



Master Thesis Projects

I would like to welcome warmly Erasmus+ mobility students from partner European Universities who wish to participate in the realization of Master Thesis Projects at the Faculty of Pharmacy, Medical University of Warsaw, Poland. For more than ninety years our Faculty has been engaged in education and research of pharmaceutical sciences, graduating several generations of well-educated pharmacists who have been working in research and development fields as well as in the healthcare system. Nowadays, our Faculty is recognized as one of the leading academic centers in Poland. As the Erasmus+ mobility students you will benefit from the innovative research projects, experienced supervisors and well-equipped laboratories which will allow you to extend the recent knowledge from the pharmaceutical and biomedical sciences and to gain additional skills. The location of our Faculty in the heart of the capital city of Warsaw is another advantage. It will give you a good opportunity to discover Polish history and culture as well as to participate in the vibrant academic life. I hope that Erasmus+ mobility to the Faculty of Pharmacy Medical University of Warsaw will contribute to your professional, social and cultural development as well as unforgettable memories.

Piotr Luliński

/Dean of the Faculty of Pharmacy
Medical University of Warsaw/

Please find below a list of Master Thesis Projects you can choose from at the Faculty of Pharmacy, Medical University of Warsaw. For all administrative issues concerning the ERASMUS exchange mobility our contact for incoming students is Ms Katarzyna Szałapska-Kręcioch from the International Relations Office (e-mail: katarzyna.szalapska@wum.edu.pl)

Title: Evaluation of the effect of *Arctii folium* on wound healing in vitro using cell based models

Supervisor: Agnieszka Bazylko

Contact: agnieszka.bazylko@wum.edu.pl

Department: Chair and Department of Pharmaceutical Biology

Faculty of Pharmacy

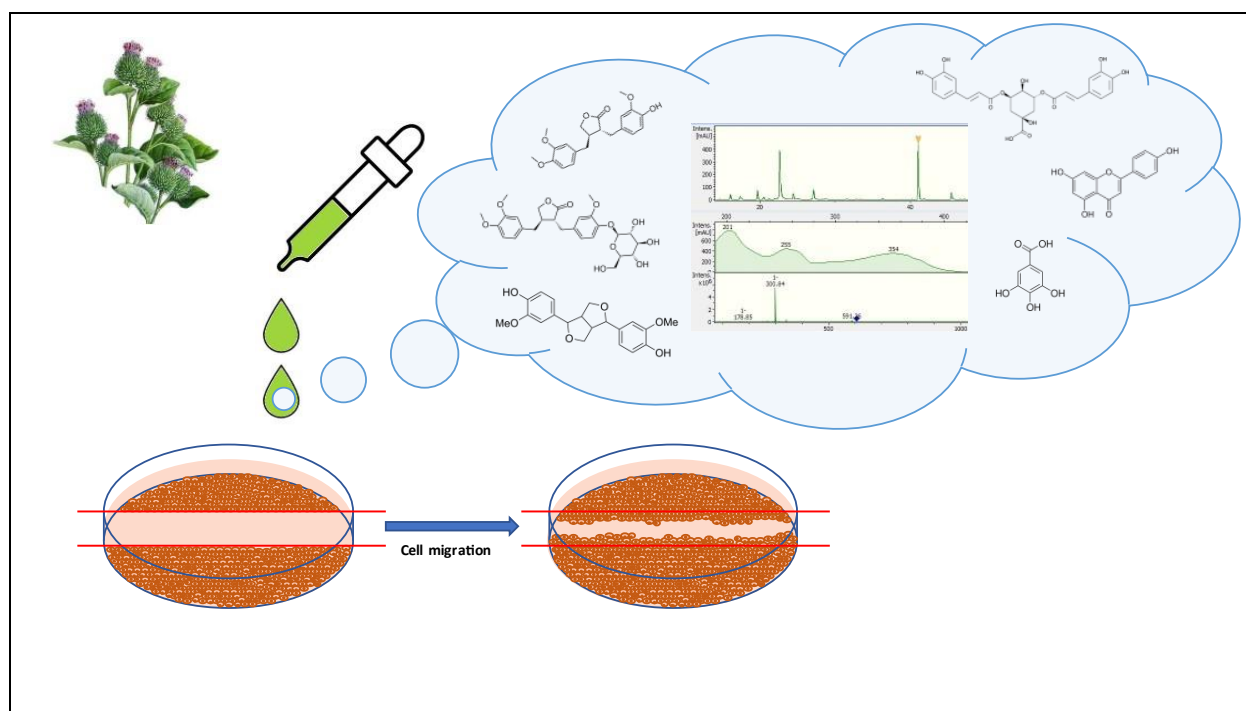
Medical University of Warsaw

Abstract

Arctium lappa also known as greater burdock is a medicinal plant material traditionally used in skin problems and as an ingredient of various cosmetic formulations present on the European market. The project will involve preparation of the extract, establishment of HPLC-DAD-MS method for the investigation of its chemical composition and evaluation of the wound healing properties of the obtained preparation. The student will have opportunity to work with state-of-the-art chromatographic equipment and will be able to learn how to perform cell cultures. Experiments will involve cytotoxicity assays on cell lines and wound healing test by scratch assay method.

Keywords: *Arctium lappa*, burdock, wound healing, scratch assay, HPLC-MS

Graphic abstract



Title: Investigation chemotaxonomic differences of chosen *Geum* species traditionally used in medicine by HPTLC method

Supervisor: Agnieszka Bazylko

Contact: agnieszka.bazylko@wum.edu.pl

Department: Chair and Department of Pharmaceutical Biology

Faculty of Pharmacy

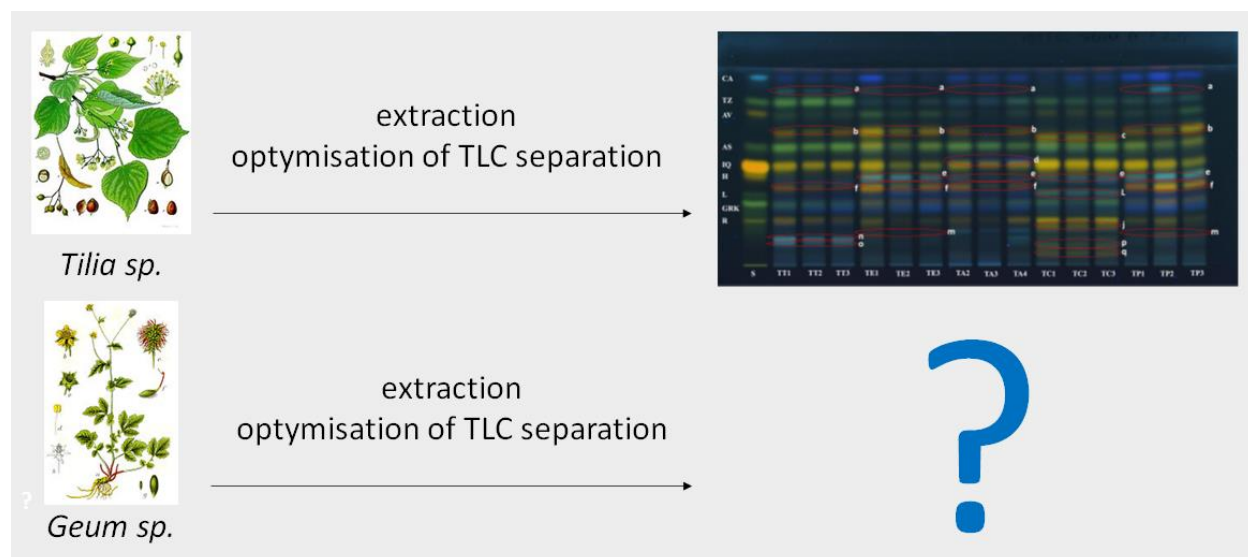
Medical University of Warsaw

Abstract

Many species belonging to *Geum* genus (Rosaceae family) are traditionally used on the phytotherapy. Differences between chemical composition of extracts prepared from different species were not established in the literature. HPTLC method is a fast and convenient solution for screening plant extracts. The student will prepare extracts in small scale from several species of *Geum*. Next the suitable separation by TLC will be established. Finally, chemical profiles will be compared using Camag equipment to determine chemotaxonomic markers of each sample.

Keywords *Geum*, thin layer chromatography, fingerprint, TLC

Graphic abstract



Title: Investigating of antioxidant and photoprotective activity of *Arnebia euchroma* extracts

Supervisor: Agnieszka Pietrosiuk

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Department of Pharmaceutical Biology

Faculty of Pharmacy

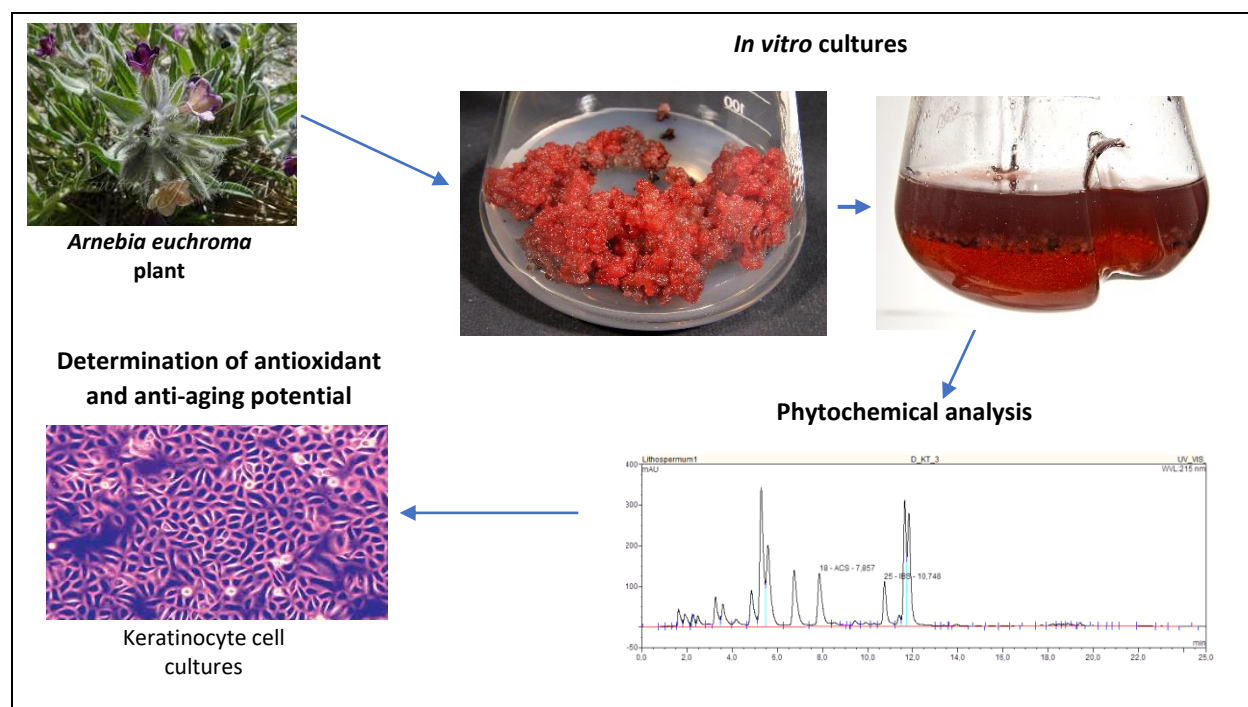
Medical University of Warsaw

Abstract

The project will include biotechnological cultures of *Arnebia euchroma* on various media. The content of bioactive phytochemicals i.e. red naphthoquinones, derivatives of shikonin, will be determined by HPLC-DAD method. The antioxidant potential of obtained material will be established using cell free models. The photoprotective activity can be checked by cell-free or cell-based models present in our laboratory.

Keywords: plant *in vitro* cultures, shikonin derivatives, antioxidant activity, photoprotective activity

Graphic abstract



Title: Mechanochemical methods of synthesis and study of physicochemical properties of new ionic crystals of active pharmaceutical substances

Supervisor: Edyta Pindelska

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Department: Department of Pharmaceutical Chemistry and Biomaterials

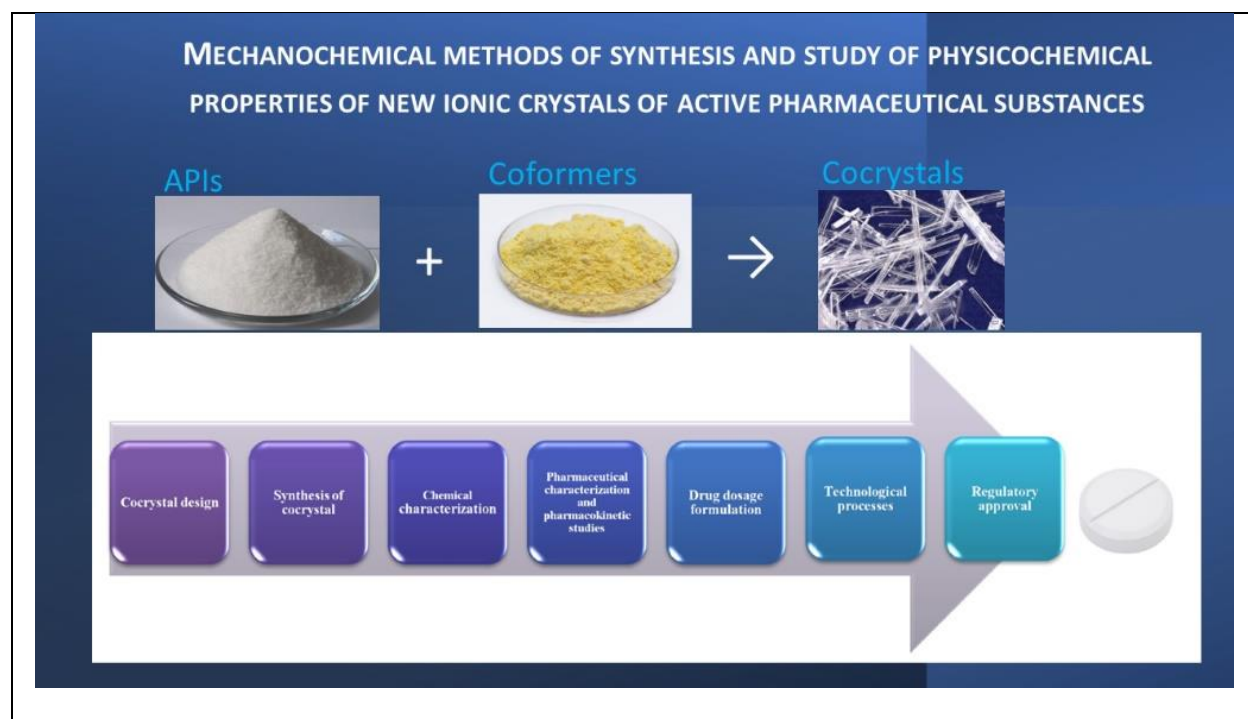
Faculty of Pharmacy, Medical University of Warsaw

Abstract

The properties of many drugs which have been available on the pharmaceutical market for a long time still need to be improved. Cocrystals are the solid state drug modification which can improve properties such as low solubility, stability and mechanical properties (e.g. compressibility). In the experimental part of the diploma thesis, new ionic cocrystals of “problematic “ active pharmaceutical substances (API) will be obtained. The structure of the obtained cocrystals will be characterized by spectroscopic and X-ray diffraction methods. The solubility in water and simulated gastric fluids for the obtained cocrystals and the rate of dissolution will be tested.

