



# PHARMACY 4.0

Transforming Education for  
Innovative Competencies

Poznań, 23–24 kwietnia 2026



# CONFERENCE BOOK

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# Pharmacy 4.0: Transforming Education for Innovative Competencies

Poznań, 23–24 kwietnia 2026

Conference Book

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Conference

Pharmacy 4.0: Transforming Education for Innovative Competencies

Poznań, 23–24 kwietnia 2026

Conference Book

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*Dear Sir/Madam,*

We are pleased to invite you to the **International Scientific and Educational Conference Pharmacy 4.0: Transforming Education for Innovative Competencies**, which will be held on April 23-24, 2026 at the Library and Congress Center of Poznan University of Medical Sciences.

The aim of the conference is to create a platform for the exchange of knowledge and experience between the academic community, pharmaceutical practice, public institutions, the pharmaceutical industry, and pharmacy students. The event is dedicated to the challenges of modern pharmacy in the context of changes in the healthcare system, technological development, and the growing expectations regarding the professional competencies of pharmacists.

How to educate pharmacists in the era of globalization? During the conference, we will compare Polish and international models of pharmaceutical education and discuss national education standards in relation to international solutions, sharing good practices and inspiration for the future. The program of the conference emphasizes the role of cooperation with external institutions and companies in the education process, which enables the resolution of economic problems and guarantees that students acquire skills and meet the needs of the labor market.

The program includes plenary lectures, scientific and teaching sessions, discussion panels, expert debates, an e-poster session and practical workshops, with a particular focus on innovative teaching methods, the internationalization of education, its interdisciplinary nature and the use of artificial intelligence in science and teaching. You are invited to attend the conference.

See you in Poznań!

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*Prof. dr hab. Anna Jelińska*

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# CONFERENCE PROGRAMME

## DAY 1 – Pharmacy Science and Education

11:00-12:00  Participants' registration

12:00-12:20  Official opening of the conference, speeches by invited guests

*Prof. dr hab. Zbigniew Krasiński, Prof. dr hab. Anna Jelińska*

12:20-13:00  Inaugural lecture: Education of Pharmacists in the Face of Global Challenges of the Pharmaceutical Industry

*Prof. dr hab. Małgorzata Sznitowska*

13:00-14:20 **Plenary Session: Pharmacy 2035 – Science, Education and Professional Practice in a Changing Healthcare System**

*Prof. dr hab. Edmund Grześkowiak, Prof. dr hab. Lucjusz Zaprutko*

 Can Technology Replace the Master? On the Limits of Modern Pharmacist Education

*Prof. dr hab. Małgorzata Kotwicka (Poznan University of Medical Sciences)*

 Modern Methods of Teaching Pharmacy Students

*Prof. dr hab. Wojciech Miłyk (Medical University of Białystok)*

 Scientific Research as an Important Element of Teaching Medicinal Chemistry and Related Disciplines

*Prof. dr hab. Roman Lesyk (Danylo Halytsky Lviv National Medical University)*

 Pharmaceutical Education in a Time of Global Challenges

*Prof. Oleksandr Kukhtenko: (National University of Pharmacy, Ukraine)*

14:20-15:10  Lunch break

15:10-16:10 **Deans' Debate of KRAUM Pharmacy Faculties: Education and competencies of pharmacists in Poland – directions for change**

facilitator: *Prof. dr hab. Dorota Zozulińska-Ziółkiewicz*

16:10-16:30  Coffee break

16:30-18:00 **Session 1: Global academic cooperation: mobility, innovation and knowledge transfer**

*Prof. dr hab. Violetta Krajka-Kuźniak*

 Academic Exchange as an Element of the Internationalization of Higher Education

*Prof. Michał Masternak (University of Central Florida, USA)*

Interface of AI and Neurodegeneration-New Ideas in Leading International Collaborations to Treat Brain Diseases

*Dr Łukasz Joachimiak (UT Southwestern Medical Center)*

American Experience and Polish Competencies – The Gains of Academic Exchange

*Anna Kertyczak (Fulbright Poland)*

Future Technologies – The Use of Science in Digital Transformation – Presentation of the BPRPM Method

*Dr inż. Filip Nowak (Łukasiewicz – Poznań Institute of Technology)*

12:00-18:00 **Poster session (e-posters)**

## **DAY 2 – Science and Practical Skills**

09:00-10:20 **Scientific Session: Interdisciplinary character of pharmaceutical research and practice**

*Prof. dr hab. Tomasz Osmalek*

The Role of the Pharmaceutical Industry in Pharmacy Education: Interdisciplinary Approaches and Collaboration with Academia and Healthcare Systems

*Prof. Nunzio Denora (The University of Bari Aldo Moro, Italy)*

Integrating Pharmacy and Industrial Pharmacy into Academic Education and Multidisciplinary Healthcare Systems

*Prof. Heli Bollström (University of Helsinki, Finland)*

Training of Pharmaceutical Scientists for Industry and Pharmaceutical Research from a UK Perspective

*Dr Sebastian Winkler (University of Nottingham, United Kingdom)*

10:20-10:40 ☕ Coffee break

10:40-12:00 **Session 3: Future competencies of pharmacists**

*Dr hab. Magdalena Waszyk-Nowaczyk*

Soft and Social Skills in Teamwork

*Dr hab. Magdalena Cerbin-Koczorowska (University of Edinburgh, United Kingdom)*

An Interprofessional Approach to Education for Future Pharmacists

*Prof. Martin Henman (Trinity College Dublin, Ireland)*

Modern Education in Pharmacy

*Dr Tanja Fens (University of Groningen, The Netherlands)*

Pharmaceutical Care as Part of Interprofessional Collaboration in Patient Therapy

*Dr Mikołaj Piekarski (University Hospital of Northern British Columbia, Canada)*

12:00-12:20 ☕ Coffee break

12:20-13:20 **Expert Panel: The labor market and professional training of pharmacists**

facilitators: *Prof. dr hab. Anna Jelińska, Prof. dr hab. Justyna Gornowicz-Porowska*

08:00-12:45 **Workshop session**

**Workshop A: Modern Teaching Methods in Pharmacy** *Prof. dr hab. Małgorzata Kotwicka*

1. **Providing Constructive Feedback** - *dr n. med. Beata Buraczyńska-Andrzejewska prof. UMP (workshop for teachers)*

2. **Effective Participation in Online Courses** - *Michał Owczarzak (workshop for students)*

3. **Learning Without Limits, or How to Effectively Use e-Learning** - *Michał Owczarzak (workshop for students)*

**Workshop B: The Pharmacist of the Future: Education and Practice in Pharmaceutical Care**

*Dr hab. Magdalena Waszyk-Nowaczyk*

**Workshop C: Application of Recent Advances in Pharmacometrics and PK/PD Modeling in Clinical Pharmacy Practice and the Pharmaceutical Industry – Practical Training in an Interprofessional Team**

*Prof. Dr. Hab. Agnieszka Bienert*

**Workshop D: Future Technologies – Modeling and Simulation of Processes as a Key to Digital Transformation in Healthcare**

*Dr inż. Jacek Krzywy & Mgr inż. Witold Statkiewicz (Łukasiewicz - Poznań Institute of Technology)*

13:20-13:45 **Closing of the conference**

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# Analysis of the Phototoxic Potential of Lomefloxacin in an Experimental Model of Prostate Cancer

Artur Beberok<sup>1\*</sup>, Zuzanna Rzepka<sup>1</sup>, Dorota Wrześniok<sup>1</sup>, Alina Drzyzga<sup>2</sup>, Ryszard Smolarczyk<sup>2</sup>, Justyna Czaplą<sup>2</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, Jagiellońska 4, 41-200 Sosnowiec, Poland

<sup>2</sup>Maria Skłodowska-Curie National Research Institute of Oncology, Wybrzeże Armii Krajowej 15, 44-102 Gliwice, Poland

\*Corresponding author e-mail: abeberok@sum.edu.pl

Prostate cancer ranks among the most frequently diagnosed malignancies in men globally and constitutes a major public health concern. Despite significant advancements in diagnostic and therapeutic approaches, there remains an ongoing need to develop novel treatment strategies aimed at enhancing therapeutic efficacy and minimizing adverse effects

Lomefloxacin, a member of the fluoroquinolone class, is an antibiotic primarily used for the treatment of bacterial infections. However, this compound also exhibits phototoxic properties, which can lead to the generation of reactive oxygen species upon exposure to UV radiation. This mechanism has attracted interest among researchers in the context of the potential use of lomefloxacin as an adjunctive agent in therapeutic strategies based on photodynamic damage to cancer cells.

The aim of this study was to evaluate the phototoxic potential of lomefloxacin in an *in vitro* model using PC3 prostate cancer cells.

To evaluate the phototoxic effect, cells were subjected to controlled exposure using a sunshine simulator that replicates the spectrum of natural UV radiation. In the experimental protocol, cells were preincubated with lomefloxacin for one hour, followed by a 30-minute irradiation period with the solar light simulator, and subsequently maintained in standard culture medium for a 24-hour post-incubation. Cell viability was determined using the WST-1 assay

Analysis of the results indicated that lomefloxacin at concentrations ranging from 1 to 200  $\mu\text{M}$  did not exhibit significant cytotoxic activity against PC3 cells, with cell viability remaining comparable to that of the control. However, under conditions of simultaneous exposure to lomefloxacin (50–200  $\mu\text{M}$ ) and UV radiation, a pronounced phototoxic effect was observed, resulting in a 45–55% reduction in cell viability, depending on the concentration of the compound applied.

The results indicate that lomefloxacin exhibits a strong phototoxic effect in the investigated *in vitro* model, while lacking inherent cytotoxic activity. These observations may serve as a basis for further studies exploring the potential use of this compound as part of combination therapy for the treatment of prostate cancer.

**Keywords:** lomefloxacin; prostate cancer; cytotoxicity; phototoxicity; solar light simulator

**Acknowledgments:** This project was funded by the National Science Centre (OPUS 27, project no. 2024/53/B/NZ5/03279) and the Medical University of Silesia in Katowice (grant no. BNP-1-035/K/5/F).

## **Inhibition of Lipid Accumulation by Withaferin A and Honokiol in an in vitro HepG2 Model of NAFLD**

Marta Belka<sup>1,2\*</sup>, Aleksandra Gostyńska-Stawna<sup>3</sup>, Maciej Stawny<sup>3</sup>, Violetta Krajka-Kuźniak<sup>1</sup>

<sup>1</sup>*Poznan University of Medical Sciences, Department of Pharmaceutical Biochemistry, Rokietnicka 3, 60-806 Poznań, Poland*

<sup>2</sup>*Poznan University of Medical Sciences, Doctoral School, Bukowska 70, 60-812 Poznań, Poland*

<sup>3</sup>*Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Rokietnicka 3, 60-806 Poznań, Poland*

\*Corresponding author e-mail: mbelka@ump.edu.pl

Non-alcoholic fatty liver disease (NAFLD), currently also defined as metabolic dysfunction-associated steatotic liver disease (MASLD), represents a growing global health challenge. This condition is characterized by excessive lipid accumulation in hepatocytes, driven by insulin resistance and metabolic disorders. In the search for new therapeutic strategies, natural compounds such as honokiol and withaferin A are being investigated for their potential to regulate fatty acid metabolism and for their anti-inflammatory effects.

This study aimed to establish an in vitro NAFLD model using the HepG2 cell line and to evaluate the effects of honokiol, withaferin A, and their combination on intracellular lipid accumulation. Steatosis was induced in HepG2 hepatocytes by exposure to a mixture of free fatty acids. Cell viability was assessed using the MTT assay, while lipid accumulation was evaluated by Nile Red staining followed by quantitative fluorescence analysis using the Celena X High-Content Imaging System. The developed in vitro NAFLD model effectively induced steatotic features in hepatocytes. Combined treatment with honokiol and withaferin A resulted in a greater reduction in intracellular lipid droplets compared to either compound alone. These findings suggest that the combined use of these natural compounds may represent a promising strategy for modulating lipid metabolism and preventing hepatocellular lipid accumulation associated with NAFLD.

**Keywords:** NAFLD; honokiol; withaferin A; HepG2

**Acknowledgments:** Research was financed from the large research grant from statutory funding for young researchers – PUMS doctoral students for 2025/2026.

# Pharmacotherapy of Acute Migraine Episodes: Comparative Effectiveness of Triptans Available in Poland with Reference to Over-the-Counter Almotriptan – A Mini Review

Wiktoria Biela<sup>1\*</sup>, Kamila Czora-Poczwardowska<sup>2</sup>, Weronika Jarczak<sup>1</sup>, Aleksandra Temblowska<sup>1</sup>, Michał Szulc<sup>2</sup>, Przemysław Mikołajczak<sup>2</sup>, Radosław Kujawski<sup>2</sup>

<sup>1</sup>*Faculty of Pharmacy, Student Scientific Society of Pharmacology, Poznan University of Medical Sciences, Rokietnicka 3 Str., 60-806 Poznan, Poland*

<sup>2</sup>*Faculty of Pharmacy, Department of Pharmacology, Poznan University of Medical Sciences, Rokietnicka 3 Str., 60-806 Poznan, Poland*

\*Corresponding author e-mail: wiktoria.biela35@gmail.com

**Introduction:** Migraine is a common neurological disorder associated with a substantial individual and societal burden. The primary goal of pharmacotherapy for acute migraine attacks is to provide rapid and sustained pain relief. Triptans remain a key therapeutic option; however, their effectiveness may vary depending on the specific compound, dose and route of administration. Recently, almotriptan, has become available as an over-the-counter (OTC) medication in Poland, potentially improving access to acute migraine treatment. Therefore, this study aimed to compare the effectiveness of triptans available in Poland and to interpret these findings in the context of the OTC availability of almotriptan and its potential clinical implications.

