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

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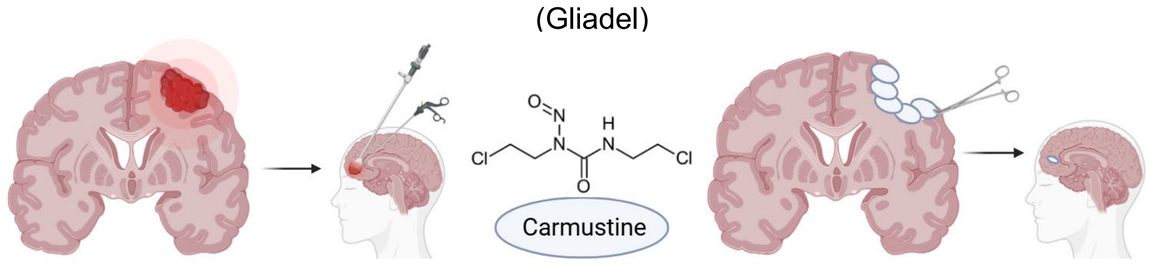
Introduction

Glioblastoma **(GBM)** 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 antineoplastic drugs. However, systemic administration damages non-tumour tissues, so local application and controlled release is being investigated (2).

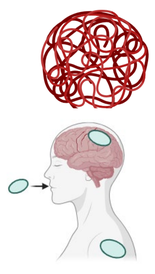
Treatment of glioblastoma

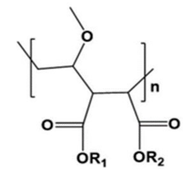
Surgery | Treatment (Gliadel) | Application



Polymeric nanofibres

- ❖Easy to synthesize (electrospinning)
- ❖Highly malleable
- ❖Oral, local or topical administration
- ❖Low-cost portability and storage

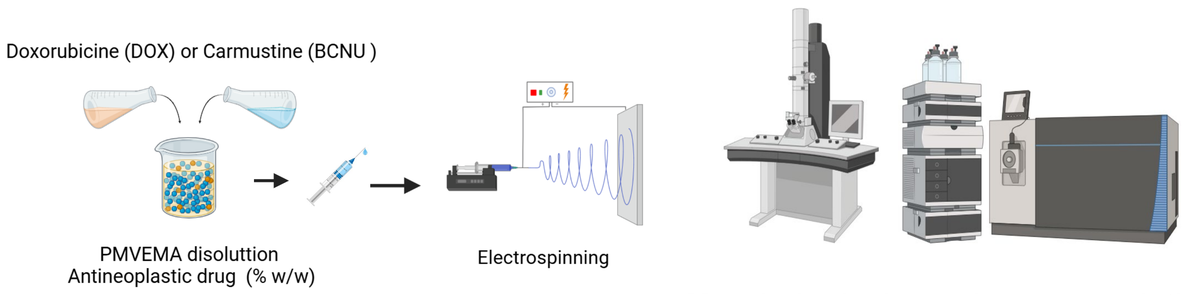




Poly (methyl vinyl ether-maleic (PVMEMA)

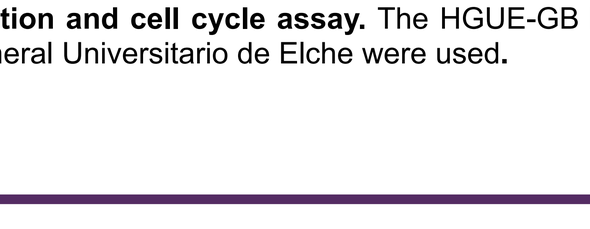
Materials and Methods

Aim: To develop and characterized electrospun polymeric nanofibers as fast realize delivery systems for antineoplastics drugs to treat glioblastoma.



Synthesis of nanofibers by electrospinning. PMVEMA-Es 25 % or Ac at 20 % in solvent with BCNU at 8 % or DOX 1 % (w/w with respect to the polymer).

