Laboratory
Laboratory of Physiology and Pathology, Centre for Preclinical research and Technology
Supervisor
Ewa Nurowska, PhD
Short description
Epileptic syndromes caused by mutations of the *SCN1A* gene, encoding a subunit of the voltage-gated Na^+ ion channel ($Na_v1.1$), are heterogeneous and phenotypically different disorders. They encompass a spectrum that ranges from epilepsies with benign symptoms to catastrophic epileptic encephalopathies, like Dravet Syndrome. Until now a clear correlation between the type/location of the mutations and the clinical presentation of the syndrome has not been established, moreover in the most cases it is not known which functions of Na^+ channel are disturbed during the course of the disease.
The aim of the study is to investigate the relationship between the type of the *SCN1A* mutations and the voltage-gated Na^+ channels' dysfunctions. Selected mutations identified in Dravet Syndrome patients will be reconstructed in cDNA of *SCN1A* gene and expressed in HEK tsA201 cells. Voltage-dependent Na^+ currents in these cells will be investigated with the use of voltage-clamp technique.

Title
1. **Porous collagen type I/apatite composite as a drug carrier for antiresorptive drugs**
2. **Modified calcium phosphates used in drug delivery systems in bone diseases.**

Department/Laboratory
Department of Analytical Chemistry
Supervisor:
Joanna Kolmas, PhD

Synthesis and physicochemical analysis of mesopores silica (SBA-16) /hydroxyapatite composite - a potential new drug delivery system.
Department/Laboratory
Department of Analytical Chemistry
Supervisor
Łukasz Pajchel, PhD

Work plan:
- synthesis of mesopores silica (SBA-16);
- synthesis of SBA-16 /hydroxyapatite composite;

- analysis of the structure, chemical composition and physicochemical properties of the composite ((PXRD, 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;