Abstract

Part-A

Curcumin has considerable neuro-protective and anti-cancer properties but is rapidly eliminated from the body. Curcumin has been shown to have the possibility of slowing the progress of Alzheimer's disease by reducing amyloid β, of delaying the onset of kainic acid-induced seizures and of inhibiting the formation of brain tumors. However, the penetration of curcumin in brain is limited due to its rapid systemic elimination and its inability to cross blood brain barrier easily. Therefore, the therapeutic efficacy of curcumin is restricted due to its short systemic retention in circulation and also in brain. Therefore, there is a need to investigate modified curcumin derivative to specifically target to the brain and evaluate the ability of curcumin derivative to cross blood brain barrier compared to the parent compound. The curcumin derivative was synthesized and compared with the curcumin for the ability to cross the blood brain barrier. The conversion of curcumin derivative and/or identification of metabolite in brain were evaluated by HPLC and LC-MS after the i.v. administration in rats. Both compounds were rapidly degraded in-vivo but the curcumin derivative was more stable and cross the blood brain barrier 10 times more as compared to the parent compound and gets converted into the parent compound in brain after the enzymatic hydrolysis. Compared with curcumin, curcumin derivative is (a) more stable; (b) less extensively metabolized in microsomal system (c) more stable in-vivo (d) cross the blood brain barrier 10 times more and finally converted into the parent compound in brain.

Key Words—Blood-brain barrier, Drug delivery, Curcumin modification
ABSTRACT

Part-B

The purpose of the present research was to develop and characterize mucoadhesive microspheres of curcumin for the potential use of treating gastric adenocarcinoma, gastric and duodenal ulcer associated with *Helicobacter pylori*. Curcumin mucoadhesive microspheres were prepared using ethyl cellulose as a matrix and carbopol 934P as a mucoadhesive polymer by an emulsion–solvent evaporation technique. Response surface methodology was used for optimization of formulation using central composite design (CCD) for two factors at three levels each was employed to study the effect of independent variables, drug:polymer:polymer ratio (curcumin: ethyl cellulose:carbopol 934P)(X₁) and surfactant concentration (X₂) on dependent variables, namely drug entrapment efficiency (DEE), percentage mucoadhesion (PM), *in vitro* drug release and particle size (PS).

Optimized formulation was obtained using desirability approach of numerical optimization. The experimental values of DEE, PS, PM, and % release after 8 h for the optimized formulation were found to be 50.256 ± 1.38%, 139.881 ± 2.56 μm, 66.23%±0.06 and 73.564 ± 1.32% respectively, which were in close agreement with those predicted by the mathematical models. The drug release was also found to be slow and extended more than 8 h and release rates were fitted to the Power law equation and Higuchi model to compute the diffusional parameters. The prolonged stomach residence time of curcumin mucoadhesive microspheres might make a contribution to *H. pylori* complete eradication in combination with other antimicrobial agents.

**Key words:** Curcumin, *Helicobacter pylori*, mucoadhesive microspheres