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Antineoplastic and cytoprotective properties of postbiotics as potential nutraceutics in adjunct therapy of central nervous system disorders

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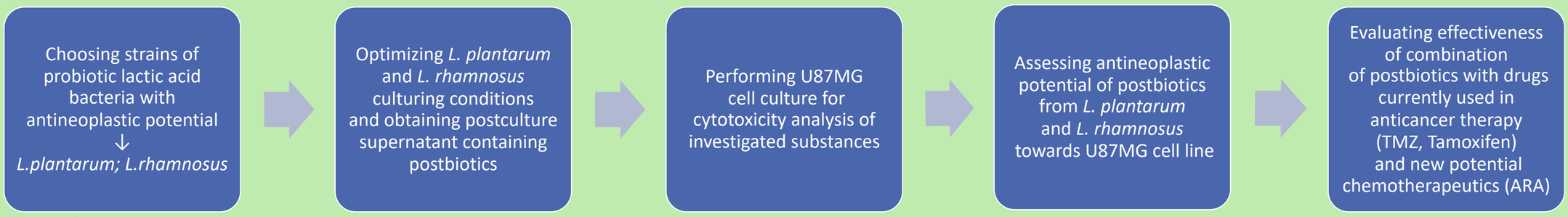
Background

Pathological mechanisms occurring in CNS, both caused by tumorigenesis and degenerative processes, still lack successful treatment, as the most frequent CNS tumor — glioblastoma (GB), has only 5% survival rate for 5 years following initial diagnosis. There is little doubt finding new compounds that will make GB therapy more effective is necessary. One group of natural compounds — postbiotics, shows promising properties as potential adjunct therapeutics.
Postbiotics are metabolites and macromolecules produced by probiotic bacteria and have been noticed to exert beneficial influence on nervous cells. Some of the metabolites were proven to pass the blood-brain barrier. In addition, postbiotics have been observed to cause cytotoxic effect towards cancer cells selectively, while having the ability to protect normal cells from various stressors.

Research aim and experimental tasks

The main aim of the investigation was a preliminary in vitro assessment of how the U87MG cell line, serving as glioblastoma model, is affected by postbiotics derived from commercially available probiotic lactic acid bacteria strains: *Lacticaseibacillus rhamnosus* and *Lactiplantibacillus plantarum.*
Following experimental schedule was designed:

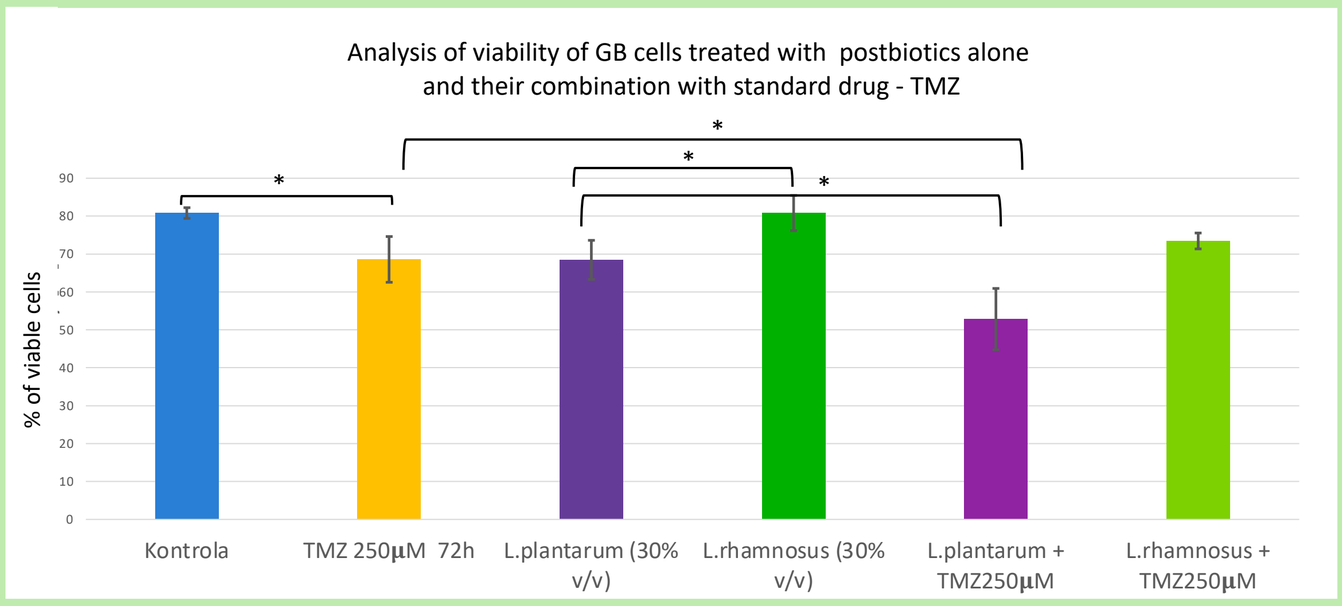


Methods

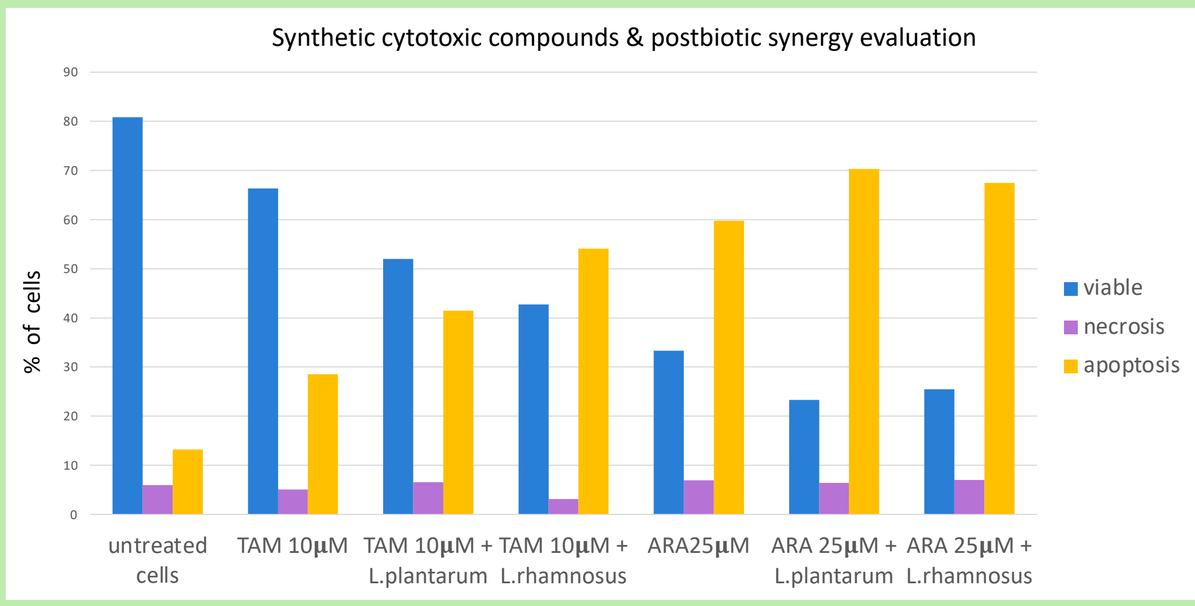
Experimental tasks were performed using following methods:

- tumor cell culture (U87MG) and bacteria culture (*L. plantarum, L. rhamnosus*) performance;
- preliminary assessment of postbiotic influence on tumor cells' viability depending on the concentration of postculture mixture (0, 10, 20, 30, 40, 50% v/v) and incubation time (24, 48, 72 h) conducted on a 96-well plate with Presto Blue assay, which allows to assess viable cells number based on fluorescence reading;
- assessment of postbiotics' influence and combination of postbiotics with synthetic cytotoxic compounds (TMZ, tamoxifen, ARA -aziridine-hydrazide hydrazone derivatives) on cells' viability and cell death processes, including necrosis and apoptosis - detection by flow cytometry of cells stained with annexin V labeled with FITC and propidium iodide;
- assessment of postbiotics influence on cell cycle progression, conducted by propidium iodide staining and flow cytometry analysis.

