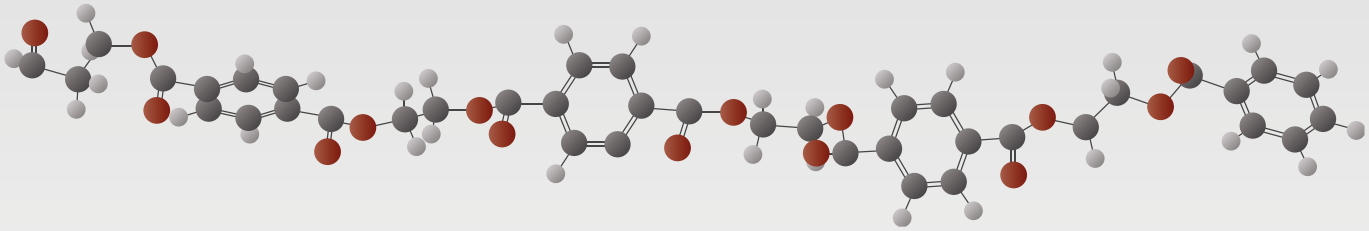
GEP-SLAP 2022



Donostia-San Sebastián

8 - 12 MAYO 2022

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GEP XVI

Reunión del Grupo Especializado de Polímeros GEP de la Real Sociedad Española de Química (RSEQ) y de la Real Sociedad Española de Física (RSEF)

Meeting of the Group Specialized in Polymers of the Spanish Royal Society of Chemistry and Spanish Royal Society of Physics

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Nanoparticles made of poly(γ-glutamic acid) derivatives for drug delivery systems

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Introduction

One of the treatments for cancer is chemotherapy but most anticancer drugs have a low therapeutic index, which causes toxicity complications in the healthy tissues [1]. To minimize these complications and improve the effect of the existing drugs, drug delivery by nanoparticles have drawn more attention as they are easy to produce and can also be prepared through biocompatible polymers [2]. Here, we report the preparation of polymer nanoparticles derived from esters of poly(γ-glutamic acid) which could be able to encapsulate hydrophobic drugs that can be used as drug delivery systems (DDS) for the treatment of different tumours. In this work, PGGA has been modified in order to improve its solubility in organic solvents and its processing capacity of this water-soluble polymer. Due to the fact that most of the anticancer drugs are lipophilic, the hydrophobic modification of PGGA will enhance the drug encapsulation [3].

Experimental

Esterification of PGGA with 4-phenylbutyl bromide was carried out in solution of *N*-methyl-2-pyrrolidone (NMP) at 60 ºC in the presence variable amounts of $NaHCO_3$ [4]. 4-phenylbutyl bromide was slowly added in the necessary amount to reach the desired conversion. The reaction was left to proceed for 48 h until no evolution was observed in the reaction and the esterified polymer was recovered by precipitation in acidified water. After that the polymer was washed with neutral water and dried under vacuum for 24 hours. An average reaction yield above 80% was obtained and the degree of esterification attained was precisely assessed by ^{1}H NMR.

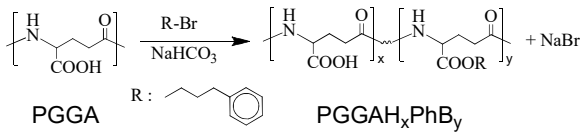

Figure 1. Modification of PGGA with 4-phenylbutyl bromide.

Results and Discussion

Spectroscopic characterization

Figure 2 displays FTIR spectra of PGGA and two $PGGAH_xPhB_y$ copolymers with different compositions. The presence of aromatic groups in the copolymer can be easily identified by the absorption bands at 3027 cm^{-1} corresponding to Ar-H stretching modes and at 746 and 698 cm^{-1} corresponding to out of plane Ar-H bending modes.

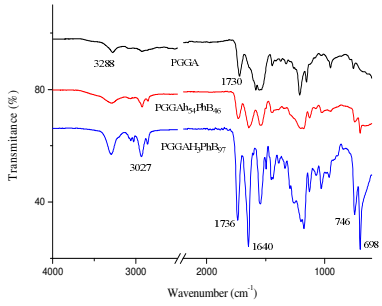

Figure 2. Infrared spectra of PGGA, $PGGAH_{54}PhB_{46}$, $PGGAH_3PhB_{97}$.

