

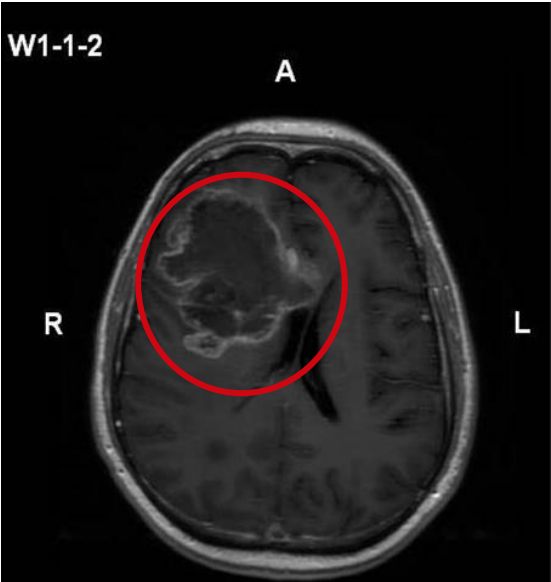
Photoactive polymeric nanofiber-based delivery systems for photodynamic therapy against glioblastoma

Pedro Valentín Badía Hernández

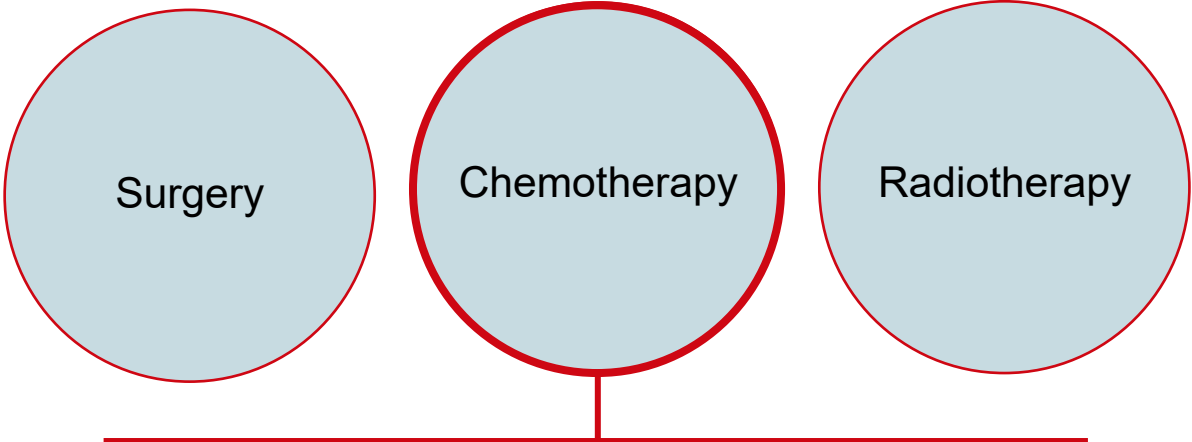
Grupo de diseño y validación de nanobiomateriales

Glioblastoma and curren treatment

Introduction



80% mortality rate



Temozolomide (TMZ)



Carmustina (BCNU)



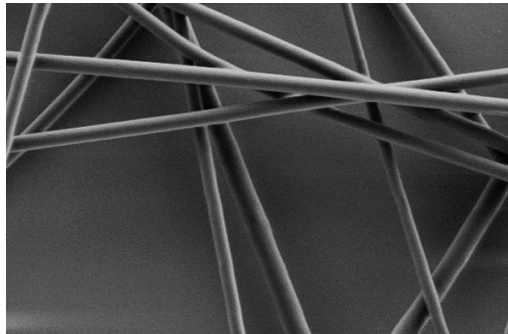
Doxorubicin (DOX)

Biomaterials for local treatment

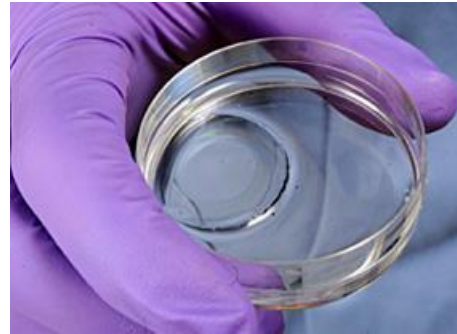
Macrostructured

Nanostructured

Nanofibers



Hydrogels

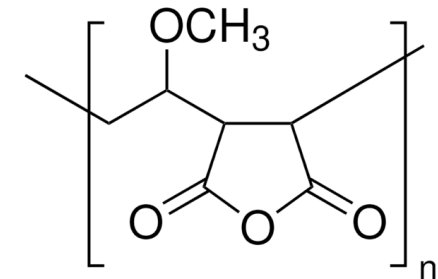


Malleable
Easy to synthesize
Administration: local, oral, or topical
Low storage and transportation costs

Introduction

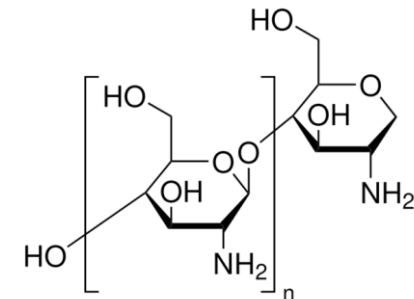
Synthetics

Poly (methyl vinyl ether-alt-maleic)
(PMVEMA)



Natural

Chitosan



Functionalized polymers for combined therapy

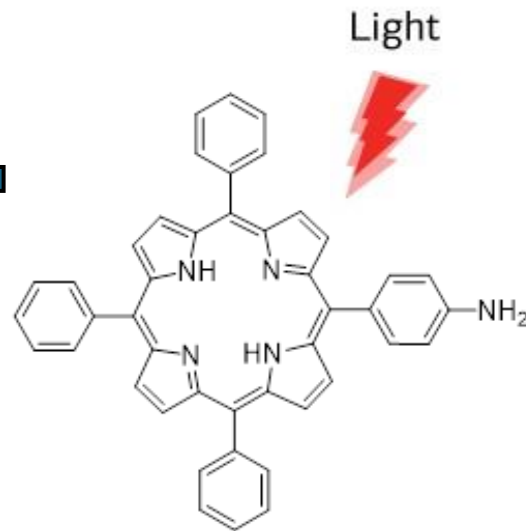
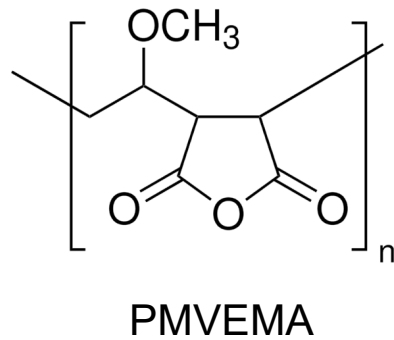
Introduction

