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COMPARATIVE ANALYSES OF STRATEGIES FOR FUNCTIONALIZATION OF POLYMER NANOPARTICLES WITH BIOMOLECULES

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Polymer nanoparticles have been widely used to formulate controlled release systems for targeting of active compounds[1]. However, one of the main challenges is finding an efficient method to functionalize the particle surface, in order to encapsulate an active and apply the system to reach a target[2]. In the present work, different strategies for chemical and physical functionalization of polymer nanoparticles based on poly(methyl methacrylate) (PMMA) with one amino acid and four proteins were compared, in order to identify effects on the efficiency and stability of adsorption of these biomolecules. In order to promote the chemical bonding between the polymer surface and the biomolecule, the activating agents 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and hexamethylenediamine (HMDA) were used.

Three polymeric nanoparticles produced using the miniemulsion polymerization technique were studied to compare the behavior of the systems when the same biomolecule is immobilized on different surfaces. From the monomers methyl methacrylate (MMA, used as the main monomer), acrylic acid (AA), and methacrylic acid (MAA), the nanoparticles of poly(methyl methacrylate) (PMMA) and the copolymers P(MMA-co-AA) and P(MMA-co-MAA) were obtained, respectively. Since they do not have chemically active functional groups on the surface, the PMMA nanoparticles were chosen as the standard system for subsequent comparison with the copolymers.

The nanoparticles were characterized by gravimetric conversion of monomer to polymer, particle diameter and electrokinetic potential, morphology, hydrogen atom bonds, molar mass distribution, maximum degradation temperature, and glass transition temperature (table 1).

Table 1: Mean sizes, zeta potentials, mean molar masses and polydispersity indices (PdI) of the prepared nanoparticles.

Polymer	Size (nm)	PdI	Zeta potential (mV)	Mw (kDa)	PdI
PMMA	57.0 ± 0.2	0.2	- 62.7 ± 0.6	313	3
P(MMA-co-AA)	53.6 ± 0.1	0.3	- 67.3 ± 0.1	292	2
P(MMA-co-MAA)	50.9 ± 0.3	0.2	- 77.8 ± 1.9	264	2

The biomolecules selected for this study were Bovine Serum Albumin (BSA), Lysine, *Candida antarctica* lipase B (CAL-B), Lysozyme, and the recombinant SARS-CoV-2 Spike Protein, tested on the studied polymers through physical adsorption or chemical adsorption (using EDC or HMDA as a chemical binding intermediary).

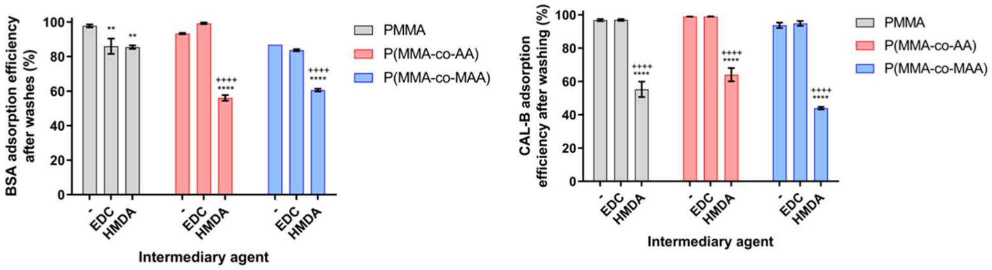

Figure 1: Comparison of adsorption efficiencies for BSA as a function of the polymer after adsorption stability tests (left). Comparison of adsorption efficiencies for CAL-B as a function of polymer after adsorption stability tests. (right).

Gray bars represent PMMA; in red, P(MMA-co-AA); and in blue, P(MMA-co-MAA). The results presented compare the adsorptions by physical and chemical means (EDC and HMDA).
** $0.001 < p < 0.01$; **** $p < 0.0001$ in relation to physical adsorption and ++++ $p < 0.0001$ in relation to adsorption with EDC.

The results indicated that larger biomolecules, such as BSA and CAL-B, were more efficiently immobilized through physical adsorption, without the need for intermediaries, while smaller biomolecules, like lysine, showed better efficiency with chemical adsorption. The performance of immobilization varied with the biomolecule size, highlighting PMMA as the best polymer for physical adsorption. It is shown that the physical adsorption route presents many competitive advantages, generally resulting in higher adsorption efficiencies and more stable products. However, the results also depend on the size of the biomolecules used, with chemical immobilization being more efficient for the functionalization of particles with smaller biomolecules.

REFERENCES

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