EVALUATION OF THE EFFICACY OF LIPID CORE NANOEMULSIONS CONTAINING TEMOZOLOMIDE COUPLED TO FERROCENES IN THE TREATMENT OF GLIOBLASTOMAS

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INTRODUCTION

Glioblastoma (GB) is the most common and aggressive neoplastic brain tumor, and its treatment has proved to be a challenge. For decades its therapy has been based on the use of temozolomide (TMZ), but the survival rate remains low. However, the discovery of the cytotoxic properties of ferrocene compounds (Fc) has suggested new approaches in the use of these ferric structures coupled to chemotherapeutics in the treatment of several cancers.

OBJECTIVES & METHODOLOGY

We investigated whether lipid core nanoemulsions (LCNE) containing TMZ and/or Fc induce a decrease in viability of T98G and U87 GB cells, which show resistant and sensible profiles against TMZ, respectively. The effects of these formulations on cell viability were investigated by neutral red uptake (NRU) assay. Next, we use the cell line which showed the highest sensitivity to treatments to investigate the mechanisms of cell death and oxidative stress through flow cytometry using specific markers for apoptosis, necrosis, superoxide anion generation and mitochondrial membrane polarization changes.

RESULTS

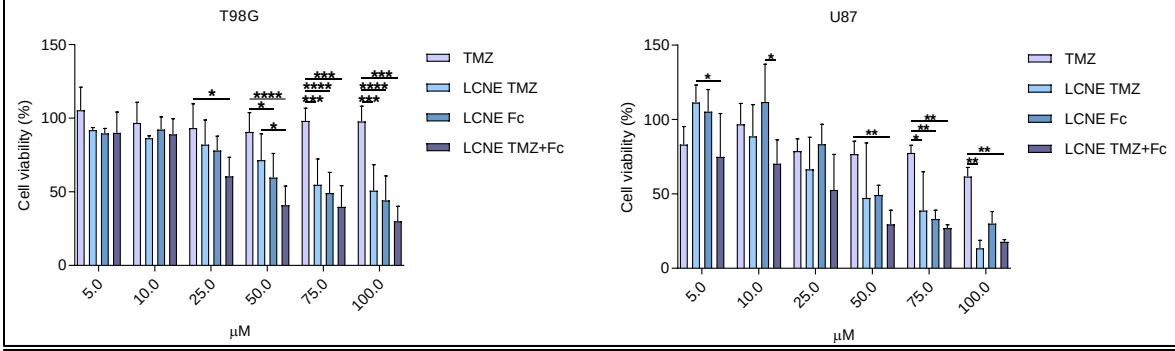

Fig 1. *In vitro* NRU cell viability assay of T98G and U87 GB cells under 24 h exposition to different treatments. Results are expressed as percentage compared to NC group growth and represent the mean ± SD of 3 independent experiments. *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001; ****p ≤ 0.0001 (Two-way ANOVA + Tukey's test).

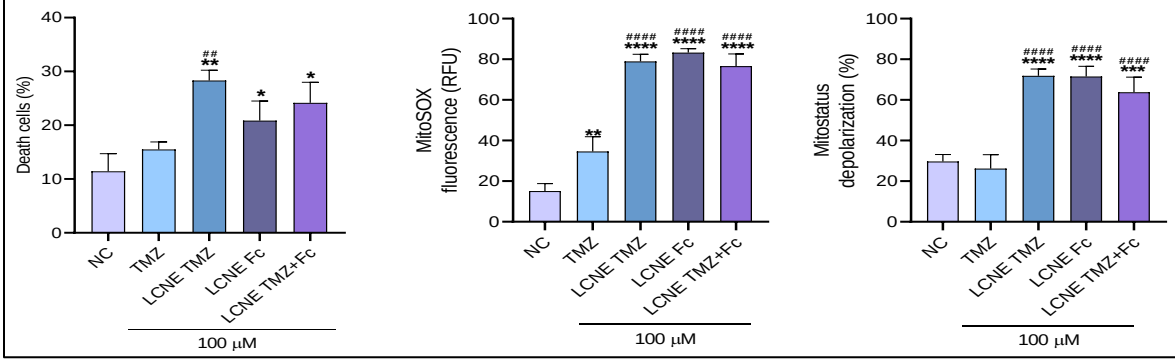

Fig 2. *In vitro* cell death, superoxide anion generation and mitochondrial membrane depolarization assays of T98G GB cells under 24 h exposition to different treatments. Results represent the mean ± SD of 3 independent experiments. *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001 and ****p ≤ 0.0001 compared to NC group. ##p ≤ 0.01 and ####p ≤ 0.0001, compared to TMZ group (One-way ANOVA).

CONCLUSIONS & PERSPECTIVES

LCNE formulations were able to reduce the cell viability in both cell lines and in a dose-dependent manner when compared to NC and TMZ treatments. Also, we observed an indication of a reversal in the resistance profile of the T98G cell line at the highest concentrations tested in a possible association with cell death and mitochondrial stress. As a next step, we intend to investigate, both *in vitro* and *in vivo*, the same compounds using polyvinyl alcohol (PVA) nanoformulations.

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