

MANUFACTURING AND PROPERTIES OF BIORESORBABLE HYDROPHILIC MICROSPHERES BASED ON POLY[(L-LACTIDE - CO - GLYCOLIDE)-BLOCK- ETHYLENE OXIDE) AND POLY(BUTYLENE SUCCINATE-BLOCK- ETHYLENE OXIDE) COPOLYMERS

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Introduction

In recent years, the attention of scientists has focused on the use of natural and synthetic polymers to produce microspheres used in the controlled release systems of various groups of active substances, including drugs.

Therefore, the research aimed to develop the composition and conditions for the synthesis of biodegradable copolymers useful in the formation of microparticles that are carriers of active substances in the processes of their controlled release. It was assumed that the polymer-carriers, obtained based on specially synthesized copolyesters and modified oligosaccharides will be characterized by favorable physicochemical properties allowing for relatively easy formation of microparticles from them, appropriate degradation time, and the release profile of model active substances optimal for the intended use, e.g. in the agrotechnical or pharmaceutical industry [1-4].

The work discusses in detail the method of formation of microspheres and the performance of studies monitoring the course of the hydrolytic and enzymatic degradation of three basic carriers: poly (L-lactide-co-glycolide-*block*-poly(ethylene oxide) terpolymers (TER); polymer blends TER/dextrin-*graft*-PCL or TER/maltodextrin-*graft*-PCL and copolymers containing blocks of butylene succinate and poly(ethylene oxide) in the chain (PUR).

Materials and Methods

Materials

Poly(L-lactide-co-glycolide)-*block*-poly(ethyleneoxide) terpolymers ($M_w = \sim 28,000$ g/mol) were obtained by ROP polymerization of glycolide with L-lactide using PEG 4600g/mol as macroinitiator and $Zr(acac)_4$ as catalyst for this reaction.

The copolymers of dextrin and/or maltodextrin with ϵ -caprolactone (CL) with various degrees of substitution dextrans with $R_{dex} = 70$ wt.% and maltodextrans with $R_{dex} = 38$ wt.%).

The macroinitiators oligo(butylene succinate) were to be obtained in a modified two-step bulk polytransesterification of a mixture of methyl succinate with 1,4-butanediol. The obtained polyesters with an average molecular weight of ~ 5000 g/mol, containing at least two active chain-terminating hydroxyl groups, were used as macroinitiators in the coupling reaction with hexamethylene diisocyanate (HDI) with poly(ethylene oxide). The weight average molecular weight of the copolymer was $\sim 21,000$ g/mol.

Methods

Forming the microspheres: The solutions of the polymer mixtures were added dropwise to a small reactor containing a 3% aqueous solution of polyvinyl alcohol (PVA) as an emulsifier. The reactor was connected to a vacuum pump, fitted with a mechanical stirrer, and placed in an oil bath at 23°C. The mixing speed was 120 rpm and the dropwise addition rate was approximately 0.3 ml/min. After the addition of all of the solutions, the temperature was lowered to 18°C while keeping the stirring speed constant. The vacuum pump was then turned on, gradually reducing the pressure to reach full vacuum. The agitation speed was reduced to about 50 rpm and the process was continued under these conditions for 6-10 hours. The obtained microspheres were washed with copious amounts of distilled water and filtered through sieves with a diameter of 150 μ m.

Hydrolytic and enzymatic degradation: During the examination of the course of the hydrolytic and enzymatic degradation of microspheres, their specific mass was packed in polypropylene dialysis bags and then each sample prepared in this way was placed in a vial filled with distilled water or activated sludge at room temperature, respectively. After the specified time: 0.5; 1; 1.5; 2; 2.5 and 3 months of the experiment, the samples were removed and placed on filter paper and washed in water carefully, but not to damage the samples. The samples were weighed completely after drying.

Results and Discussion

The developed and applied method of forming microspheres allowed for the preparation of microparticles with a relatively regular spherical shape, a fairly smooth and uniform surface, and a relatively narrow diameter distribution with good reproducibility. As expected, with the increase in the degradation time, an increasing weight loss of the samples was observed.

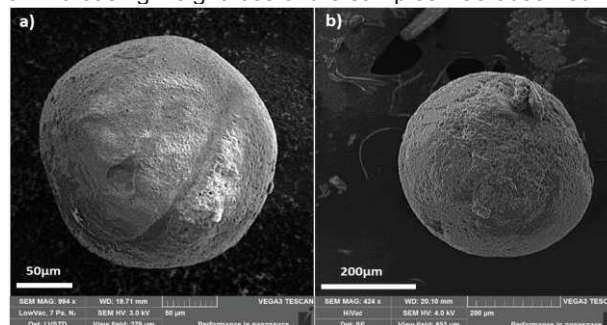


FIG. 1. SEM images of the microspheres with a) Terpolymer, b) copolymers containing blocks of butylene succinate and poly(ethylene oxide) in the chain.

Conclusions

Understanding the mechanism of degradation of these microspheres is a key step in starting research on their use as carriers of active substances in controlled release systems. The obtained microspheres are planned to be used as carriers of active substances, used in the formulation of cosmetics and dermatological preparations.

Acknowledgments

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References

- [1] T. Kemala, E. Budianto *et al.*, Arab. J. Chem. 5 (1) (2012) 103-108.
- [2] H.K.Makadia, S.J. Siegel, Polymers (Basel). 3 (3) (2011) 1377-1397.
- [3] K.S. Meghna, M.P. Krishna, *et al.*, Int. J. Novel Trends Pharm. Sci. 7 (2017) 109-11
- [4] K. Lewicka, P. Dobrzynski, *et al.*, Materials 13 (2020) 2778.