Further characterization was assessed by ^{1}H-NMR, where the degree of modification could be easily determined by integration of the aromatic signals that appear at 7.2 ppm and the signal of main chain CH protons appearing at 4.3 ppm (Figure 3).

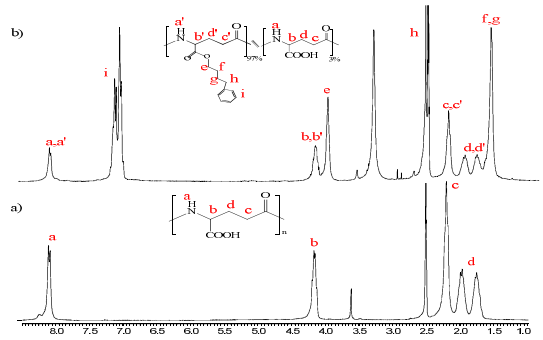

Figure 3. ^{1}H NMR spectra of a) PGGA and b) PGGAH$_3$PhB$_{97}$

Thermal properties

The TGA analysis revealed the weight loss concomitant to degradation is seen to occur between 200 ºC and 330 ºC. The thermal stability was observed to be enhanced with the degree of modification. As shown in Figure 4 and Table 1, the residual material left at the end of the test was different but it decreases in most of the cases as the degree of modification increased.

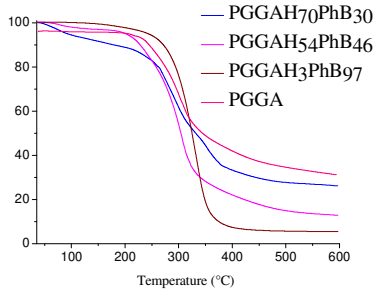

Figure 4. TGA traces recorded of PGGA and PGGAH$_x$PhB$_y$ copolymers.

Table 1. Thermal behaviour of PGGAH$_x$PhB$_y$ copolymers & PGGA

Polymers	[a] T_{d1} /T_{d2}/T_{d3} (ºC)	[b] RW (%)
PGGA	*299*/311	*31.25*
PGGAH$_{89}$PhB$_{11}$	*309.2*/215.7	*27.53*
PGGAH$_{54}$PhB$_{46}$	*303.9*/308/240	*12.81*
PGGAH$_{25}$PhB$_{75}$	*331*	*4.36*
PGGAH$_3$PhB$_{97}$	*332*	*5.4*

[a] Maximum rate decomposition temperature. [b] Remaining weight at 600 ºC.

Nanoparticles formation and characterization

Nanoparticles with sizes around 200 nm have been prepared using the nanoprecipitation-dialysis and emulsion/evaporation methods as revealed by DLS (Figure 5) and SEM (Figure 6). The resulting nanoparticles were loaded with Doxorubicin (DOX) and release of the drug was carried out in two environments (pH ≈4.2 and 7.2) and as expected, it was released faster at pH 4.2.

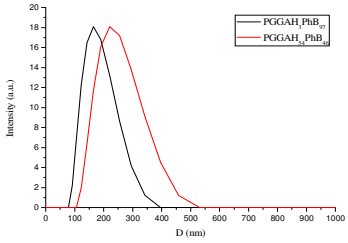

Figure 5. Particle size distribution of nanoparticles (DLS) obtained from PGGAH$_{54}$PhB$_{46}$ by dialysis and from PGGAH$_3$PhB$_{97}$ by emulsion solvent evaporation.

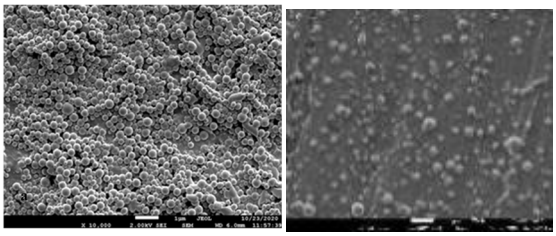

Figure 6. SEM micrographs PGGAH$_{54}$PhB$_{46}$ (left), PGGAH$_3$PhB$_{97}$ (right).

Acknowledgements

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References

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