Alginate/chitosan core-shell beads with bioactive functionalities

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Aims and objectives

The number of Multi-Drug Resistant bacterial strains (MDR) has been rapidly increasing[1]. Drug resistance is the main cause of prolonged infections which enhances the risk of dangerous illnesses such as wound infections, osteomyelitis, septic arthritis, endocarditis. In general, acute infections are known to be caused by planktonic bacteria, which are usually treated with antibiotics. In contrast, in case of biofilm forming strains, infections often show up to be untreatable and usually develop into chronic[2]. Thus, since overused antibiotics become ineffective, innovative approaches are required in the search of alternative biocidal agents and therapies. Among a number of strategies, polymeric particles as drug carriers have attracted lately a lot of researchers attention.

Present study focuses on alginate/chitosan submicroparticles (Fig.1) constructed of polymeric core loaded with antibiotic (ciprofloxacin) and polymeric shell prone for further lytic enzyme immobilization. Several synthetic approaches were conducted in order to obtain stable and uniform core-shell beads (Table 1).

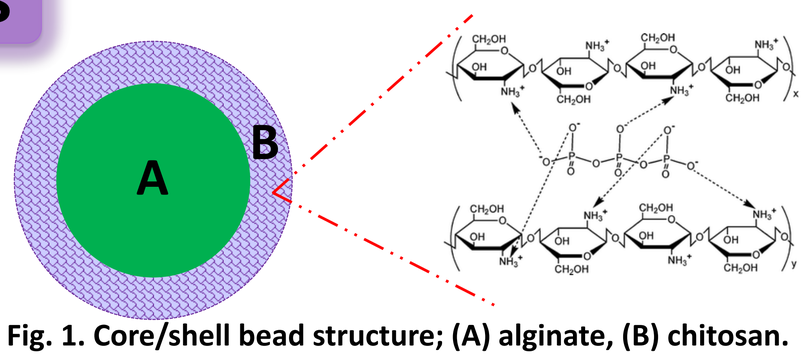

Fig. 1. Core/shell bead structure; (A) alginate, (B) chitosan.

Table. 1. Main synthetic parameters.

Sample	Water/Oil volume ratio [%]	n_{acid}/n_{Ca2CO3}
NS1; NS1@CSL	20	1,25
NS2; NS2@CSL	20	1,75
NS3; NS3@CSL	20	2,50
NS4; NS4@CSL	30	2,50
NS5; NS5@CSL	40	2,50

RESULTS

Size and Zeta potential

Table. 2. Beads hydrodynamic diameter and Zeta potential.

	Size / nm	Zeta Potential / mV		
NS1	201 ± 2	-32,1 ± 0,8	**NS1@CSL**	5,1 ± 0,4
NS2	202 ± 14	-32,8 ± 1,5	**NS2@CSL**	5,5 ± 0,3
NS3	134 ± 12	-23,6 ± 1,1	**NS3@CSL**	5,8 ± 0,5
NS4	177 ±13	-29,5 ± 2,1	**NS4@CSL**	5,3 ± 0,2
NS5	156 ±24	-29,5 ± 2,5	**NS5@CSL**	5,0 ± 0,4

Antibiotic release profiles

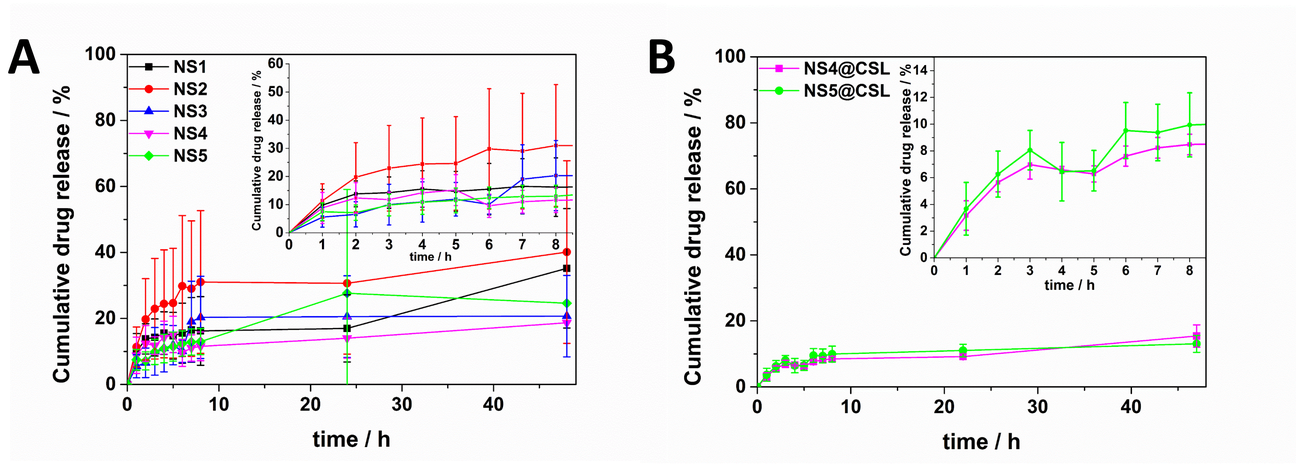

Fig. 2. Cumulative drug release profiles for core (A) and core/shell (B) beads loaded with ciprofloxacin.

