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Oral administration of Fe-bLf loaded nanocapsules for colon cancer therapy

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Oral administration of bio-macromolecules is an uphill task and the challenges presented in the gut milieu, from varying pH and enzymatic activity, are difficult to overcome. In this regard, nanotechnology promises a new hope and offers advantages such as controlled release, target specific delivery, combinatorial therapy with lower doses and abolished toxicities.

Aim: This study aims to develop polymeric-ceramic nanocapsules in order to achieve oral delivery of the anti-cancer neutraceutical protein iron saturated bovine lactoferrin (Fe-bLf).

Methodology: A formulation of novel anti-cancer nanocapsules was prepared using combination of polymers and ceramics. Alginate enclosed chitosan coated enclosing Fe-bLf or paclitaxel (taxol) adsorbed onto nanocores of calcium phosphate nanocapsules (AEC-CP-Fe-bLf NCs or AEC-CP-taxol NCs), were made by combination of ionic gelation and nanoprecipitation techniques to encapsulate the anti-cancerous therapeutics. Size distribution, morphology, internalization and release profiles of the NCs under varying pH along with in vitro and in vivo anti-cancer efficacies were evaluated. Paclitaxel was used as positive anti-cancer drug to compare the effectiveness with our natural anti-cancer protein, Fe-bLf.

Results: AEC-CP-Fe-bLf NCs obtained spherical morphology and showed enhanced anti-cancer efficacy in vitro. Further, these NCs were efficiently taken up by the colon cancer (Caco-2) and didn't effect the mucosal integrity during transcytosis. AEC-CP-Fe-bLf NCs were supplemented in AIN 93G diet with 1.2%w/w of Fe-bLf, by replacing casein and fed to mice, in both prevention and treatment xenograft colon cancer models. Nanoformulated Fe-bLf diet when given orally, as a pre-treatment, one week before Caco-2 cell injections, was found to be highly effective. None of the mice fed with the AEC-CP-Fe-bLf NCs diet, developed tumours, or show any signs of toxicity, while the mice fed control AIN-93G diet, showed normal tumour growth. When taxol or Fe-bLf were given orally as a nanoformulations post tumour development, a significant regression in the tumour size was observed and completely rejected in 35 days, while intra tumoural injection of taxol just delayed the growth of tumours. The pharmacokinetic and bioavailability studies indicate that nanoformulated Fe-bLf predominantly present on tumour cells as compared to non-nanoformulated Fe-bLf. These NCs can thus be used for future targeted protein/peptide or nucleic acid based drug delivery to treat difficult diseases including cancer. Fe-bLf loaded NCs were found to help in absorption of iron thus may have utility in enhancing the iron uptake during iron deficiency without interfering with the absorption of calcium.

Conclusion: With the promising results of our study, the future potentials of the NCs loaded Fe-bLf, in chemoprevention and in the treatment of human colon cancer, deserve further investigations for translational research and preclinical studies of other malignancies.

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