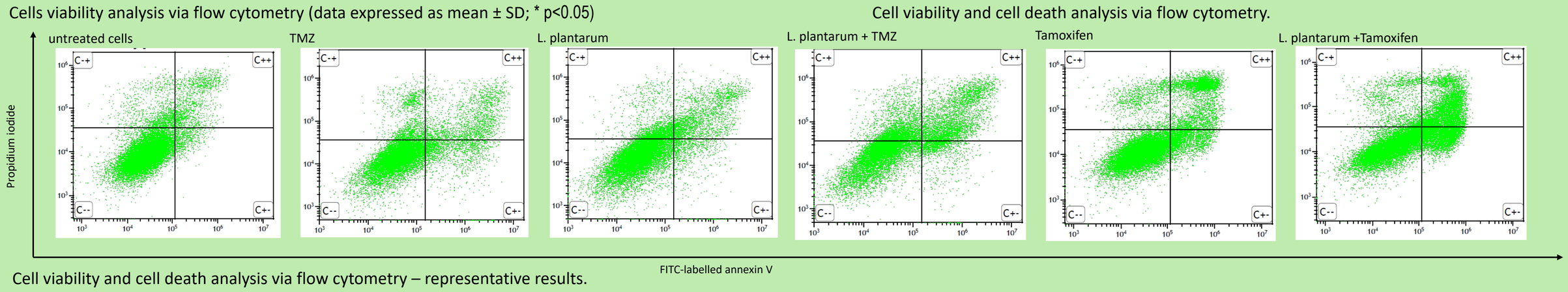
Results



Cells viability analysis via flow cytometry (data expressed as mean ± SD; * $p<0.05$)



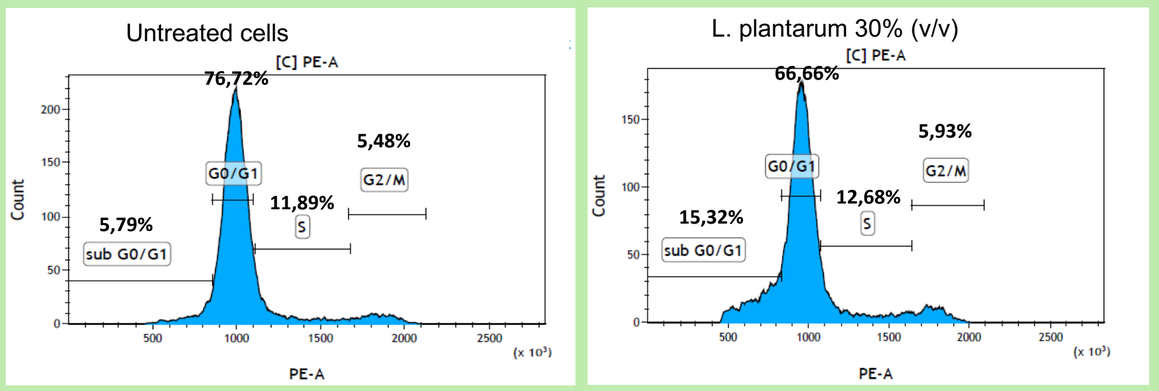
Cell viability and cell death analysis via flow cytometry.



Cell viability and cell death analysis via flow cytometry – representative results.

Conclusion

- Postbiotics obtained from examined LAB strains exert different effects on GB cells, detected as cytotoxicity of *L. plantarum* and lack of harmful influence of *L. rhamnosus.*
- Postbiotics have potential to enhance cytotoxic effect of synthetic chemotherapeutics; however, the final effect of postbiotic-drug combination seems to depend on type of applied chemical and the mechanism of its activity towards the cells.
- Perspectives:
  - evaluation of influence of LAB-derived postbiotics on broader spectrum of GB cell lines and normal cells of CNS to verify selectivity of cytotoxic effects,
  - analysis of postbiotic influence on molecular and cellular processes involved in drug response and resistance of tumor cells,
  - evaluation of cytoprotective potential of postbiotics towards normal cells of CNS in context of cellular processes underlying pathogenesis of neurodegeneration.



Cell cycle analysis – representative results.