



## KEY WORDS

- ✓ Glioblastoma
- ✓ Temozolomide
- ✓ Rutin
- ✓ Local treatment
- ✓ Hybrid layered composite nanofiber webs

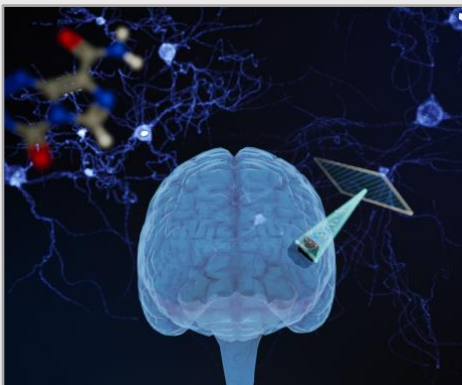
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## DESIGN AND ANALYSIS OF USABILITY OF COMBINED DRUG LOADED LAYERED NANOFIBER SURFACES IN GLIOBLASTOMA TREATMENT

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## THESIS ABSTRACT

In the current doctoral thesis, a hybrid layered composite nanofiber network (LHN) loaded with temozolomide (TMZ) and rutin was designed with controlled release capability to suppress the aggressiveness of the remaining cells after surgical resection in the glioblastoma (GB) tumor region for local treatment. In addition, it aimed to evaluate these nanofibers in terms of their effects on the aggressiveness of GB cells in vitro, reveal the associated protein network, and determine the effects on GB tumor progression, systemic side effect risk, and inflammatory response using an in-vivo orthotopic GB rat model. It was determined that loaded nanofibers slowed the growth of GB cells, while the combination of LHN<sup>TMZ+rutin</sup> significantly reduced the sphere size compared to untreated cells ( $p < 0.0001$ ). In the GB rat model, LHN<sup>TMZ+rutin</sup> treatment showed a more significant tumor reduction effect than LHN<sup>TMZ</sup> ( $p < 0.005$ ). Structural changes in tumor mitochondria, decreased membrane potential, and decreased PARP expression indicated activation of apoptotic pathways in tumor cells. Local administration of LHNs in the GB model attenuated aggressive tumor features without causing local tissue inflammation or adverse systemic effects. Our findings suggest that LHN<sup>TMZ+rutin</sup> is a promising biocompatible model for the local treatment of GB.

## APPLICATION AREAS OF THE THESIS RESULTS

The developed rutin and TMZ-loaded nano drug delivery system was shown to be a promising model for developing a new treatment approach for the local treatment of GB tumors.

## ACADEMIC ACTIVITIES

1. [Ercelik, M., et al. \(2023a\)](#). Olea europaea Leaf Phenolics Oleuropein, Hydroxytyrosol, Tyrosol, and Rutin Induce Apoptosis and Additionally Affect Temozolomide against Glioblastoma: In Particular, Oleuropein Inhibits Spheroid Growth by Attenuating Stem-like Cell Phenotype. *Life*(Basel, Switzerland), 13(2), 470.
2. [Ercelik, M., et al. \(2023b\)](#). Co-loading of Temozolomide with Oleuropein or rutin into polylactic acid core-shell nanofiber webs inhibit glioblastoma cell by controlled release. *International journal of biological macromolecules*, 253(Pt 2), 126722.
3. [Ercelik, M., et al. \(2024\)](#). A new nano approach to prevent tumor growth in the local treatment of glioblastoma: temozolomide and rutin-loaded hybrid layered composite nanofiber. *Asian Journal of Pharmaceutical Sciences*. Accepted
4. A national patent application has been made with the name "Drug Delivery System in Layered Hybrid Nanofiber Structure Loaded with Chemotherapy Drug and/or Bioactive Molecule for Local Use in Surgical Resection Area to Prevent Recurrence in Brain Tumors" with the application number 2023/018556 and an international patent application with the application number PCT/TR2024/050617.