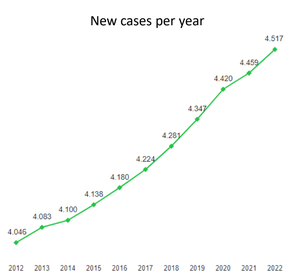
Development of novel drug delivery systems based on polymeric nanofibers for the treatment of glioblastoma

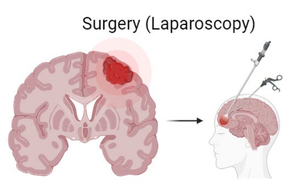
Pedro Valentín Badía[a], Maria Fuentes[a], Marta Fernández-Oliver, Joan Moll Carrió[a], Rocío Díaz-Puertas[a], Enrique Rodríguez-Cañas[a], María del Pilar García[a], Miguel Saceda[a], Ricardo Mallavia[a]

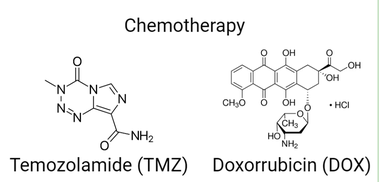
[a] Instituto de Investigación, Desarrollo e Innovación en Biotecnología Sanitaria de Elche of Research, (IDiBE), Universidad Miguel Hernández (UMH), Elche, España

Glioblastoma

Glioblastoma is a type of glioma with a low incidence but a high mortality rate due to its malignancy (1). Current treatments for glioblastoma focus on surgery followed by chemotherapy with antineoplastics drugs. However, the systemic administration damages non-tumorous tissues, so their local application and controlled release is being investigate (2).







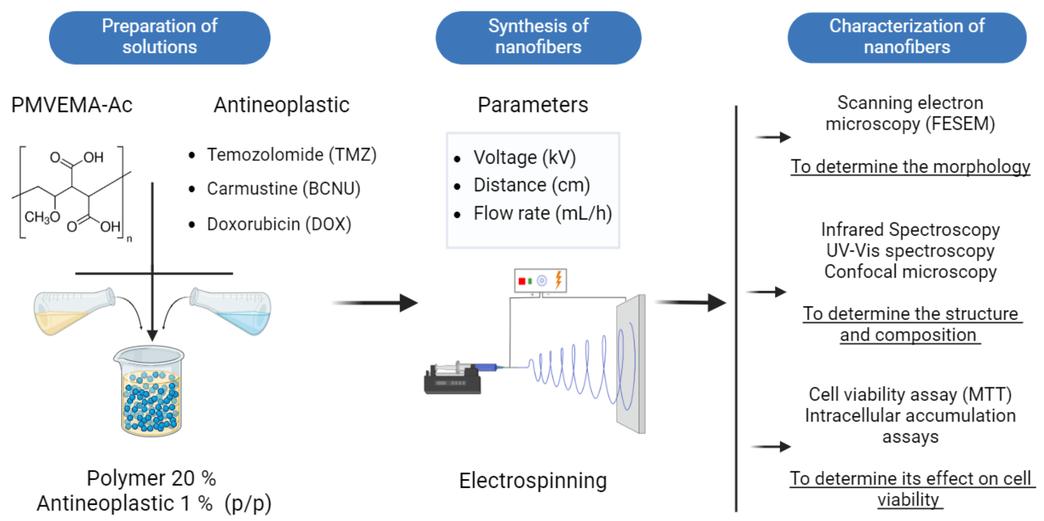
Polymeric nanofibers

- ❖Controlled release
- ❖Increase drug bioavailability
- ❖Easy to synthesize (electro-spinning)
- ❖Oral, local or topical administration
- ❖Low-cost portability and storage

(3)

Objective: To synthesize and characterize polymeric nanofibers as antineoplastic drug delivery systems.

Materials and Method



Results

Morphology

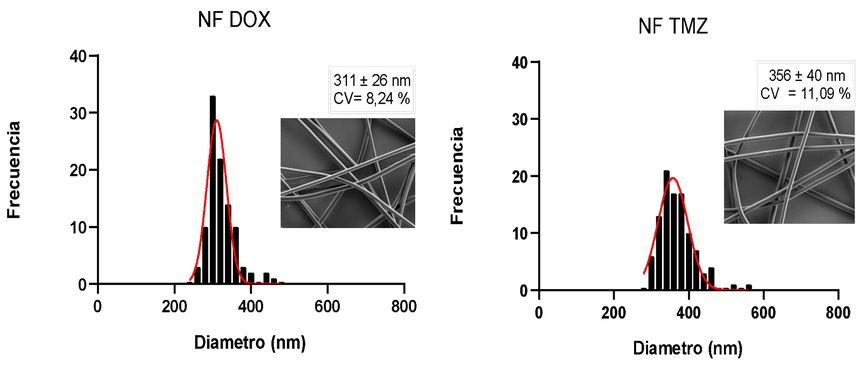


Figure 1. Histograms of the diameter of the PMVEMA-Ac/antineoplastic 1% nanofibers. Diameter is shown with standard, coefficient of variation (CV) and its photograph taken through FESEM microscopy. deviation

