ABSTRACT

Colonic local pathological state such as “Melanosis Coli” develops in the intestinal region (colon) due to prolonged intake of anthraquinone laxatives. Present study was designed to evaluate the potential of curcumin (CUR) for the prophylactic action / treatment of Melanosis coli via optimization of colon targeted drug delivery systems. Present work is focused toward the development and optimization of various novel drug delivery systems namely nanoemulsifying preconcentrate (SNP), polymeric Self-emulsifying nanocapsules (PSN), and polymeric enteric nanospheres using CUR. Optimization of formulations were undertaken by experimental design technique (Box-Behnken design). Impact of formulation variables such as oil, polymer, adsorbent, surfactant and cosurfactant concentration on encapsulation efficiency, drug loading, particle/globule size, surface morphology and in vitro drug release was evaluated. In vitro studies revealed that selected formulations released the drug after 5 h lag time corresponding to the time to reach the colonic region. Roentgenography study was conducted to confirm the presence of carrier in specified GI conditions at different time intervals. Observed results conferred that developed formulation(s) can be used as a promising approach to deliver CUR to colonic sites.

Further, in vivo localization of optimal formulation was investigated using a colitis guinea pig model to mimic Melanosis coli environment (induced by sennosides administration). Efficacy of formulation(s) was characterized by change in body weight, stool consistency, level of tumour necrosis factor in tissues and histopathogical changes (as a marker of pathology) of animals kept under test conditions. Animals treated with sennosides had passed soft stool during the study, whereas, no such (laxative) effects were seen in control group. A continuous decrease in body weight was observed in animals of positive control and standard prevention group, in contrast, insignificant weight loss was observed in the animals kept under prevention group (treated with CUR loaded polymeric Self-emulsifying nanocapsule formulation). Autopsy studies showed uniform mucous membrane in control group, whereas, disrupted membrane was observed in the positive control group. Results showed that animals kept under prevention group (administered PSN formulation and sennosides simultaneously) were maintained their normal physiology in comparison to standard prevention group (administered reference formulation and sennosides simultaneously). Reference formulation failed to maintain the normal physiology of animals. Therefore, it was concluded that polymeric Self-emulsifying nanocapsule formulation presents as a favorable delivery system for colonic pathologies such as Melanosis coli, in comparison to reference formulation.