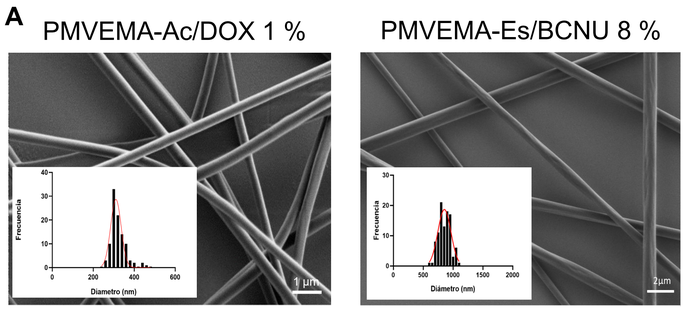
Morphological and encapsulation efficiency (EE) analysis. Scanning electron microscopy (FESEM), confocal microscopy and high-performance liquid chromatography (HPLC).



MTT cell proliferation and cell cycle assay. The HGUE-GB lines from patients at the Hospital General Universitario de Elche were used.

Resultados

A

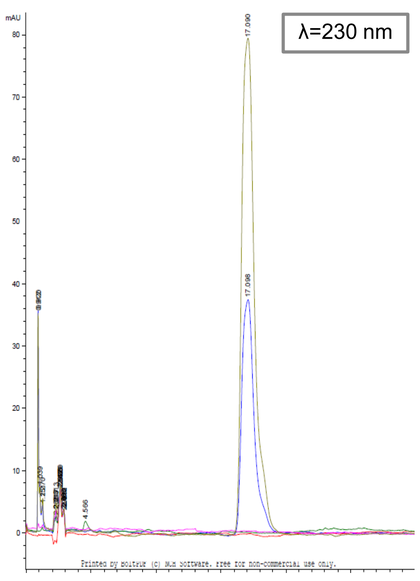


311 ± 26 nm | 855 ± 99 nm

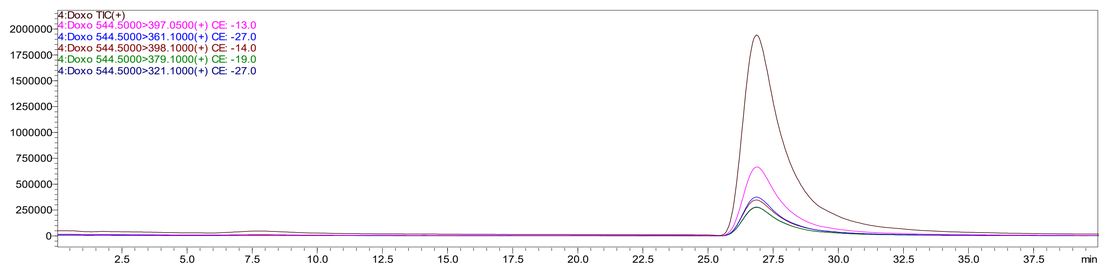
B

	[Real] (mg/mL)	Area under the curve (AUC)	[Theoretical] (mg/mL)	EE (%)
NF BCNU 8 %	0.575	5370.9	0.8	71.9
NF DOX 1 %	0.125	224378.5	0.125	100

