Introduction
Floating drug delivery system (FDDS) is one of gastroretentive dosage forms which could prolong GRT to obtain sufficient drug bioavailability. It is useful for drugs that act in the proximal part of gastrointestinal tract such as antibiotic administration for *Helicobacter pylori* eradication. The system floats in the gastric fluid because of its lower bulk density.

Objectives
The main objectives of the present studies are listed below:

A. To develop a stomach specific multiple unit particulate formulation of clarithromycin, this floats in the stomach, for long time by the principle of buoyancy and releases the antibiotic for longer period of time. It was also proposed to enhance the efficacy of clarithromycin by providing less degradation in the acidic environment by proton pump inhibition by pantoprazole.

B. To formulate a Eudragit S100 enteric coated pantoprazole sodium sesquihydrate, a proton pump inhibitor formulations using mainly natural polymers such as sodium alginate and low methoxy pectin. It was also planned to evaluate the formulation *in vitro* for its physicochemical properties including the drug release characteristics in the alkaline pH and final selection of the best formulation.

Optimization and evaluation
I. To effectively utilize the $3^2$ full factorial design tool for development and optimization of both clarithromycin and pantoprazole formulations.

II. To study the enhancement of CL concentration *in situ* by the formulation of PSS using wistar rats.

III. To study the gastroretentive property of CL formulation for better efficacy by *in situ* gastro retention studies in wistar rats.

IV. To study the pharmacokinetics of clarithromycin and pantoprazole from the formulations using *albino* rabbits.
Materials and methods

Clarithromycin, Pantoprazole sodium sesquihydrate, chitosan, sodium alginate, pectin (LM) were used for the formulations. The clarithromycin floating formulations were prepared based on the interaction of chitosan, with the trisodium citrate by ionotropic gelation followed by freeze drying. The pantoprazole formulations were prepared using cation induced ionotropic gelation method using alginate, pectin, and a combination of alginate and pectin and subsequent coating with enteric polymer Eudragit S 100. The product optimization tool, a $3^2$ factorial design was employed efficiently to study the effects of independent variables in the formulations. Various main parameters evaluated are in vitro dissolution studies, in vitro buoyancy of clarithromycin, micromeritics, in vitro drug release, in situ floating properties, and in situ drug concentration in the gastric mucosa using wistar rats, pharmacokinetics using albino Rabbits

Results and discussions

In the pre formulation studies, DSC, FTIR, and XRD, analysis showed that there is no interaction between the drug, polymer and the other excipients used in the formulations. Out of nine formulations prepared for clarithromycin, CLCH6 (drug to polymer ratio 1:1 and 2% w/v of trisodium citrate) was found to be the best among the nine formulations as it fulfilled the response requirement within the criteria selected for various factors in the factorial design. Nine formulations each were prepared for pantoprazole at varying drug to polymer ratios and % Eudragit coating using alginate, pectin, and a combination of alginate and pectin. The formulation ALG-PECT6 (drug to polymer ratio 1:3 and 5% coating) was found to be the best among the nine formulations as it fulfilled the response (100% drug released in 8 h) requirement within the criteria selected for various factors in the factorial design. The clarithromycin formulations were evaluated for in vitro buoyancy it was found that CLCH6 has a maximum percentage buoyancy of 55.82% in 8 h. The apparent particle density of freeze dried clarithromycin chitosan beads found to be less than 1; hence these formulations have buoyancy in the aqueous GI fluids. SEM analysis of clarithromycin beads showed that large porous cavities formed inside the beads which help particles to float in the GI medium. The particle Volume weighted
mean particle sizes of clarithromycin beads were showed that the higher polymer concentration will have an opposite effect on the particle size. Surface weighted mean particle size of Eudragit coated PSS alginate beads ranged between 922.10 μm to 1342.67 μm and that of Eudragit coated PSS pectin beads were between 754.80 μm to 1281.36 μm. The combination of alginate and pectin produced microbeads of size ranging between 853.24μm to 1142.37 μm. The formulation CLCH 6 has shown a first order concentration dependent kinetics, and the diffusion exponent close to Fickian kinetics was selected for in situ and in vivo studies Among the Pantoprazole the maximum % CR was obtained for formulations ALG-PECT6 and the kinetic models revealed that a first order model with a case II transport mechanism. The formulation ALG-PECT6 and CLCH6 were subjected for long term stability testing as per ICH guidelines, which revealed that the product remains stable for a period of one year. The in situ gastro retention study showed a significant (P<0.05) amount of CLCH9 remained in the rat stomach after 1, 2, and 4 h respectively. The gastric mucosal concentration of clarithromycin from CLCH6 in presence of the pantoprazole beads, were significantly high (P<0.5) compared to CLCH6 alone clarithromycin suspension. Similar results were obtained for study of clarithromycin concentration in the blood of the rats. The plasma CL concentrations obtained for the CLCH6 beads, it was found that there were significantly (p<0.05) higher level of plasma concentrations compared with that of CL suspensions. In the pharmacokinetics studies various pharmacokinetic parameters such as $C_{\text{max}}$, $T_{\text{max}}$, and AUC were established for ALG-PECT6 and CLCH6.

Conclusions
The in vitro studies conducted on the clarithromycin loaded chitosan formulations proved that it has a potential as a floating delivery system. The in vivo and in situ animal studies have shown an enhanced gastric mucosal and plasma concentration of clarithromycin in the presence of enteric coated pantoprazole formulations. Hence the present study needs to be extended to healthy volunteers to prove its worthiness as dosage form in human use.
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