PAQ-12

DRUG DELIVERY SYSTEMS BASED ON POROUS CHITOSAN/POLYACRYLIC ACID MICROSPHERES

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The ionisable amino groups present in the structure of chitosan, makes possible (at suitable pH ranges) the formation of interpolyelectrolite complexes with polyanionic macromolecules as alginate or polyacrylic acid. This polymer complexes can be considered as physically crosslinked matrices or hidrogels able to respond to pH and other environmental factors. They currently have considerable interest in the preparation of controlled release systems and other biomedical applications. This work deals with the preparation of chitosan/polyacrylic acid microspheres by a one-step method involving inverse suspension/template polymerization using sunflower oil as continuous phase.

MATERIALS AND METHODS

Chitosan was obtained from shells of lobsters (*Panulirus argus*) as described elsewhere[1]. Acrylic acid (AA, Fluka) was distilled before using. Ammonium persulfate (Aldrich) and meclofenamic acid (Parke-Davis) were used as received.

Polymerization was carried out by a suspension template method in a 250 mL flask fitted with a mechanical stirrer using sunflower oil 2% Span 80 as continuous phase. The reaction product, spherical beads, was washed with acetone and ethanol and dried under vacuum for 24 h.

Samples were characterized by FTIR. The morphology of the surface was observed using a environmental scanning electronic microscope (Phillips XL30). The size and size distribution of the microspheres were determined by means of an optical microscope (Nikon Eclipse E-400).

RESULTS AND DISCUSSION

Some estimative compositional data can be taken out from the absorption bands ratio A1728/A1082 of the FTIR spectra according to the literature and to a previous work[1], in despite of the described low reliability of this calibrate at high chitosan compositions. Using this ratio, it has been estimate

that the microspheres have a poly-acrylic acid content in the range 45-50 wt %, which correspond to a 65-70 % molar content.

Although the polymerization begins with a clear acrylic acid excess (94 molar percent), the final material is a semi-IPN composed of chitosan and a 65-70 % molar content of complexed acrylic acid (because the FTIR exhibits the COO^- as well as the NH_3^+ and the COOH bands). The acrylic suspension polymerization in the presence of chitosan can be therefore considered as a template polymerization. The acrylic acid and the corresponding poly(acrylic acid) are partially soluble in the suspension media (sunflower oil) and therefore during the polymerization process is produced a distribution or partition of the acrylic acid or poly-acrylic acid content in the reacting beads and in the suspension media. This behaviour explains the decrease in composition of the acrylic acid component in the beads after the polymerization.

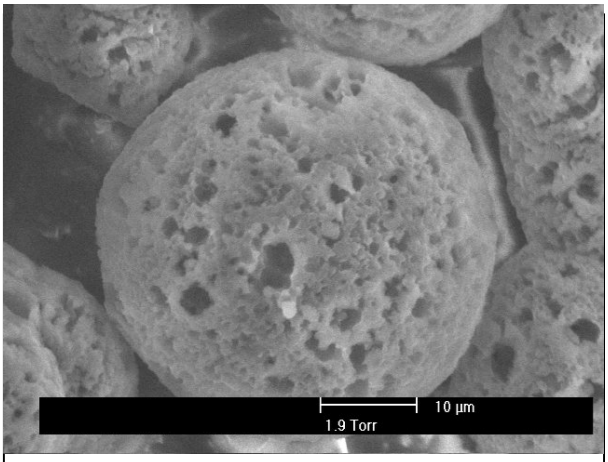

Figure 1. ESEM micrograph of a microsphere

In addition the microspheres have a porous structure (see Figure 1). What happens is that only the partially complexed polyacrylic chains remain in the microspheres after the polymerization and isolation process. Thus, the water and the non-complexed PAA behave as true porogens leading to the formation of chitosan-based porous structures. Porosity can be a very attractive property for some biomedical application as in the design of some particular drug delivery systems. The porosity of the particles obtained in this work is obtained from the extraction or solubilization of some of the components, and therefore, it can be tailored at some extent by controlling the initial ratio chitosan/acrylic acid/water. Besides, the obtained microparticles are not completely spherical and their size range from 10 to 60 μm.

REFERENCES

[1] C. Peniche, W. Argüelles-Monal, N. Davidenko, R. Sastre, A. Gallardo and J. San Román, Self-curing membranes of chitosan/PAA IPNs obtained by radical polymerization : preparation, characterization and interpolymer complexation, Biomaterials 20, 1999, 1869-1878