Keywords: Crystal Engineering, Pharmaceutical Ionic Cocrystals, Crystal Structure, Physicochemical Properties, Pharmaceutical Properties;

Graphic abstract



Title: Synthesis of triterpene derivatives with antitumor and antiviral activity preceded by *in silico* research

Supervisor: Edyta Pindelska

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Department: Department of Pharmaceutical Chemistry and Biomaterials
Faculty of Pharmacy Medical University of Warsaw

Abstract

Triterpenes are common in many plant species. These compounds are characterized by multidirectional pharmacological activity. The antiviral and cytotoxic properties are of most interest. Compounds from this chemical group are characterized by poor solubility in water and poor bioavailability. Chemical modifications of the triterpenes structure can also improve the biological activity in relation to the parent substances. Theoretical studies will allow designing chemical modifications to obtain compounds with the expected biological activity. In addition, these modifications will take into account improvements in stability, water solubility and bioavailability. In the experimental part of the work, triterpene derivatives will be obtained. Structural studies confirming the structures will be performed for the newly synthesized compounds. The obtained derivatives will be tested for the determination of physicochemical properties such as solubility in various media and permeability testing using the Franz chamber.

Keywords: triterpenes, *in silico* studies, pro-drug, solubility, permeability

Graphic abstract



Title: Synthesis of new cannabidiol derivatives and their physicochemical and pharmaceutical characteristics

Supervisor: Edyta Pindelska

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Department: Department of Pharmaceutical Chemistry and Biomaterials

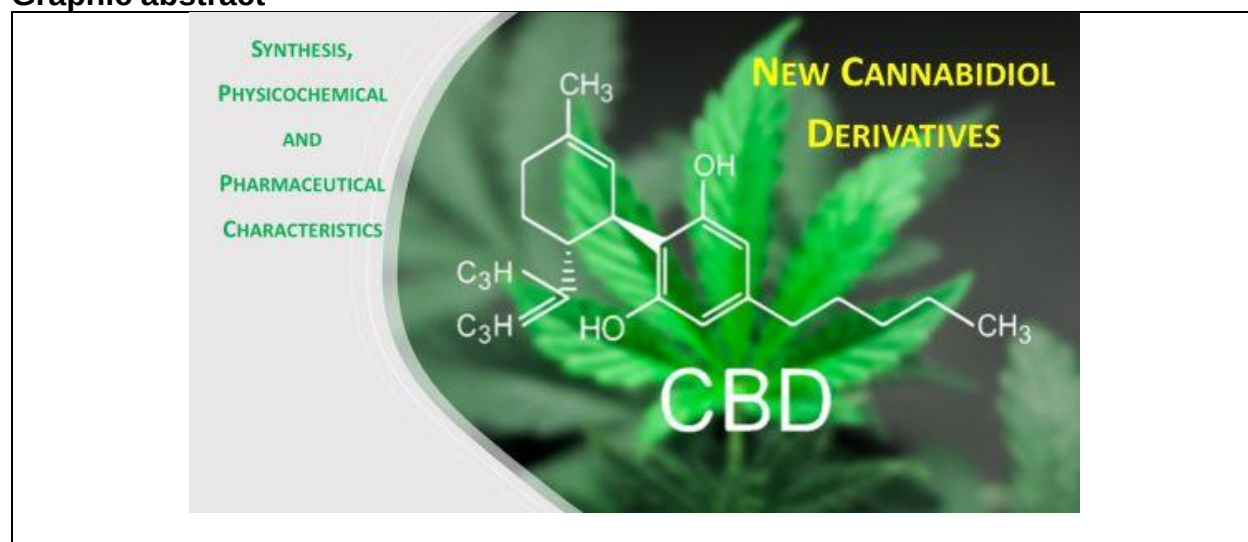
Faculty of Pharmacy Medical University of Warsaw

Abstract

Hemp (*Cannabis sativa* L.) is an interesting subject of pharmacological research due to its rich content of active substances with diverse biological activity. One of the most interesting chemical components of this plant is cannabidiol (CBD). Due to its physicochemical properties and chemical reactivity, cannabidiol requires structural modifications. CBD under the influence of oxygen from the air is slowly oxidized. As a result of oxidation, colored products are formed, causing discoloration on the surface of the pure substance and the tablets containing it. Chemical modifications are aimed at improving water solubility and chemical stability in the developed forms of drugs. These modifications will consist in the introduction of polar elements into the structure of CBD, which can form stable water-soluble salts. In the experimental part of diploma thesis, a derivative with the expected physicochemical properties will be synthesized. The structure of the obtained new pro-drug will be characterized by spectroscopic and X-ray diffraction methods.

Keywords: hemp, cannabidiol, solubility, synthesis, stability

Graphic abstract



Title: Selected aspects of the quality of dietary supplements recommended for cancer prevention

Supervisor: Joanna Giebułtowicz

Contact: joanna.giebultowicz@wum.edu.pl

Department: Department of Drug Chemistry

Faculty of Pharmacy

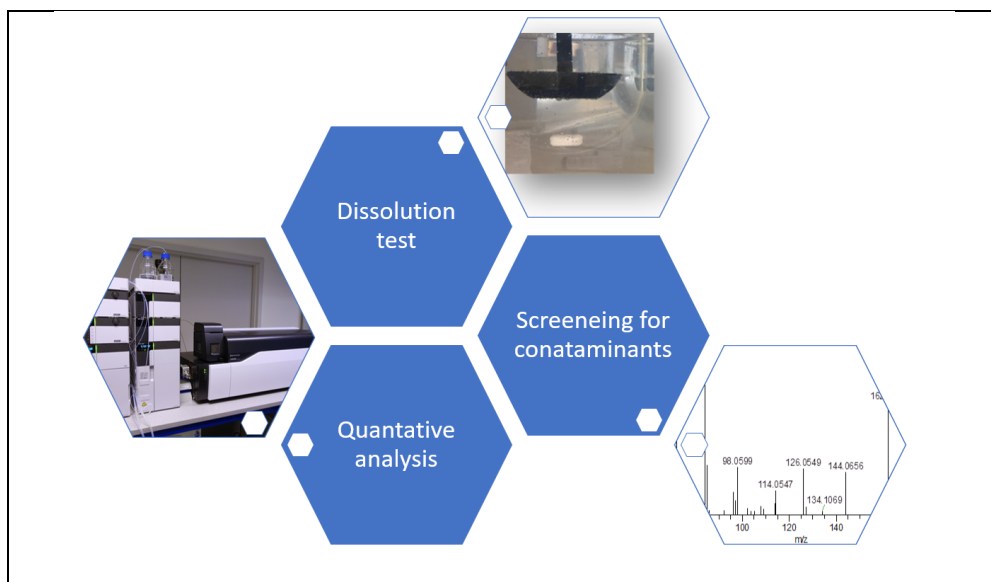
Medical University of Warsaw

Abstract

Dietary supplements are widely used throughout the world. Advertisements of these products can be found in the mass media, i.e. radio, television, newspapers and the Internet. All pharmacies offer a variety of supplements; in addition, one can also purchase them on the Internet. According to a statistical report, almost 72% of Poles declare to take dietary supplements. Although dietary supplements are classified as food, they are sold in pharmaceutical dosage forms such as tablets, capsules, sachets and others intended to be taken in small and defined unit quantities. Based on their similarity to pharmaceuticals, consumers mistakenly believe that dietary supplements have also been validated for safety and efficacy before being marketed. However, unlike medicinal products, dietary supplements are not tested for stability, interactions or pharmacovigilance. Studies on the quality of dietary supplements confirm that these products often contain undeclared ingredients, or the amount of the substance is different than declared, or the substance is not released from pharmaceutical formulation.

Keywords: dietary supplements, dissolution test, LC-MS/MS, food quality

Graphic abstract



Title: Use of liquid chromatography associated with mass spectrometry (LC-MS/MS) to determine the composition of illegal pharmaceutical products containing anabolic-androgenic steroids

Supervisor: Joanna Giebułtowicz

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Department: Department of Drug Chemistry

Faculty of Pharmacy

Medical University of Warsaw

Abstract

Falsified medicinal products are a current and very important public health problem worldwide. A large percentage of all counterfeit drugs in the world are products containing anabolic androgenic steroids. Formulations from illegal sources are not manufactured by the principles of Good Manufacturing Practice (GMP). Very often their composition differs significantly from that declared on the packaging. The presence of undeclared active substances and their analogues, impurities, and incorrect dosing can lead to serious side effects that threaten the life or health of patients. Very rarely, such illegal products are analyzed for the presence of ingredients not declared on the package. The aim of the work will be an attempt to identify undeclared ingredients (including impurities) in counterfeit medicinal products containing anabolic androgenic steroids. The research material will consist of medicinal products from various cases conducted by law enforcement authorities. The tested pharmaceuticals will be anabolic-androgenic steroids containing oxandrolone. The scope of the research will include a qualitative analysis of medicinal products in terms of the content of active substances and potential contaminants using the LC-MS/MS method.

Keywords: illegal pharmaceutical products, LC-MS/MS, anabolic androgenic steroids

Graphic abstract



Title: Application of laccase as the alternative method of removal of antidepressants from wastewaters

Supervisor: Joanna Giebułtowicz

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Department: Department of Drug Chemistry

Faculty of Pharmacy

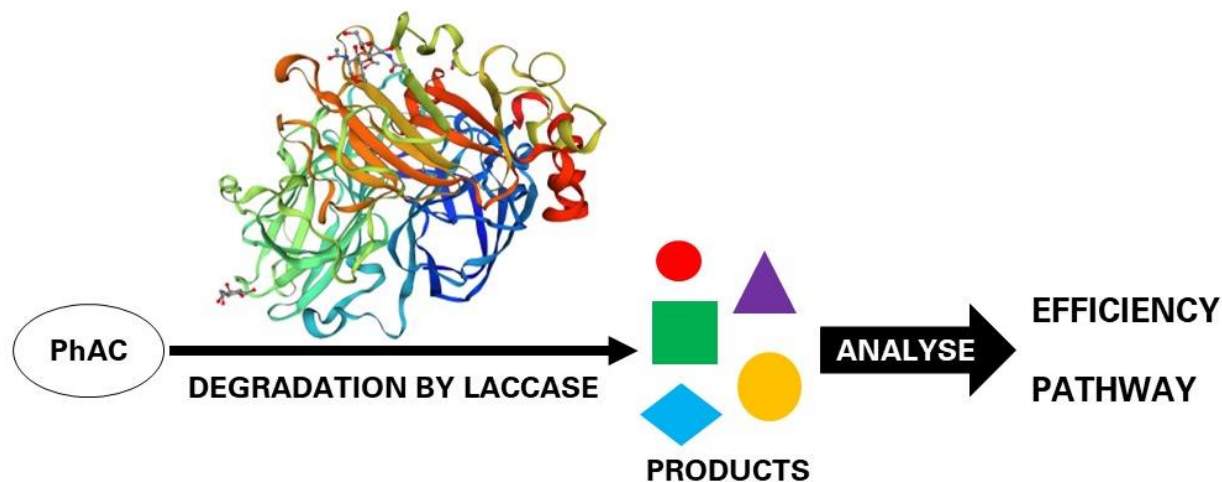
Medical University of Warsaw

Abstract

The pharmaceutical industry manufactures significant quantities of pharmaceuticals (PhACs) used to treat various diseases. After administration to patients, PhACs undergo ADME processes and are eliminated with urine and/or feces as parent drug or metabolites. Unfortunately, pharmaceuticals and their metabolites are difficult to remove from wastewater and are released with treated sewage into the environment, e.g., to rivers, where they pose a risk for aqueous biota. Laccase is an enzyme that can be used in wastewater treatment as the alternative to conventional methods. Laccase is a biocatalyst produced mainly by the white-rot fungi (e. g. *Pleurotus ostreatus*, “oyster mushroom”). Its most important advantage is its ability to degrade many chemical substances, including PhACs. In this project we aim to test the ability of commercial laccase to degrade selected pharmaceuticals, including novel antidepressants. Besides the removal efficiency, we will determine the tentative metabolites and create possible pathways of PhACs enzymatic degradation. We will mainly use liquid chromatography coupled with mass spectrometry as the analytical method.