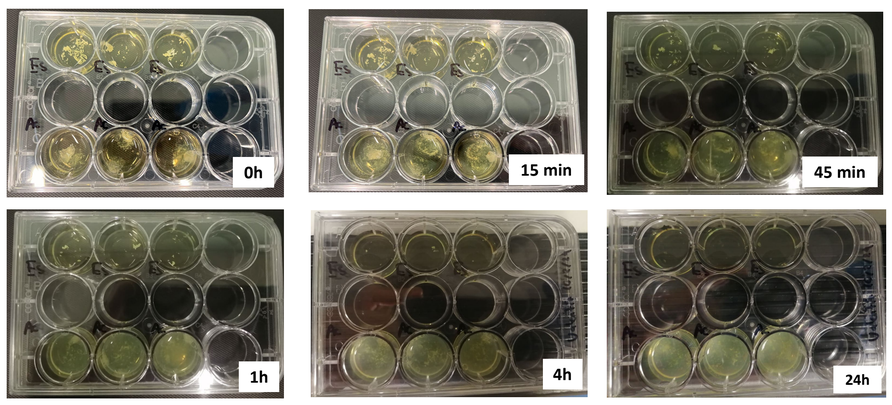


Figure 4. Degradation of polymer nanofibers of PMVEMA-AC (Ac) and its variant PMVEMA-Es (Es) at different times. A visible change in the size of the nanofibers is observed in the first hour, reaching its complete degradation at 24h. Observing visible differences between Ac and Es. The nanofibers were dissolved in cell culture medium F12 at 12 mg/ml.

Composition

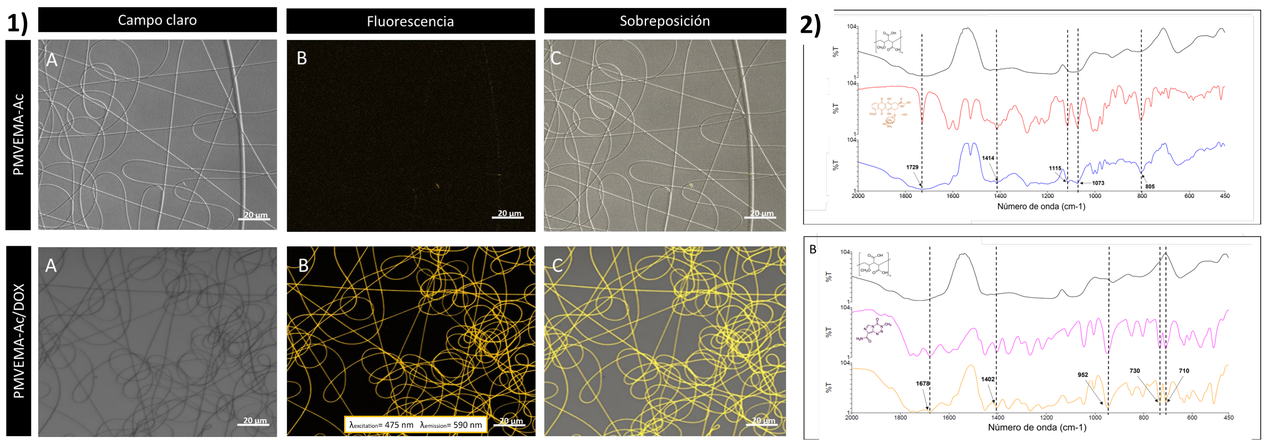


Figure 2. Composition of polymeric nanofibers loaded with 1% antineoplastic. 1) Photographs taken by confocal microscopy of PMVEMA-Ac/DOX 1 % nanofibers. 2) Fingerprint of the infrared spectra of A) PMVEMA-Ac (black), DOX (red) and PMVEMA-Ac/DOX (blue). B) PMVMEA-Ac (black), TMZ (purple) and PMVEMA/TMZ (yellow). Representative frequencies of each compound are identified with dotted lines (cm-1).