**Materials and methods:** A literature review was conducted using PubMed, Google Scholar, and the Cochrane Library. English-language meta-analyses and clinical trials published within the last 10 years evaluating the effectiveness of triptans in the treatment of acute migraine attacks were included (state of knowledge as of May 2025). After removal of duplicates, eight publications were included in the final analysis.

**Results:** Triptans provide effective pain relief and pain freedom at both 2 and 24 hours. Their efficacy varies according to the specific agent, dose, and route of administration, with oral eletriptan (40 mg) and subcutaneous sumatriptan (6 mg) showing the highest effectiveness. Combination therapy with sumatriptan and naproxen enhances both efficacy and tolerability compared with monotherapy. Almotriptan (12.5 mg) demonstrates slightly lower efficacy than standard-dose sumatriptan (50 mg), still appears more effective than naratriptan and frovatriptan in most studies.

**Conclusions:** Triptans are effective for acute migraine attacks with their particular choice and route of administration to be tailored to the patient. Although the availability of almotriptan as an OTC medication improves access to treatment, the use of all mentioned triptan representatives carries a risk of adverse events, particularly with higher doses, which requires careful consideration.

**Keywords:** migraine; triptans; acute treatment

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# Thin-Film Hydration Method for the Synthesis of Nobiletin-Loaded Mixed Micelles

Kamila Buzun<sup>1\*</sup>, Izabela Żółnowska<sup>1</sup>, Barbara Jadach<sup>2</sup>, Maciej Stawny<sup>1</sup>

<sup>1</sup>*Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry,  
Rokietnicka 3 Street, Poznan, Poland*

<sup>2</sup>*Poznan University of Medical Sciences, Department of Pharmaceutical Technology,  
Rokietnicka 3 Street, Poznan, Poland*

\*Corresponding author e-mail: kbuzun@ump.edu.pl

Nobiletin is a natural compound occurring in citrus peels, leaves, and stems. This bioactive flavonoid has a broad spectrum of activity, including antioxidant, anticancer, antidiabetic, and anti-inflammatory. In recent years, nobiletin has attracted numerous preclinical studies investigating its mechanism of action and potential therapeutic applications. However, due to its poor water solubility, the potential use of nobiletin in medicine and pharmacy is limited.

The aim of this study was to synthesize nobiletin-loaded mixed micelles. Nobiletin (5 mg), phosphatidylcholine (100 mg), and sodium deoxycholate (50 mg or 100 mg) were dissolved in 10 mL of absolute ethanol in a round-bottom flask. In the next step, the solvent was evaporated under reduced pressure using a rotor evaporator (50 °C, 125 rpm) to obtain a thin layer of nobiletin, phosphatidylcholine, and sodium deoxycholate. After ethanol evaporation, the samples were kept at room temperature (RT) for two hours and frozen (-20 °C). Subsequently, the film was hydrated with 12 mL of sterile water (RT, 70 rpm), and the mixed micelles suspension was stabilized using a horizontal shaker (20 min, 200 rpm). All samples were frozen for 24h (-20 °C) and lyophilized. Measurements of particle size and zeta potential were conducted two times – directly after synthesis and after lyophilization.

Directly after synthesis, the nobiletin-loaded mixed micelles exhibited average particle sizes in the range of 13.37–16.38 nm, with zeta potential values between -34.20 and -41.20 mV. After lyophilization, the average particle size ranged from 12.89 to 15.99 nm, while the zeta potential ranged from -34.40 to -45.60 mV.

The obtained nobiletin-loaded mixed micelles exhibit good solubility in aqueous media. The applied synthesis method enabled the preparation of mixed micelles with the desired physicochemical properties.

**Keywords:** nobiletin; polyphenols; mixed micelles; nanoparticles

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# Polymeric Mixed Micelles as Carriers for Fisetin: Development and Stability Evaluation

Joanna Czerniel<sup>1\*</sup>, Tomasz Przybylski<sup>1,2</sup>, Maciej Stawny<sup>1</sup>

<sup>1</sup>*Department of Pharmaceutical Chemistry, Poznan University of Medical Sciences, Rokietnicka 3, 60-806 Poznan, Poland*

<sup>2</sup>*Doctoral School, Poznan University of Medical Sciences, Poznan, Poland*

\*Corresponding author e-mail: jczerniel@ump.edu.pl

**Introduction:** Fisetin (FIS) is a natural polyphenolic compound found in small amounts in fruits and vegetables such as strawberries, apples, and onions. Chemically known as 3,7,3',4'-tetrahydroxyflavone, it is a yellow crystalline compound characterized by low water solubility and high lipophilicity. FIS exhibits antioxidant, anti-inflammatory, antiangiogenic, and anticancer properties and can inhibit tumor growth, migration, and autophagy while promoting cell-cycle arrest and programmed cell death. However, its therapeutic application is limited by low bioavailability resulting from rapid metabolism and a short half-life. Nanotechnology-based delivery systems, such as mixed micelles, can enhance drug solubility, stability, and therapeutic efficacy.

**The aim of this study** was to develop three-component mixed polymeric micelles to enhance the solubility and bioavailability of FIS. The systems were based on Poloxamers, Kolliphor, and a bile salt. Their physicochemical properties and stability over 28 days were evaluated, and selected formulations were analyzed for thermal behavior and crystalline structure.

**Materials and methods:** Eight formulations containing different ratios of bile salts, Poloxamer, and Kolliphor were prepared using the thin-film hydration method and stored as lyophilizates at  $4 \pm 1$  °C.

**Results:** All formulations showed high encapsulation efficiency (64.8–74.8%) on the first day. After 28 days, systems containing Kolliphor HS15 maintained the highest values (>72%). Stability assessment based on mean droplet diameter and zeta potential identified three formulations (FM2, FM4, FM6) for further analysis. DSC results indicated the formation of a solid dispersion, while XRPD analysis confirmed structural reorganization and amorphization of FIS.

**Conclusions:** The developed micellar systems showed high encapsulation efficiency and good physical stability over 28 days. Thermal and structural analyses confirmed interactions within the polymer matrix and the transition of FIS from crystalline to amorphous form, which may enhance its biopharmaceutical performance.

**Keywords:** mixed micelles; fisetin; Poloxamer; Kolliphor; bile salts

**Acknowledgments:** This work was funded by grant OPUS No. 2022/45/B/NZ7/01056 from the National Science Centre, Poland.

## A Biomimetic Nanocarrier for Honokiol

Katarzyna Dominiak<sup>1,2\*</sup>, Aleksandra Majchrzak-Celińska<sup>3</sup>, Violetta Krajka-Kuźniak<sup>3</sup>,  
Maciej Stawny<sup>1</sup>

<sup>1</sup> Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Rokietnicka 3, 60-806 Poznan, Poland

<sup>2</sup> Poznan University of Medical Sciences, Doctoral School, Bukowska 70, 60-812 Poznan, Poland

<sup>3</sup> Poznan University of Medical Sciences, Department of Pharmaceutical Biochemistry, Rokietnicka 3, 60-812 Poznan, Poland

\*Corresponding author e-mail: katarzyna.dominiak@student.ump.edu.pl

Coating nanoparticles with red blood cells (RBC) membranes is a promising biomimetic strategy that combines the benefits of nanocarriers with those of natural cell membranes. Nanoparticles (NPs) can deliver poorly water-soluble compounds efficiently and improve stability and bioavailability, while RBC membranes enhance biocompatibility and biodegradability. This approach is particularly promising for compounds with clinical potential whose application is limited by their unfavourable physicochemical properties. One such compound is honokiol (HON), which modulates multiple signaling pathways and receptors and exhibits anti-inflammatory, antioxidant and anticancer activities.

The aim of this study was to develop honokiol-loaded nanoparticles (HON-loaded-NPs) coated with RBC membranes.

First, polymeric NPs were prepared and subsequently combined with RBC membranes. HON polycaprolactam NPs were obtained using an emulsification method involving ultrasonic sonication, followed by solvent evaporation. Prior to coating, the RBC membranes were sonicated and extruded through filters with a pore diameter of 200 nm. The final formulation was obtained by combining RBC membranes with HON-loaded-NPs at a ratio of 2:1, followed by sonication in an ultrasonic bath for 10 minutes. The physicochemical properties of the NPs (MPS, PDI and ZP) were evaluated, and haemolysis and cytotoxicity assays were performed.

The HON-loaded-NPs coated with RBC membranes exhibited desirable physicochemical properties. The MPS values ranged from 197 to 226 nm, which confirms an increase following RBC membrane coating. The zeta potential values became more negative (by up to 5.2 mV), which indicates successful membrane coating. Haemolysis tests showed that uncoated nanoparticles caused 17.2% haemolysis, whereas this value decreased to 1.13% after coating, which is within the safe range < 5%. Cytotoxicity studies on the glioblastoma cell lines U87 revealed reduced viability of the cells.

The results of the present study suggest that HON-loaded-NPs-RBC may exhibit improved safety and anti-cancer activity, supporting their potential as candidates for further investigation.

**Keywords:** nanoparticles; honokiol; erythrocyte

**Acknowledgments:** This project was funded by the Poznan University of Medical Sciences Doctoral School grant (No. 148/MGB/2024) from statutory funds.

# Population Pharmacokinetics of Mycophenolic Acid in Children with Nephrotic Syndrome

Julia Gabliczak<sup>1</sup>, Danuta Ostalska-Nowicka<sup>2</sup>, Jacek Zachwieja<sup>2</sup>, Joanna Sobiak<sup>1\*</sup>

<sup>1</sup>*Department of Physical Pharmacy and Pharmacokinetics, Poznan University of Medical Sciences, Rokietnicka 3, Poznań, 60-806, Poland*

<sup>2</sup>*Department of Pediatric Nephrology and Hypertension, Poznan University of Medical Sciences, Szpitalna 27/33, 60-572, Poznan, Poland*

\*Corresponding author e-mail: jsobiak@ump.edu.pl

Mycophenolate mofetil (MMF) is converted into its active form, mycophenolic acid (MPA), which exhibits strong plasma protein binding, undergoes enterohepatic recirculation, and has a narrow therapeutic range. Therefore, therapeutic drug monitoring (TDM) is recommended, with population pharmacokinetics as one of the approaches. This study aimed to develop a population pharmacokinetic model of MPA in children with nephrotic syndrome (NS).

The analysis was performed using MonolixSuite2024R1 and nonlinear mixed-effects modeling with the SAEM algorithm. The study included 62 pediatric patients (aged 3–17 years; 30 girls, 32 boys), providing 424 total MPA (tMPA) and 352 free MPA (fMPA) concentration measurements. Model development involved structural model selection, residual error modeling, covariate analysis, and model evaluation using Visual Predictive Checks, observed vs. predicted plots, Objective Function Value, and corrected Bayesian Information Criterion.

A two-compartment model with double first-order absorption and linear elimination best described the data. A combined error model was used for tMPA, and a proportional error model for fMPA. Log-transformed body weight (logWT) was identified as a significant covariate affecting clearance. Estimated pharmacokinetic parameters differed from literature values, including the first absorption rate (2.87 1/h), the second absorption rate (0.20 1/h), first lag time (0.22 h), difference between the first and second lag times (8.12 h), clearance (4.18 L/h), central compartment volume (6.03 L), and peripheral compartment volume (430 L). The free drug fraction was very low (0.004).

The analysis showed that logWT was the only significant factor influencing MPA clearance. High interindividual variability was observed, particularly in absorption rates, lag times, and intercompartmental clearance. Differences from published data and variability among patients highlight the need for individualized MPA therapy in children with NS.

**Keywords:** mycophenolic acid; nephrotic syndrome; population pharmacokinetics; therapeutic drug monitoring

# Use of Dietary Supplements by Patients with Prostate Cancer During Oncological Therapy – Survey Study

Paulina Gieremek<sup>1,2\*</sup>, Julia Pipowska<sup>1</sup>, Katarzyna Regulska<sup>2,4</sup>, Tomasz Kolenda<sup>3,4</sup>,  
Katarzyna Wawrzyniak<sup>2</sup>, Marcin Michalak<sup>5</sup>, Beata J. Staniszl<sup>1</sup>

<sup>1</sup> *Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Rokietnicka 3 Street, Poznan, Poland*

<sup>2</sup> *Pharmacy, Greater Poland Cancer Centre, Garbary 15 Street, Poznan, Poland*

<sup>3</sup> *Microbiology Laboratorium, Greater Poland Cancer Centre, Garbary 15 Street, Poznan, Poland*

<sup>4</sup> *Research and Implementation Unit, Greater Poland Cancer Centre, Garbary 15 Street, Poznan, Poland*

<sup>5</sup> *Surgical, Oncological and Endoscopic Gynaecology Department, Greater Poland Cancer Centre, Garbary 15 Street, Poznan, Poland*

\*Corresponding author e-mail: paulina.gieremek@wco.pl

Prostate cancer is one of the most frequently diagnosed malignancies in men worldwide and remains a major public health concern. In 2022, it was the most commonly diagnosed cancer among men over the age of 49 in approximately 66% of countries, with over 20,000 new cases reported in Poland. Modern oncological treatment, including oral therapies, is often associated with adverse effects that may negatively affect patients' quality of life. As a result, many patients seek additional methods, such as dietary supplementation, to alleviate symptoms or improve overall well-being. However, the use of supplements during cancer treatment may pose a risk of drug–supplement interactions, potentially influencing the safety and efficacy of therapy.

The aim of this study was to assess the prevalence of dietary supplement use among patients undergoing oral treatment for prostate cancer, identify the most commonly used preparations, and evaluate patients' awareness of their potential impact on anticancer therapy. The study was conducted using a proprietary questionnaire among 105 patients treated at the Pharmacy of the Greater Poland Cancer Center. Data included supplement use, sources of information, and adverse effects related to treatment. Statistical analysis was performed using the Shapiro–Wilk and chi-square tests.