Keywords: environmental pollution, laccase, white rot fungi; pharmaceutical; wastewater

Graphic abstract



Title: Novel multifunctional bone substitutes containing zinc and metformin

Supervisor: Joanna Kolmas

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Department: Department of Pharmaceutical Chemistry and Biomaterials

Faculty of Pharmacy

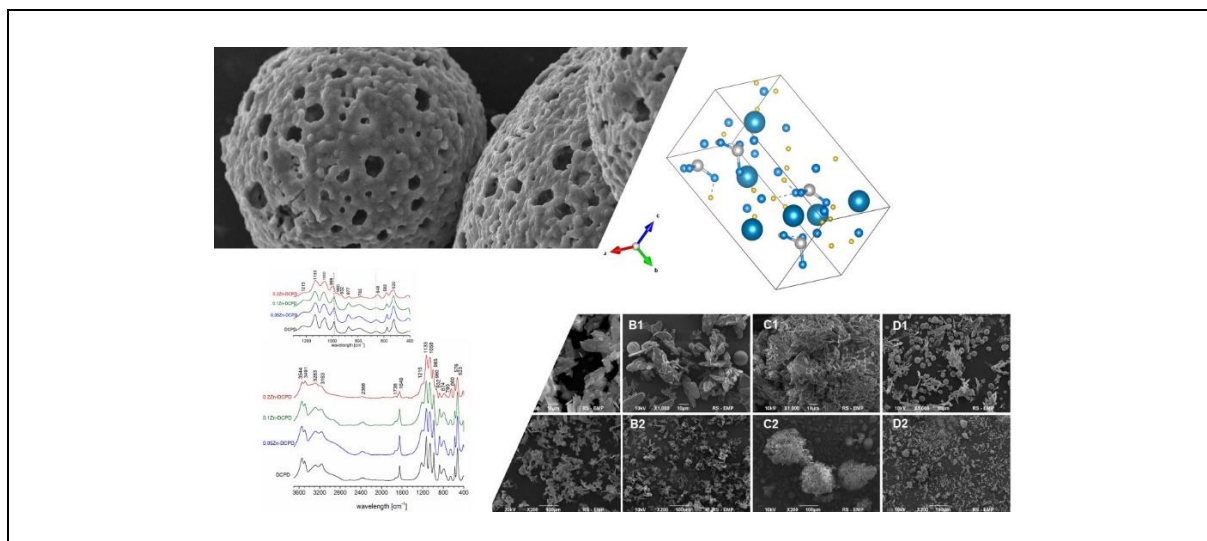
Medical University of Warsaw

Abstract

The main aim of this project is to develop new bioceramics for potential applications in the treatment of bone diseases. The planned materials will be based on different calcium phosphates enriched in zinc ions, nanosized zinc oxide and/or zinc phosphates and will be used as metformin delivery systems. Zn is essential for healthy bones' growth, development, and maintenance. Moreover, Zn is well known for exhibiting antibacterial activity, and osteogenic, and angiogenic potential. Metformin is a widely used drug for type II diabetes, with the ability to enhance osteogenesis and angiogenesis by promoting cell migration and differentiation. Metformin promotes mineralization and bone defect regeneration. The obtained bioceramic materials will be physicochemically tested using various methods: FT-IR spectroscopy, Raman spectroscopy, TEM microscopy, X-ray diffractometry, and AAS spectrometry. The release of Zn ions and metformin will be analyzed using AAS and HPLC, using AAS and HPLC, respectively. The preliminary cytotoxicity tests (*in vitro*) are planned.

Keywords: biomaterials, drug delivery systems, bone diseases, physicochemical analysis

Graphic abstract



Title: Novel biomaterials containing boron and fluoride as potential delivery systems for metformin

Supervisor: Joanna Kolmas

Contact: joanna.kolmas@wum.edu.pl

Department: Department of Pharmaceutical Chemistry and Biomaterials

Faculty of Pharmacy

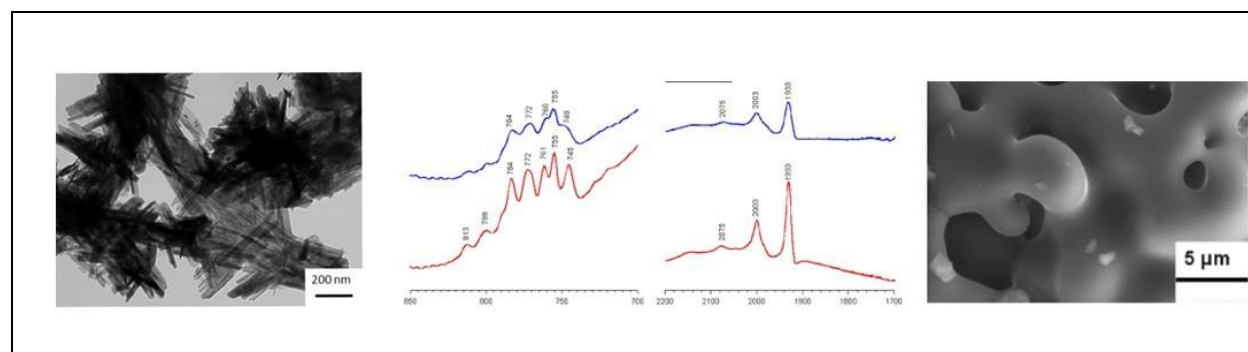
Medical University of Warsaw

Abstract

The main aim of this project is to develop new bioceramics for potential applications in the treatment of bone diseases. The planned materials will be based on different calcium phosphates enriched in borate and/or fluoride ions. Boron plays an important role in osteogenesis, and its deficiency has been shown to adversely impact bone development and regeneration. Recent research indicates that fluoride may improve bone formation by osteoblastic stimulation, especially trabecular bone, and increases spinal bone density. Metformin is a widely used drug for type II diabetes, with the ability to enhance osteogenesis and angiogenesis by promoting cell migration and differentiation. Metformin promotes mineralization and bone defect regeneration. The physicochemical analysis will be performed using various methods: FT-IR spectroscopy, Raman spectroscopy, TEM microscopy, X-ray diffractometry, and AAS spectrometry. The release of borate and fluoride ions and metformin will be analyzed using potentiometry, ICP-OES and HPLC, respectively. The preliminary biological tests (*in vitro*) will also be performed.

Keywords: biomaterials, drug delivery systems, bone diseases, physicochemical analysis

Graphic abstract



Title: Determining interactions of *Cannabis sativa* with human gut microbiota.

Supervisor: Jakub Piwowarski

Contact: jakub.piwowarski@wum.edu.pl

Department: Microbiota Lab, Department of Pharmaceutical Biology

Faculty of Pharmacy

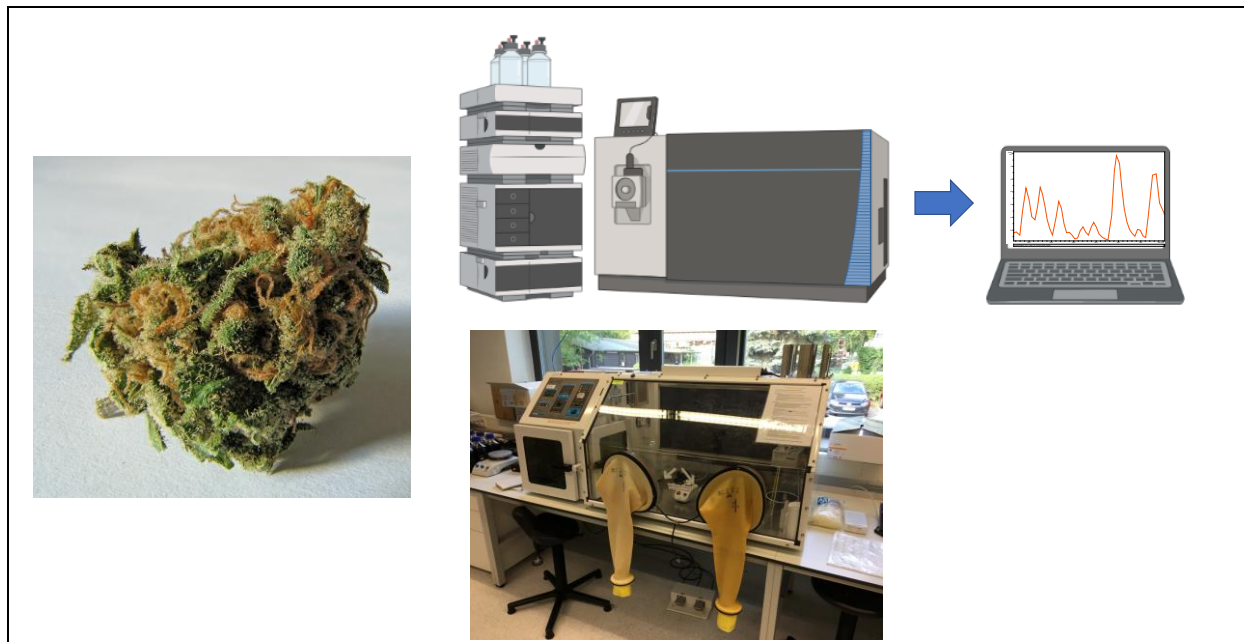
Medical University of Warsaw

Abstract

The aim of the project is to establish the possible metabolism of compounds contained in extracts prepared from *Cannabis flos* by human gut microbiota *ex vivo*. The students will be involved in the preparation of the extract its chemical analysis using HPLC-DAD-MS. Samples of the extract will later be incubated *ex vivo* in anaerobic chamber with human colon microbiota collected from healthy volunteers. Metabolism of extract constituents will be evaluated by HPLC-DAD-MS.

Keywords: Cannabis, microbiota, metabolism, chromatography

Graphic abstract



Title: How procyanidins can influence processes associated with leaky gut syndrome.

Supervisor: Jakub Piwowarski

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Department: Microbiota Lab, Department of Pharmaceutical Biology

Faculty of Pharmacy

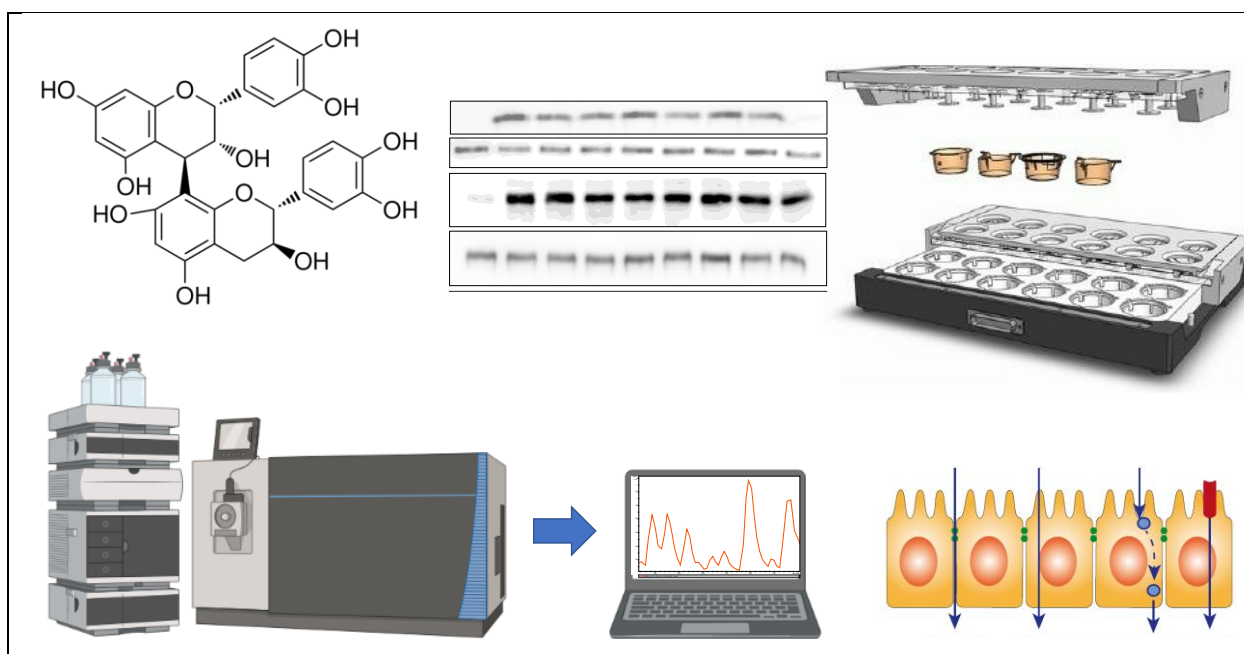
Medical University of Warsaw

Abstract

The project is focused on the evaluation of the influence of procyanidins rich plant extracts on the condition of monolayers of Caco-2 cells in vitro. The student will have to prepare extract from chosen plant material. Establish its chemical composition by chromatographic methods (HPLC-DAD-MS). If needed certain compounds will be purified from the raw material and their chemical structure will be checked. Finally, after getting suitable experience and skill the students might be involved in the biological assays with Caco-2 cells including cell layers integrity experiments or permeability assays.

Keywords: Procyanidins, Caco-2, leaky gut syndrome, chromatography

Graphic abstract



Title: Do selenated polysaccharides affect the growth of fungal and bacterial strains in submerged cultures?

Supervisor: Jadwiga Turło

Contact: jadwiga.turlo@wum.edu.pl

Department: Department of Drug Technology and Pharmaceutical Biotechnology

Faculty of Pharmacy

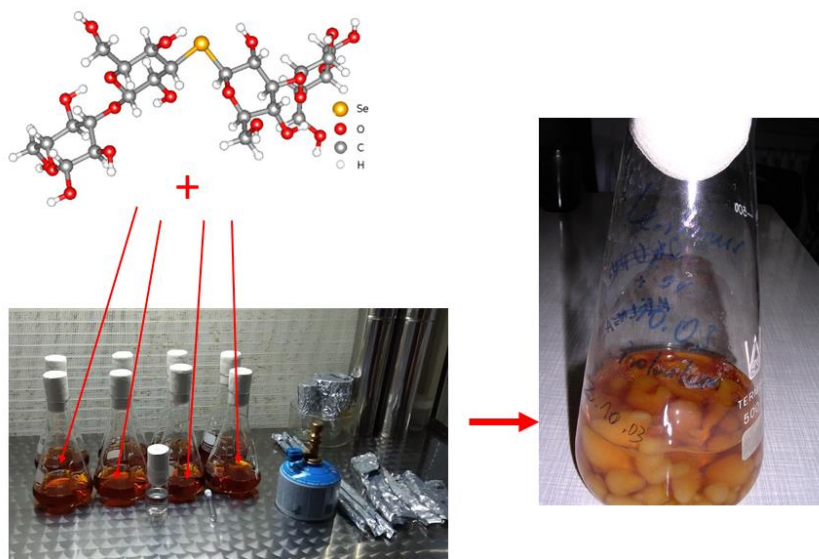
Medical University of Warsaw, Poland

Abstract

In our previous research we obtained, by biotechnological methods, the polysaccharides with selenium incorporated into the molecule. These compounds have shown strong antioxidant and growth-stimulating effects on animal cell lines. It is interesting, whether these compounds can stimulate the growth of actinomycetes and fungi strains, used in the pharmaceutical biotechnology for biosynthesis of the drugs. If so, it would be technologically significant.

