ABSTRACT

The phenomenon of mucoadhesion, however, is unpredictable due to varying turnover time and composition of mucus, different behavior of mucoadhesive devices over the pH range, and disease conditions. The lack of specificity in adhering to specific mucous tissue seriously limits drug delivery/targeting through this technique, thus mucoadhesive polymers in many cases are not proven to be effective as pharmaceutical glue. Chitosan is a natural polycationic copolymer consisting of glucosamine & N-acetylglucosamine units. The polymer has valuable properties as a biomaterial because it is considered to be mucoadhesive, biocompatible, biodegradable and non-toxic. The objective of present study is to enhance the mucoadhesion of chitosan by thiolating chitosan with various thiolating agents which are capable of forming covalent disulfide bonds between thiomers and cysteine-rich subdomains of mucus glycoproteins & enhance mucoadhesion of tablet. The derivatizations of the primary amino groups of chitosan with thiolating agents like Thioglycolic acid & L-Cysteine leads to the formation of thiolated chitosan where the reaction was mediated by EDAC. To evaluate the mucoadhesive property of thiolated chitosan, methotrexate & cefuroxime axetil was chosen as model drug. Mucoadhesive tablets of thiolated chitosan were prepared by direct compression method & prepared formulations were subjected to evaluations like in vitro adhesion, water uptake studies, in vitro drug release studies & in vivo residence studies. In vitro dissolution studies of thiolated chitosan tablet indicated non-Fickian diffusion controlled drug release mechanism and was best fitted into Korsmeyer–Peppas equation. In vitro mucoadhesion was up to 48.13 ± 0.31 hours for MTXF6 formulation & 48.38 ± 0.04 for CF6 where as In vivo radiographic studies conducted in rabbits for optimized formulation indicated over 36 hours retention of tablet in the stomach region for MTXF6 formulation. Hence from the above result we found that thiolated chitosan has enhanced mucoadhesion than its parent molecule.

Key words: Mucoadhesion, Chitosan, Thioglycolic acid, L-Cysteine, Methotrexate, Cefuroxime axetil, Mucus