CHITOSAN MICROCAPSULES OBTAINED BY WET METHOD AS POTENTIAL CARRIERS FOR ACTIVE SUBSTANCE

JAN STARTEK[1], EWA DZIERZKOWSKA[1], JULIA GOLAŃSKA[2], EWA STODOLAK-ZYCH[2]*, ALICJA RAPACZ-KMITA[2]

[1] FACULTY OF ELECTRICAL ENGINEERING, AUTOMATICS, COMPUTER SCIENCE AND BIOMEDICAL ENGINEERING, AGH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KRAKOW, POLAND
[2] FACULTY OF MATERIALS SCIENCE AND CERAMICS, AGH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KRAKOW, POLAND
*E-MAIL: STODOLAK@AGH.EDU.PL

[ENGINEERING OF BIOMATERIALS 148 (2018) 92]

Introduction

Hydrogel biomaterials are attractive carriers for many active substances in modified drug release systems. Unfortunately, only few such systems have been introduced to the clinical market. The reason for this is a large number of factors affecting the release of the active compound from this type of carrier [1]. The lack of so-called bioavailability results in a lowering of the therapeutic effect and revocation of the tested system from further basic and clinical trials. The response to these problems is the use of biocompatible and biodegradable hydrogel materials based on natural compounds. An example of such a biopolymer is chitosan, which is characterized by biocompatibility, enzymatic degradation under in *vitro/in vivo* conditions, and its degradation products are non-toxic [2]. An additional advantage of chitosan is its hydrophilicity, the multitude of functional groups undergoing controlled reactions (e.g. combining into a carrier-drug system) and the cationic nature of the chain, which allows to combine chitosan with drugs, nucleotides, proteins or peptides. The release kinetics of the active compound from the chitosan carrier are, however, also influenced by a variety of factors. One of them is the type of cross-linking agent, particle size of the closed (encapsulated) active compound in the polymer network space, or the molecular weight of chitosan alone [3]. Chitosan makes also possible to match the form of the carrier to the place and time of drug release. It can be formed and shaped into micro and nanocapsules, micro and nanometer fibers, or coat the other carriers with a chitosan layer (e.g. by electrospraying).
Bearing in mind the above, a series of chitosan microcapsules was obtained in this study, in which gentamycin was additionally introduced. Various conditions for forming capsules have been used: a different composition of the precipitation bath (NaOH or a mixture of NaOH:KCl) and a different cross-linking agent (carrageen/agar).

Materials and Methods

The microcapsules were prepared from low molecular weight chitosan (Sigma-Aldrich), and carrageen and agar (Sigma-Aldrich) were used as the crosslinking agents. A 5% NaOH solution and 0.3 M KCl solution (POCH) were used to prepare the precipitation bath. The chitosan solution was mixed in a weight ratio of 2:1: with 2.5% agar or 2.5% carrageenan and homogenized for 30 minutes on a magnetic stirrer. A 5% gentamycin (Pharma Cosmetics) was introduced into part of the solution. The coagulation process was carried out at 10°C using NaOH precipitant solution or a 1:1 mixture of NaOH:KCl. The obtained capsules were stabilized for 24h at 15°C, and then the excess of coagulation agents were rinsed with water (until it reached a constant conductivity). The prepared capsules were frozen at -80°C for 24 h, and then lyophilized (-50°C/ 0.3 Torr). Microcapsules were characterized for their morphology and composition (SEM / EDS). Structural studies of chitosan-carrageen (KR) and chitosan-agar (AR) systems were carried out using the FTIR-ATR technique. The size was estimated by determining the equivalent diameter of the microcapsule. The possibility of release of active compounds from the porous surface of the capsule was confirmed by monitoring the release of gentamycin (GS) by the ES-ICP method.

Results and Discussion

The size of CS microcapsules depends on the cross-linking agent used: microcapsules with a larger equivalent diameter were obtained in CS-KR (260 μm) systems than in CS-AR (230 μm) systems, where the precipitating factor was NaOH / KCl solution. The crosslinking agent used did not affect the morphology and shape of the microcapsule. The type of coagulation bath did not affect the microcapsules shape too.
The introduction of 5% gentamicin into chitosan led to an increase and change in the shape of microcapsules (from oval to spherical). A similar trend was retained, as in the case of reference materials (CS-AR, CS-KR): larger microcapsules were obtained in CS-KR-GS systems, where the precipitating factor was a mixture of NaOH / KCl solutions (increase from 260 to 290 μm for the CS-KR-GS system and increase from 230 to 250 μm for the CS-AR-GS system). The introduction of gentamicin increased the surface development of microcapsules, and their roughness. The conducted release tests showed that CS-AR-GS and CS-KR-GS systems release the drug faster than the same materials, however precipitated in NaOH solution.

Conclusions

The preliminary results obtained show that properties such as: morphology, size and rate of drug release can be modeled already at the stage of obtaining materials, through the selection of cross-linking agents or coagulation solutions. The fastest release occurs when chitosan is not cross-linked. The stronger crosslinking agent is carrageen compared to agar, thus the release of the drug from the systems enriched with the KR occurs in the slowest way.

Acknowledgments

This work was performed within the framework of funding for statutory activities of AGH University of Science and Technology in Krakow, Faculty of Materials Science and Ceramics (11.11.160.182).

References

[1] A. Kidane, P.P. Bhatt, Recent advances in small molecule drug delivery, Curr. Opin. Chem. Biol. 9 (2005) 347–351.
[2] T.R. Wang, Drug delivery: principles and applications, John Wiley and Sons, NJ, 2005.
[3] A.S. Hoffman, Hydrogels for biomedical applications, Adv. Drug Deliv. Rev. 54 (2002) 3–12.