Keywords: Se-polysaccharides, growth-stimulators, pharmaceutical biotechnology

Graphic abstract



Title: Investigation of the ability of mycelial cultures of *Inonotus obliquus* (Chaga mushroom) of biosynthesis of anticancer polysaccharides

Supervisor: Jadwiga Turło

Contact: jadwiga.turlo@wum.edu.pl

Department: Department of Drug Technology and Pharmaceutical Biotechnology

Faculty of Pharmacy

Medical University of Warsaw, Poland

Abstract

Inonotus obliquus (Chaga mushroom) is one of the medicinal mushroom widely used in China, Russia, Korea, and some occidental countries to prepare anticancer preparations. In water extracts from *I. obliquus*, the polysaccharide fraction - IOPS is supposed to be one of the major bioactive components. It possess antitumor, antioxidant, anti-virus, hypoglycemic, and hypolipidemic activities. It is interesting to investigate whether mycelial cultures of this fungus are also capable of effective biosynthesis of IOPS fraction. Thus, the aim of the project is to check whether IOPS can be obtained by biotechnological methods.

Keywords: *Inonotus obliquus*; anti-tumor polysaccharides

Graphic abstract



Title: Investigation of the ability of white-rot fungi mycelial cultures to decompose pharmaceutical-derived pollutants

Supervisor: Jadwiga Turło

Contact: jadwiga.turlo@wum.edu.pl

Department: Department of Drug Technology and Pharmaceutical Biotechnology

Faculty of Pharmacy

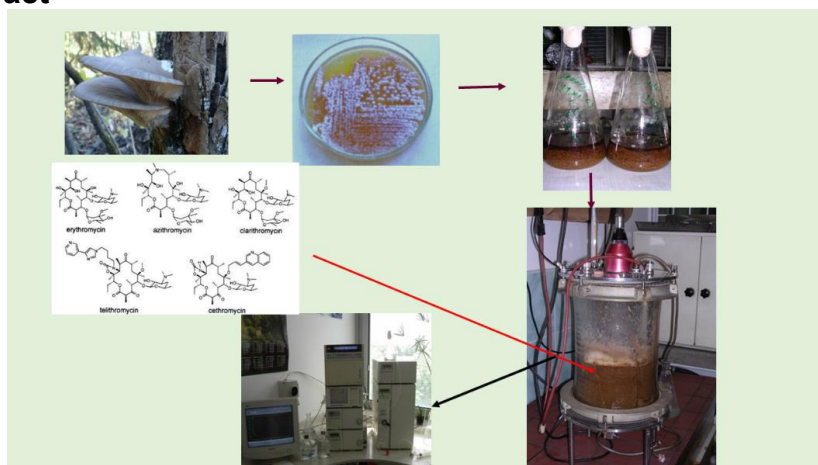
Medical University of Warsaw

Abstract

The problem of environmental pollution is being discussed with a rising frequency in both science and politics. Pollution is most often associated with something tangible that can be easily noticed, such as household waste. However, recently more attention is being paid to micropollutants, which, although not visible, pose an equally dangerous threat to the environment and ourselves as its part. The micropollutants include pharmaceuticals that penetrate uncontrolled into soil and water as a result of incorrect disposal methods. The methods currently used in wastewater treatment plants are not effective in removing micropollutants. This leads to the release of these compounds into water of everyday use and their accumulation in the environment. Employing white-rot fungi in the mycoremediation process gives a promising alternative to the methods currently used in wastewater treatment plants, however, the implementation of this technology on an industrial scale remains a challenge. The aim of the study is to test the ability of the fungus *Armillaria mellea* to degrade drug contaminants present in the aquatic environment in properly designed laboratory conditions and to optimize an alternative, low-cost growth medium for the species.

Keywords: mycoremediation, drug pollutants white-rot fungi

Graphic abstract



Title: Coumarin as an interesting compound with a different biological effect

Supervisor: Kinga Ostrowska

Contact: kinga.ostrowska@wum.edu.pl

Department: Department of Organic and Physical Chemistry

Faculty of Pharmacy

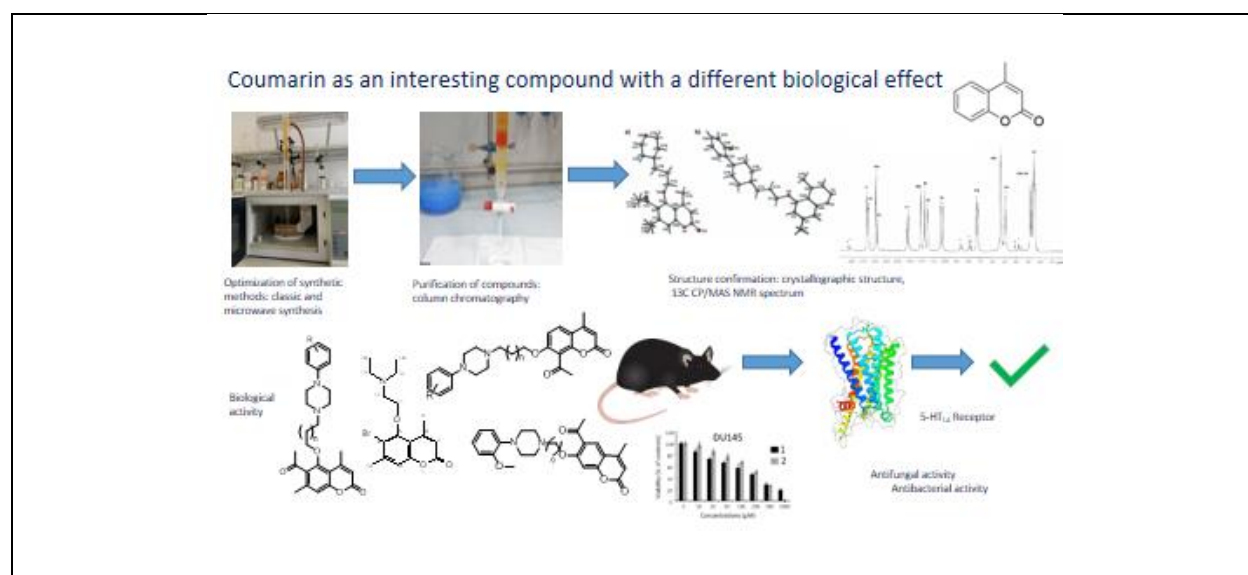
Medical University of Warsaw

Abstract

Coumarin derivatives from natural and synthetic sources are useful in a number of fields and are commonly used in medicine, often in the form of glycosides. Numerous efforts, including the isolation and purification of naturally occurring coumarins from a variety of plants as well as laboratory synthesis of coumarin derivatives with novel structures and properties, have been focusing on the research and development of coumarins as potential drugs. So far a number of coumarins such as warfarin, acenocoumarol, armillarisin A, carbochromen and hymecromone have been approved for therapeutic purposes in clinic. In the Organic Chemistry Laboratory, we have been researching coumarin derivatives for several years. We have been involved in the design, synthesis and purification of new coumarin derivatives. Now, we synthesize new derivatives using classical and microwave methods, purify them using column chromatography, confirm structures using spectral (^1H , ^{13}C NMR, HRMS) and crystallographic methods. Then, as a part of extensive cooperation, our compounds are tested for anticancer, microbiological or central nervous system effects.

Keywords: coumarin, biological activity, microwave synthesis

Graphic abstract



Title: Exploring of the antioxidant and anti-aging potential of *Larrea tridentata* extracts

Supervisor: Katarzyna Syklowska-Baranek

Contact: Katarzyna.syklowska-baranek@wum.edu.pl

Department of Pharmaceutical Biology

Faculty of Pharmacy

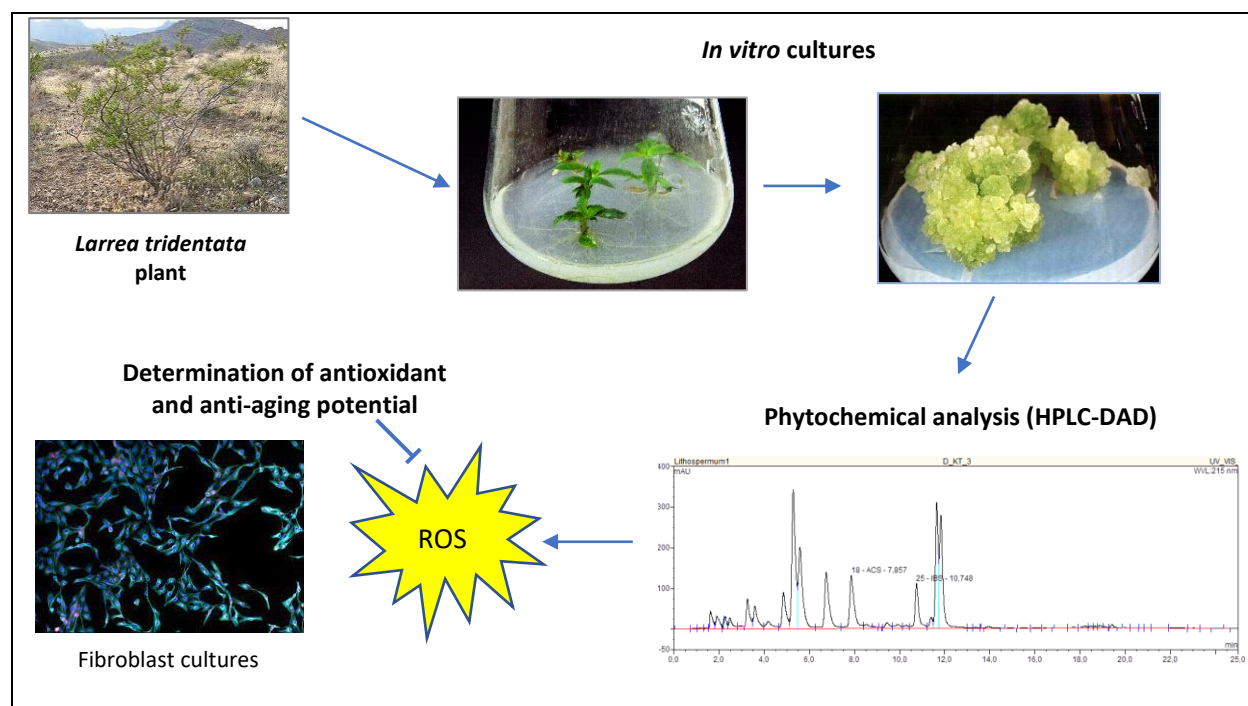
Medical University of Warsaw

Abstract

The students will be involved in carrying out the *in vitro* cultures of callus and suspension cultures of *Larrea tridentata* (Chaparral, Creosote bush). The resulted plant material will later be extracted, and the content of certain biologically active compounds will be checked by HPLC-DAD. Finally, the antioxidant and anti-aging properties of resulted extracts of diverse composition will be evaluated in cell-free models including anti-elastase, anti-hyaluronidase and anti-collagenase activity. Students also might be involved in bioassays on fibroblasts.

Keywords: plant suspension cultures, anti-aging activity, antioxidant activity, phenolic compounds

Graphic abstract



Title: Optimization of total polyphenol content and antioxidant properties of the extracts from the selected agri-food by-products

Supervisor: Katarzyna Zawada

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Department: Organic and Physical Chemistry

Faculty of Pharmacy

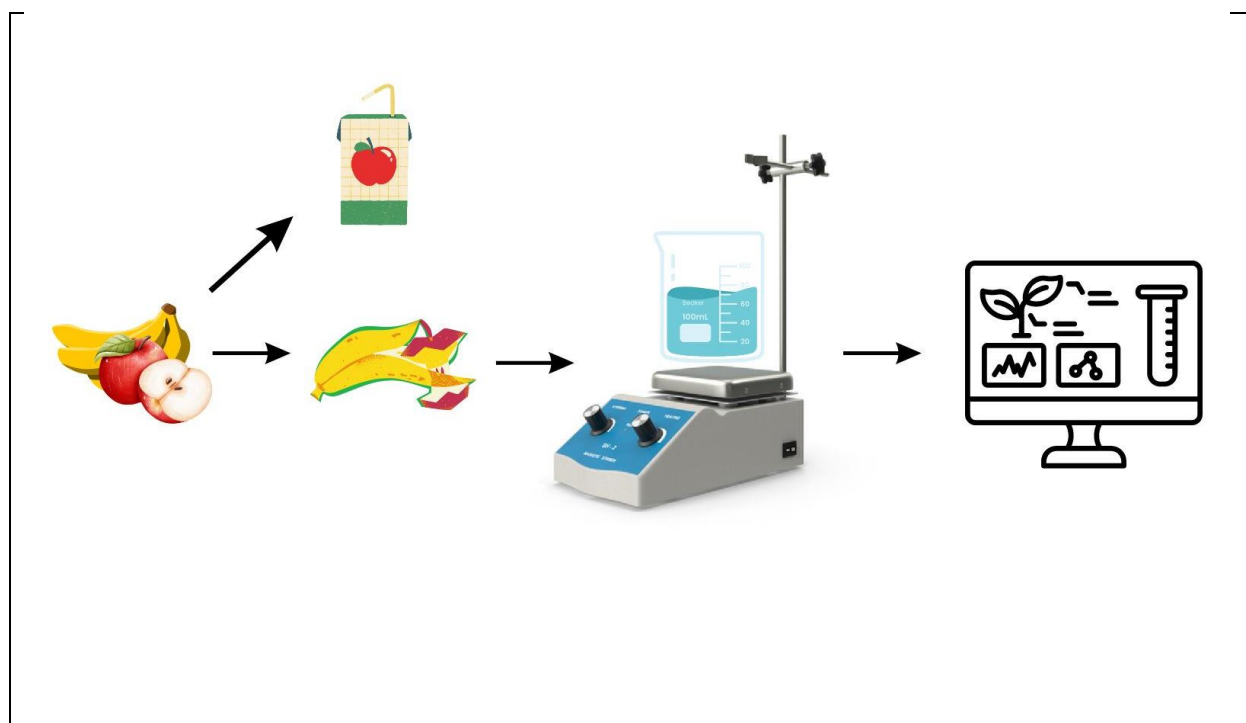
Medical University of Warsaw

Abstract

The project will concentrate on the optimization of the total polyphenol content and antioxidant activity of the selected agri-food by-products, such as fruit and vegetable pomace, spent coffee grounds and others. Agri-food by-products are rich in bioactive compounds such as polyphenols. With proper extraction of the bioactive compounds from agri-food by-products, they could be further used in animal feed or for the production of high-quality dietary supplements and cosmetics. During this work, student will learn step-by-step: different techniques of extract preparation, antioxidant activity tests (FRAP, ORAC, DPPH), data analysis, advanced statistical and chemometric methods for the analysis of experimental data, advanced techniques for visuals (figures and tables) preparation, presentation techniques to present the results of the project

Keywords: antioxidants, agri-food by-products, ORAC, FRAP, polyphenols

Graphic abstract



Title: Use of silicate molecular sieve/hydroxyapatite composites as drug delivery systems for bone infections treatment.