Macrostructured

Nanostructured

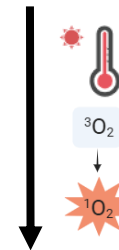
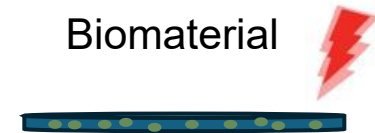
Photosensitizer conjugation

Photodynamic therapy (PDT)



5-(4-Aminophenyl)-10,15,20-triphenylporphyrin (TPP/NH₂)

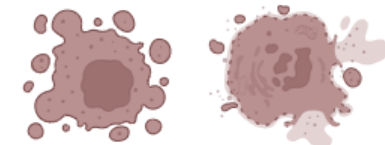
Biomaterial



Tumor cell death

Apoptosis

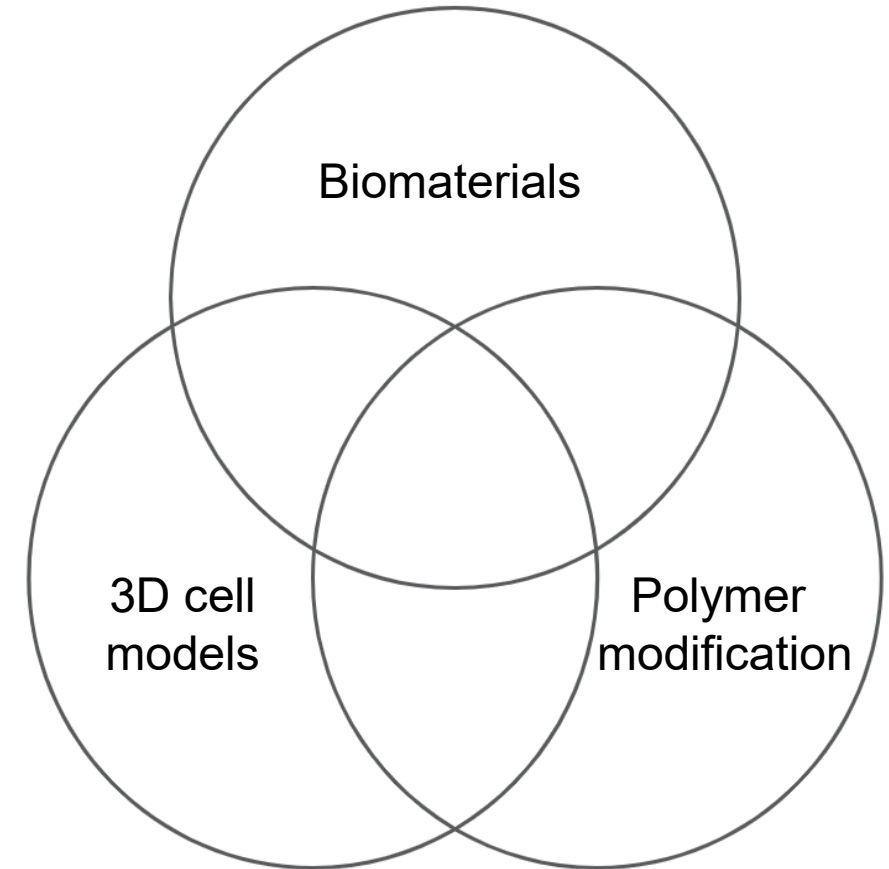
Necrosis



Main aim

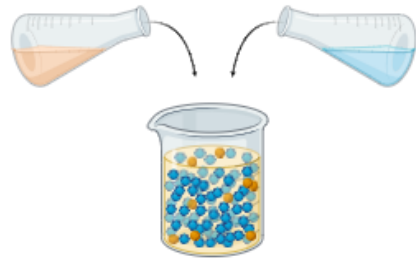
Developing photoactive delivery systems based on biopolymers for the administration of glioblastoma treatments

- Development and characterization of electrospun PMVEMA nanofibers as drug deliver systems for antineoplastic DOX and BCNU.
- Evaluation of their effect in cell models.
- Development of 3D cell models of glioblastoma.
- Functionalization of PMVEMA with porphyrins for PDT.



Material and Methods

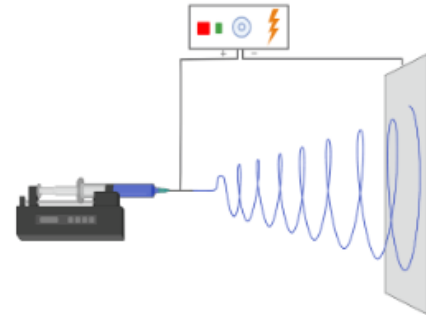
Doxorubicine (DOX) or Carmustine (BCNU)



PMVEMA dissolution
Antineoplastic drug (% w/w)

PMVEMA dissolutions (w/w):

- PMVEMA-Ac at 20 % in water
- PMVEMA-Es at 25 % in ethanol



Synthesis by
Electrospinning

Parameters considered:

- Voltage (kV)
- Distance (cm)
- Flow (mL/h)

Characterization of nanofibers

→ Scanning electron
microscopy (FESEM)
Confocal microscopy

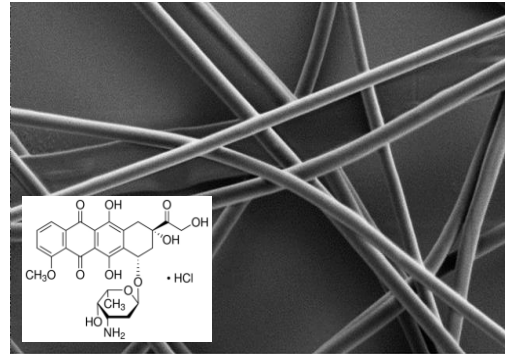
Morphology and composition

→ Liquid chromatography
(HPLC-UV)

