Molecularly imprinted drug reservoir for targeted glioblastoma cell treatment: *in vitro* and *in vivo* characterization

Alexandra-Iulia Bărăian[1], Bogdan-Cezar Iacob[1], Olga Soriță[2], Cosmin Pește[3], Alexandru Florian[4], Sergiu Șușman[5,6], Ede Bodoki[1], Ștefan Florian[4]

[1]*Department of Analytical Chemistry, Faculty of Pharmacy, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania;*

[2]*Laboratory of Tumor Cell Biology and Radiobiology, Institute of Oncology "Prof Dr. Ion Chiricuță", Cluj-Napoca;*

[3]*Department of Anesthesiology and Surgical Propaedeutics, University of Agricultural Sciences and veterinary Medicine, Cluj-Napoca;*

[4]*Department of Neurosurgery, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca;*

[5]*Department of Morphological Sciences, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca;*

[6]*Department of Pathology, IMOGEN Research Centre, Cluj-Napoca;*

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INTRODUCTION

Glioblastoma (GBM) is recognized as one of the most intricate and aggressive types of central nervous system tumours [1]. Conventional treatment involving surgery, chemo- and radiotherapy faces challenges due to the tumour's diffuse nature, resulting in limited survival time [2],[3].

This study aimed to address the existing limitations of chemotherapy in GBM treatment by designing a molecularly imprinted drug reservoir. The objective was to achieve sustained release of the antitumor agent ruxolitinib (RUX, a JAK/STAT-3 inhibitor) within the tumour post-resection cavity to target residual infiltrative cancer cells while minimizing toxicity. Four distinct molecularly imprinted polymers (MIPs) were successfully developed and characterized, with one progressing to the *in vivo* assessment stage.

MATERIALS AND METHODS

The synthesis of MIPs involved precipitation polymerization, using acrylamide, trifluoromethacrylic acid, methacrylic acid, and styrene as functional monomers. *In vitro* characterization, as described in our recent paper [4], included analysis of particle size, morphology, drug loading and release profiles. Cytotoxic efficacy was evaluated through the Alamar Blue cell viability assay on C6 GBM cells. Additionally, an *in vivo* assessment was performed using an orthotropic model in Wistar rats.

RESULTS AND DISCUSSION

The *in vitro* characterization of MIPs, as reported previously [4], demonstrated favourable properties when employing trifluoromethacryilic acid (TFMAA) as the functional monomer. Out of the four tested RUX-loaded imprinted polymers, the TFMAA-based one revealed the most favourable risk-benefit profile over the course of 96 hours, exhibiting superior efficacy against GBM cells, while its non-imprinted counterpart showed low toxicity. Within the *in vivo* evaluation, the treatment with this drug-loaded MIP significantly extended the survival time of animals from 20 to 50 days.

CONCLUSIONS

Selection of MIPs for *in vivo* studies was guided by the Alamar Blue assay, considering both the efficacy and potential toxicity of residual monomers. The TFMAA-based RUX-loaded MIP emerged as the most effective one, significantly prolonging animal survival by 30 days.

ETHICAL STATEMENTS

Study adhered to ethical regulations for animal experimentation, in accordance with the guidelines and regulations set forth by the Ethics Committee of Iuliu Hațieganu University of Medicine & Pharmacy.

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