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ACCEPTED MANUSCRIPT

Alginate coated chitosan core-shell nanoparticles for efficient oral delivery of naringenin in diabetic animals - an *in vitro* and *in vivo* approach

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Research highlights:

- Naringenin loaded chitosan/alginate core-shell nanoparticles were prepared.
- They were characterised by DLS, SEM, FTIR, XRD and pH dependent dialysis study.
- Mucoadhesive nanoparticles showed drug encapsulation efficiency of 91%.
- They produced significant antidiabetic responses following oral delivery in rats.
- Peroral treatment with these polymeric nanoparticles showed no systemic toxicity.

Abstract:

The chemical synthesis of this study targets for development of a bio-safe polymeric nano-vehicle for improvising the solubility of the flavanone naringenin in antidiabetic animal study. Nanoparticles were prepared from two cost-effective carbohydrate biopolymers - chitosan and alginate for successful encapsulation of naringenin. Dual crosslinked nanoparticles were synthesized by using Na₂SO₄ and CaCl₂ as crosslinkers. The nanoparticles were characterized by DLS, FTIR, XRD and SEM. The prepared nano-formulations exhibited significant naringenin entrapment of > 90% and pH-responsive slow and sustained release of the flavonoid. *In-vivo* studies revealed significant hypoglycemic effect after oral delivery of the nanoparticles to streptozotocin-induced diabetic rats. Histopathology and several blood parameters indicated that oral administrations of nanoparticles were free from toxicity. Other studies also suggested that polymeric formulations were quite effective for oral delivery of the flavonoid as a therapeutic agent in the treatment of dyslipidemia, hyperglycemia and haemoglobin iron-mediated oxidative stress in type 1 diabetic model.

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