Supervisor: Łukasz Pajchel

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Department: Department of Pharmaceutical Chemistry and Biomaterials

Faculty of Pharmacy

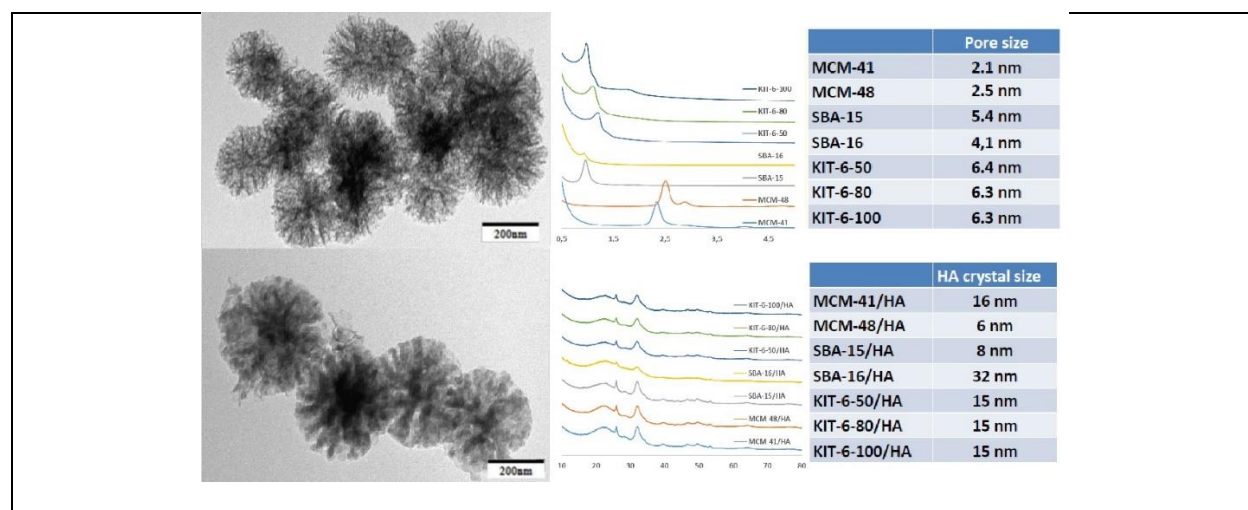
Medical University of Warsaw

Abstract

Hydroxyapatite with the formula $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ belongs to the group of calcium phosphates and is the most similar to natural osseous apatite. Mesoporous silica materials have emerged as promising drug vehicles, primarily due to their unique mesopores structure that while preserving a level of chemical stability, surface functionality and biocompatibility ensures the controlled release of a variety of drug molecules, so they are very useful for bone tissue regeneration. Gentamicin and ciprofloxacin are antibiotics frequently used in bone and joint infections. The problem with the treatment of bone infections is the low blood supply to this tissue, which makes it difficult for systemic antibiotics to reach this tissue. Therefore, local delivery of the antibacterial drug to the bone using a slow-release system is advisable. The aim of the project will be to test the utility of silicate molecular sieve/hydroxyapatite composites as drug delivery systems for antibiotics delivery. The Student's task will be to produce six composites: MCM-41/HA, MCM-48/HA, SBA-15/HA, SBA-16/HA, Kit-6/HA and KCC-1/HA differing in pore size and crystal morphology; characterisation of the materials using spectroscopic (PXRD, FT-IR, Raman) and microscopic (TEM, SEM) methods. A student will load then two antibiotics gentamycin and ciprofloxacin and analyze their release profile by HPLC method.

Keywords bone biomaterials, silica molecular sieve, hydroxyapatite, drug delivery systems, antibiotics

Graphic abstract



Title: Application of molecular modeling methods in the studies of inclusion complexes formed between borneol and cyclodextrins.

Supervisor: Łukasz Szeleszczuk

Contact: lukasz.szeleszczuk@wum.edu.pl

Department: Department of Organic and Physical Chemistry

Faculty of Pharmacy

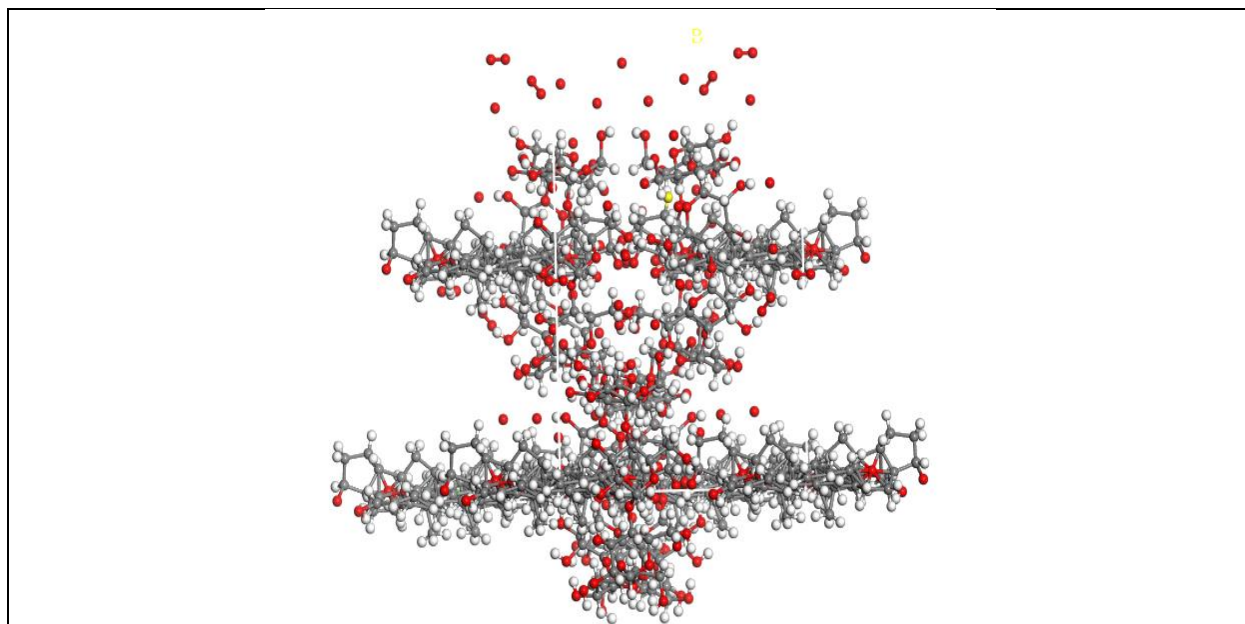
Medical University of Warsaw

Abstract

Cyclodextrins are cyclic oligosaccharides widely used to form inclusion complexes with hydrophobic drugs by the host-guest interaction, improving the solubility, dissolution rate and bioavailability of the including APIs. In order to effectively plan the synthesis routes as well as to explain the experimental results at the molecular level the molecular modeling methods are now commonly used in the pharmaceutical sciences. The aim of this work is to apply the molecular modelling methods in the studies of the complexes formed between the borneol and chosen cyclodextrins. The idea is to explain the difference in the stability constants, determined experimentally, between the α and β cyclodextrin's complexes with borneol. The study will include the geometry optimization of the complexes and calculations of chosen properties, such as thermodynamic values and simulation of molecular dynamics.

Keywords: cyclodextrin, borneol, molecular modeling, DFT, calculations

Graphic abstract



Title: Accessing a new space of biologically active compounds with multicomponent reactions

Supervisor: Maciej Dawidowski

Contact: maciej.dawidowski@wum.edu.pl

Department: Chair and Department of Drug Technology and Pharmaceutical Biotechnology

Faculty of Pharmacy

Medical University of Warsaw

Abstract

MultiComponent Reactions (MCRs) are chemical processes, in which three or more starting materials combine together, to give complex products of relevance to drug discovery, that would be difficult to be obtained by other means. Mostly, these product are complex in nature but can be obtained in a relatively straightforward manner. Therefore, MCRs are of increasing interest for pharma industry to develop new biologically active compounds. Moreover, due to their exceptional 'atom economy', they are more and more widely employed in large-scale manufacturing of active pharmaceutical ingredients (APIs), according to the principles of 'green chemistry'. In this project, students will gradually gain experience in synthetic medicinal chemistry using MCRs. They will be responsible for execution of chemical pathways leading to a number of biologically interesting scaffolds. This will be done using our *state-of-the-art* medicinal chemistry laboratories. The structure-reactivity analysis will be performed according to the obtained results. The obtained compounds will be characterized (NMR, MS) and assayed for their chemical purity (NMR, LC/MS).

Keywords: Multicomponent reactions (MCRs), drug discovery, medicinal chemistry, biologically active compounds, organic chemistry

Graphic abstract



Title: New, unnatural amino acid derivatives for drug discovery

Supervisor: Maciej Dawidowski

Contact: maciej.dawidowski@wum.edu.pl

Department: Chair and Department of Drug Technology and Pharmaceutical Biotechnology

Faculty of Pharmacy

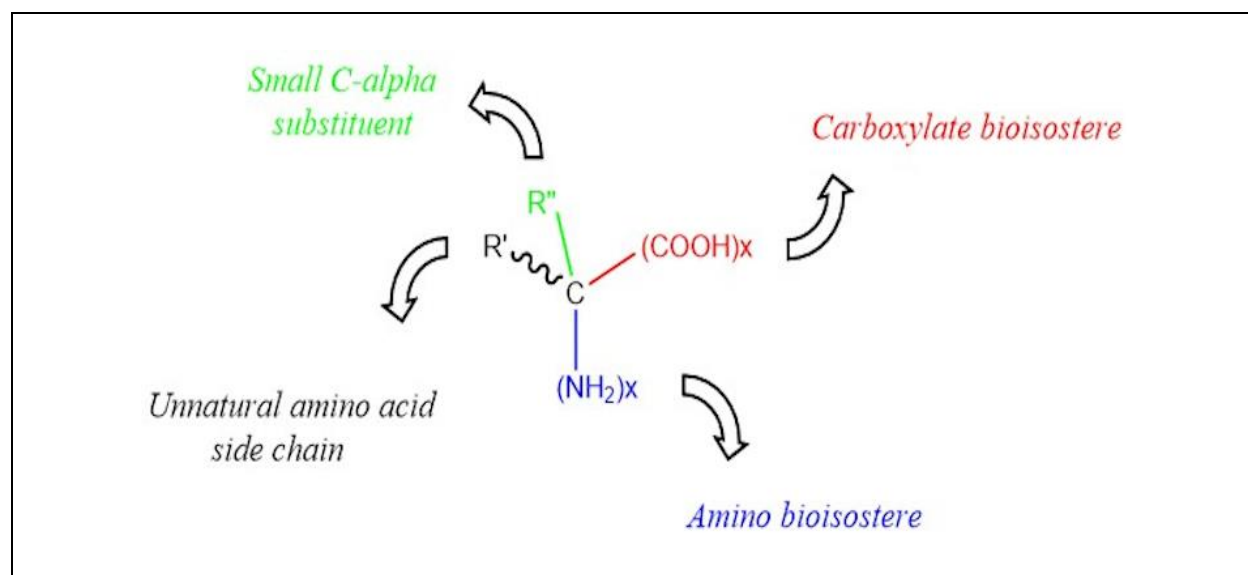
Medical University of Warsaw

Abstract

Amino acids constitute an important class of building blocks for drug discovery and for cellular studies. Unnatural amino acids are of particular interest, due to their use in design of compounds mimicking natural peptides. Such derivatives often have increased metabolic stability and display more optimal pharmacochemical profiles with regard to their naturally occurring counterparts. In this project, students will perform chemical synthesis of biologically relevant unnatural amino acid derivatives. This will be done using our *state-of-the-art* scientific medicinal chemistry infrastructure. The obtained scaffolds will be characterized (NMR, MS), assayed for their chemical purity (NMR, LC/MS) and used in the future as key building blocks for peptidomimetics.

Keywords: Drug discovery, peptidomimetics, organic chemistry, medicinal chemistry, amino acids

Graphic abstract



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

Supervisor: Maciej Dawidowski

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Department: Chair and Department of Drug Technology and Pharmaceutical Biotechnology

Faculty of Pharmacy

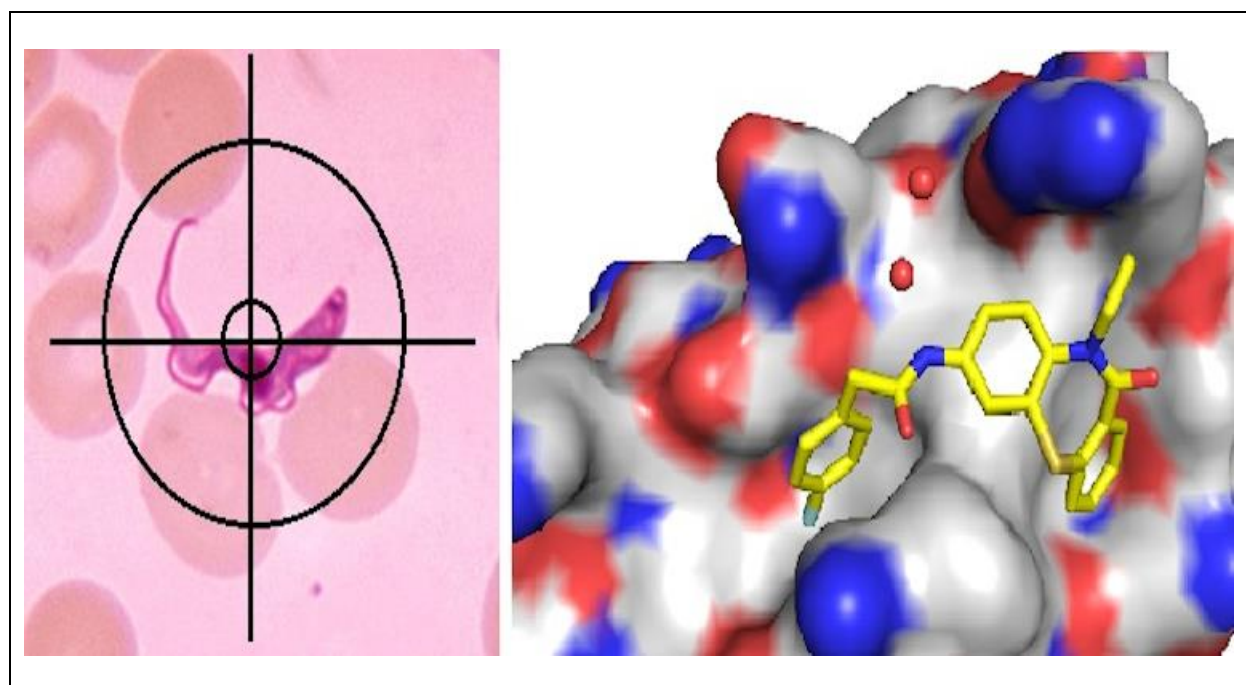
Medical University of Warsaw

Abstract

African Sleeping Sickness and Chagas disease are the major neglected tropical diseases (NTDs), 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).

