UNIWERSYTET
MIKOŁAJA KOPERNIKA
W TORUNIU
Collegium Medicum
im. Ludwika Rydygiera w Bydgoszczy

Bydgoszcz, dnia 18.09.2025 r.

Paulina Szeliska
(Imię i nazwisko doktoranta)

STRESZCZENIE ROZPRAWY DOKTORSKIEJ

Dyscyplina naukowa: Nauki Farmaceutyczne

Tytuł rozprawy doktorskiej:

Evaluation of the effectiveness of a selected pharmacotherapy for glioblastomas on the basis of metabolomic and lipidomic profiling of cell lines derived from patients as a step towards personalizing therapy

Streszczenie rozprawy doktorskiej:

The aim of this dissertation was to integrate a pharmaco-metabolomic approach to glioblastoma (GBM) by outlining best practices for in-vitro metabolic studies and their translation, developing a biocompatible, high-throughput solid-phase microextraction (SPME) workflow, and characterizing GBM responses to gallium maltolate (GaM) in 2D and 3D culture models. The review component synthesizes key determinants of GBM metabolic readouts (culture dimensionality, hypoxia, media composition, stem-like state), discusses sample-preparation strategies and analytical platforms that support reliable in vitro–in vivo extrapolation, and provides practical guidance to avoid common pitfalls in supervised modelling. The methodological component introduces an upgraded system enabling repeated, in-incubator sampling from 96-well cultures with minimal perturbation and reduced solvent/plastic use, offering a scalable route for metabolomics in pharmaceutical testing. The research component evaluated GaM across established (A-172, U-87 MG) and patient-derived (3005, 3019, 3034, 3048, 3073) GBM lines grown in 2D and 3D, combining dose–response modelling (IC10/IC50/IC90), transferrin receptor (TFRC) quantification, oxygen consumption rate (OCR), and metabolomics with liquid chromatography combined with mass spectrometry (LC-MS).

GaM reduced viability in all models, with a consistent rightward shift of dose–response and stronger OCR suppression in 3D than in 2D, indicating greater microenvironment-driven tolerance and heightened mitochondrial stress. Baseline TFRC associated with GaM sensitivity in 2D (significant TFRC–IC50 correlation) but not in 3D, underscoring context-dependent biomarker performance. Multivariate analyses showed line-specific drivers of variance: treatment-dominant separation in 3005/3048, culture format dominance in 3019/3034, and time effects in A-172/U-87 MG/3073. The observed metabolomic alteration mainly involved tryptophan, methionine, uracil, and allantoin and pointed to coordinated perturbations in amino-acid, one-carbon/nucleotide, and redox pathways alongside mitochondrial dysfunction. Collectively, the findings identify culture dimensionality as a primary determinant of GaM response and support 3D, patient-derived systems with integrated OCR and metabolomics as more predictive platforms for efficacy assessment, mechanism elucidation, and biomarker development. Moreover, the proposed SPME method, which is simple to use and more ecological, allows for easy integration with cell cultures and traditional assays, which facilitates the design of studies combining pharmacology with metabolomics.

Key words: gallium maltolate; glioblastoma; 3D culture; Solid Phase Micorextraction, Pharmacometabolomic

Paulina Szeliska

(czytelny podpis doktoranta)