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Hydrophobically Modified Maleic Copolymers for Preparation of Microspheres

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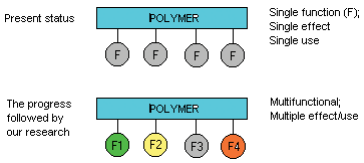
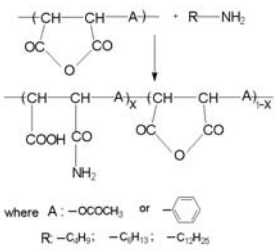
In the last decades, it can be seen an increase of the interest for synthesis, analysis, application and interactions of maleic copolymers with various molecules, macromolecules, particles and surfaces [1-3]. The use of maleic copolymers as drugs or drug carriers, supports for enzymes or protein modifiers became also important [4-6].



The properties of maleic copolymers as multifunctional materials were not yet developed neither in Romania, nor in the other countries. So the research in this topic is highly new/original, as presented below.



Scheme 1. Reaction of MA copolymers with amines at low temperature without catalyst

In this paper are presented some aspects concerning the synthesis of hydrophobically modified polymers from maleic anhydride binary or ternary copolymers by reaction with aliphatic amines at low temperature without catalyst. In these conditions mainly a monoamidation reaction occur, as described in Scheme 1.The behavior in aq. solution and tensioactive properties of the amides was also investigated. Finally the obtention of microspheres by ionic crosslinking is described.

Hemiamides were obtained with 62 - 100% conversion. The behavior of amide derivatives in aqueous solution is typical for weak polyelectrolyte and some of derivatives exhibit tensioactive properties (Fig. 1) proved by surface tension measurements. Preliminary attempts to obtain microspheres loaded with a enzyme by ionic crosslinking of amide derivatives with $CaCl_2$ aq. solution were satisfactory (Fig. 2).

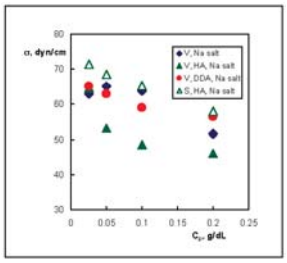


Figure 1. Influence of polymer concentration and alkyl length on the surface tension of aqueous solutions of semiamides

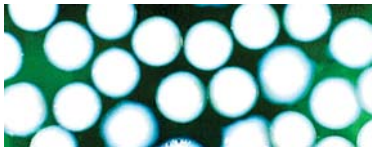


Figure 2. Pattern of microspheres prepared by ionic crosslinking of SAV3 sodium salt. The diameter of microspheres is ~ 0.1 mm

References

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Modified Poly(e-caprolactone)s and Their Use for Drug Encapsulating Nanoparticles

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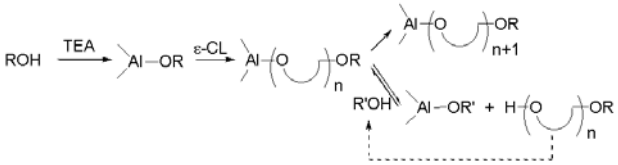
Poly(e-caprolactone) is well known as a biocompatible and biodegradable polymer. Moreover, its biodegradability can be enhanced by copolymerization. It is a relatively hydrophobic material with a crystalline structure. A quite large amount of work was recently dedicated to the use of polycaprolactones and of their linear or crosslinked copolymers as vehicles for slow release of drugs or as biodegradable-biocompatible ceramers appropriate for the repairing of skeletal tissues. Nanoparticles based on amphiphilic copolymers containing poly(ethylene oxide) and polycaprolactone sequences have been proved to be able to encapsulate various bioactive principles or even to present a stimuli (temperature) - responsive drug release behavior.

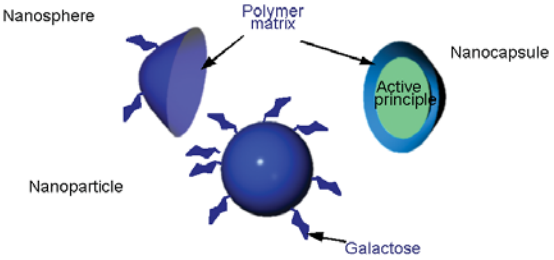
On the other hand, polysiloxanes, especially polydimethylsiloxane, are interesting hybrid organic-inorganic polymers possessing a quite unique combination of properties. Polysiloxanes are characterized by biocompatibility (physiological inertness), high gas permeability, good oxidative, thermal and UV stability. Different types of functional polysiloxanes and siloxane copolymers were synthesized and used as blend compatibilizers and surface modifiers or as biomaterials (contact lenses, implants, transdermal penetration enhancers).

The bilateral project Roumania - France (partially developed in the framework of CNRS-Romanian Academy agreement) was concerned with the preparation of modified polycaprolactones and with their use as polymeric supports in the preparation of nanoscaled biologically active conjugates. Poly(e-caprolactone)-polydimethylsiloxane di- and triblock copolymers and poly(e-caprolactone-co-(4-ethylcaprolactone)) random copolymers were prepared through the homogeneously catalyzed coordinated anionic polymerization of e-caprolactone and the copolymerization of e-caprolactone with 4-ethyl-e-caprolactone in the presence of hydroxy-terminated polysiloxanes or allyl alcohol as chain transfer agents, respectively (Scheme 1). Polysiloxane precursors having hydroxypropyl or hydroxyethyl propyl ether end groups were obtained by the hydrosilation of the appropriate unsaturated alcohol with mono- or difunctional hydro-terminated polysiloxanes of different molecular weights. As proved by DSC analysis, the presence of siloxane blocks and of ethylcaprolactone units determines diminished copolymer crystallinity as seen in reduced melting temperatures and enthalpy of fusion as compared to pure polycaprolactone. Both types of copolymers were found to form, in the presence of Pluronic emulsifier, monodisperse and stable nanoparticles able to encapsulate different types of bioactive compounds (Vitamin E or indomethacin). More complex copolymer structures, containing monosaccharide groups, were also envisaged as molecular recognition supports for nanoencapsulation of biologically active principles in targeting delivery conjugates (Scheme 2).



Scheme 1. Synthesis of caprolactone copolymers

e-CL can be replaced by either ethyl-e-CL or a mixture of both components; ROH: differently substituted HO-polysiloxanes for caprolactone-siloxane block copolymers or allyl alcohol for caprolactone-ethylcaprolactone random copolymers



Scheme 2. Targeting nanoparticles - schematic representation