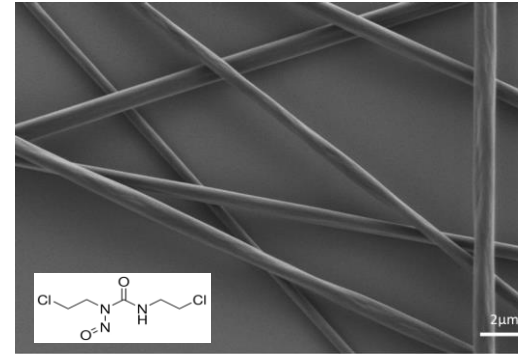
Encapsulation efficiency and
release kinetics

Cell viability assay (MTT)

→ Effect on glioblastoma
patient cell lines from the
Hospital General
Universitario de Elche (HGUE-
GB) and 3D model
development



PMVEMA-Ac/DOX 1 %

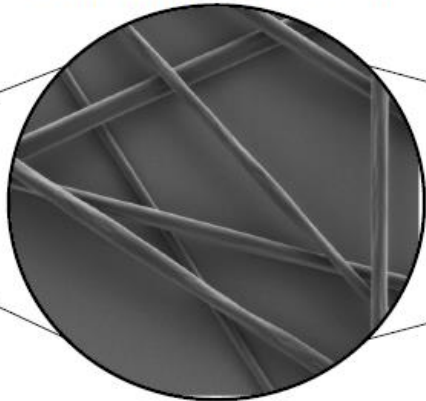


PMVEMA-Es/BCNU 8 %

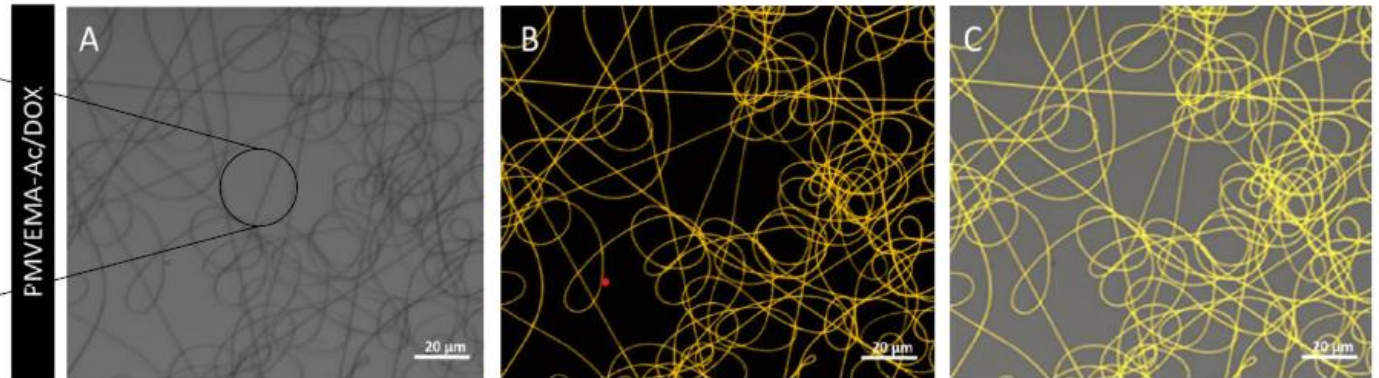
Veil



Nanofibers by FESEM

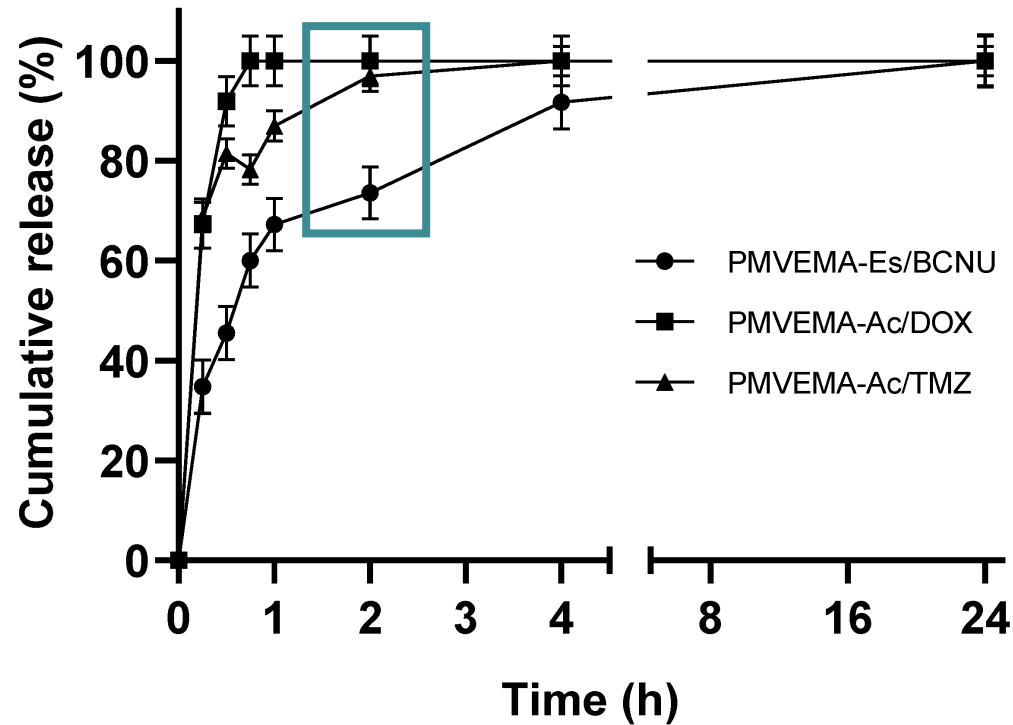


Confocal microscopy of nanofibers with encapsulated DOX