Keywords: Drug discovery, medicinal chemistry, Trypanosoma, Sleeping Sickness, Chagas Disease,

Graphic abstract



Title: Biotechnological approach on obtaining woundhealing naphthoquinone pigments in *Anchusa officinalis* L. root *in vitro* culture

Supervisor: Małgorzata Jeziorek

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Faculty of Pharmacy

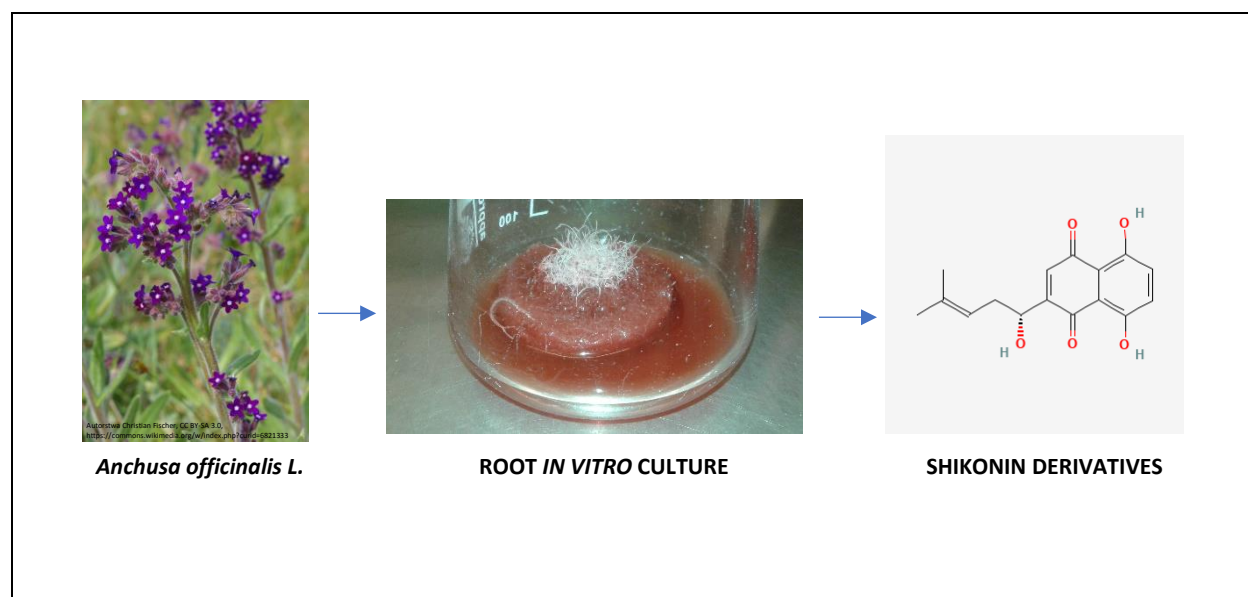
Medical University of Warsaw

Abstract

Anchusa officinalis L., commonly known as alkanet, is a species belonging to Boraginaceae family, which roots contain several red naphthoquinone pigments of shikonin/alkannin type. The aim of the project will be to obtain root *in vitro* cultures of *A. officinalis* producing significant amounts of shikonin derivatives, which are well known for their woundhealing activity and also can be used in the cosmetic industry. The laboratory work will include biotechnological methods in conducting root *in vitro* cultures, phytochemical investigation of root extracts and if needed isolation of pure compounds performed with preparative HPLC method.

Keywords: *Anchusa officinalis* L., *in vitro* roots, shikonin, alkannin

Graphic abstract



Title: Polyurethane anti-cancer drug delivery systems - synthesis, structural and application research

Supervisor: Marcin Sobczak

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Department: Department Pharmaceutical Chemistry and Biomaterials

Faculty of Pharmacy

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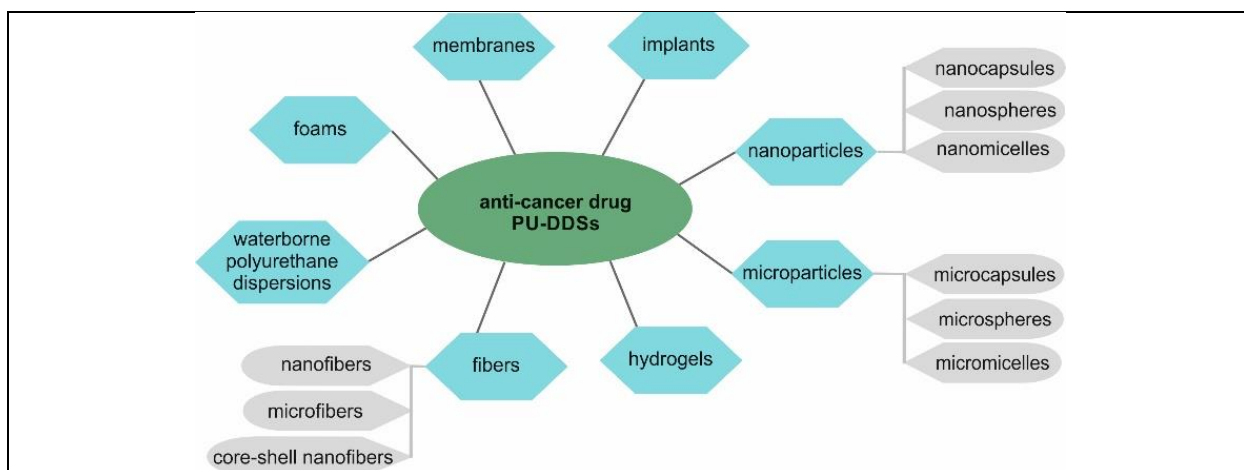
Abstract

With the intensive development of polymeric biomaterials in recent years, research using drug delivery systems (DDSs) has become an essential strategy for cancer therapy. Various DDSs are expected to have more advantages in anti-neoplastic effects, including easy preparation, high pharmacology efficiency, low toxicity, tumor-targeting ability, and high drug-controlled release. Polyurethanes (PUs) are a very important kind of polymers widely used in medicine, pharmacy, and biomaterial engineering. Biodegradable and non-biodegradable PUs are a significant group of these biomaterials.

In the experimental part of the diploma thesis, biodegradable PU DDSs containing paclitaxel will be obtained. The structure of the obtained DDSs will be characterized by spectroscopic methods. The kinetics of the drug release from the obtained DDSs will also be tested.

Keywords: biomaterials, drug delivery systems, anti-cancer drug delivery systems, biomedical polyurethanes, biodegradable polyurethanes,

Graphic abstract



Title: Enzyme-responsive hydrogels as anti-cancer drug delivery systems - synthesis, structural and application research

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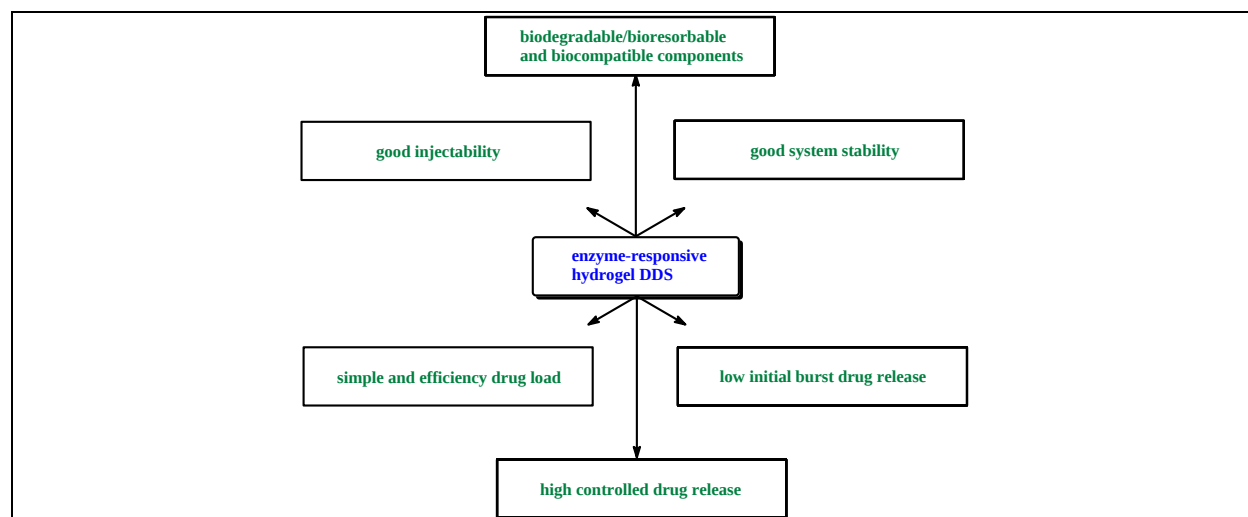
Abstract

Fast advances in polymer science have provided new hydrogels for applications in drug delivery. Among modern drug formulations, polymeric type stimuli-responsive hydrogels (SRH), also called smart hydrogels deserve special attention as they revealed to be a promising tool useful for a variety of pharmaceutical and biomedical applications. In fact, the basic feature of this system is the ability to change their mechanical properties, swelling ability, hydrophilicity, bioactive molecules permeability, etc., influenced by various stimuli, particularly enzymes. An enzymatic stimulus-responsive hydrogels (ERH) is highly attractive field of research due to its many potential biomedical applications (e.g., in controlled release, drug delivery, and other areas of biomaterial sciences).

In the experimental part of the diploma thesis, ERH containing paclitaxel will be obtained. The structure of the obtained ERH will be characterized by spectroscopic methods. The kinetics of the drug release from the obtained drug delivery systems will also be tested.

Keywords: biomedical hydrogels, stimuli-responsive hydrogels, enzyme-responsive hydrogels, drug delivery systems, controlled release

Graphic abstract



Title: Impact of FTO genotypes on radical weight loss after bariatric surgery

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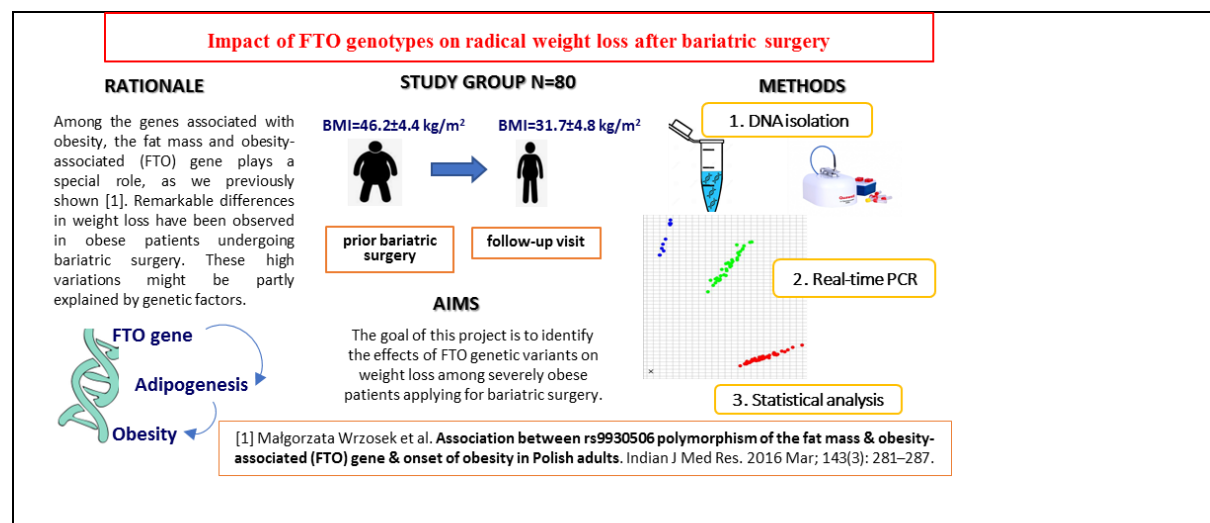
Abstract

Rationale: Among the genes associated with obesity, the fat mass and obesity-associated (FTO) gene plays a special role. In humans, it was first identified in 2007 in Genome-Wide Association Study (GWAS). The FTO gene is one of the genes recognized as associated with enhanced adiposity and seems to influence the risk of obesity, as we previously shown [1]. Remarkable differences in weight loss have been observed in obese patients undergoing bariatric surgery. These high variations might be partly explained by genetic factors. The goal of this project is to identify the effects of FTO genetic variants on weight loss among severely obese patients applying for bariatric surgery. **Materials and methods:** 80 participants with extreme obesity, prior bariatric surgery and follow-up visit. Body weight and body mass index (BMI), metabolic profile in relation to obesity, lipid and carbohydrate metabolism disturbances were measured at before bariatric surgery and after surgery at the 12 month. All 80 individuals will be analyzed for the FTO rs9939609 and rs9930506 gene polymorphisms. DNA will be isolated and Real-time PCR with Taq Man probes will be used. Genetic tests prior to bariatric surgery can help clinicians predicting the weight loss for severely obese patients in short-term follow-up.

[1] Indian J Med Res. 2016 Mar; 143(3): 281–287. Association between rs9930506 polymorphism of the fat mass & obesity-associated (FTO) gene & onset of obesity in Polish adults. Małgorzata Wrzosek et al.

