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# THE DOCTORAL RESEARCH ABSTRACTS

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**Title :** NANOPARTICLES-IN-BEADS MADE OF ALGinate AND CHITOSAN DERIVATIVES AS ORAL INSULIN CARRIER

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This project aimed to design nanoparticles-in-beads made of alginate, chitosan and their derivatives as oral insulin carrier. In the first part of the study, the calcium alginate beads were prepared using the vibratory nozzle extrusion microencapsulation technique through concurrent core and coat formation with chlorpheniramine maleate as a model drug. These beads were coated with chitosan/chitosan-oleic acid conjugate of which the latter was synthesized via covalent reaction. The formability of beads was optimized through varying alginate solution concentration, alginate/chitosan solution flow rate and nozzle vibrational frequency. The size, shape, morphology, swelling, erosion, water uptake, drug content, drug release and matrix molecular profiles of beads were characterized. Spherical discrete coated beads were produced through critical interplay of nozzle vibrational frequency and polymeric solution flow rate. The conjugate-coated beads had their swelling and water uptake tendency negated through the introduction of tripolyphosphate ions as a crosslinking agent to attract the conjugate to the alginate core interface for coacervation to take place. The drug release propensity of tripolyphosphate-crosslinked, chitosan-oleic acid conjugate-coated beads was unexpectedly higher than the uncoated beads. This was attributed to reduced drug-alginate interaction as a result of alginate coacervating with chitosan-oleic acid conjugate and loss of calcium alginate crosslinkage to tripolyphosphate species. In the second part of the study, nanoparticles of simple calcium alginate, calcium alginate-stearic acid, and calcium alginate-C18 conjugate were prepared by nanospray

drying technique. Alginate-C18 conjugate was chemically synthesized with the aim of introducing a hydrophobic segment to the polymer chain for drug release modulation. The nanoparticles size, zeta potential, surface morphology, drug content, drug encapsulation efficiency, drug release, matrix molecular characteristics, mucus penetration, HT-29 cell line cytotoxicity and intracellular trafficking profiles were evaluated. Where applicable, the nanoparticles were loaded into calcium alginate beads and had their *in vivo* blood glucose lowering and insulin bioavailability profiles determined. The calcium alginate-C18 conjugate nanoparticles were characterized by non-toxicity, reduced size and zeta potential thus enhanced mucus penetration and intracellular trafficking, with minimal insulin readsorption tendency as a result of active COOH/COO<sup>-</sup> sites of alginate being occupied by C18 conjugate. Loading of such nanoparticles into tripolyphosphate-crosslinked, chitosan-oleic acid conjugate-coated beads had their drug release reduced in the simulated gastric phase with the majority of insulin being transported transmucosally in the form of nanoparticles at the intestinal region. The combination of nanoparticles and coated beads increased the blood glucose lowering extent of rats synergistically, and insulin bioavailability instead of nanoparticles alone.