The results showed that nearly 82% of respondents used over-the-counter preparations, with vitamin D3 and calcium being the most common. Physicians were the main source of information (46.6%). Despite widespread use, supplementation generally did not significantly affect anticancer therapy.

In conclusion, most patients were aware of the need to consult healthcare professionals and were willing to use supplements to reduce treatment-related side effects. However, awareness of pharmaceutical care remains limited, highlighting the need to improve its availability and integration into clinical practice.

**Keywords:** prostate cancer; dietary supplements; drug-supplement interactions

**Acknowledgments:** We would like to thank the Director of Geater Cancer Center in Poznan, Prof. Julian Malicki, for enabling us to conduct the survey.

## Evaluation of the Activity of Bis-Heteroaryl Derivatives in Combination with Ultrasound against Melanoma Cells

Jan Grzegorzewski<sup>1,2</sup>, Aleksandra Majchrzak-Celińska<sup>2</sup>, Violetta Krajka-Kuźniak<sup>2</sup>,  
Daniel Ziental<sup>3\*</sup>

<sup>1</sup> Doctoral School, Poznan University of Medical Sciences, Bukowska 70, 60-812 Poznan, Poland

<sup>2</sup> Department of Pharmaceutical Biochemistry, Poznan University of Medical Sciences, Rokietnicka 3, 60-806 Poznan, Poland

<sup>3</sup> Chair and Department of Inorganic and Analytical Chemistry, Poznan University of Medical Sciences, Rokietnicka 3, 60-806 Poznan, Poland

\*Corresponding author e-mail: dziental@ump.edu.pl

Sonodynamic therapy (SDT) is an emerging non-thermal modality that uses ultrasound-activated sonosensitizers to generate mainly reactive oxygen species (ROS) within tumor tissue, enabling deep-tissue penetration and spatially confined cytotoxicity. The investigated bis-heteroaryl derivatives (BHADs) are small-molecule kinase inhibitors, originally developed as protein kinase C (PKC) inhibitors, with documented activity in modulating survival pathways, apoptosis, and stress-response signaling in cancer cells. Despite their pronounced kinase-inhibitory and pro-apoptotic effects, these BHADs have not yet been evaluated in context of SDT or ultrasound-responsive cytotoxic compounds. Melanoma is an aggressive skin cancer with high metastatic potential, and although modern therapies have improved outcomes, advanced or resistant cases still present treatment challenges – making it a promising target for modalities like SDT.

In this study, we investigated selected BHADs as potential sonosensitizers in human melanoma lines HTB-140 and MICH-2. A WST-8-based cytotoxicity assay was performed with and without ultrasound exposure, and parallel experiments were performed on healthy human fibroblasts (MRC-5) to assess tumor-selective toxicity. Statistical analysis was performed using Student's t-test ( $p < 0.05$ ).

In the absence of ultrasound, nearly all BHADs significantly reduced HTB-140 viability at 20  $\mu\text{M}$  and markedly decreased MRC-5 viability. Notably, 15  $\mu\text{M}$  BHADs combined with ultrasound further enhanced cytotoxicity in HTB-140, while 10  $\mu\text{M}$  BHADs plus ultrasound reduced viability by over 50% in this line. MICH-2 viability was not significantly altered under either condition. Interestingly, although 20  $\mu\text{M}$  BHADs were highly cytotoxic to MRC-5 cells without ultrasound, lower concentrations (5–15  $\mu\text{M}$ ) combined with ultrasound were associated with increased fibroblast proliferation compared to controls without BHADs. The results indicate that tested BHADs in combination with ultrasound exhibit promising anti-cancer effects in HTB-140 cells, whereas healthy MRC-5 fibroblasts are not killed and may even show increased proliferation under the same conditions.

**Keywords:** melanoma; bis-heteroaryl derivatives; sonodynamic therapy; PKC

# A Promising Strategy in Anticancer Drug Design: New Oleanolic Acid-Cinnamic Acid Derivatives

Zuzanna Grześkowiak\*, Jakub Kąkolewski, Barbara Bednarczyk-Cwynar

*Department of Organic Chemistry, Faculty of Pharmacy, Poznan University of Medical Sciences, Collegium Pharmaceuticum, Rokietnicka 3, 60-806 Poznan, Poland*

\*Corresponding author e-mail: zuzanna.grzeskowiak@student.ump.edu.pl

Naturally occurring compounds are often used to synthesize new molecules with pharmacological activity. The goal is to obtain products with higher biological activity. Appropriate modification can also result in drugs with radically different effects. Examples of such compounds include derivatives of oleanolic acid and cinnamic acid (Wang et al., 2019). Education at the Poznan University of Medical Sciences, besides usual activities according to the study program, includes the participation of students in scientific research conducted within the framework of a student scientific society. The purpose of the research conducted in our group is the synthesis of new triterpenoid ester-type derivatives with a cinnamic acid residue. As both oleanolic acid and cinnamic acid exhibit anticancer activity, we decided to synthesize derivatives of these acids to verify whether their effects would be superior to those of oleanolic acid and cinnamic acid.

Syntheses using derivatives of oleanolic acid and cinnamic acid have been performed in dioxane, and DCC and DMAP were used as acylation initiators. Synthesis was tracked through thin-layer chromatography. NMR spectroscopy and mass spectrometry were used to confirm the structures of the synthesized derivatives, and their basic physicochemical properties were determined. The correlation between structure and pharmacological activity was investigated based on calculations.

The structures of the obtained derivatives have been confirmed, and their pharmacological activity has been predicted, showing their potential anticancer activity. The compounds obtained will be tested for cytotoxic activity against selected cancer cell lines. Screening studies and investigations into the mechanisms underlying this activity will be conducted at the Lviv National Medical University. Our study shows that simple syntheses using natural-based substrates can be carried out based on chemical reactions that do not require expensive or toxic reagents. The reactions are fast and proceed at room temperature, which gives potential for their commercialization.

**Keywords:** triterpenes; oleanolic acid; cinnamic acid; cytotoxic activity

**Acknowledgments:** The research is funded by Poznan University of Medical Sciences

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# UPLC–MS/MS Method for the Simultaneous Quantification of Ruxolitinib and Its Metabolites in Blood Plasma

Julia Kerner<sup>1,2\*</sup>, Jan Trąbka<sup>1</sup>, Marta Karaźniewicz-Łada<sup>1</sup>

<sup>1</sup> Faculty of Pharmacy, Poznan University of Medical Sciences, Department of Physical Pharmacy and Pharmacokinetics, Rokietnicka 3, 60-806 Poznan, Poland

<sup>2</sup> Poznan University of Medical Sciences, Doctoral School, Bukowska 70, 60-812 Poznan, Poland

\*Corresponding author e-mail: juliakerner1405@gmail.com

Ruxolitinib, as a Janus kinase inhibitor, participates in the regulation of hematopoiesis and the immune response. It is used in the treatment of graft-versus-host disease and myeloproliferative neoplasms [1]. Its metabolites, M18 and M27, are responsible for a significant part of the drug's activity. Due to the high variability of response following drug administration, pharmacokinetic analysis is necessary. Currently, there is no literature describing a method for the simultaneous determination of all these compounds in blood plasma.

The study aimed to develop and validate a simple UPLC-MS/MS method for the determination of the concentrations of ruxolitinib and its main metabolites, M18 and M27.

Chromatographic separation of all compounds was obtained using a Luna Phenyl-Hexyl column, and the mobile phase consisted of 0.1% formic acid in water and acetonitrile, delivered in gradient mode. For sample preparation, simple protein precipitation with methanol, followed by filtration, was applied. Detection was performed in positive ion mode using multiple reaction monitoring. Deuterated ruxolitinib was used as an internal standard. The applicability of the method was confirmed using clinical samples collected from patients treated with the drug.

We confirmed the linearity of the method in the concentration range of 0.2-200 ng/mL and 0.5-20 ng/mL for ruxolitinib and its metabolites, respectively. The limit of quantification was 0.2 ng/mL for all compounds, and no carry-over effect was observed. The method demonstrated acceptable interday and intraday accuracy and precision. The effect of matrix components on analyte ionization was observed. The stability of the compounds was confirmed after 3 hours at room temperature, 24 hours, and 14 days at -80°C, as well as after three freeze-thaw cycles. The developed sensitive UPLC-MS/MS method for the determination of ruxolitinib and its metabolites met validation guidelines and can be applied in clinical practice.

**Keywords:** ruxolitinib; M18-ruxolitinib; M27-ruxolitinib; pharmacokinetic analysis

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# Knowledge, Usage, and Educational Needs of Polish Pharmacists Regarding Artificial Intelligence (AI)

Wiktor Klimek<sup>1\*</sup>, Karolina Morze<sup>2</sup>, Łucja Zielińska-Tomczak<sup>1</sup>

<sup>1</sup>*Poznan University of Medical Sciences, Student Scientific Society, Students' Scientific Club of Medical Education, Department of Medical Education and Communication, Poznan, Poland*

<sup>2</sup>*Poznan University of Medical Sciences, Department of Clinical Pharmacy and Biopharmacy, Poznan, Poland.*

<sup>3</sup>*Poznan University of Medical Sciences, Department of Medical Education and Communication, Poznan, Poland*

\*Corresponding author e-mail: 85501@student.ump.edu.pl

**Background:** Artificial Intelligence (AI) is increasingly permeating the healthcare sector, yet the readiness of the pharmaceutical workforce to integrate these tools remains under-explored. This pilot study aimed to evaluate the current level of knowledge, practical application, and educational needs concerning AI tools among pharmacists in Poland.

**Methodology:** A cross-sectional survey was conducted among Polish pharmacists (n=35). Data were collected regarding digital competencies, AI usage patterns, professional attitudes, and perceived educational gaps.

**Results:**

Regarding educational background, 97.6% of pharmacists did not encounter AI topics during their university studies, and 84.2% had never participated in formal AI-related training. While 32.4% of participants expressed unfamiliarity with basic AI terminology, "Generative AI" and "Machine Learning" were the most recognized concepts. Currently, AI is used sporadically by 43.2% of pharmacists, while 32.4% plan to implement it in the future. Existing usage is primarily for private purposes (45.2%) or administrative professional tasks (29.0%). The general attitude toward AI is moderately positive (59.5%), though respondents identified significant barriers including a lack of knowledge (30.6% high impact), concerns regarding legal liability for errors (28.0%), and data reliability (29.0%). Despite these concerns, pharmacists identified the highest potential for AI in enhancing patient safety (31.5% high agreement) and optimizing pharmaceutical care (29.6% high agreement).

**Conclusions:** There is a significant educational gap in the Polish pharmaceutical sector regarding AI. Despite low formal training, pharmacists recognize AI as a permanent shift in the profession. There is high demand for certified training (65.7% interested) focusing on practical applications in pharmaceutical care and the critical evaluation of AI-generated content.

**Keywords:** Artificial Intelligence (AI); pharmacist; pharmacy, pharmaceutical care

# Advanced LC-MS/MS Approaches for the Determination of Glucocorticoids in Pharmaceutical Research

Marta Kowalska<sup>\*</sup>, Agnieszka Zgoła-Grześkowiak, Robert Frankowski

*Faculty of Chemical Technology, Poznan University of Technology, Poznan, Poland*

<sup>\*</sup>Corresponding author e-mail: marta.kowalska@doctorate.put.poznan.pl

Glucocorticoids are amongst one of the most rapidly growing groups of contaminants of emerging concern in the environment. These steroid hormones have a great physiological impact on the aquatic ecosystems, making them an increasing threat to all living organisms [1]. Glucocorticoids are a group of corticosteroids that are present in the environment through natural and synthetic routes. They exist in nature in the form of cortisol and cortisone, which are two chemicals naturally occurring in living organisms as glucose-regulating agents, stress response mediators, and a factor in an organism's immune response [2]. Glucocorticoids, like dexamethasone and prednisone, are synthetic anti-inflammatory drugs used to treat asthma, rheumatoid arthritis, as well as in autoimmune diseases or even as cancer therapy [1]. In this work, an analytical procedure based on liquid chromatography combined with tandem mass spectrometry (LC-MS/MS) was established for the determination of selected glucocorticoids. The conditions of chromatographic separation and the parameters of mass spectrometric detection were optimized to ensure high sensitivity and selectivity of the analysis. Method validation was performed by evaluating essential analytical characteristics such as linearity, limits of detection (LOD), and limits of quantification (LOQ). The method demonstrated good linearity across the concentration range of 0.0005–0.5  $\mu\text{g ml}^{-1}$ , with correlation coefficients ( $R^2$ ) between 0.9986 and 0.9997. The calculated LOD and LOQ values ranged from below 0.0001 to 0.0002  $\mu\text{g ml}^{-1}$  and from 0.0001 to 0.0008  $\mu\text{g ml}^{-1}$ , respectively. The results obtained indicate that LC-MS/MS is a highly effective analytical technique for the determination of glucocorticoids. The proposed method may be useful in pharmaceutical studies and could enhance the monitoring of these compounds in different types of matrices.