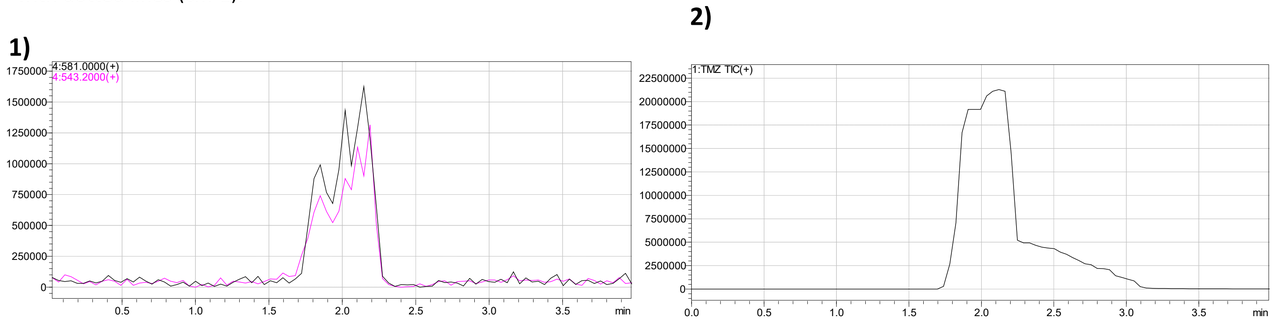
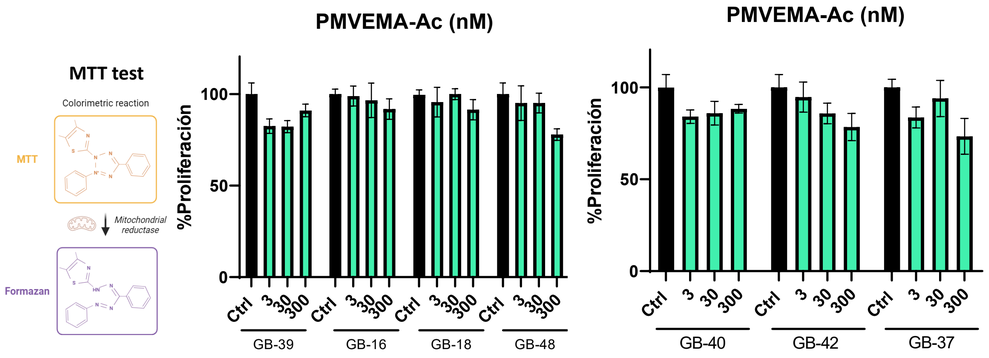


Figure 3. Chromatograms of DOX and TMZ encapsulated in polymeric nanofibers obtained by HPLC MS. 1) The peaks of DOX-hydrochloride with Mw=581 and DOX with Mw= 543.2 were detected, confirming drug encapsulation. 2) TMZ peak was detected with Mw= 194.15, confirming drug encapsulation. Samples were analyzed using an Agilent LC 1100 series HPLC (Agilent Technologies, Inc., Palo Alto, CA, USA) and 50:50 isocratic water/acetonitrile method was used.

Biological effect



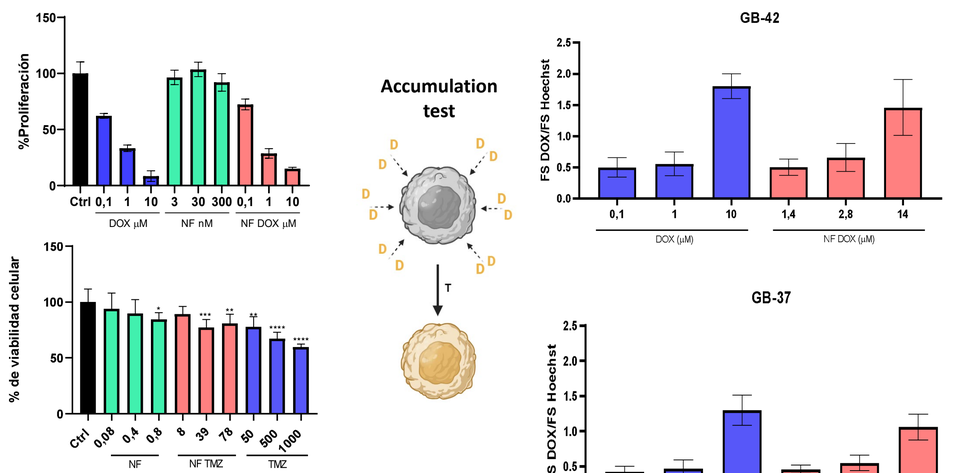


Figure 5. Effect of nanofibers alone and loaded with DOX on the viability of glioblastoma cells from patients of the Hospital General Universitario de Elche (HGUE-GB-N). The cells were treated with different concentrations (µM) of free antineoplastic (red) nanofibers (yellow) and NF loaded with antineoplastic (orange).

Figure 6. Intracellular accumulation in HGUE-GB-37 and GB-42 lines of encapsulated DOX. Cells were treated with different concentrations (µM) of free (blue) and encapsulated (red) DOX at 20 min. The fluorescence intensity of DOX was normalized to that of Hoechst (Y-axis).

Conclusions

- PMVEMA-Ac polymer at its concentration of use does not decrease cell viability of HGUE glioblastoma lines.
- The synthesis of PMVEMA-Ac nanofibers by electrospinning allows the encapsulation of antineoplastic drugs, highlighting PMVEMA-Ac/DOX nanofibers.
- The encapsulated antineoplastic drugs TMZ, BCNU and DOX decrease the viability of glioblastoma cell lines.

Bibliography

1. Melhem JM, Detsky J, Lim-Fat MJ, Perry JR. Updates in IDH-Wildtype Glioblastoma. Neurotherapeutics. octubre de 2022;19(6):1705-23.
2. Martínez-Lacaci I, García Morales P, Soto JL, Saceda M. Tumour cells resistance in cancer therapy. Clin Transl Oncol. enero de 2007;9(1):13-20.
3. Singh B, Kim K, Park MH. On-Demand Drug Delivery Systems Using Nanofibers. Nanomaterials. 16 de diciembre de 2021;11(12):3411.