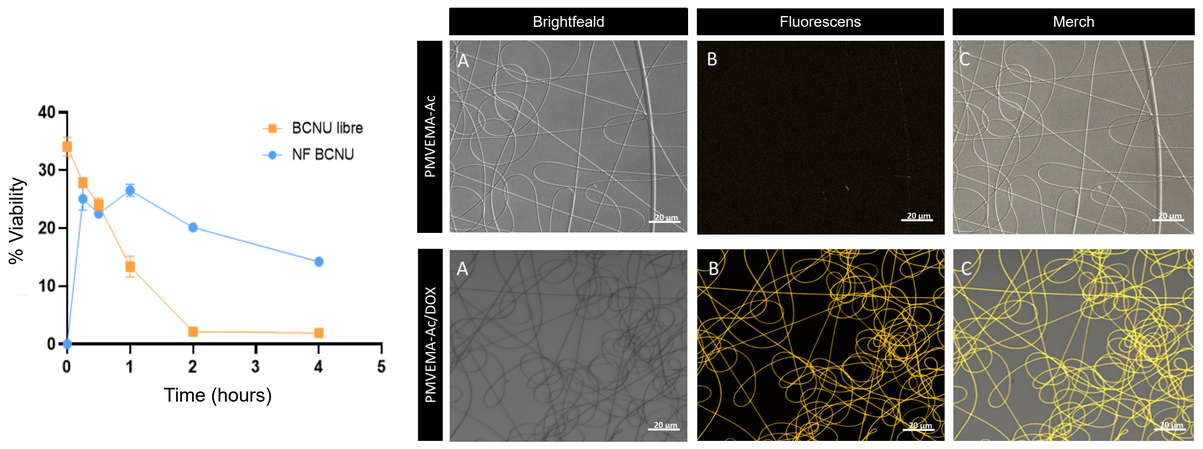
B1



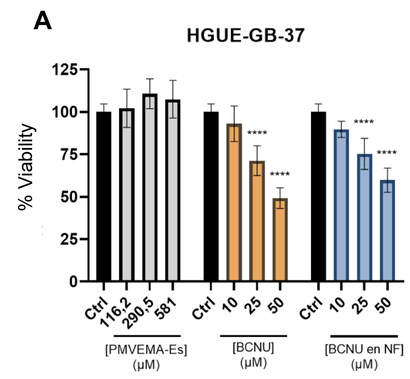
B2



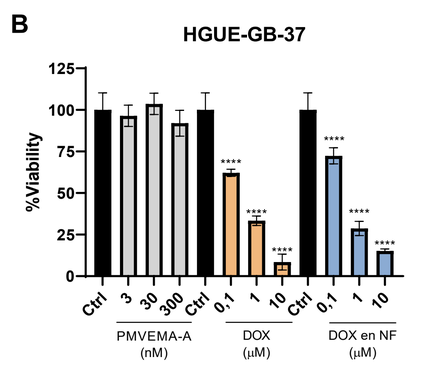
Diameter of PMVEMA/Drug 1 and 8 % nanofibers and their encapsulation efficiency. (A) FESEM photographs, diameter n=100. **(B1)** HPLC-UV method BCNU: Algilent C18 column at 10°; mobile phase (MP): 30 % ACT, at a flow rate of 1 ml/min and an injection volume of 10 µL. **(B2)** HPLC-MS/MS method DOX: column at 50º; MP: 60 % methanol, 1 % formic acid an injection volume of 1 µL. The results obtained were integrated in the equation of the line.



Realize assay of encapsulated BCNU and confocal microscopy of encapsulated DOX. (A) The assay was performed in DMEM/F12 cell medium at 30°. n=3 (mean ± SD), with a maximum time realize of 1h. **(B)** Photographs taken by confocal microscopy of PMVEMA-Ac/DOX 1 % nanofibers. A) Bright field B) Fluorescence C) Merge of A and B. **λexc** = 475 nm, **λem** = 590 nm.



[BCNU] (µM)	[PMVEMA-Es] (µM)
10	116,2
25	290,5
50	581



Effect of encapsulated BCNU (A) and DOX (B) on HGUE-GB lines. Treated with different concentrations (µM) of nanofibres without drug (grey), free drug (orange) and nanofibres with drug (blue). Percentage of cell proliferation is shown relative to untreated control (*p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001). n=6 (mean ± SD).

Conclusión

The synthesis of PMVEMA nanofibers allowed the encapsulation of 100% and 70% of drugs with a release time of 1h, without modifying their properties on cell proliferation. Work will continue with their characterization in 3D cellular models.

References

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Financing

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