**Keywords:** glucocorticoids; liquid chromatography - mass spectrometry; ecotoxicity

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## Dual role of mitoxantrone as an anticancer drug and an antibiotic

Szymon Krawczyk<sup>1,2\*</sup>, Chih-Wei Chen<sup>3,4</sup>, Haaris A. Safdari<sup>5</sup>, Martino Morici<sup>5</sup>, Marta Leśniczak-Staszak<sup>1,2</sup>, Clifford Yerby<sup>3,4</sup>, Jasbir Dalal<sup>6</sup>, Max J. Berger<sup>5</sup>, Ewelina Gowin<sup>7</sup>, Pavel Ivanov<sup>8,9</sup>, Shawn M. Lyons<sup>6,10</sup>, Yury Polikanov<sup>3,4</sup>, Daniel N. Wilson<sup>5</sup>, Witold Szaflarski<sup>1</sup>

<sup>1</sup> Department of Histology and Embryology, Poznan University of Medical Sciences, Poznań, Poland

<sup>2</sup> Doctoral School, Poznan University of Medical Sciences, Poznań, Poland

<sup>3</sup> Department of Pharmaceutical Sciences, University of Illinois at Chicago, Chicago, IL 60607, USA

<sup>4</sup> Center for Biomolecular Sciences, University of Illinois at Chicago, Chicago, IL 60607, USA

<sup>5</sup> Institute for Biochemistry and Molecular Biology, University of Hamburg, Hamburg, Germany

<sup>6</sup> Department of Biochemistry, Boston University School of Medicine, Boston, MA, USA

<sup>7</sup> Clinic of the Children's Diseases, Poznan University of Medical Sciences, Poznań, Poland

<sup>8</sup> Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Boston, MA 02115, USA

<sup>9</sup> Department of Medicine, Harvard Medical School, Boston, MA 02115, USA

<sup>10</sup> The Genome Science Institute, Boston University School of Medicine, Boston, MA 02118, USA

\*Corresponding author e-mail: [szymonkrawczyk627@gmail.com](mailto:szymonkrawczyk627@gmail.com)

**Background/Aim:** Mitoxantrone (MIT) is a clinically approved anthracenedione used in the treatment of malignancies and autoimmune diseases, classically described as a DNA intercalator and topoisomerase II inhibitor. The aim of this study was to determine whether MIT also affects translation through direct ribosome targeting and to define the molecular basis of this activity.

**Methods:** We combined cellular, biochemical, and structural approaches to investigate the effect of MIT on translation in human and bacterial systems. Protein biosynthesis was assessed in multiple mammalian cell types, bacterial cells, and cell-free translation systems. Ribopuromycylation assays and polysome profiling were used to evaluate translational activity, while high-resolution X-ray crystallography and cryo-electron microscopy were applied to identify the ribosomal binding mode of MIT.

**Results:** MIT potently inhibited protein biosynthesis in mammalian, bacterial, and cell-free systems, indicating an evolutionarily conserved mechanism of action. Ribopuromycylation and polysome profiling confirmed global suppression of translation, largely independent of canonical stress-response pathways. Structural analyses revealed that MIT binds within the nascent polypeptide exit tunnel (NPET), where its planar aromatic rings form a  $\pi$ - $\pi$  stacked arrangement that sterically obstructs the tunnel and likely interferes with translation elongation. Unlike established tunnel-binding antibiotics, MIT appears to engage the ribosome through a distinct multimeric stacking mode, suggesting an unusual mechanism of translational arrest.

**Conclusions:** These findings identify the ribosome as a clinically relevant target of MIT and expand its known pharmacological spectrum beyond DNA-directed activity. MIT therefore exhibits a dual mode of action, functioning as both an anticancer drug and an antibiotic-like translational inhibitor. More broadly, this study highlights the therapeutic and mechanistic relevance of ribosome-targeting small molecules outside conventional antimicrobial applications.

**Keywords:** mitoxantrone; ribosome; nascent polypeptide exit tunnel (NPET); translation inhibition; anticancer drug

## Linking drug chemistry to stress granule diversity

Shuyi Liu<sup>1,2</sup>, Marta Leśniczak-Staszak<sup>1,2</sup>, Antonina Sikora<sup>1</sup>, Hanna Kasprzak<sup>1</sup>,  
Mohamed Abouzid<sup>1</sup>, Martino Morici<sup>3</sup>, Ewelina Gowin<sup>4</sup>, Daniel N. Wilson<sup>3</sup>,  
Witold Szaflarski<sup>1\*</sup>

<sup>1</sup> *Department of Histology and Embryology, Poznan University of Medical Sciences, Poznań, Poland*

<sup>2</sup> *Doctoral School, Poznan University of Medical Sciences, Poznań, Poland*

<sup>3</sup> *Institute for Biochemistry and Molecular Biology, University of Hamburg, Hamburg, Germany*

<sup>4</sup> *Clinic of the Children's Diseases, Poznan University of Medical Sciences, Poznań, Poland*

\*Corresponding author e-mail: witold@ump.edu.pl

**Background/Aim:** Stress granules (SGs) are dynamic ribonucleoprotein assemblies formed in response to cellular stress, but the extent to which their formation and diversity depend on the chemical properties of stress-inducing compounds remains poorly understood. The aim of this study was to determine how bioactive small molecules shape SG assembly and whether specific chemical classes are associated with distinct SG phenotypes.

**Methods:** We performed a systematic screen of a curated library of more than 500 bioactive compounds, including approved antiparasitic drugs, antibiotics, and other small molecules, to identify SG inducers in mammalian cells. Compounds that reproducibly triggered SG formation were further analyzed by comparative imaging. SG morphology, size, and intracellular distribution were assessed, and SG-inducing compounds were grouped into drug families to examine relationships between biological activity and shared chemical or functional features.

**Results:** Among the screened compounds, 55 robustly induced SG formation in mammalian cells. Comparative imaging analyses showed that drug-induced SGs are morphologically diverse and differ substantially in size and cellular distribution, indicating that SG assembly is not a uniform response but depends on the nature of the inducing compound. Grouping SG-inducing molecules into drug families revealed associations between SG phenotypes and shared chemical and functional properties. A particularly informative pattern emerged for antibiotics: although many activated kinases involved in eIF2 $\alpha$  phosphorylation, they generally failed to induce SGs. This likely reflects their direct inhibition of ribosomal function and rapid suppression of protein biosynthesis, which prevents the cellular conditions required for canonical SG assembly.

**Conclusions:** Our results show that the ability of drugs to induce SGs depends not only on stress signaling but also on their chemical and functional properties. This study provides new insight into the chemical determinants of SG formation and demonstrates that distinct classes of compounds promote different SG states. These findings establish a framework for identifying the structural principles underlying stress granule diversity.

**Keywords:** stress granules; drug screening; eIF2 $\alpha$  phosphorylation; translation inhibition; chemical biology

# Evaluation of Photodynamic Properties and Biological Activity of a Novel Zinc Chlorin

Maciej A. Michalak<sup>1, 2\*</sup>, Daniel Ziental<sup>1</sup>, Jolanta Długaszewska<sup>3</sup>, Marcin Ptaszek<sup>4</sup>,  
Łukasz Sobotta<sup>1</sup>

<sup>1</sup>Chair and Department of Inorganic and Analytical Chemistry, Poznan University of Medical Sciences, Rokietnicka 3, 60-806 Poznan, Poland

<sup>2</sup>Doctoral School, Poznan University of Medical Sciences, Bukowska 70, 60-812 Poznan, Poland

<sup>3</sup>Chair and Department of Genetics and Pharmaceutical Microbiology, Poznan University of Medical Sciences, Rokietnicka 3, 60-806 Poznan, Poland

<sup>4</sup>Department of Chemistry, Biochemistry University of Maryland, Baltimore County (UMBC), 1000 Hilltop Circle, Baltimore, MD 21250, USA

\*Corresponding author e-mail: maciej.michalak2@student.ump.edu.pl or [michalakm500@gmail.com](mailto:michalakm500@gmail.com)

**Overview:** This study evaluates the photodynamic potential of a novel zinc chlorin modified with methyl benzoate, phenylacetylenes, and methyl groups for use in antimicrobial photodynamic therapy (aPDT). The research focused on characterizing the photochemical properties and biological efficacy of the compound against various pathogens.

**Methodology:** Photochemical characterization involved UV-VIS spectroscopy and the assessment of photostability and singlet oxygen generation ( $\Phi\Delta$ ), and photostability studies ( $\Phi P$ ) in dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). Singlet oxygen yield was measured indirectly using Rubrene as a quencher. Microbiological activity was tested against *Candida albicans*, *Escherichia coli*, and methicillin-resistant *Staphylococcus aureus* (MRSA). We tested the compound at concentrations of  $10^{-4}$  and  $10^{-5}$  mol/L and irradiated with LED (650 nm corresponding  $A_{max}$ ) light at doses of 30 and 60 J/cm<sup>2</sup>.

**Results and Conclusion:** The zinc chlorin demonstrated high  $\Phi\Delta$  of 0.49 in DMF and 0.32 in DMSO, which correlates with a high theoretical potential for bactericidal activity. Moreover, photostability was sufficient in both solvents, reaching  $\Phi P = 7.72 \cdot 10^{-5}$  (DMF), and  $\Phi P = 6,81 \cdot 10^{-6}$  (DMSO). In microbiological assays, the compound at a concentration of  $10^{-4}$  mol/L showed significant efficacy. At a light dose of 30 J/cm<sup>2</sup>, the treatment achieved a reduction of 5.97 log for *E. coli* and 6.02 log for *C. albicans*, exceeding the standard requirements for disinfection. Effectiveness against MRSA reached a 4.9 log reduction at 60 J/cm<sup>2</sup>. These findings confirm the high antimicrobial activity of presented zinc chlorin, particularly against *E. coli* and *C. albicans*. The research provides a strong foundation for the future development of effective antiseptic or disinfectant products.

**Keywords:** chlorins; photodynamic therapy; MRSA; *E. coli*; *C. albicans*

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# Vitamin D Receptor Gene Polymorphisms and Vitamin D Concentration in Patients With Hashimoto's Thyroiditis - A Pilot Study

Aniceta A. Mikulska-Sauermann<sup>1\*</sup>, Aleksandra Hozakowska<sup>1</sup>, Dorota Filipowicz<sup>2</sup>,  
Marek Ruchała<sup>2</sup>, Franciszek K. Główka<sup>1</sup>, Matylda Resztak<sup>1</sup>

<sup>1</sup>Department of Physical Pharmacy and Pharmacokinetics, Poznan University of Medical Sciences,  
Rokietnicka 3, 60-806 Poznan, Poland

<sup>2</sup>Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical  
Sciences, Przybyszewskiego 49, 60-355 Poznan, Poland

\*Corresponding author e-mail: amikulska@ump.edu.pl

Hashimoto's thyroiditis (HT) is the most common autoimmune disease and a leading cause of hypothyroidism. Its development involves both genetic and environmental factors, including excessive iodine intake and low vitamin D levels.

The aim of the study was to determine vitamin D concentrations and analyze specific polymorphisms of the vitamin D receptor (VDR) gene in patients with HT and compare to healthy individuals.

The study included 36 women: 15 with HT and 21 without thyroid disease (control group), recruited at the Department of Endocrinology, Metabolism, and Internal Medicine of the Poznań University of Medical Sciences.

Biochemical tests included thyroid profile (TSH, fT4, fT3, TPOAb, and TgAb), lipid profile (TC, TG, HDL and LDL cholesterol), fasting blood glucose, and insulin level, performed by standard laboratory methods. Vitamin D concentrations were determined by LC-MS/MS. VDR gene polymorphisms (*TaqI*, *ApaI*, *BsmI*, *FokI*) were identified using PCR-RFLP. Anthropometric analyses and body composition analysis were also performed.

No significant differences in vitamin D levels were found between groups ( $26.5 \pm 13.0$  ng/ml in HT vs.  $27.8 \pm 14.1$  ng/ml in controls). However, 73.3% of women with HT and 65.0% of the control group had vitamin D levels below the reference value (<30 ng/ml). The T/T *TaqI* polymorphism was associated with higher anti-TG values. In the entire study population the G/G genotype of the *ApaI* polymorphism correlated with higher BMI, TC, LDL cholesterol, TG, glucose, and insulin levels, indicating increased risk of obesity and metabolic disorders. Additionally, the *FokI* heterozygote was linked to a higher risk of overweight and obesity in whole study group.

A pilot study indicated that VDR gene polymorphisms may influence the autoimmune activity and the metabolic profile in patients with HT. The results suggest a potential role of VDR gene variation in modulating the clinical phenotype, independent of vitamin D levels.

**Keywords:** Hashimoto's thyroiditis; vitamin D; VDR gene polymorphisms

# Behavioral Interactions of Fluoxetine and Withanolides from *Withania Somnifera* in *Danio Rerio* Larvae – a Pilot Study

Maria Miotk<sup>1</sup>, Michał Szulc<sup>2</sup>, Dorota Józefowicz<sup>1</sup>, Joanna Cebrat<sup>1</sup>, Sandra Mazurkiewicz<sup>1</sup>, Wiktoria Biela<sup>1</sup>, Gracjan Ziółkowski<sup>1</sup>, Magda Tomczak<sup>1</sup>, Błażej Borysewicz<sup>1</sup>, Kamila Czora-Poczwardowska<sup>2</sup>, Weronika Jarczak<sup>2</sup>, Przemysław Mikołajczak<sup>2</sup>, Radosław Kujawski<sup>2\*</sup>

<sup>1</sup>Faculty of Pharmacy, Student Scientific Society of Pharmacology, Poznan University of Medical Sciences, Rokietnicka 3 Str., 60-806 Poznan, Poland

<sup>2</sup>Faculty of Pharmacy, Department of Pharmacology, Poznan University of Medical Sciences, Rokietnicka 3 Str., 60-806 Poznan, Poland

\*Corresponding author e-mail: radkuj@ump.edu.pl

**Introduction:** Fluoxetine (FLU), a selective serotonin reuptake inhibitor (SSRI), is one of the most widely prescribed antidepressants, yet its clinical use is associated with notable limitations including delayed onset of action and adverse effects. Withanolides from *Withania somnifera*, including withanolide A (WitA) and withaferin A (WTF), exhibit anxiolytic properties through modulation of GABA-A receptors and the HPA axis. The aim of this study was to evaluate the behavioral interaction between FLU and withanolides in *Danio rerio* larvae using the Light-Dark Test (LDT) and thigmotaxis assay.