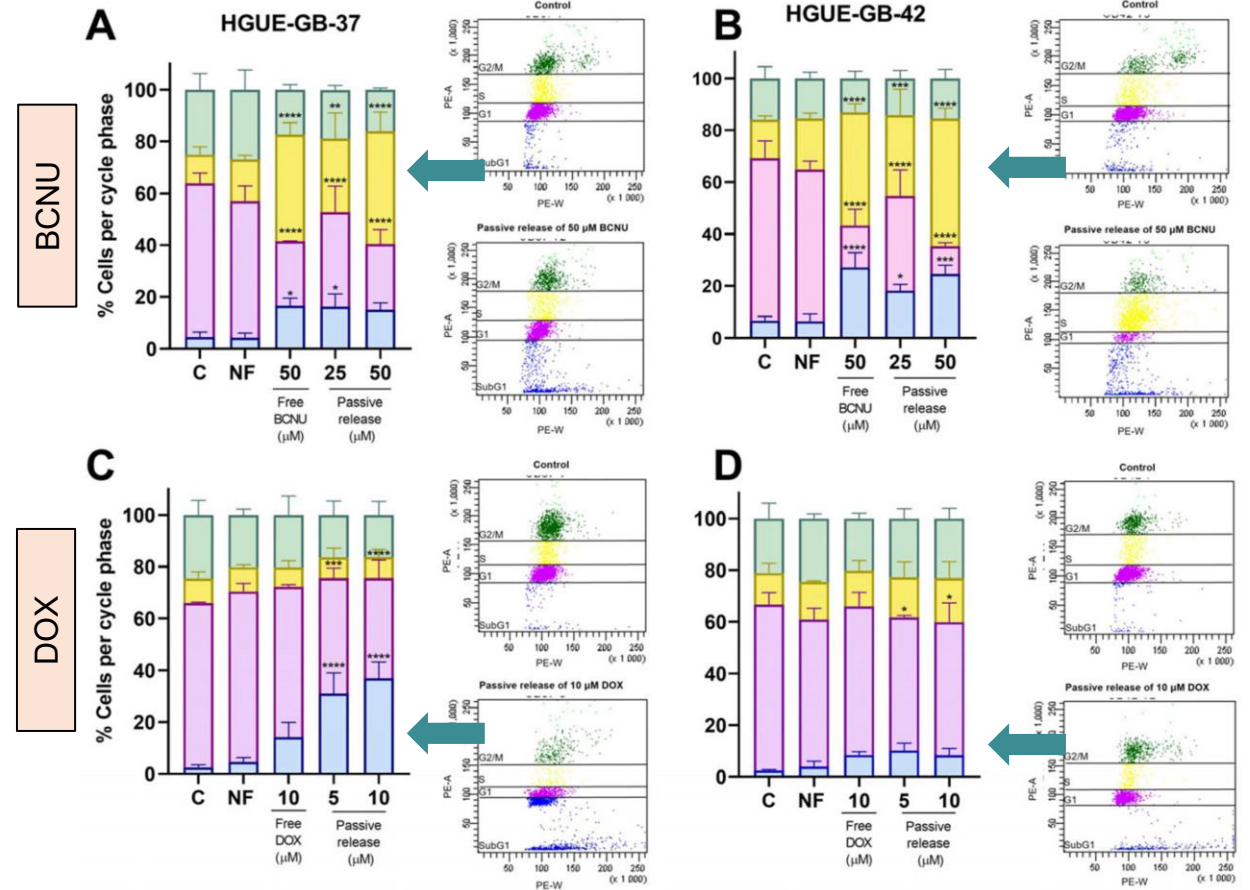


Kinetic release and effect on cell cycle

Results



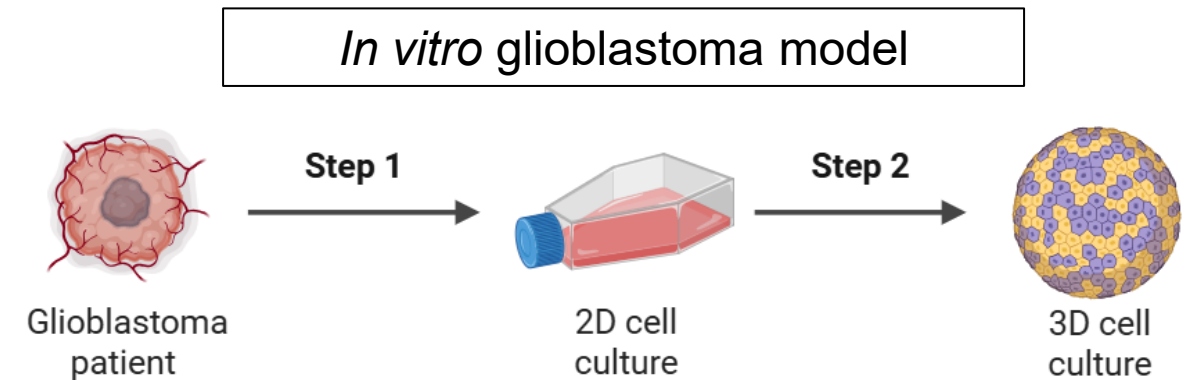
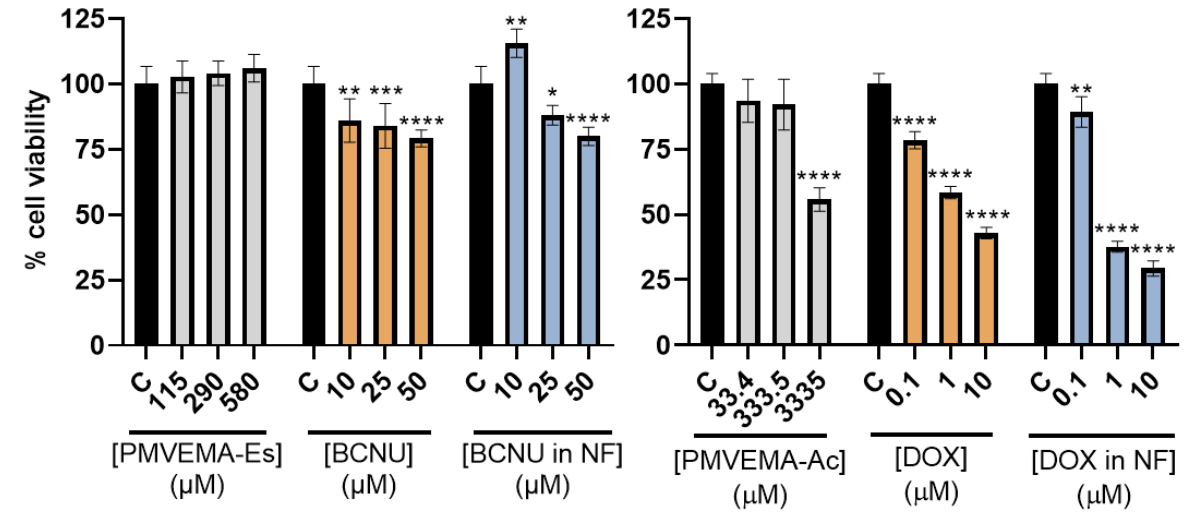
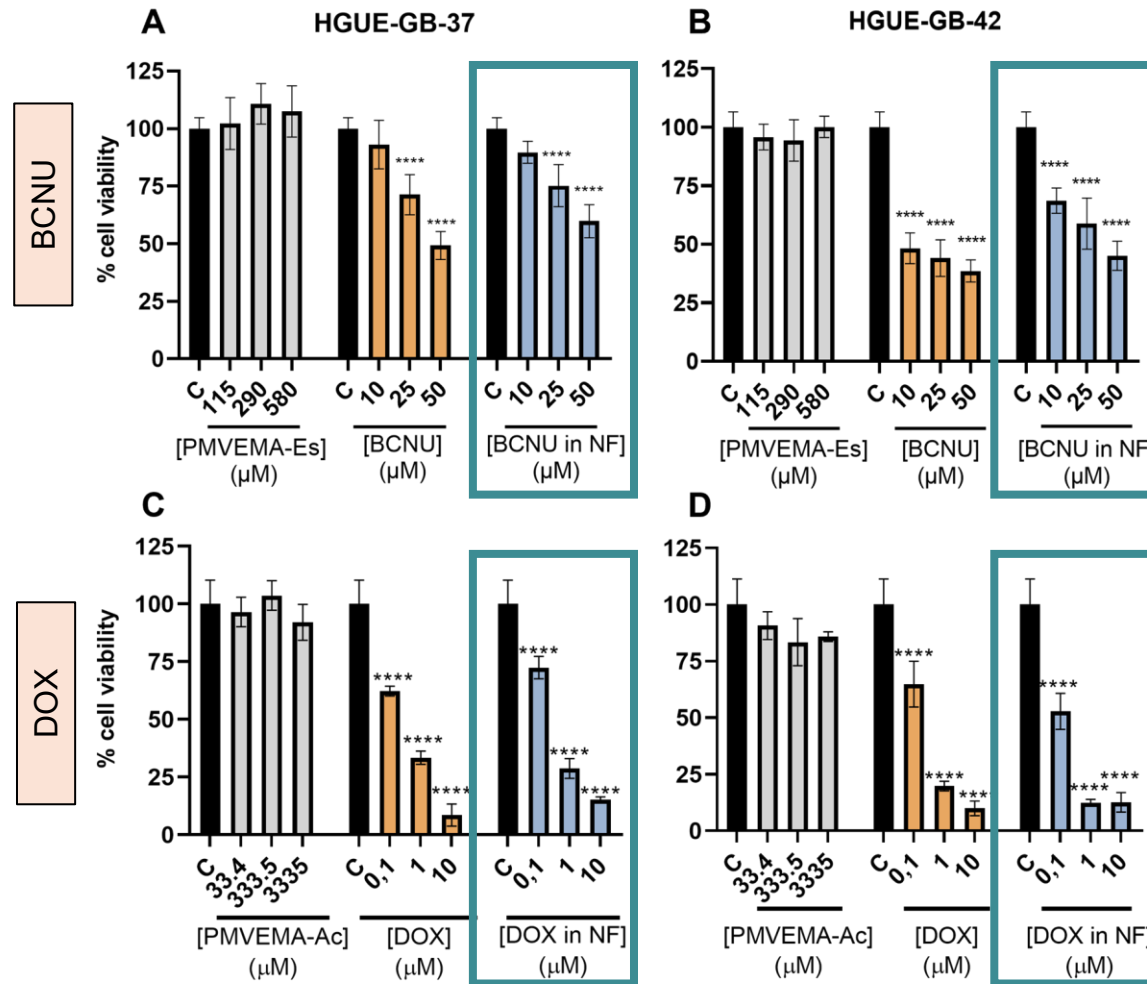
Conditions: 37°; PBS; pH 7.4



