ALGINATE/CHITOSAN HYBRID MATERIALS LOADED WITH CIPROFLOXACIN

AGNIESZKA KYZIOŁ[1]*, ALEKSANDRA MAZGAŁA[1], JUSTYNA MICHNA[1], ANNA REGIEL-FUTYRA[1], IVAN MORENO[2,3], VICTOR SEBASTIAN[2,3], SILVIA IRUSTA[2,3]

[1] FACULTY OF CHEMISTRY, JAGIELLONIAN UNIVERSITY, POLAND
[2] DEPARTMENT OF CHEMICAL ENGINEERING AND ENVIRONMENTAL TECHNOLOGY, INSTITUTE OF NANOSCIENCE OF ARAGON (INA), UNIVERSITY OF ZARAGOZA, SPAIN
[3] NETWORKING RESEARCH CENTER ON BIOENGINEERING, BIOMATERIALS AND NANOMEDICINE, CINER-BBN, SPAIN
*E-MAIL: KYZIOL@CHEMIA.UJ.EDU.PL

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Introduction

Constantly growing bacteria drug resistance, connected with the possibility of formation by them multicellular community (biofilms), is one of the most serious global public health problems and a huge threat to modern medicine. For the past two decades, biopolymers and among them alginate (AL) and chitosan (CS) were the subject of the intense research related to various medical applications such as materials for regenerative medicine and tissue engineering, nevertheless, as well for inhibition of bacterial biofilm formation [1-3].

Both AL and CS are well-known because of their biocompatibility, biodegradability, non-antigenicity, nontoxicity under the normal physiological conditions, as well as muco- and bioadhesiveness [1]. Thus, they are ideal candidates for preparation of novel biomaterials. Alginate/chitosan formulations (*i.e.* spheres, capsules, core-shell composites, fibers, *etc.*) have been proposed in particular for drug delivery systems. Such biopolymer-based drug carriers offer an alternative approach to effective and controlled delivery of many drugs (*e.g.*, antibiotics), even with improvement of their pharmacological and therapeutic properties [4].

Materials and Methods

Ciprofloxacin-loaded alginate beads (AL_CP) were prepared by adopting the method of Silva *et al.* based on emulsification/internal gelation with some modifications [5]. Freeze-dried alginate cores were coated with chitosan, and subsequently cross-linked with sodium tripolyphosphate (AL_CP_CS).

Alginate-based electrospun fibers loaded with ciprofloxacin hydrochloride were fabricated with application of an Yflow 2.2 D500 electrospinner. After electrospinning fibers were stabilized in ethanol and ionically crosslinked by calcium ions. As well, alginate fibers loaded with CP were covered by chitosan by application of coaxial setup.

The resulting materials were characterized in detail by application of such techniques as: (*i*) size was studied by nanoparticle tracking analysis (NTA), (*ii*) zeta potential was investigated by dynamic light scattering technique (DLS), (*iii*) the presence of chitosan on the alginate core and interactions between a polymer and antibiotic were confirmed by infrared spectroscopy, (*iv*) morphology of obtained materials was analysed by scanning electron microscopy (SEM), (*v*) drug loading efficiency and cumulative drug release profiles were evaluated with UV-Vis spectrophotometry.

Results and Discussion

Herein, we present a comprehensive study focused on optimization of method of preparation of alginate/chitosan hybrid materials – beads and fibers. Beads were constructed of alginate core and chitosan shell. Sodium alginate electrospun nanofibers were prepared by blending alginate with poly(ethylene oxide). Beads and fibers were loaded with ciprofloxacin, a fluoroquinolone antibiotic widely used for wound healing.

Spherical in shape AL_CP and AL_CP_CS beads with a mean diameter *ca.* 160 and 250 nm for AL_CP and AL_CP_CS, respectively and encapsulation efficiency *ca.* 75 % were successfully synthesized. Cumulative drug release studies revealed the extended over time antibiotic release profiles.

AL fibers were electrospun and coated with CS with co-axial technique application. The resulting fibers exhibited a core–sheath structure, revealed by TEM analysis. The average diameter of the AL_CP_CS fibers was less than 200 nm, depending on the composition and electrospinning parameters.

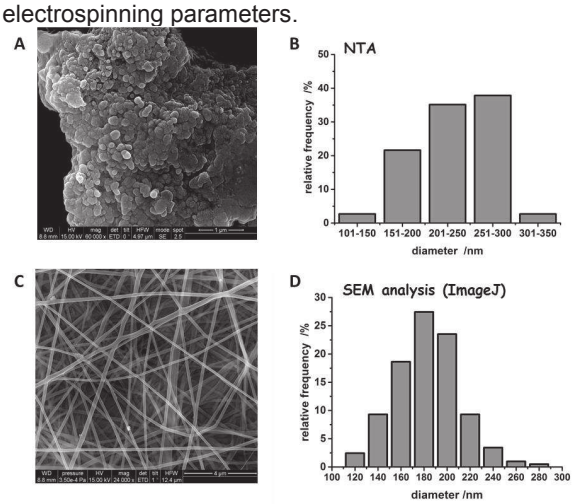

FIG. 1. SEM images and the relative frequency of diameter of obtained materials: alginate loaded with ciprofloxacin beads (A and B) and fibers (C and D), respectively.

Conclusions

In conclusion, four hybrid formulations based on application of biocompatible and biodegradable polymers – alginate and chitosan, both Food and Drug Administration approved biopolymers, were proposed as effective drug delivery systems to fight down multi-drug resistant bacteria. The resulting materials loaded with antibiotic (*i.e.* ciprofloxacin): (*1*) alginate beads, (*2*) alginate beads covered by chitosan, (*3*) alginate fibers and (*4*) alginate fibers covered by chitosan were prepared and characterized.

Acknowledgments

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