**Materials and methods:** *D. rerio* larvae (3-4 dpf) were incubated in test substance solutions and subjected to a 40-minute LDT protocol (alternating 10-min dark-light phases) with locomotor activity recorded using the Noldus EthoVision XT system. Summing up, eleven groups were examined: E3 control, FLU (0.1, 0.2, 1.0, 10, and 100 µg/L), and combinations of FLU (0.1 and 1.0 µg/L) with WitA or WTF (100 µg/L). Total distance, activity during light and dark phases, and the Zone/Arena ratio (thigmotaxis) were analyzed. The Kruskal-Wallis test and Mann-Whitney U test were applied ( $\alpha = 0.05$ ).

**Results:** FLU significantly reduced dark-phase hyperactivity (anxiolytic effect) at studied concentrations ( $p < 0.05$ – $0.001$  vs. E3). The strongest effect was observed in FLU 1.0 + WitA group with a significant reduction in dark-phase distance (~90% vs. E3;  $p < 0.001$ ) without affecting light-phase activity ( $p = 0.24$ ), suggesting a synergistic enhancement of the anxiolytic effect.

**Conclusions:** The results indicate that especially WitA may additively or synergistically enhance the anxiolytic effect of FLU in *D. rerio* larvae. Whether this interaction involves complementary modulation of serotonergic (SERT/5-HT<sub>1A</sub>) and GABAergic (GABA-A) pathways requires molecular verification. The selective profile of the FLU + WitA combination, suggesting anxiety reduction without general sedation, is particularly promising. These findings provide a rationale for further experimental and mechanistic studies.

**Keywords:** fluoxetine; withanolides; *Danio rerio*; Light-Dark Test; anxiolytic interaction

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# Comparison of the Effects of Commercial Intravenous Lipid Emulsions on NF- $\kappa$ B and Nrf2 Signaling Pathways in an *in vivo* Model

Olga Obrzut<sup>1</sup>, Aleksandra Gostyńska-Stawna<sup>2</sup>, Joanna Czerniel<sup>2</sup>, Michał Szulc<sup>3</sup>,  
Violetta Krajka-Kuźniak<sup>1\*</sup>

<sup>1</sup>Poznan University of Medical Sciences, Department of Pharmaceutical Biochemistry, Rokietnicka 3, 60-806 Poznan, Poland

<sup>2</sup>Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Rokietnicka 3, 60-806 Poznan, Poland

<sup>3</sup>Poznan University of Medical Sciences, Department of Pharmacology, Rokietnicka 3, 60-806 Poznan, Poland

\*Corresponding author e-mail: vkrajka@ump.edu.pl

Long-term parenteral nutrition can cause metabolic complications, including the most serious condition, intestinal failure-associated liver disease (IFALD). The development of IFALD is closely associated with liver inflammation and oxidative stress, both of which are affected by the composition of intravenous fat emulsions (IVFEs). Plant-based oils containing high concentrations of phytosterols and an imbalanced omega-3 to omega-6 fatty acid ratio in IVFEs are considered critical triggers of liver injury through the modulation of the NF- $\kappa$ B and Nrf2 signaling pathways.

The study aimed to evaluate and compare the impact of different lipid profiles of two commercial IVFEs - Intralipid (soybean oil-based) and Smoflipid (a mixture of soybean oil, medium-chain triglycerides, olive oil, and fish oils) on the activation of inflammatory and antioxidant markers in rat liver tissue.

Rats were randomly assigned to three groups: a control group receiving a multi-electrolyte solution and two experimental groups receiving parenteral nutrition containing either Intralipid or Smoflipid, all administered for 10 days. Cytosolic and nuclear extracts were isolated from rat liver tissue and prepared for molecular analysis. The levels of NF- $\kappa$ B p50, NF- $\kappa$ B p65, COX-2, Nrf2, GPx1/2, HO-1, and SOD-1 were determined by Western blot analysis.

Both Smoflipid and Intralipid affected the Nrf2 signaling pathway. The expression levels of HO-1, SOD-1, and GPx1/2 differed from those observed in the control group. Notably, levels of SOD-1 and GPx1/2 were significantly higher in rats treated with Smoflipid than in those receiving Intralipid. Furthermore, the two emulsions affected inflammatory markers; specifically, Intralipid altered COX-2 levels and NF- $\kappa$ B (p50 and p65) nuclear translocation.

Both IVFEs interact with the Nrf2-mediated antioxidant defense system; however, Smoflipid and Intralipid exhibit divergent profiles regarding the NF- $\kappa$ B signaling pathway, with the results trending in favor of Smoflipid's superior anti-inflammatory potential. These findings suggest that the balanced composition of Smoflipid, particularly its omega-3 to omega-6 fatty acid ratio, may better mitigate the risk of IFALD.

**Keywords:** IFALD; Smoflipid; Intralipid; NF- $\kappa$ B; Nrf2

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# Pharmaceutical Care Considerations in the Use of Levocetirizine-based Medicines for Allergic Rhinitis Treatment

Inna Otrishko<sup>1\*</sup>, Viktoriia Propisnova<sup>2</sup>

<sup>1</sup>*Department of Pharmacology and Clinical Pharmacy, National University of Pharmacy,  
53 Skovorody St, Kharkiv, Ukraine, 61002*

<sup>2</sup>*Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences,  
3 Rokietnicka St, Poznań, 80-806 Poland*

\*Corresponding author e-mail: innaotrishko@gmail.com

Pharmaceutical care plays a crucial role in optimizing the use of levocetirizine-based medicines in the treatment of allergic rhinitis among pharmacy visitors in Ukraine. An observational evaluation involving 60 pharmacy visitors with seasonal and perennial allergic rhinitis demonstrated that administration of levocetirizine 5 mg once daily for 14 days resulted in significant symptom relief, including reduction of nasal congestion, sneezing, and rhinorrhea in the majority of participants. In this study, levocetirizine was used in commonly available dosage forms, including film-coated tablets and oral drops, allowing individualized selection based on age and person's preference. Improvement was noted as early as day 7 in approximately 85% of pharmacy visitors, with continued progress by the end of therapy. The incidence of adverse drug reactions was low, with mild sedation (10%) and dry mouth (8%) being the most commonly reported effects, none of which required discontinuation of therapy. Importantly, pharmacist-led interventions, including counseling and regular follow-up, substantially improved adherence rates from 70% to 92%, highlighting the value of pharmaceutical care in clinical outcomes. Special attention should be given to visitor-specific factors such as age, renal function, and concomitant medications, as levocetirizine is primarily eliminated via the kidneys and may require dose adjustments in individuals with renal impairment. Counseling on the optimal timing of administration, preferably in the evening, and warning about potential drowsiness can reduce risks and improve tolerability. Visitors should also be advised to avoid alcohol and other central nervous system depressants during treatment. In conclusion, levocetirizine is an effective and well-tolerated option for allergic rhinitis management when accompanied by structured pharmaceutical care in community pharmacy settings. Pharmacists should actively engage in education, adherence monitoring, and safety assessment. Regular follow-up is recommended to evaluate therapeutic response and ensure rational use, ultimately improving quality of life and treatment success.

**Keywords:** allergic rhinitis; levocetirizine-based medicines; pharmaceutical care

# Assessment of Quality of Life in Persons Undergoing Hormone-replacement Therapy for Hypothyroidism

Inna Otrishko<sup>1\*</sup>, Tatiana Sakharova<sup>2</sup>, Viktoriiia Propisnova<sup>3</sup>

<sup>1</sup>*Department of Pharmacology and Clinical Pharmacy, National University of Pharmacy,  
53 Skovorody St, Kharkiv, Ukraine, 61002*

<sup>2</sup>*Department of General and Clinical Pharmacy, Odesa I.I. Mechnikov National University,  
14 Universytetska St, Odesa, Ukraine, 65026*

<sup>3</sup>*Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences,  
3 Rokietnicka St, Poznań, 80-806 Poland*

\*Corresponding author e-mail: innaotrishko@gmail.com

Assessment of quality of life in individuals with hypothyroidism receiving hormone-replacement therapy remains clinically relevant, particularly in real-world settings. The aim of this study was to evaluate quality of life and identify factors influencing patient-reported outcomes among pharmacy visitors receiving levothyroxine therapy. The study included 36 pharmacy visitors (mean age  $46.1 \pm 11.4$  years; 78% female) who had been taking levothyroxine for at least 6 months and were surveyed during routine pharmacy visits. Quality of life was assessed using the ThyPRO-39 questionnaire, along with collection of self-reported thyroid-stimulating hormone control, body mass index, and disease duration. The results demonstrated reduced quality of life across all domains, with the greatest impairment in fatigue ( $60.8 \pm 13.7$ ) and emotional instability ( $56.9 \pm 12.5$ ). During the observation period, dose adjustments were performed by physicians, while pharmacists evaluated therapy effectiveness, safety, and adherence. After 2 months of follow-up, a subgroup of visitors ( $n = 24$ ) reported improvement, with overall quality of life scores increasing by 22% ( $p < 0.05$ ). Fatigue decreased by 18%, and cognitive complaints by 15%. However, 44% of visitors continued to report persistent symptoms despite reporting thyroid-stimulating hormone within the target range. No significant association between thyroid-stimulating hormone levels and quality of life was identified, while higher body mass index showed a weak positive correlation with improvement ( $r = 0.31$ ). These findings indicate that quality of life in hypothyroidism is influenced by factors beyond biochemical control. Hormone-replacement therapy improves patient well-being but does not fully eliminate symptoms in a substantial proportion of individuals. The results highlight the role of pharmacists in assessing effectiveness, safety, and adherence, while treatment decisions remain physician-led. Routine quality of life monitoring, personalized counseling, and interdisciplinary collaboration are recommended to optimize therapeutic outcomes and improve overall well-being.

**Keywords:** quality of life; levothyroxine-based hormone replacement therapy; hypothyroidism

# One Tumor, Two Strategies: Atorvastatin and Regorafenib Target Angiogenesis in a Zebrafish Xenograft Model of Metastatic Colorectal Cancer

Filip Otto<sup>1\*</sup>, Konrad Sarnowski<sup>1</sup>, Natalia Lisiak<sup>2</sup>, Ewa Totoń<sup>2</sup>,  
Małgorzata Chmielewska-Krzysińska<sup>3</sup>, Joanna Dybalska-Szczepanek<sup>3</sup>, Piotr Podlas<sup>3</sup>,  
Edyta Szafek<sup>1</sup>, Agnieszka Karbownik<sup>1</sup>

<sup>1</sup>Department of Clinical Pharmacy and Biopharmacy, Faculty of Pharmacy, Poznan University of Medical Sciences, Poznan, Poland

<sup>2</sup>Department of Clinical Chemistry and Molecular Diagnostics, Faculty of Pharmacy, Poznan University of Medical Sciences, Poznan, Poland

<sup>3</sup>Department of Pathophysiology, Forensic Veterinary Medicine and Administration, Faculty of Veterinary Medicine, University of Warmia and Mazury in Olsztyn, Poland

\*Corresponding author e-mail: f.otto@ump.edu.pl

**Introduction:** Atorvastatin (ATO), a widely used HMG-CoA reductase inhibitor, has been increasingly recognized for its potential anticancer properties. Regorafenib (REG), an oral multikinase inhibitor targeting pathways involved in angiogenesis and tumor proliferation, is approved for the treatment of metastatic colorectal cancer (mCRC). The aim of this study was to evaluate the effect of ATO on the antitumor activity of REG in a zebrafish xenograft model (ZfXM) of mCRC.

**Materials and Methods:** The *in vivo* stage of the study was preceded by *in vitro* experiments using the MTT assay to evaluate the potential synergistic cytotoxic effects of the two xenobiotics. A transgenic zebrafish line, *Tg(Fli1a:GFP)*, was used throughout the study. At 2 days post-fertilisation, mCherry-labelled Caco-2 cells were microinjected into the perivitelline space. Larvae ( $N=30$ ) were randomly assigned to five groups: a non-injected control group (-), a cancer cell-injected control group (I<sub>REG+ATO</sub><sup>-/-</sup>), and three cancer cell-injected treatment groups (II<sub>REG+ATO</sub><sup>+/-</sup>, III<sub>REG+ATO</sub><sup>-/+</sup>, IV<sub>REG+ATO</sub><sup>+/+</sup>). Larvae ( $n=6$ /group) were incubated for 24 h at 32 °C in media containing REG (50 nM) and/or ATO (0.05 nM). Tumor-associated angiogenesis was assessed using confocal microscopy (LSM 700, Zeiss). Quantitative analysis of angiogenic changes was performed based on subintestinal venous plexus (SIVP) cytoarchitecture, including vessel area, branching, and sprout formation.

**Results:** In the ZfXM, compared with the control group I, the treatment groups II–IV showed changes in the surface area of SIVP:  $0.20\pm 0.10$ ;  $0.23\pm 0.14$ ;  $0.28\pm 0.07$ ; and  $0.19\pm 0.09$  mm<sup>2</sup>, respectively. The number of SIVP branches was  $18.7\pm 7.1$ ;  $27.8\pm 11.8$ ;  $22.6\pm 6.9$ ; and  $28.8\pm 9.8$  respectively. However, in both parameters the differences between groups were not statistically significant ( $p>0.05$ ).

**Conclusions:** These findings suggest a complementary interaction between REG and ATO, with REG suppressing sprouting angiogenesis and ATO promoting vascular branching in the SIVP. Their combined activity may indicate a potential synergistic effect and highlights this combination as a promising therapeutic strategy.

