CHAPTER 5

CONCLUSION

The present experiments were designed to provide a pharmacological basis for the use of curcumin in gastrointestinal inflammatory diseases. The results showed that curcumin definitely inhibited the development of acute reflux esophagitis and acute gastritis in different rat models, and also accelerated the healing of chronic gastric ulcer induced by acetic acid in rat model. Curcumin exerted less potent antiulcer effect than lansoprazole against acid reflux esophagitis, but exerted more potent antiulcer effect than lansoprazole against mixed reflux esophagitis. The prevention of acute esophagitis or gastric damage by curcumin was more effective at doses lower than 40 mg/kg/day probably by involvement of its antioxidant nature, inhibition of iNOS and/or mucus secretory action. The accerelation of healing of chronic gastric ulcer by curcumin was more effective at doses between 40-160 mg/kg/day by mechanisms involving the inhibition of TNF-α and iNOS production and the up-regulation of healing-related factors. The potency of the ulcer healing for curcumin was almost the same as that of cimetidine but slightly higher than that of aminoguanidine. Curcumin has been demonstrated to inhibit multiple intra-cellular pathways associated with multiple pro-inflammatory cytokine expression. This suggests that curcumin may be an alternative broad based anti-inflammatory agent for treating acute and chronic inflammatory diseases. It also seems likely that curcumin may be clinically beneficial as a potential therapeutic agent for preventing and treating upper gastrointestinal inflammatory diseases.

Curcumin exerted a potent inhibitory activity on iNOS and TNF-α production, whereas its active metabolite (tetrahydrocurcumin) or its active degradation product (vanillin) had only weak or no inhibitory activity on these pro-inflammatory cytokines. Therefore, curcumin directly attenuates the development of upper gastrointestinal inflammatory diseases even though it has low systemic bioavailability following oral dosing.

Importantly, curcumin can exert opposite effects between prevention and exacerbation of gastrointestinal inflammation or ulcer healing and ulcer relapse depending on the timing of administration (prophylactic vs therapeutic), the type of gastrointestinal inflammation (acute vs chronic; mild or severe), and the dose-effect relationship.