S phase – Cytostasis
SubG1 phase – Cytotoxic

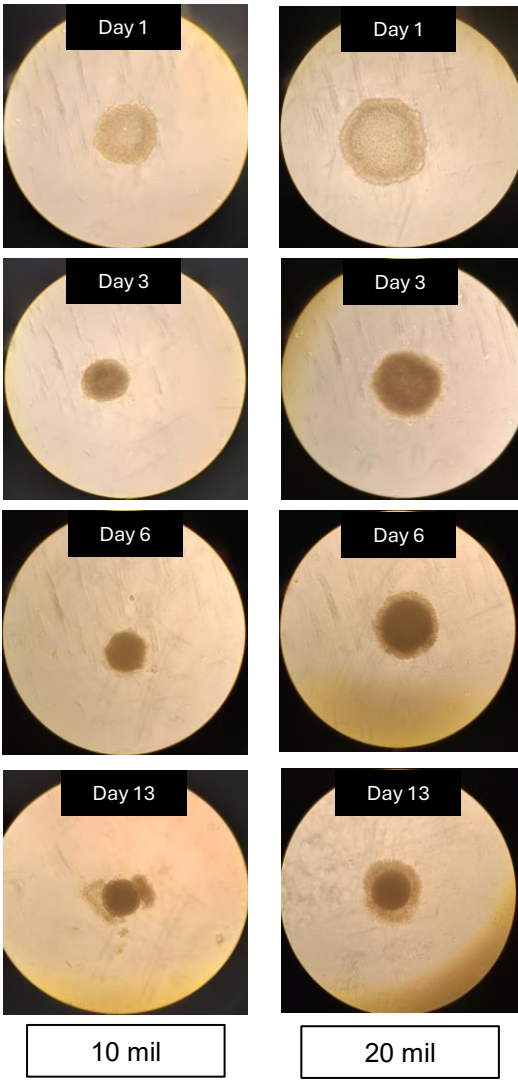
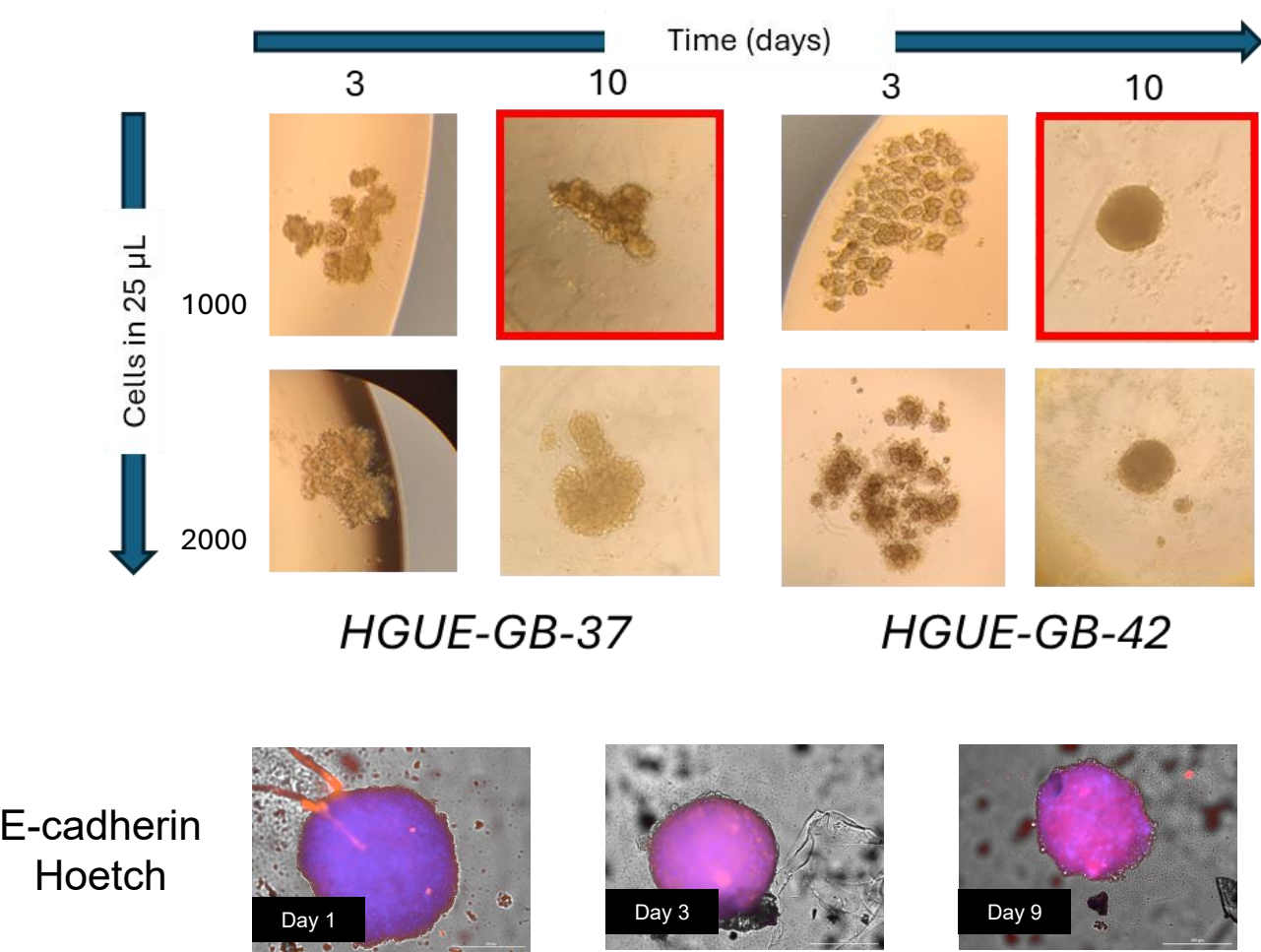
Cell models testing and developing

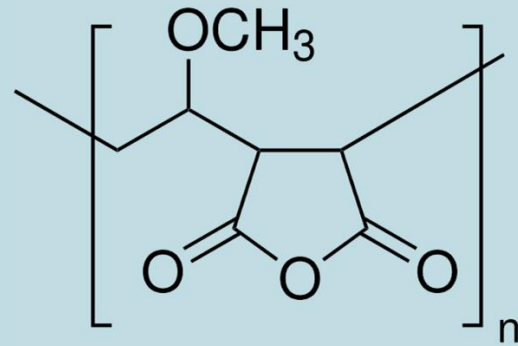
Results



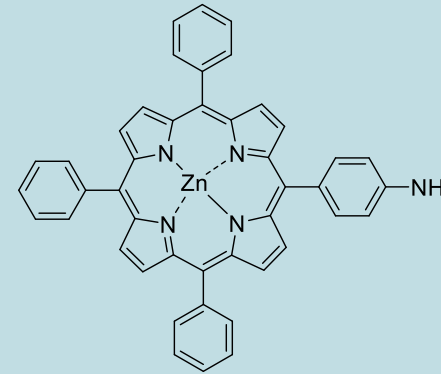
Development of 3D cell models of glioblastoma

Results





PMVEMA-Anh



TPP/NH₂-Zn

Synthesis:

Microwave reaction

- Molar ratio: 1:0.25

-Conditions:

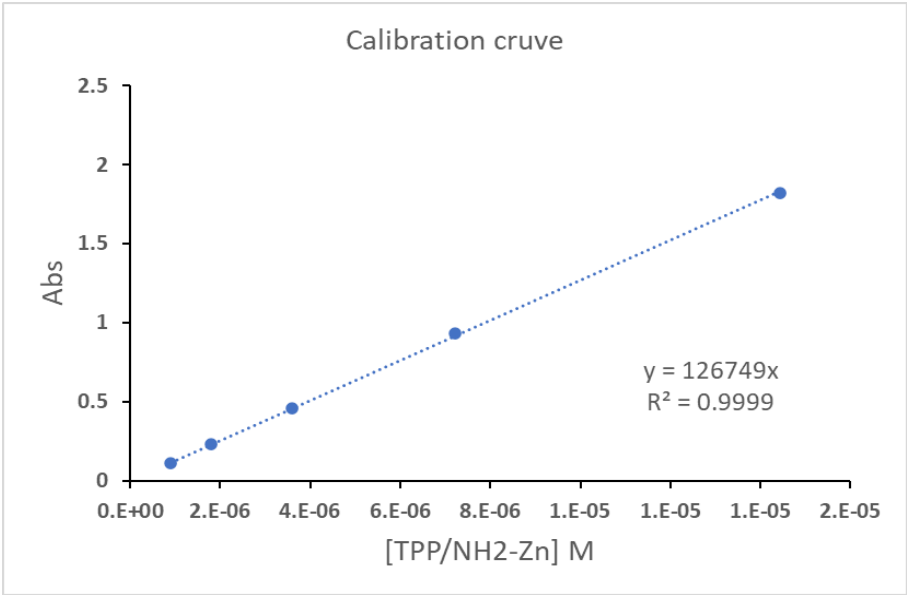
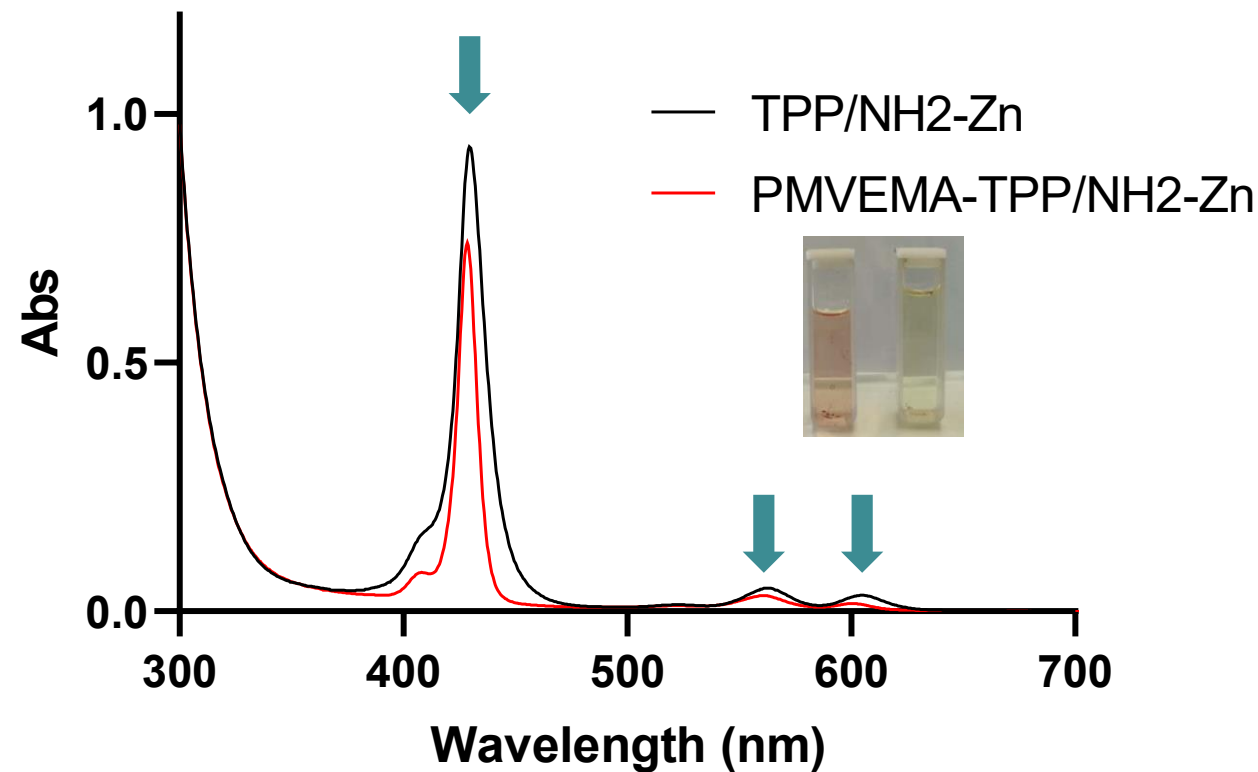
4 mL DMF, 175°C
and 20 min



Characterization:

- UV
- FTIR
- NMR
- Cell viability

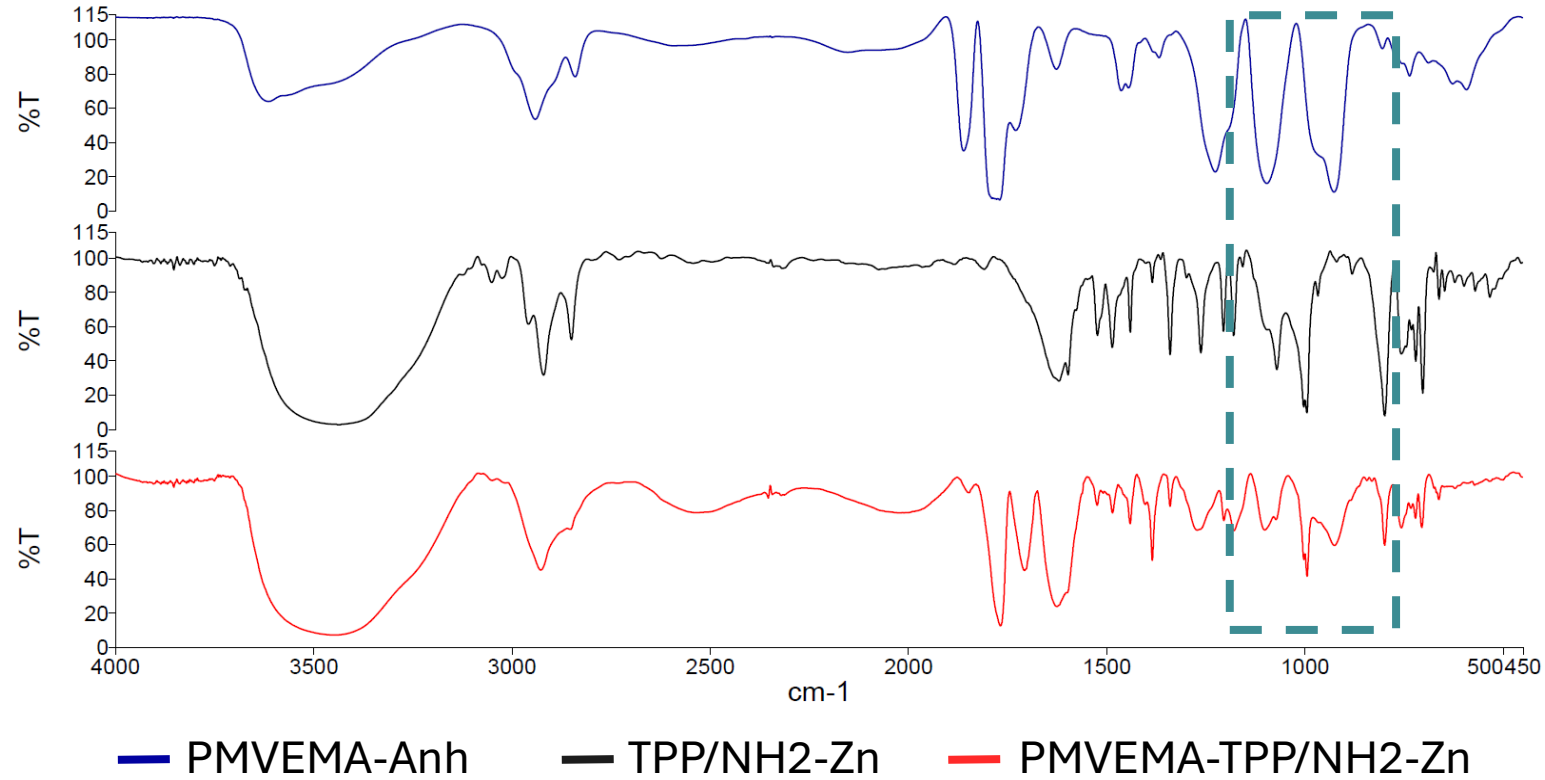




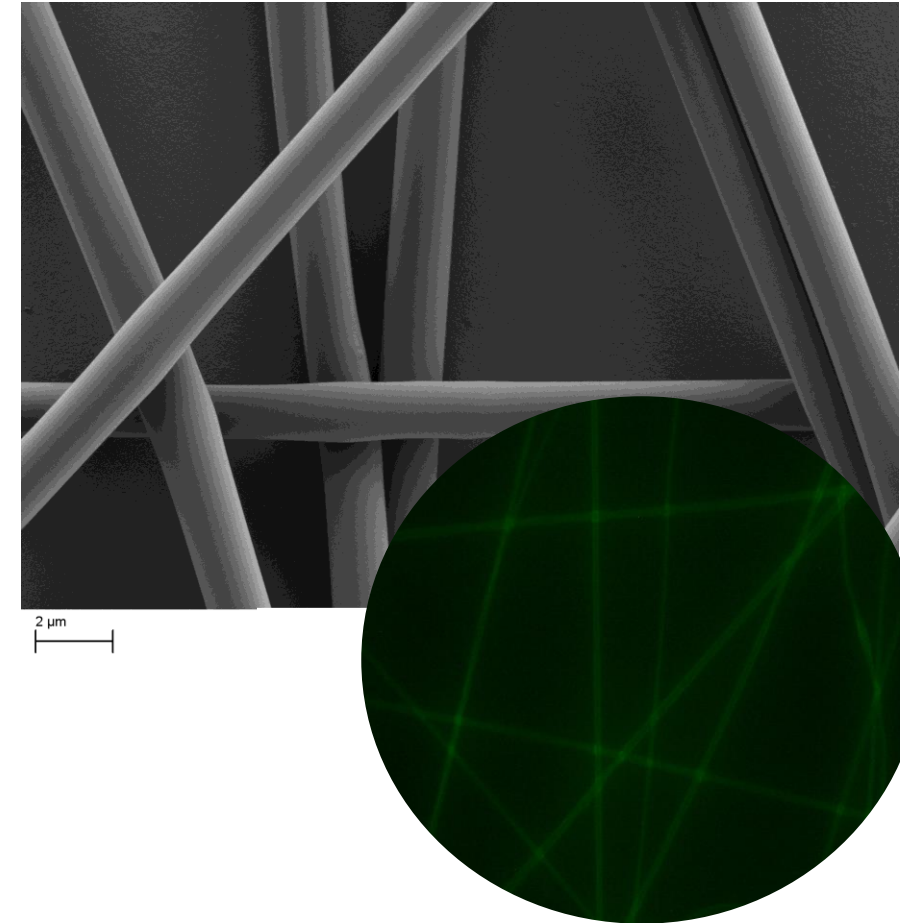
PMVEMA-TPP/NH2-Zn		
Abs 429.5	0.705	u.a.
[PM-TPP]	0.005	mg/mL
Ratio Porf/Polym	770.7	mgPorf/1g Polym
w/w	77.1	%

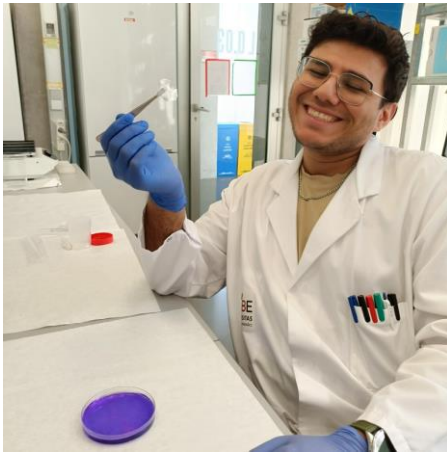
FTIR characterization of PMVEMA-TPP/NH2-Zn

Results



PMVEMA-TPP/NH2-Zn as copolymer in NF synthesis



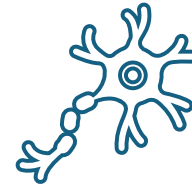


Conclutions



- Biomaterials

Electrospun PMVEMA-derivate nanofibers were able to encapsulate DOX and BCNU with a loading efficiency comparable to clinically approved versions of drug delivery systems.



- *In vitro* glioblastoma model

The loaded drugs keep their antitumor activity and reduces glioblastoma cell viability with minimum effects in human astrocytes.

HGUE-GB-42 cell line at a cell density of 20,000, it is proposed to establish a glioblastoma mixed cell model.



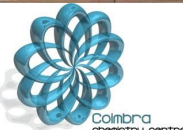
- Polymer modification

PMVEMA has been successfully functionalized, further characterization should be performed to use it for PDT treatment.

Acknowledgements



MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



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