**Keywords:** regorafenib; atorvastatin; zebrafish xenograft model; angiogenesis; metastatic colorectal cancer

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# The Influence of Polymorphisms in the CYP3A4, CYP2J2, and ABCB1 Genes on the Pharmacokinetics of Rivaroxaban and Coagulation Parameters

Kornel Pawlak<sup>1,2\*</sup>, Marta Karażniewicz-Łada<sup>1</sup>

<sup>1</sup>*Poznan University of Medical Sciences, Department of Physical Pharmacy and Pharmacokinetics, 3 Rokietnicka Street, 60-806 Poznan, Poland*

<sup>2</sup>*Doctoral School, Poznan University of Medical Sciences, 60-812 Poznan, Poland*

\*Corresponding author e-mail: 76772@student.ump.edu.pl

**Introduction:** Rivaroxaban (RIV) is a direct oral anticoagulant (DOAC) and selective inhibitor of Factor Xa. Overall two-thirds of the oral dose of rivaroxaban is metabolized by CYP enzymes (mainly by CYP2J2 and CYP3A4 cytochromes) [1]. Rivaroxaban is also a substrate of P-glycoprotein (P-gp, ABCB1), which is engaged in its membrane transport. Hence, genetic polymorphisms of CYP3A4, CYP2J2 and ABCB1 may affect the functionality of the encoded proteins and thereby influence the pharmacokinetics and therapeutic response to rivaroxaban [2].

The main aim of this study is to determine the influence of polymorphisms in the CYP3A4 (rs2242480), CYP2J2 (rs890293), and ABCB1 (rs1045642, rs2032582) genes on the pharmacokinetics of rivaroxaban and coagulation parameters (INR, aPTT).

**Materials and methods:** DBS samples for analysis were prepared using previously published method [3]. We used PCR-RFLP method for genotyping. The following PCR conditions were used: initial denaturation at 95°C for 5 min, denaturation at 95 °C for 30 s, annealing for 45 s, elongation at 72 °C for 45 s, and final elongation at 72°C for 7 min. Restriction products were separated on 3.0% agarose gel (5 V/cm) containing SimplySafe dye (EURx, Poland; 5 µl/100 mL of agarose). We analyzed DBS and DNA samples collected from 43 patients treated with 20 mg of rivaroxaban.

**Results:** Statistical analysis revealed that carriers of CT genotype of rs2242480 in the CYP3A4 gene had significantly higher aPTT values than patients with the CC genotype (44.63±7.20 vs. 37.36±5.64 s, respectively; p = 0.0231). Carriers of the G allele of rs2032582 had lower INR and AUC<sub>0-12h</sub> values than non-carriers (INR: 1.32±0.21 vs. 1.62±0.45, p = 0.0113; AUC<sub>0-12h</sub>: 1817.43±703.7 vs. 2442.96±691.13 ng·h/mL, p = 0.0369).

**Discussion:** Among the studied polymorphisms, the G allele of rs2032582 may be associated with lower rivaroxaban exposure and decreased efficacy of the therapy. For rs2242480, the CT genotype was associated with higher aPTT values and may therefore increase the risk of bleeding

**Keywords:** anticoagulants; genetic variability; drug metabolism; P-glycoprotein

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# Rapid Molecular Diagnostics in the Microbiology Laboratory – Must Have or Luxury?

Paulina Pecyna<sup>1,2</sup>, Sylwia Kobyłka<sup>2</sup>, Maria M. Mielcarek<sup>2</sup>, Magdalena Lenckowska<sup>2</sup>,  
Marzena Gajęcka<sup>2,3\*</sup>

<sup>1</sup>Department of Genetics and Pharmaceutical Microbiology, Poznan University of Medical Sciences,  
3 Rokietnicka St. 60-806 Poznan, Poland

<sup>2</sup>S.T. Dabrowski Hospital in Puszczykowo, 11 Kraszewskiego St. 62-041 Puszczykowo, Poland

<sup>3</sup>Institute of Human Genetics, Polish Academy of Sciences, 32 Strzeszynska St. 60-479 Poznan, Poland

\*Corresponding author e-mail: [gamar@man.poznan.pl](mailto:gamar@man.poznan.pl)

**Introduction:** In recent years, despite the availability of vaccinations for children (mandatory vaccination schedule), a high number of Invasive Pneumococcal Disease (IPD) cases have been observed. According to statistics from the National Reference Centre for Diagnosis of Bacterial Infections of the Central Nervous System (KOROUN) in 2025, pneumococcal infections largely concerned patients aged 25 and older. Due to the high mortality rate caused by IPD, reaching over 17%, diagnostics are crucial as they can contribute to the rapid implementation of targeted treatment.

**Objective:** The aim of this study was to identify the etiological factor responsible for an invasive infection in a 44-year-old female patient admitted to the Emergency Department in serious condition.

**Materials and Methods:** The study samples included blood, cerebrospinal fluid (CSF) and blood cultures. The indication for the above diagnosis was the occurrence of earache, headache and neck stiffness one week before the hospitalization episode. The Meningitis/Encephalitis (ME) Panel (Biofire, FilmArray, Biomerieux) was used for rapid CSF diagnosis.

**Results:** Blood biochemistry results revealed high levels of inflammatory markers: CPR 274 mg/dL and PCT 2.16 ng/ml, and a high leukocyte count of 24.8 g/l. General PRM examination revealed turbidity, high pleocytosis of 492 cells/ $\mu$ l, significantly elevated protein level of 4.32 g/l, and decreased glucose level. Immediately after collection, the CSF was also submitted to the microbiology laboratory. Gram-stained specimens revealed Gram-positive cocci arranged in diplococci. The patient's blood cultures were identified as positive within a short time of being placed in the blood culture machine. *Streptococcus pneumoniae* was detected in the molecular diagnostic panel.

**Conclusions:** Rapid molecular diagnostics is an essential tool in modern microbiological diagnostics, enabling implementation of targeted antibiotic therapy. However, classical microbiology methods are essential for assessing phenotypic drug susceptibility as a gold standard.

**Keywords:** pneumococcal infections, molecular diagnostics, invasive infections

# Identification of Virulence Genes and Assessment of Synergism Between Selected Antibiotics Among Carbapenem-Resistant *Acinetobacter baumannii* Strains

Paulina Pecyna<sup>1</sup>, Wiktoria Nowicka<sup>1</sup>, Klaudiusz Kaźmierczak<sup>1</sup>, Marcelina Maria Jaworska<sup>2</sup>, Marzena Gajęcka<sup>1,3\*</sup>

(1) Department of Genetics and Pharmaceutical Microbiology, Poznan University of Medical Sciences, 3 Rokietnicka St. 60-806 Poznan, Poland

(2) The hospital of Baptism Monument of Poland, 37 Maja St. 62-002 Gniezno, Poland

(3) Institute of Human Genetics, Polish Academy of Sciences, 32 Strzeszyńska St. 60-479 Poznan, Poland

\*Corresponding author e-mail: [gamar@man.poznan.pl](mailto:gamar@man.poznan.pl)

**Introduction:** Carbapenem-resistant *Acinetobacter baumannii* (CRAB) was included on the WHO Bacterial Priority Pathogens List (BPPL) of the year 2024. In 2025, multidrug-resistant (MDR) strains of *A. baumannii* accounted for approximately 45% of all *A. baumannii* strains worldwide, causing numerous deaths. These data indicate a serious challenge in implementing effective therapies against this pathogen.

**Objective:** This study aimed to evaluate the presence of the *AriI*, *OmpA*, and *Omp33-36* genes, which determine carbapenem resistance and virulence among *A. baumannii*. Furthermore, the synergistic *in vitro* antibacterial effect of the antibiotics meropenem and tigecycline, as well as ceftazidime/avibactam and aztreonam were verified.

**Materials and Methods:** *A. baumannii* strains (n=45) isolated from patients hospitalized at the hospital of Baptism Monument of Poland in Gniezno were used in this study. The procedure for thermal isolation of bacterial DNA was developed at the PUMS. The presence of genes encoding selected virulence factors was assessed using PCR techniques. Co-action of antibiotics was assessed using the disk diffusion method.

**Results:** Among the 45 *A. baumannii* isolates tested, the presence of the *AriI* gene was confirmed in 33% of the strains, while the *OmpA* and *Omp 33–36* genes were identified in 27% and 20% of the bacteria tested, respectively. All three genes were detected in one isolate. Only one strain demonstrated a synergistic effect between ceftazidime/avibactam and aztreonam. No synergistic effect between meropenem and tigecycline was observed in any of the tested microorganisms.

**Conclusions:** The presence of the *AriI*, *OmpA*, and *Omp33-36* genes in the genomes of the studied *A. baumannii* strains is not clearly associated with carbapenem resistance. Further studies are necessary to identify the synergistic antibacterial effects of various antibiotics before using them in combination therapy *in vivo*.

**Keywords:** *Acinetobacter spp.*, carbapenems, synergism

# LC-MS/MS as an Ideal Tool for the Determination of Trace Antifungal Compounds from the Azole Group

Julia Płatkiewicz\*, Robert Frankowski, Agnieszka Zgoła-Grześkowiak

*Faculty of Chemical Technology, Poznan University of Technology, Berdychowo 4, 60-965 Poznan, Poland*

\*Corresponding author e-mail: julia.platkiewicz@doctorate.put.poznan.pl

Azole antifungals constitute an important class of pharmaceuticals widely used in the treatment of fungal infections in humans. Their mechanism of action is based on the inhibition of lanosterol 14 $\alpha$ -demethylase, a key enzyme in ergosterol biosynthesis, which results in disruption of fungal cell membrane [1]. Azole compounds are commonly applied in systemic and topical therapies against broad spectrum of fungal infections, including candidiasis, cryptococcosis and blastomycosis [2]. Their extensive use may lead to the presence of azoles in the environment, for instance fluconazole, which undergoes limited metabolism (approximately 11.4% of the administered dose) and is excreted largely unchanged (>90%), increasing the likelihood of its environmental occurrence [3]. Therefore, the need for reliable analytical methods for detecting and quantifying trace concentrations of azole compounds in complex samples in both pharmaceutical analysis and environmental studies has increased.

In this study, an analytical method based on liquid chromatography coupled with tandem mass spectrometry (LC–MS/MS) was developed for the determination of selected azoles, including clotrimazole, climbazole, econazole, fluconazole, ketoconazole, and miconazole. The chromatographic separation conditions and mass spectrometry detection parameters were optimized to achieve high sensitivity and selectivity. The developed method was validated by determining key analytical parameters, including linearity, linear range, limits of detection (LOD), and limits of quantification (LOQ). The method showed satisfactory linearity within the concentration range of 0.0005 – 0.5  $\mu\text{g ml}^{-1}$ , with correlation coefficients ( $R^2$ ) ranging from 0.9995 to 1.0000. The obtained LOD and LOQ values varied from 0.00001 to 0.00006  $\mu\text{g ml}^{-1}$  and from 0.00003 to 0.00021  $\mu\text{g ml}^{-1}$ , respectively.

The obtained results highlight the potential of LC–MS/MS as a powerful analytical tool for the determination of medically relevant azole antifungal agents. The developed approach may support pharmaceutical analysis and contribute to improved monitoring of antifungal compounds in various matrices.

**Keywords:** azole antifungals; LC–MS/MS; trace analysis; analytical method validation;

**Acknowledgments:** The research was supported by the Ministry of Science and Higher Education, research project 0911/SBAD/2606.

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# Design of Polymeric Micelle-Based Nanocarriers for the Topical Delivery of Fisetin in Skin Disease Therapy

Tomasz Przybylski<sup>1,2\*</sup>, Joanna Czerniel<sup>1\*</sup>, Aleksandra Majchrzak-Celińska<sup>3</sup>,  
Violetta Krajka-Kuźniak<sup>3</sup>, Maciej Stawny<sup>1</sup>

<sup>1</sup>*Department of Pharmaceutical Chemistry, Poznan University of Medical Sciences,  
Rokietnicka 3, 60-806 Poznan, Poland*

<sup>2</sup>*Doctoral School, Poznan University of Medical Sciences, Poznan, Poland*

<sup>3</sup>*Poznan University of Medical Sciences, Department of Pharmaceutical Biochemistry, 3  
Rokietnicka, 60-802 Poznan, Poland*

\*Corresponding author e-mail: tomasz.przybylski@student.ump.edu.pl

**Introduction:** Fisetin (FIS) is a naturally occurring bioactive flavonoid that exhibits well-established antioxidant and anti-inflammatory activities. However, its clinical and pharmaceutical applicability is limited by poor aqueous solubility and pronounced lipophilicity, which adversely affect its bioavailability. Consequently, the development of nanotechnology-based delivery systems represents a promising strategy to enhance the therapeutic potential of this compound.

**Aim of the study:** In the present study, micellar nanocarriers were formulated to improve the bioavailability of FIS and to enhance its therapeutic efficacy in the management of skin disorders.

**Materials and methods:** Eight formulations (F1 – F8) with varying ratios of bile salts, Poloxamers, and Kolliphors were prepared using the thin-film hydration method and subsequently stored as lyophilized samples at  $4 \pm 1$  °C. The effect of FIS and its nanoformulations on the viability of MICH-2 and MRC-5 cells was evaluated using the MTT assay.

**Results:** Based on physicochemical characteristics and stability data, three formulations (F2, F4, and F6) were selected for subsequent biological evaluation. In MICH-2 melanoma cells, free FIS induced a gradual decrease in cell viability, whereas micellar formulations exhibited enhanced cytotoxicity at lower concentrations. Among them, F2 demonstrated the strongest effect, followed by F6, while F4 showed moderate activity. In contrast, MRC-5 fibroblasts maintained higher overall viability, particularly upon treatment with free FIS and the F4 formulation.