Keywords: FTO variants, bariatric surgery, obesity; metabolic disturbances

Graphic abstract



Title: Antioxidant/pro-oxidant properties of selected agri-food by-products in vivo in zebrafish embryos model

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Faculty of Pharmacy

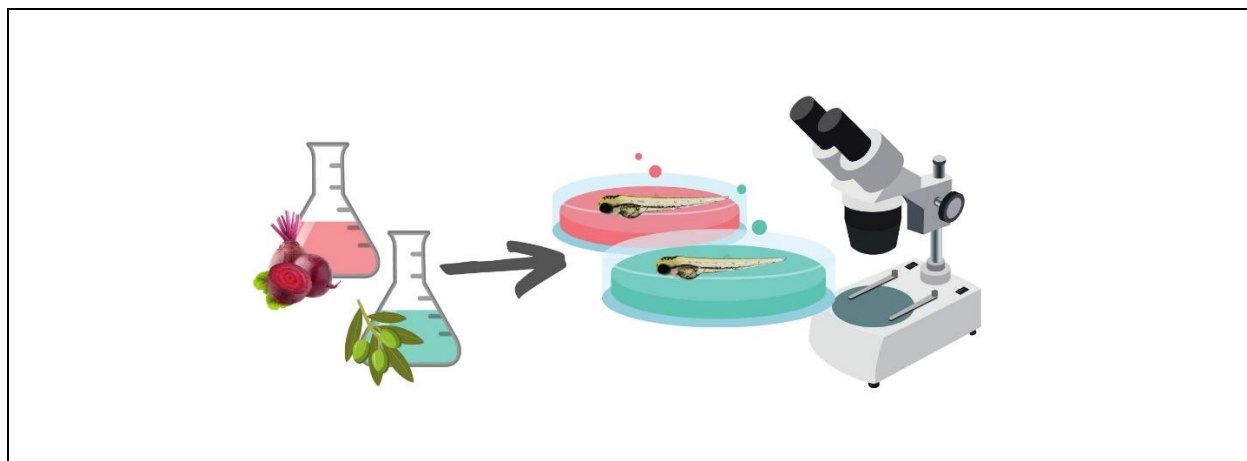
Medical University of Warsaw

Abstract

The project will concentrate on antioxidant/prooxidant properties of selected agri-food by-products, such as fruit or vegetable pomace, spent coffee grounds and others. One of the main problems with agri-food products is that they are rich in bioactive compounds. These compounds in general have antioxidant properties, but in some circumstances can have a pro-oxidant effect on aquatic animals, and thus should not be directly disposed in the environment. On the other hand, with proper extraction of the bioactive compounds from agrifood by-products, they could be further used to protect aquatic animals from oxidative stressed caused by pesticides and microplastic. During this work, student will learn step-by-step: different techniques of extract preparation and sample preparation for the zebrafish experiments, *in vivo* zebrafish embryos toxicity model, which is widely used for screening potential toxicants, various bioactive compounds and potential new drugs. Student will work with zebrafish embryos from 4 hours post fertilization till 3 days post fertilization and use microscope for the observation of zebrafish development, data analysis and advanced statistical methods for the analysis of zebrafish development data, advanced techniques for visuals (figures and tables) preparation, presentation techniques to present the results of the project

Keywords: antioxidants, pro-oxidants, zebrafish embryos, agri-food by-products

Graphic abstract



Title: Theoretical study of the mechanism of substituted thalidomide racemization

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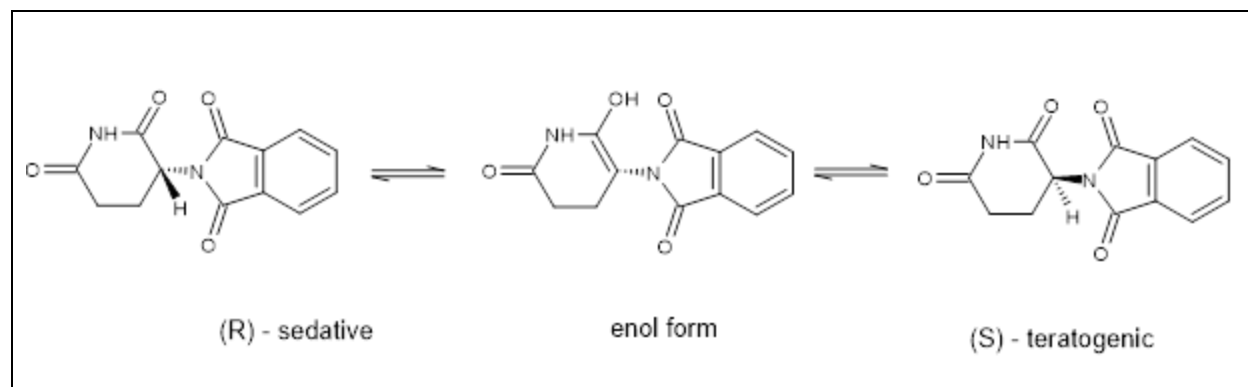
Medical University of Warsaw

Abstract

The thalidomide exists as two enantiomers – (R) - sedative medicine and (S) - teratogenic form. The process of racemisation is realized via the enol form. It is possible to determine the structure and thermodynamic stability of the enantiomers, the transition product (enol) and the transition states, by means of quantum-chemical calculations. The most important information obtained is the activation barrier which determines the speed of the racemization. This barrier can be raised by proper substitution of the molecule. Therefore the aim of this study is to perform the calculations first for the original thalidomide as the reference molecule, and then for pomalidomide and lenalidomide as two other developed drugs to check how the structural modifications influenced the stability of transition product and transition states. Next, the thalidomide molecule will be substituted by several selected substituents (for example: NH₂, Cl, CN, CF₃) in order to determine which of them could be potentially applied to raise the activation barrier of transition states and make the process of racemization very difficult or even impossible. That would result in making thalidomide-like medicine without teratogenic isomer present. The calculations will be performed by using the Gaussian 16 software, DFT and CCSD(T) methodologies.

Keywords: thalidomide, racemization, quantum-chemical calculations, keto-enol tautomerism, substituent effect

Graphic abstract



Title: Molecularly imprinted polymers based drug delivery devices

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Faculty of Pharmacy

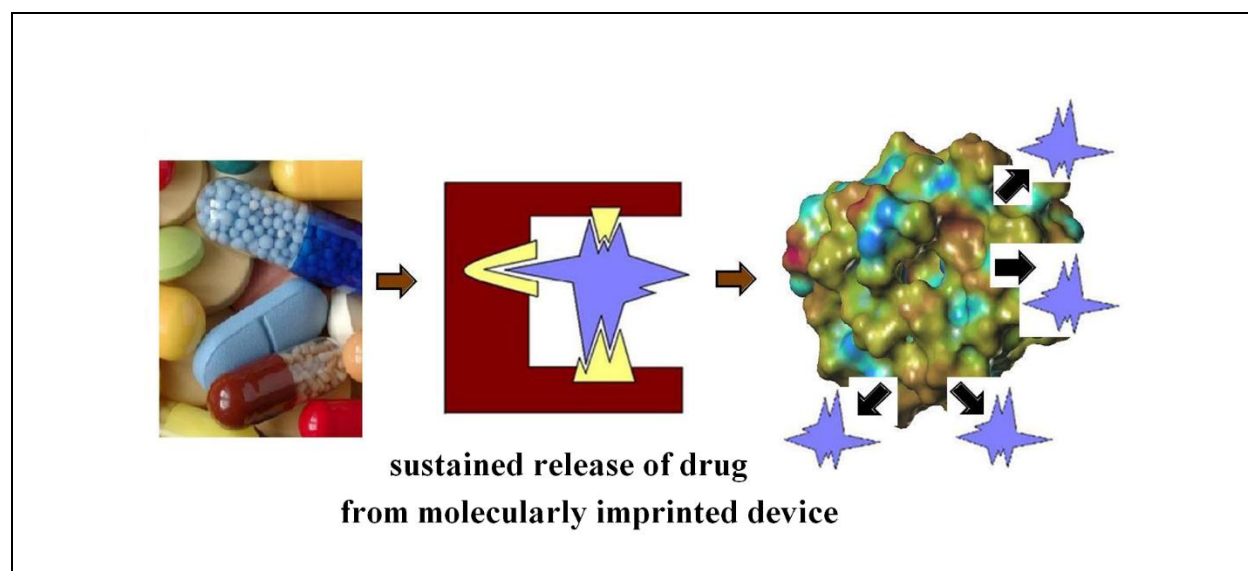
Medical University of Warsaw

Abstract

Molecularly imprinted polymers are promising materials in the construction of drug delivery devices because they can provide improved delivery profiles and longer release time as well as extended residency of the drug. This class of polymers could also release the drugs in the feedback regulated way, which could be extremely important in a modern model of pharmacotherapy oriented towards the delivery of the best suited drug to a single patient in the right place and at the right time. During the project, various synthetic approaches will be carried out to obtain the molecularly imprinted drug delivery device and special attention will be paid on biocompatibility and biodegradability of the material. The physicochemical characterization of the resulted polymer will be provided. The model drugs will be selected from various therapeutic groups to verify the applicability of molecularly imprinted drug delivery device.

Keywords: drug delivery, molecularly imprinted polymer, drug release

Graphic abstract



Title: Investigation of the chemical composition and gut microbiota metabolism of extracts from lemon balm leaves (*Melissa officinalis*)

Supervisor: Sebastian Granica

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Department: Department of Pharmaceutical Biology

Faculty of Pharmacy

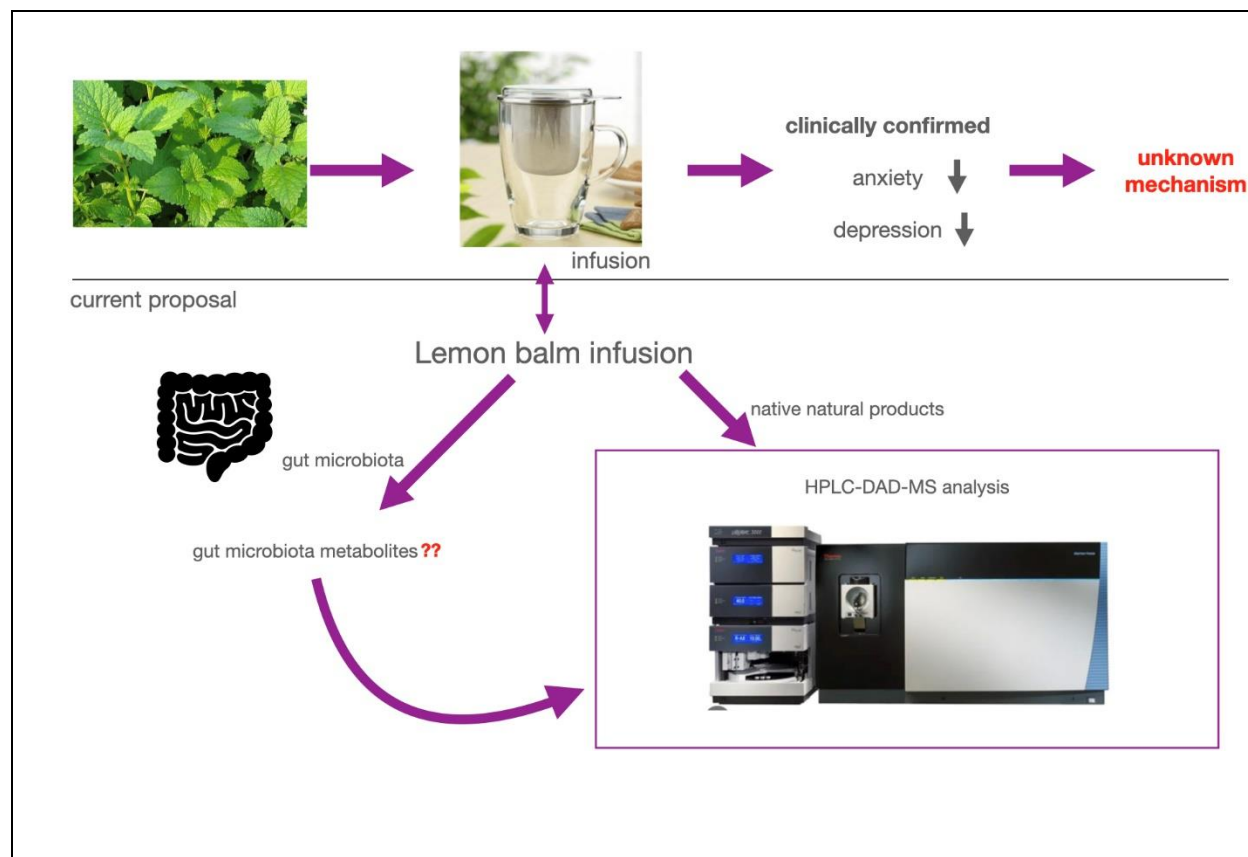
Medical University of Warsaw

Abstract

The aim of the project is to establish the possible metabolism of compounds contained in extracts prepared from lemon balm by human gut microbiota ex vivo. The students will be involved in the preparation of the extract its chemical analysis using HPLC-DAD-MS. Samples of the extract will later be incubated with human colon microbiota collected from healthy volunteers and changes in the composition will be checked by HPLC-DAD-MS.