Morphology

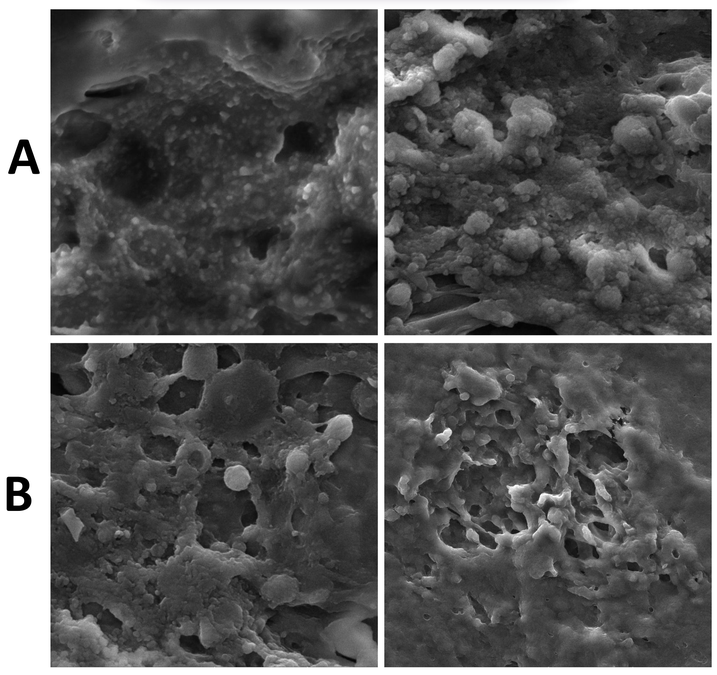

Fig. 3. Scanning electron micrograpghs of core (A) and core/shell (B) beads.

Biological test: cytotocixity assay

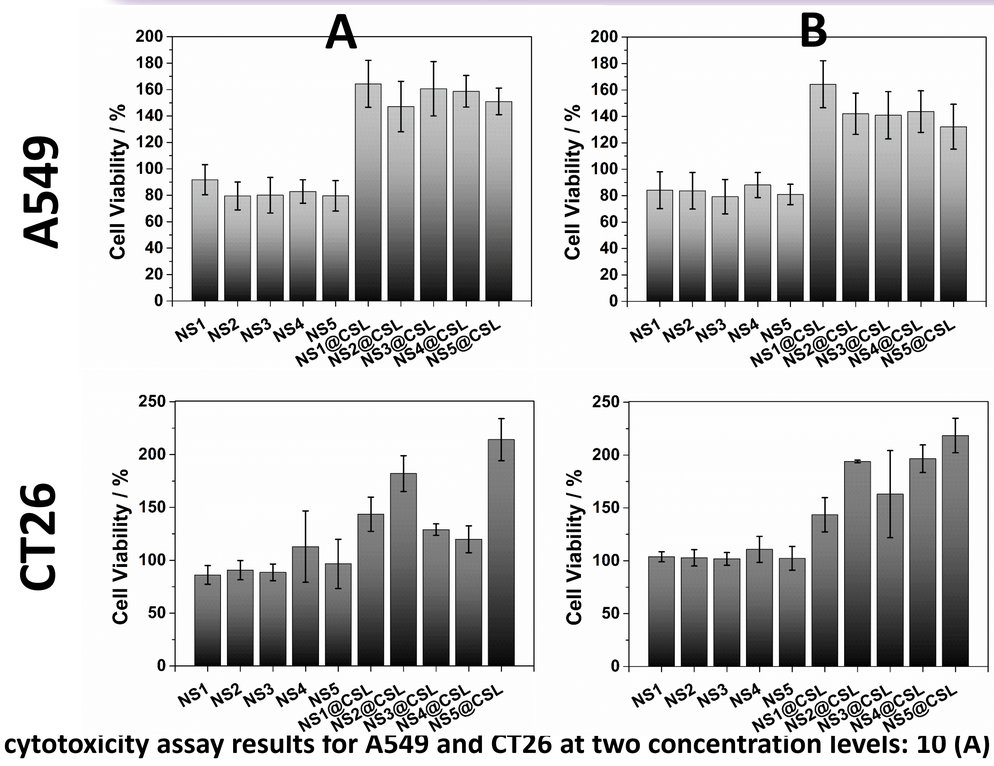

Fig. 4. MTT cytotoxicity assay results for A549 and CT26 at two concentration levels: 10 (A) and 50 mg/mL (B).

Conclusions

1. Synthesis of alginate/chitosan core-shell beads was optimized (synthesis in microemulsion/ionic gelation technique);
2. Cumulative drug release studies revealed the extended over time ciproflaxine release profiles;
3. Spherical shape of beads was confirmed by SEM technique;
4. No significant cytotoxic effect *in vitro* was observed. Interestingly, in case of core-shell beads even proliferative effect was observed (experiments in progress).

1. Høiby, N.; Bjarnsholt, T.; Givskov, M.; Molin, S.; Ciofu, O., Antibiotic resistance of bacterial biofilms. *International Journal of Antimicrobial Agents 35* (4), 322-332.
2. Bjarnsholt, T., The role of bacterial biofilms in chronic infections. *APMIS* **2013,***121*, 1-58.

This work was supported by Polish Foundation of Science within POMOST project "Alginate/chitosan core-shell beads with bioactive functionalities" (POMOST/2013-7/7).

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FNP Foundation for Polish Science
EUROPEAN UNION EUROPEAN REGIONAL DEVELOPMENT FUND