**Conclusions:** The present study demonstrates that the type of poloxamer significantly influences the biological performance of FIS-loaded mixed micelles. Furthermore, nanoencapsulation enhanced the cytotoxic activity of FIS against melanoma cells compared to the free compound while maintaining acceptable safety toward normal fibroblasts.

**Keywords:** mixed micelles; fisetin; skin diseases; MTT assay

# Assessment of Anticancer Effects of CBD and Celecoxib Co-Loaded in Single-Lipid POPC Liposomes

Anna Rybarczyk<sup>1,2\*</sup>, Aleksandra Majchrzak-Celińska<sup>2</sup>, Ludwika Piwowarczyk<sup>3</sup>,  
Violetta Krajka-Kuźniak<sup>2</sup>

<sup>1</sup> Poznan University of Medical Sciences, Doctoral School, Bukowska 70, 60-812 Poznań, Poland

<sup>2</sup> Poznan University of Medical Sciences, Department of Pharmaceutical Biochemistry, Rokietnicka 3, 60-806 Poznań, Poland

<sup>3</sup> Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Rokietnicka 3, 60-806 Poznań, Poland

\*Corresponding author e-mail: anna.rybarczyk@student.ump.edu.pl

Glioma remains one of the most difficult-to-treat malignant brain tumors, with limited long-term survival. The exploration of novel drug combinations is a promising strategy to enhance therapeutic outcomes. Non-intoxicating cannabidiol (CBD) demonstrates the potential to enhance cell death in cancer cells while preserving healthy tissue. Its therapeutic potential may be enhanced when co-administered with anti-inflammatory drugs such as celecoxib (CELE). Furthermore, an additional advantage of liposomal delivery systems is increased stability of the compounds. This study was designed first to assess the cytotoxicity of CBD, CELE, and their combination in non-cancerous astrocytes and U-87 MG tumor cells, and subsequently to evaluate POPC liposomal formulations of these compounds in U-87 MG cells.

The MTT assay was employed to determine the cytotoxicity of the free compounds and their liposomal formulations. The pro-apoptotic and pro-oxidative potential of CBD-, CELE-, and mixture-loaded liposomes in the U-87 MG glioma cells was subsequently assessed using the Annexin V & Dead Cell Kit<sup>®</sup> and the Oxidative Stress Kit<sup>®</sup>.

After 48 h of exposure, the CBD+CELE combination showed an IC<sub>50</sub> above 10 μM in human astrocytes, whereas in U-87 MG cells, the IC<sub>50</sub> at the same time point was 7.9 μM. The liposomal formulations of CBD, CELE, and co-loaded CBD+CELE at 1 and 5 μM reduced the metabolic activity of U-87 MG cells and induced pro-apoptotic effects. These reports were accompanied by elevated ROS levels, particularly in cells treated with 5 μM CELE and CBD+CELE liposomes.

Overall, the findings suggest that POPC liposomes allowed efficient encapsulation of CBD and CELE as well as co-encapsulation, however, the toxicity of the liposomal formulations was less pronounced compared with the free compounds. Future studies should include drug release profiling and long-term exposure experiments to assess the potential of POPC carriers for these agents.

**Keywords:** cannabidiol (CBD); celecoxib; glioma; liposomes; combination

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## **Patient with Anxiety in the Pharmacy: Pharmacist Competencies (Pilot Study)**

Tetiana Sakharova<sup>1</sup>, Viktorii Propisnova<sup>2\*</sup>, Inna Otrishko<sup>3</sup>, Kateryna Vietrova<sup>3</sup>

<sup>1</sup>*Department of General and Clinical Pharmacy, Odesa I.I. Mechnikov National University,  
14 Universytetska St., Odesa, Ukraine, 65026*

<sup>2</sup>*Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences, 3  
Rokietnicka St, Poznań, 80-806 Poland*

<sup>3</sup>*Department of Pharmacology and Clinical Pharmacy, National University of Pharmacy,  
53 Skovorody St, Kharkiv, Ukraine, 61002*

\*Corresponding author e-mail: vpropisnova@ump.edu.pl

In the modern civilized world, feelings of anxiety and inner tension are integral companions of everyday life. Under certain conditions, anxiety as a typical psycho-emotional response may acquire a negative character and lead to pathological mental and morphofunctional disorders. In conditions of limited access to specialized care, a significant proportion of patients turn to pharmacies as the first point of contact within the healthcare system. This increases the role of pharmacists in identifying and supporting such patients. The aim of this study was to assess pharmacists' adherence to the current requirements of the Ministry of Health of Ukraine regarding pharmaceutical care for patients with symptoms of anxiety. The study employed sociological (survey), analytical-synthetic, and statistical methods. Frontline pharmacists (n = 12) from the pharmacy chain LLC "ROST" in Kharkiv (Ukraine) participated in the study. The questionnaire included three sections: self-assessment of clinical knowledge, awareness of "red flags" of anxiety conditions, and criteria for selecting symptomatic treatment and non-pharmacological interventions. All respondents reported being able to recognize anxiety symptoms and perform initial differentiation. Half of the participants considered it necessary to clarify the frequency of anxiety episodes, clinical manifestations, and treatments used by patients. Screening for "red flags" requiring referral to a physician was performed by two-thirds (n = 8) of pharmacists. Herbal sedatives predominated among over-the-counter recommendations (58%), followed by non-prescription anxiolytics (34%) and homeopathic remedies (8%). Patient counseling mainly focused on dosage regimens and duration of use. Only 20% of pharmacists provided non-pharmacological recommendations, while others cited lack of time and increased workload associated with pharmacy operations under martial law conditions. In conclusion, high levels of communication and clinical competencies among pharmacists are essential for improving pharmaceutical care and patient safety, but require continuous development in mental health care adapted to rapidly changing conditions.

**Keywords:** anxiety; pharmaceutical care; professional competencies

# Developing Clinical Competencies of Pharmacy Students Through Simulation and Clinical Reasoning

Jan Sobczyński<sup>1\*</sup>, Aleksandra Szopa<sup>1</sup>

<sup>1</sup>*Department of Clinical Pharmacy and Pharmaceutical Care, Medical University of Lublin,  
Al. Raclawickie 1, Lublin, Poland*

\*Corresponding author e-mail: jan.sobczynski@umlub.edu.pl

Modern pharmacy education must adapt to the evolving realities of clinical practice and the expectations of new generations of learners. The expanding role of the clinical pharmacist, legislative changes, digital transformation in higher education, and global trends in medical teaching all necessitate a shift away from traditional lecture-based models toward active, practice-oriented, and competency-focused instructional methods. This presentation introduces a comprehensive educational framework implemented in the Pharmacy program at the Medical University of Lublin, integrating medical simulation, clinical reasoning, and interprofessional education.

Medical simulation—delivered through low-, medium-, and high-fidelity scenarios—provides students with a safe environment in which to practice clinical, communication, and analytical skills. Activities involving standardized patients, educational videos, realistic case scenarios, and simulated care settings enable students to develop pharmaceutical care competencies, identify drug-related problems, and make therapeutic decisions without risk to actual patients. A core component of the curriculum is clinical reasoning, taught through a structured process involving data collection, clinical assessment, therapeutic planning, and therapy monitoring. This approach strengthens critical thinking, evidence-based decision-making, and prioritization skills, particularly in cases involving multimorbidity and polypharmacy.

Interprofessional education, delivered jointly with medical students, further enhances readiness for real-world clinical practice. These sessions foster understanding of professional roles, improve communication within therapeutic teams, and support the implementation of patient-centered care and emerging clinical pharmacy services. The approach aligns with national recommendations for modern medical education.

This multidimensional model integrates contemporary educational tools, advances key competencies required of future pharmacists, and responds to healthcare system challenges. Experience to date demonstrates that these methods effectively prepare students for collaborative clinical practice, responsible patient care, and the complex decision-making required in modern pharmacy.

**Keywords:** medical simulation; clinical reasoning; interprofessional education

# Optimization of Sonication Conditions and Short-Term Stability of Cholesterol-Based Niosomes

Jagoda Szkudlarek<sup>1,2\*</sup>, Gabriela Anglart<sup>1</sup>, Dariusz T. Młynarczyk<sup>3</sup>, Anna Jelińska<sup>1</sup>,  
Ludwika Piwowarczyk<sup>1</sup>

<sup>1</sup> *Poznan University of Medical Sciences, Chair and Department of Pharmaceutical Chemistry, Rokietnicka 3, 60-803 Poznań, Poland*

<sup>2</sup> *Doctoral School, Poznan University of Medical Sciences, 70 Bukowska, 60-812 Poznań, Poland*

<sup>3</sup> *Poznan University of Medical Sciences, Chair and Department of Chemical Technology of Drugs, Rokietnicka 3, 60-803 Poznań, Poland*

\*Corresponding author e-mail: jszkudlarek@ump.edu.pl

Niosomes are versatile drug delivery systems that have attracted considerable interest due to their biocompatibility, stability, and capacity to improve the delivery of active substances. In this study, niosomal formulations composed of cholesterol and selected surfactants were prepared by the thin-film hydration method and subsequently sonicated to optimize vesicle properties. Two sonication approaches, differing in duration and intensity, were evaluated to improve particle size distribution and formulation homogeneity. Particle size and polydispersity index (PDI) were used as key parameters for process assessment. The optimized formulation was further characterized by nanoparticle tracking analysis (NTA), and its stability was assessed over 21 days using dynamic light scattering (DLS) and electrophoretic light scattering (ELS). The modified sonication conditions yielded smaller, more homogeneous vesicles than the initial protocol, indicating improved process performance. Additional characterization confirmed the nanoscale size range of the optimized formulation. Stability studies demonstrated that the formulation retained acceptable physicochemical properties during storage. These findings suggest that optimization of the sonication step can significantly improve niosomal formulation quality and process.

**Keywords:** niosomes; vesicular carriers; thin-film hydration; sonication; physicochemical stability

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# The Analysis of the Factors Influencing the Efficiency of the Cloud Point Extraction for Levofloxacin and Ciprofloxacin under Acidic Conditions

Bartosz Sznek<sup>1,2\*</sup>, Andrzej Czyrski<sup>1</sup>

<sup>1</sup>*Department of Physical Pharmacy and Pharmacokinetics, Poznań University of Medical Sciences, Rokietnicka 3 Street, 60-806 Poznań (Poland),*

<sup>2</sup>*Doctoral School, Poznan University of Medical Sciences, Bukowska 70, Poznań 60–812, Poland*

\*Corresponding author e-mail: bartosz.sznek@gmail.com

**Introduction:** With growing environmental awareness, industries are increasingly adopting eco-friendly practices. Cloud point extraction (CPE) aligns with green chemistry principles, offering a sustainable alternative for drug extraction.

**The aim of the study:** To analyze the effect of the independent variables on the recovery of ciprofloxacin and levofloxacin for CPE with the Central Composite Design (CCD).

**Materials and methods:** The study included 27 experiments with a threefold central-point repetition. The following independent variables were analyzed: TX-114 (surfactant) concentration, HCl and NaCl concentrations, and incubation temperature, each coded at five levels. HPLC analyzed samples, and the data were processed using Statistica software. The polynomial equations were developed to predict recovery values, and response surface methodology was used to interpret the impact of the analyzed factors.

**Results:** Statistical analysis indicated that all the factors were significant to the model. TX-114 concentration has the greatest effect on recovery, although HCl concentration also plays a significant role. The optimal conditions for ciprofloxacin recovery included TX-114 concentration of 8.5%, no NaCl addition, HCl concentration of 0,1M, and an incubation temperature of 45 °C. The estimated recovery was 53%. For levofloxacin, optimal conditions included a TX-114 concentration of 9%, no NaCl addition, an HCl concentration of 1,5 M, and an incubation temperature of 60 °C. It resulted in a 43% recovery.

**Conclusion:** TX-114 concentration was indicated as the most significant independent variable. Results demonstrated the validity of the CCD model for analyzing the impact of the analyzed factors on the recovery of both analytes. It enabled the detailed analysis and optimization of factors affecting the process.

**Keywords:** aqueous matrices; cloud point extraction; green chemistry; optimization; sample preparation

# Size-Dependent Changes in Selected Oxidative Stress Markers in Rat Liver Following Exposure to Manganese-Containing Polydopamine Nanoparticles

Marta Szukalska<sup>1\*</sup>, Radosław Mrówczyński<sup>2</sup>, Patrycja Sujka-Kordowska<sup>3</sup>,  
Izabela Miechowicz<sup>4</sup>, Tomasz Zalewski<sup>5</sup>, Michał Nowicki<sup>3</sup>, Ewa Florek<sup>1</sup>

<sup>1</sup> Laboratory of Environmental Research, Department of Toxicology, Poznan University of Medical Sciences, 3 Rokietnicka Street, Poznań, 60-806, Poland

<sup>2</sup> Faculty of Chemistry, Adam Mickiewicz University, Uniwersytetu Poznańskiego 8, Poznań, 61-614, Poland

<sup>3</sup> Department of Histology and Embryology, Poznan University of Medical Sciences, 6 Świącickiego Street, Poznań, 60-781, Poland

<sup>4</sup> Department of Computer Science and Statistics, Poznan University of Medical Sciences, 7 Rokietnicka Street, Poznań, 60-806, Poland

<sup>5</sup> NanoBioMedical Centre, Adam Mickiewicz University, Wszechnicy Piastowskiej 3, Poznań, 61-614, Poland

\*Corresponding author e-mail: martan@ump.edu.pl

Manganese-modified polydopamine nanoparticles (PDA@Mn NPs) are increasingly studied as multifunctional nanomaterials with potential applications in drug delivery and magnetic resonance imaging (MRI). However, their *in vivo* safety profile still requires further investigation. The aim of this study was to evaluate size-dependent changes in selected oxidative stress markers in rat liver following exposure to PDA@Mn nanoparticles.