Keywords: lemon balm, gut microbiota, phytochemical analysis, natural products

Graphic abstract



Title: The influence of chosen plant extracts on the inflammatory response of keratinocytes and/or fibroblasts in the context of their traditional use in skin diseases

Supervisor: Sebastian Granica

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Faculty of Pharmacy

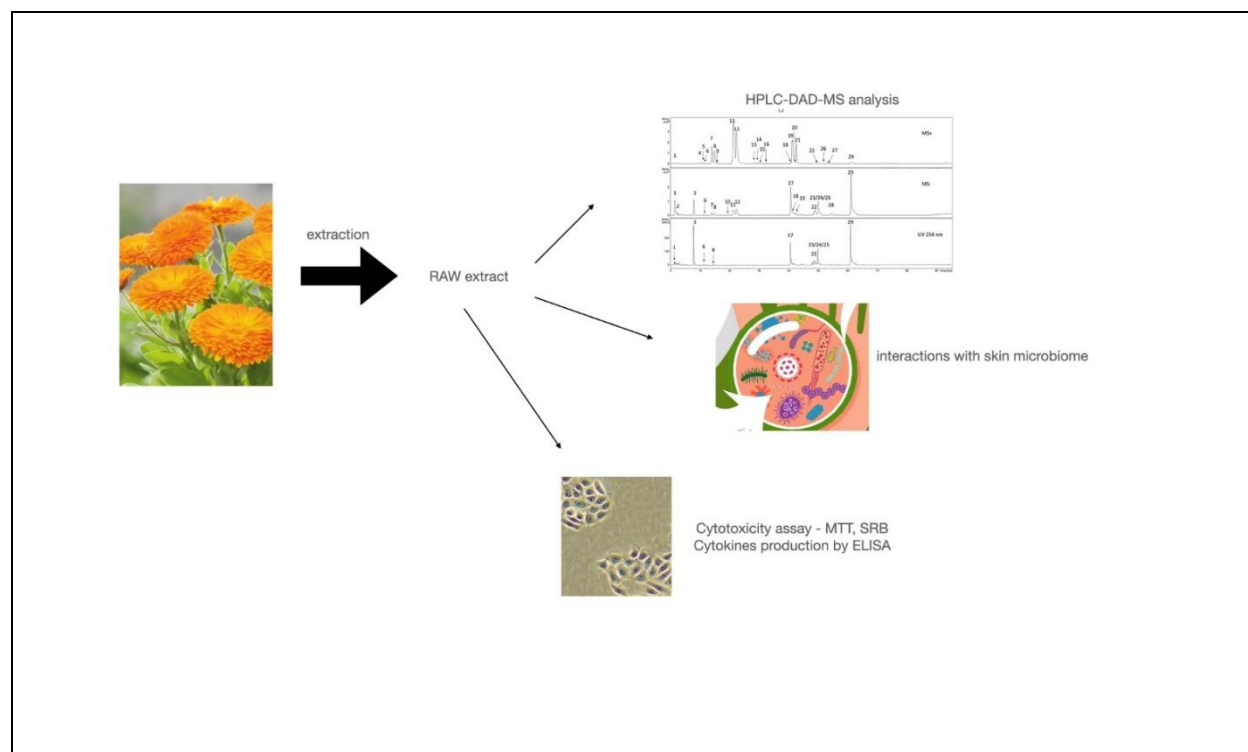
Medical University of Warsaw

Abstract

The project is focused on the preparation of plant extracts from one or two chosen plant materials commonly used in the treatment of skin diseases. The extracts will be chemically characterized by HPLC-DAD-MS method. Later the cytotoxicity of obtained material will be evaluated by SRB or MTT test using cell cultures present in our lab. Finally, the anti-inflammatory potential should be checked by the evaluation of the influence of extracts on proinflammatory functions of keratinocytes or/and fibroblasts.

Keywords: skin diseases, skin microbiota, plant extracts, phytochemical analysis, cell cultures

Graphic abstract



Title: Evaluation of the toxicity of selected antidepressant on the several fish cell lines

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Faculty of Pharmacy

Medical University of Warsaw

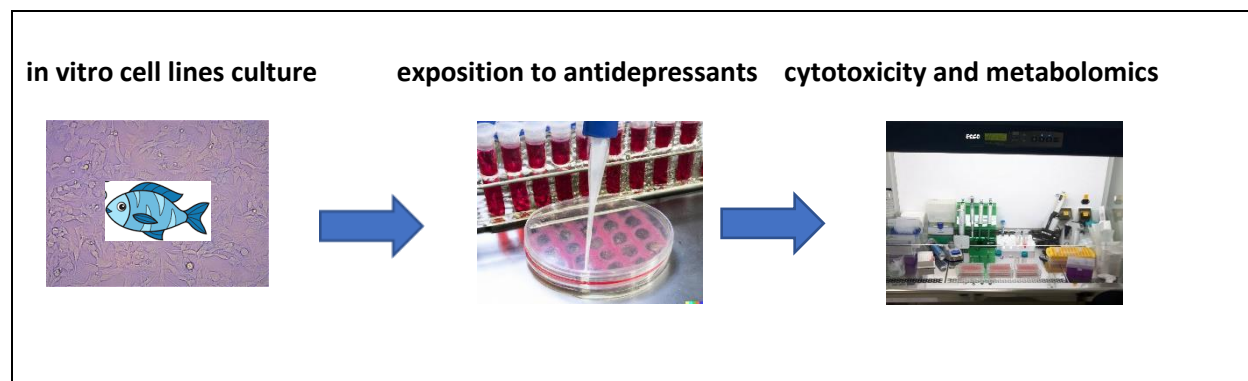
Abstract

During the last years, the number of studies on the occurrence of active pharmaceutical ingredients (API) in the environment has increased significantly. Antidepressants are a frequently detected group of drugs. Studies of acute and chronic toxicity have shown a significant effect of antidepressants in environmental concentrations on aquatic organisms. However, it is still unknown how API and their mixture affect the metabolism. This study aims to determine whether selected APIs: fluoxetine, paroxetine, sertraline and mianserin and their mixtures affect the metabolism of various fish cell lines.

During the project, several techniques will be used. Fish lines will be cultured *in vitro*, the cytotoxicity will be assessed in MTT assay or assay for cell proliferation with trypan blue. The metabolic changes will be evaluated using metabolomics.

Keywords: environment, antidepressants, toxicity, *in vitro*, cell lines, metabolomics

Graphic abstract



Title: The pharmaceutical availability of hydrogels with plant extracts of anti-inflammatory properties

Supervisor: Katarzyna Paradowska

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Department: Department of Organic and Physical Chemistry

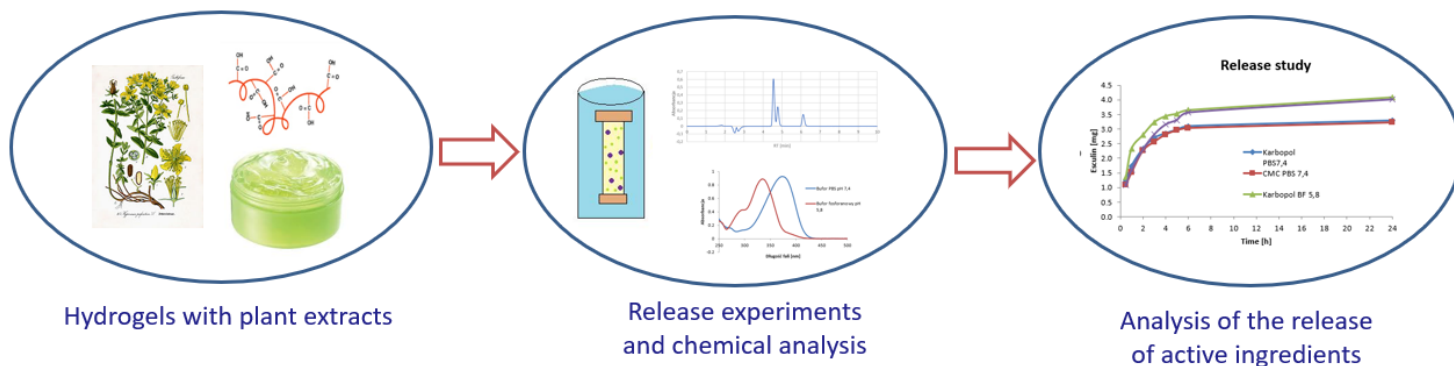
Faculty of Pharmacy, Medical University of Warsaw

Abstract

Plant extracts, due to the versatility of biologically active compounds are often used in cosmetic products, natural drugs, as well as food supplements. They are components with a multifunctional effect. An important issue for the pharmaceutical and cosmetics industry, which determines the effectiveness of the active substance, is its penetration into the skin. The penetration of active substances deep into the skin is determined by factors such as the condition of the skin, the physicochemical nature of the compound, and the type of the base. Penetration can be accelerated by using substances that provide relaxation of stratum corneum cells, including alcohols or glycols. A modern method determining the availability of active ingredients contained in a pharmaceutical or cosmetic product is the study of release kinetics from formulations, such as emulsions or gels. This experiment allows the assessment of the ability of the active substance to diffuse from the substrate through the membrane into a suitable solution. The aim of the present research is to characterize the chemical profile of plants extracts of anti-inflammatory properties, and their antioxidant activities, and to assess the diffusion capacity of plant extracts from self-prepared hydrogels.

Keywords: antioxidant, pharmaceutical availability, plant extract, hydrogels

Graphical abstract



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

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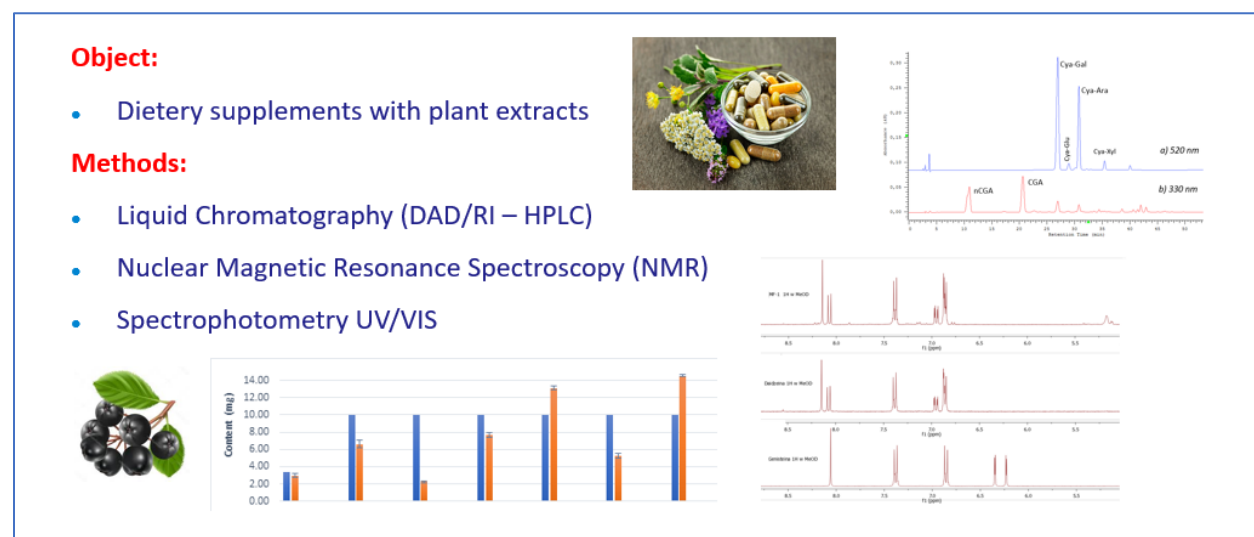
Faculty of Pharmacy, Medical University of Warsaw

Abstract

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.

Keywords: dietary supplements, DAD/RI-HPLC, NMR, plant extracts

Graphical abstract



Title: The preparation, physicochemical characterization, and *in vitro* dissolution of a selected anticancer drug-cyclodextrin inclusion complexes

Supervisor: Ewa Oledzka

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Department: Department of Pharmaceutical Chemistry and Biomaterials

Faculty of Pharmacy

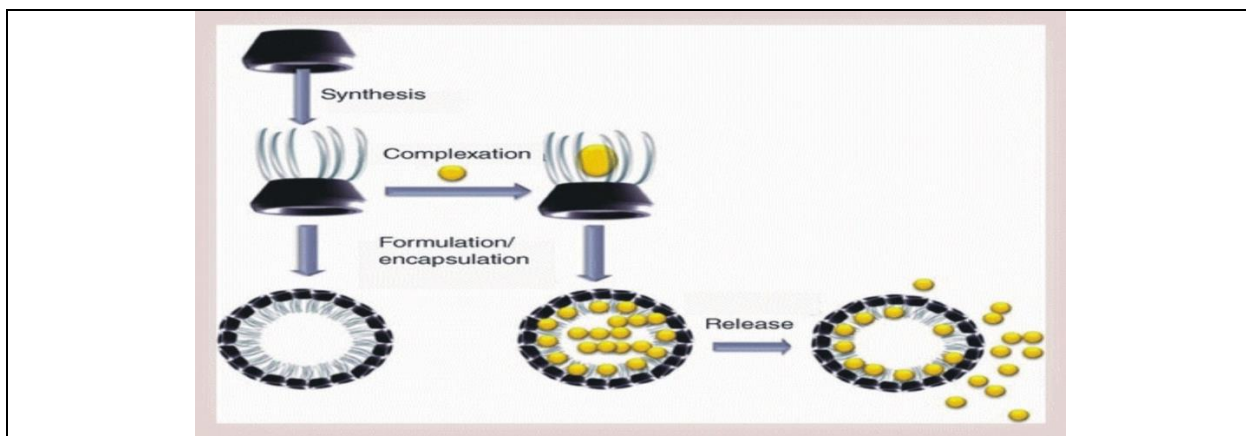
Medical University of Warsaw

Abstract

The goal of the research will be to develop new inclusion complexes of the selected cyclodextrins and their derivatives with a natural anticancer agent. In the pharmaceutical industry, cyclodextrins are used to increase the water solubility of lipophilic compounds, alter drugs, and improve bioavailability, solid phase stability, and absorption following oral, rectal, or transdermal administration. The experimental part of the work will consist of the synthesis and structural, physicochemical, and biological properties of the produced guest-host complex for various molar ratios of the reagents. The *in vitro* release profile of the anticancer agent will also be evaluated, and the results will be matched to specified kinetic models in order to analyze the control and release mechanism of the pharmacologically active compound from the produced complexes. The use of cyclodextrin in combination with an anticancer agent can improve drug encapsulation and its delivery, hence improving its therapeutic efficacy. Cyclodextrin inclusion complexes may also be a viable strategy for lowering therapeutic dosage levels, increasing the safety and curative potential of chemotherapeutic agent.

Keywords: cyclodextrin, anticancer drug, inclusion complex, controlled release, methods for host inclusion

Graphic abstract:



Title: Evaluation of the effectiveness of innovative biodegradable carrier for use in propranolol controlled release system

Supervisor: Ewa Oledzka

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Department: Department of Pharmaceutical Chemistry and Biomaterials

Faculty of Pharmacy

Medical University of Warsaw

Abstract

Synthetic biodegradable and/or biocompatible polymers are frequently employed in medicine and pharmacy due to their unique features. Aliphatic polyesters are of particular relevance because to their relatively easy degradation over a period of months to years. The goal of the research will be to synthesize and characterize novel polyester matrices as propranolol micro- and nanocarriers for the treatment of hypertension. Various spectroscopic techniques will be used to characterize the resulting polymeric materials, and the release profile of the active substance from the obtained system will be determined. Because of the repeatable and well-controlled drug release rate, as well as biodegradability and biosafety, the proposed system appears promising as a short-, middle-, or long-term drug delivery system with potential application in the treatment of hypertension.

Keywords: propranolol, nanoparticles, biodegradable copolymers, antihypertensive drug, hypertension, drug delivery system

Graphic abstract

