Chitosan-based polyelectrolyte complexes for drug delivery

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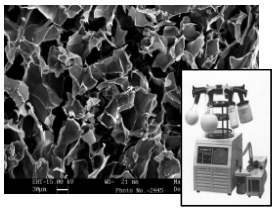
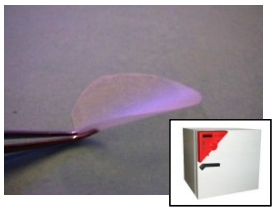
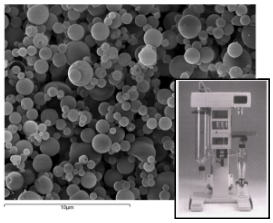
Among different polymers, chitosan, the N-deacetylated product of the polysaccharide chitin, is gaining increasing importance in medical and pharmaceutical applications due to its good mucoadhesion and absorption enhancing ability. Moreover, chitosan shows the ability to form hydrogels able to control the rate of drug release from the delivery system as well as protect the drug from chemical and enzymatic degradation in the administration site. In particular, when chitosan is cross-linked or complexed with an oppositely charged polyelectrolyte, a three-dimensional network is formed in which the drug can be incorporated in order to control its release.



Porous structure of freeze-dried chitosan/pectin nasal insert



Chitosan/hyaluronate transdermal film obtained by film casting



Spray–dried chitosan/pectin microspheres

1. Description of the product

Chitosan-based polyelectrolyte complexes have been developed for local or systemic administration of drugs and biodrugs. In particular, our research has been focused on the study of different dosage forms (micro-nanoparticles, inserts and films) for oral, buccal, nasal, vaginal and intravenous administration of drugs with unfavourable biopharmaceutical properties (peptide and protein, nucleic acids, antipsychotic substances and antihypertensive drugs). Great attention has been given to the choice of (1) suitable polyelectrolyte complex: chitosan deacetylation degree and molecular weight, kind of polyanion (hyaluronic acid, alginic acid, pectin and gelatin), chitosan/polyanion molar ratio; (2) preparative technologies (spray-drying, freeze-drying, film casting and coacervation); (3) functional properties of the carriers (morphological aspect, size distribution, loading efficiency, swelling ability, mucoadhesion properties, site specificity, drug release kinetics and drug permeation across biological membranes).

2. Innovative aspect of the product

Precise drug delivery requires that the triggering mechanism in the delivery system only respond to the physiological or pathological conditions particular to the treatment site. Hence, continuous efforts have been focused on designing delivery systems with improved site specificity and versatile drug release kinetics to accommodate different therapeutic needs. Our research concerns the development of innovative drug delivery systems based on new natural polymeric materials and innovative preparative technologies.

In particular the systems studied include: (1) pH-dependent spray-dried microspheres based on chitosan/pectin complexes for colon delivery of vancomycin; (2) freeze-dried inserts based on chitosan/hyaluronic acid complexes for nasal delivery of vancomycin and insulin; (3) freeze-dried inserts based on chitosan/pectin complexes for nasal delivery of chlorpromazine; (4) chitosan, chitosan/tripolyphosphate and chitosan/hyaluronic acid nanoparticles, obtained by simple and complex coacervation, for siRNA delivery; (5) chitosan/gelatine films, obtained by film casting, for buccal delivery of propranolol; (6) freeze-dried inserts based on chitosan/alginate for vaginal delivery of chlorhexidine.

3. Main advantages of the offer

The choice polyelectrolyte complexes, based on natural polymeric materials, with specific functional properties such as good mucoadhesion and absorption enhancing ability as well as good control of drug

release, associated with the application of appropriate preparative methodologies, has led to the development of innovative pharmaceutical systems for the delivery of nucleic acids, peptidic and protein drugs and, in general, drugs with unfavourable biopharmaceutical properties. In particular, the selection of suitable preparative conditions during chitosan/polyanion complexes is a novel strategy for the realization of pharmaceutical systems with interesting functional properties (drug loading ability, stability and drug delivery) and allow the modulation of the delivery system behaviour at the administration or therapeutic site. Moreover, the definition of the adequate preparative technology, generally innovative, and of the final dosage form, is another hallmark of the work. In fact, nano and micro preparative technologies for the realization of pharmaceutical carriers are a state-of-the-art approach to ensure the therapeutic success of drug treatments. Another interesting aspect of the research is the versatility of these vectors which can be employed as pharmaceutical, cosmetic, herbal and food products.

4. Technology key words

Chitosan; polyelectrolyte complexes; drug delivery strategies; innovative preparative technologies.

5. Current Stage of Development

Completed research: pH-dependent spray-dried microspheres based on chitosan/pectin complexes for colon delivery of vancomycin; freeze-dried inserts based on chitosan/hyaluronic acid complexes for nasal delivery of vancomycin and insulin; freeze-dried inserts based on chitosan/pectin complexes for nasal delivery of chlorpromazine; chitosan, chitosan/tripolyphosphate and chitosan/hyaluronic acid nanoparticles, obtained by simple and complex coacervation, for siRNA delivery; chitosan/gelatine films, obtained by film casting, for buccal delivery of propranolol; freeze-dried inserts based on chitosan/alginate for vaginal delivery of chlorhexidine. Work in progress: chitosan/ialuronate films for transdermal delivery of tiocolchicoside; chitosan/carboxymethylcellulose inserts for vaginal delivery of chlorhexidine; chitosan nanoparticles for nasal delivery of sodium chromoglicate.

6. Intellectual Property Rights

The product of the research is not covered by patent.

Technical and scientific publications

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