Nanoparticles with average diameters of approximately 50, 100, and 200 nm were synthesized and characterized using scanning electron microscopy (SEM) to confirm their morphology and size distribution. Animals received nanoparticles at doses of 15 or 45 mg/kg body weight, and liver samples were collected after 1 h, 24 h, 7 days, and 28 days.

A histological evaluation of tissues was conducted. Liver homogenates were analyzed for oxidative stress biomarkers, including reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and thiobarbituric acid reactive substances (TBARS). The results showed a size-dependent response. Exposure to smaller nanoparticles (~50 nm) led to early depletion of GSH and increased lipid peroxidation, indicating enhanced oxidative stress shortly after administration. At the same time, changes in SOD and CAT activity suggest activation of cellular antioxidant defense mechanisms.

In contrast, nanoparticles with an intermediate diameter (~100 nm) caused smaller changes in both enzymatic and non-enzymatic markers, suggesting better hepatic tolerance. Larger nanoparticles (~200 nm) produced moderate but more persistent oxidative changes at later time points, particularly at the higher dose.

These findings indicate that nanoparticle size plays an important role in shaping oxidative stress responses in the liver. Since manganese incorporation gives these nanoparticles potential MRI contrast properties, careful optimization of nanoparticle size and dose may be important for balancing biomedical usefulness with biological safety.

**Keywords:** polydopamine nanoparticles; oxidative stress; liver; manganese nanoparticles; nanotoxicology

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# The Role of Pharmaceutical Support in Optimising the Treatment of Functional Constipation in Preschool Children

Kateryna Vietrova<sup>1</sup>, Viktoriia Muzyka<sup>1</sup>, Viktorii Propisnova<sup>2\*</sup>

<sup>1</sup>*Department of Pharmacology and Clinical Pharmacy, National University of Pharmacy,  
53 Skovorody St, Kharkiv, Ukraine, 61002*

<sup>2</sup>*Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences,  
3 Rokietnicka St, Poznań, 80-806 Poland*

\*Corresponding author e-mail: vpropisnova@ump.edu.pl

This study aims to substantiate the role of pharmaceutical support in improving the efficacy and safety of treating functional constipation in pre-school children, who are the group most affected by the disorder in recent years. A survey was conducted with 16 pharmacists working in pharmacies in Kyiv.

Up to 44% of pharmacists are frequently approached by parents asking for a laxative to treat constipation in pre-school children. 68.75% always ask if the child has not had a bowel movement for more than 48 hours beyond what is normal for them. 75% always investigate causes that may lead to constipation in children. The same proportion of pharmacists always rule out 'alarming symptoms' that require a doctor consultation. Most pharmacists prefer to prescribe lactulose-based preparations for pre-school children. The preferred dosage forms are syrups and rectal suppositories. Most pharmacists provide pharmaceutical care when dispensing laxatives and 87.5% are aware of lactulose's contraindication in acute inflammatory bowel diseases. Only 81.25% know that sodium picosulphate is not prescribed to children under four and 93% are aware of drug-laxatives interactions. 75% provide advice on non-pharmacological treatment and prevention of constipation in pre-school children.

The pharmacist plays a vital role in managing children's constipation with laxatives. At the start of pharmaceutical care, the pharmacist should ask how long the child has been constipated and rule out 'alarming' symptoms. It is also necessary to identify the cause of the constipation. Often, addressing the cause leads to normal bowel movements.

If there are no symptoms, a safe and effective laxative may be selected. Child representatives must be advised on how to use it, the side effects and drug interactions, and offered other ways to treat and prevent constipation. If the treatment is ineffective, or if 'alarming' symptoms appear or side effects occur, a doctor must be consulted immediately.

**Keywords:** constipation; children; pharmacist

# Clinical Perspectives on the Safety of Palbociclib, Ribociclib and Abemaciclib in HR-positive Breast Cancer

Katarzyna Wawrzyniak<sup>1,2\*</sup>, Katarzyna Regulska<sup>1,2</sup>

<sup>1</sup> Pharmacy, Greater Poland Cancer Centre, Garbary 15 Street, 61-866 Poznań, Poland

<sup>2</sup> Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences, Poznan, Poland, Collegium Pharmaceuticum, Rokietnicka 3 Street, 60-806 Poznań, Poland

\*Corresponding author e-mail: katarzyna.wawrzyniak@wco.pl

Cyclin-dependent kinase 4 and 6 inhibitors - palbociclib, ribociclib, abemaciclib - constitute a contemporary class of agents used in combination with endocrine therapy for hormone receptor-positive, HER2-negative breast cancer. Although their antitumor efficacy is broadly comparable, they differ in safety profiles and interaction potential. These distinctions may be clinically relevant when selecting an optimal agent as part of an individualized treatment approach.

A questionnaire-based study was conducted in a cohort of 157 patients with hormone-dependent breast cancer. Among them, 106 patients received endocrine therapy combined with one of three CDK4/6 inhibitors, while 49 patients formed a control group treated with endocrine therapy alone.

The combination of CDK4/6 inhibitors with endocrine therapy was associated with a lower overall risk of adverse events compared with endocrine therapy alone (OR < 1; p < 0.05). Among individual agents, the likelihood of adverse effects was highest for abemaciclib, followed by ribociclib, and lowest for palbociclib (p < 0.05). In the abemaciclib group, adverse events were more frequently observed in patients with BMI < 30 compared to those with BMI ≥ 30.

CDK4/6 inhibitors enhance the tolerability of endocrine therapy in breast cancer. Abemaciclib is associated with the highest risk of adverse effects among the analyzed agents. In patients with BMI ≥ 30, its pharmacological activity may be diminished. Patients receiving CDK4/6 inhibitors should undergo medication review with consideration of cumulative toxicity and potential interactions involving cytochrome enzymes and membrane transporters.

**Keywords:** palbociclib; ribociclib; abemaciclib; adverse drug reactions

## The New Medicine Service in Practice

Dobrosława Wiśniewska<sup>1\*</sup>, Olga Sierpniowska<sup>1</sup>, Magdalena Jasińska-Stroschein<sup>2</sup>,  
Magdalena Waszyk-Nowaczyk<sup>1</sup>

<sup>1</sup> *Pharmacy Practice and Pharmaceutical Care Division, Chair and Department  
of Pharmaceutical Technology, Poznan University of Medical Sciences, Rokietnicka 3 St., 60-806,  
Poznan, Poland*

<sup>2</sup> *Department of Biopharmacy, Medical University of Lodz, T. Kosciuszko 4 St., 90-419, Lodz, Poland*

\*Corresponding author e-mail: [dobrosława.w@gmail.com](mailto:dobrosława.w@gmail.com)

**Background:** Medication non-adherence remains a significant public health concern and is particularly common during the initiation phase of chronic pharmacotherapies. To address this issue, Poland introduced the New Medicine Service (NMS), a structured, pharmacist-led intervention aimed at improving patient safety, supporting therapeutic continuity, and enhancing long-term medication persistence.

**Objective:** To evaluate the impact of the NMS professional service on patient adherence and to address the increasing systemic demand for advanced pharmaceutical care services beyond clinical settings.

**Methods:** A cohort study was conducted involving 54 patients (median age: 70 yrs) initiating newly prescribed chronic pharmacotherapies in the period between (January 2025-January 2026). Standardized NMS documentation was utilized throughout the intervention. The protocol comprised: (i) an initial drug-use assessment to identify potential barriers to appropriate medication intake, (ii) an education session including practical demonstrations of correct administration techniques, and (iii) a follow-up consultation to evaluate adherence and address emerging drug-related problems (DRPs).

**Results:** The majority of pharmacological interventions involved cardiovascular and lipid-lowering medications, reflecting the high clinical burden of these conditions. Analysis of the NMS forms confirmed that patients who completed the consultation achieved high levels of health literacy. During NMS, personalized instruction on dosing regimens and side-effect management was provided to all participants. Structured pharmacist-led education significantly reduced patient anxiety regarding the new therapy and improved patient adherence.

**Conclusion:** There is substantial patient demand for NMS consultations, which help reduce the workload of primary care providers. To maximize clinical and system-level benefits, broader integration of pharmaceutical care services into the national healthcare reimbursement framework is essential for effective long-term adherence management.

**Keywords:** pharmaceutical care, adherence, interprofessional collaboration, patient service

# Assessment of the Cytotoxic and Phototoxic Potential of Doxycycline in an *in vitro* Experimental Model Using A253 Salivary Gland Carcinoma Cells

Dorota Wrześniok<sup>1\*</sup>, Zuzanna Rzepka<sup>1</sup>, Artur Beberok<sup>1</sup>, Alina Drzyzga<sup>2</sup>,  
Ryszard Smolarczyk<sup>2</sup>, Justyna Czapla<sup>2</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences in Sosnowiec,  
Medical University of Silesia in Katowice, Jagiellońska 4, 41-200 Sosnowiec, Poland

<sup>2</sup>Maria Skłodowska-Curie National Research Institute of Oncology, Wybrzeże Armii Krajowej 15,  
44-102 Gliwice, Poland

\*Corresponding author e-mail: dwresniok@sum.edu.pl

Doxycycline, a semi-synthetic antibiotic from the tetracycline group, in addition to its antibacterial activity, exhibits properties that modulate cellular processes, including effects on the proliferation, migration, and apoptosis of cancer cells. Previous studies conducted using cell lines of breast, lung, colorectal cancer, and melanoma indicate that doxycycline may have anticancer potential. Its effects include inhibition of cancer cell proliferation, migration, and invasion, induction of apoptosis, and modulation of extracellular matrix metalloproteinase activity. Simultaneously, doxycycline is classified as a compound with a high phototoxic potential, suggesting that concurrent exposure to UV radiation may enhance its biological effects.

The aim of the study was to evaluate the cytotoxic and phototoxic potential of doxycycline in an *in vitro* model using human A253 salivary gland carcinoma cells.

As part of the assessment of the phototoxic effect, the cells were subjected to controlled exposure using a sunshine simulator generating a spectrum similar to natural UV radiation. The following experimental model was applied: cells were preincubated with doxycycline for one hour, then exposed for 30 minutes to radiation generated by the solar simulator, followed by a 24-hour post-incubation in standard culture medium. Cell viability was analyzed using the WST-1 assay.

The demonstrated results indicate that doxycycline, within the concentration range of 1–100  $\mu\text{M}$ , did not exhibit a cytotoxic effect leading to a reduction in the viability of A253 cells compared to the control. However, under conditions of simultaneous exposure to doxycycline (10–100  $\mu\text{M}$ ) and UV radiation, a significant phototoxic effect was observed—cell viability decreased by 25–75%, depending on the applied drug concentration.

The obtained results confirm the phototoxic activity of doxycycline in the investigated *in vitro* model, which may provide a basis for further studies on its potential application in the treatment of salivary gland cancer.

**Keywords:** doxycycline; pharyngeal squamous cell carcinoma; cytotoxicity; phototoxicity; sunshine simulator.

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# Human Serum Albumin Nanoparticles Co-Loaded with Lycopene and Lutein: Development and Cytocompatibility of an Intravenous Nanoformulation

Izabela Żółnowska<sup>1,2,\*</sup>, Violetta Krajka-Kuźniak<sup>3</sup>, Maciej Stawny<sup>1</sup>

<sup>1</sup>Poznan University of Medical Sciences, Department of Pharmaceutical Chemistry, Rokietnicka 3, 60-806 Poznan, Poland

<sup>2</sup>Poznan University of Medical Sciences, Doctoral School, Bukowska 70, Poznan 60-812, Poland

<sup>3</sup>Poznan University of Medical Sciences, Department of Pharmaceutical Biochemistry, Rokietnicka 3, 60-806 Poznan, Poland

\*Corresponding author e-mail: izabela.zolnowska@student.ump.edu.pl

Modern pharmaceutical research increasingly integrates nanotechnology to design safer therapeutic strategies and improve the formulation and delivery of poorly water-soluble compounds. Such approaches may also be valuable for natural bioactive molecules, including carotenoids such as lutein and lycopene, which exhibit promising biological activity but remain difficult to formulate for intravenous administration due to their hydrophobic nature. The aim of this study was to develop a nanoformulation based on human serum albumin nanoparticles co-loaded with lutein and lycopene and to evaluate its physicochemical properties and cytocompatibility.

The nanoformulation containing lutein and lycopene (1:1) was prepared using a method inspired by nab technology applied in the production of the anticancer drug Abraxane. The developed nanoparticles exhibited a mean diameter of  $123.5 \pm 6.9$  nm and a polydispersity index of  $0.193 \pm 0.006$ , as determined by dynamic light scattering. Freeze-drying followed by reconstitution did not affect particle size, and the formulation maintained colloidal stability for at least four weeks. Cytocompatibility of the formulation was assessed using the MTT assay in THLE-2 human hepatocytes. Treatment with the free lutein–lycopene mixture (1:1) resulted in a clear dose-dependent decrease in cell viability within the tested concentration range (1–100  $\mu$ M). In contrast, carotenoid-loaded albumin nanoparticles demonstrated good cytocompatibility at corresponding carotenoid concentrations, as the viability of THLE-2 cells exposed to the nanoformulation for 48 h remained above 70%, suggesting a protective effect of the albumin matrix.

These findings demonstrate that albumin nanoparticles enable the simultaneous encapsulation of two hydrophobic carotenoids while maintaining good cytocompatibility, highlighting their potential as a nanotechnology-based strategy for intravenous delivery of poorly water-soluble antioxidants.

**Keywords:** non-provitamin A carotenoids; drug delivery; human serum albumin; nanoparticles

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