Formulation and Evaluation of Glycyrrhizin Alginate Beads for Stomach-Specific Delivery

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ABSTRACT: Gastric irritation is a very common problem with various stomach related disorders. The present research was undertaken to formulate floating calcium alginate beads of glycyrrhizin for targeting the gastric mucosa and prolonging their gastric residence time. Glycyrrhizin is the chief sweet tasting active constituents of the plant *Glycyrrhiza glabra* which belongs to the family Fabaceae. Glycyrrhizin is used for the treatment of ulcer and also now-a-days used as natural sweetening agent. The beads were prepared by suspending glycyrrhizin in calcium alginate solution. The beads were prepared using calcium alginate and glycyrrhizin (1:1) and were evaluated. The mean diameter, drug loading and entrapment efficiency were evaluated. Thus, the present investigation aimed in formulating stomach specific drug delivery useful in the treatment of gastric problems.

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INTRODUCTION

Gastric ulcers are one of the serious health problems in almost all developing countries like India with a considerable economic burden associated with its high morbidity and mortality rates. Any therapeutic drug must therefore be able to penetrate the gastric mucus layer and maintain a concentration sufficient for antibacterial activity at the infected site for a suitable length of time (Goodman and Cockburn, 2001; de Sousa Falcão et al., 2008).

Calcium Alginate (CA) has been used to treat the symptoms of reflux esophagitis and the results showed that the alginate was more effective, and costs less than cisapride for the treatment of symptoms presented by patients suffering from reflux without severe oesophagitis Literature reports have indicated the widespread use of CA for achieving sustained release of drugs, targeting gastric mucosa, and increasing the bioavailability of drugs, due to the ability of alginate to form a stable and bio adhesive gel with calcium ions (Zhang et al., 2011).

In addition, the alginate bead preparation method involves the use of aqueous solvents, avoiding exposure of ingredients to high temperatures and toxic organic solvents. Moreover, the resulting preparation is nonimmunogenic, with bioadhesive and floating properties that could be appropriate for stomach targeted drug delivery (Murata et al., 2007; Whitehead et al., 2000). Glycyrrhizin (or glycyrrhizic acid or glycyrrhizinic acid) is the chief sweet-tasting constituent of *Glycyrrhiza glabra* (liquorice) root. Structurally it is a saponin and has been used as an emulsifier and gel-forming agent in foodstuff and cosmetics (Dwivedi, 2009; Dwivedi and Kaul, 2010). Its aglycone is enoxolone and it has therefore been used as a prodrug for that compound, for example it is used in Japan to prevent liver carcinogenesis in patients with chronic hepatitis C (Sato et al., 1996). The floating delivery system strategy allows the local delivery of a drug to the stomach, making it a promising vehicle for Glycyrrhizin.

The work described here is concerned with the formulation of Glycyrrhizin floating CA beads. Such a dosage form for Glycyrrhizin would remain buoyant in the stomach without affecting the gastric emptying time for a prolonged period of time and localize the drug at the *H. pylori* infection site on the gastric epithelium. Furthermore, such treatment may lead to drug dose reduction which will

be an additional valuable advantage (Vani et al., 2010). Some of the eminent Scholar (Zam et al., 2014 and Rijo et al., 2014) have studied the plant extract and their utility for formation of beads. Thus, the objective of this study was to encapsulate the plant extract glycyrrhizinic in CA beads to be incorporated as an additive in pharmaceutical products.

MATERIALS AND METHODS

Preparation of floating glycyrrhizin beads

CA was dissolved in the distilled water and added to Glycyrrhizin. The Glycyrrhizin mixture was then added to the CA solution. The resulting suspension was dropped through a 12 mm inner diameter syringe needle from a height of 7 cm into calcium chloride solution (2% w/v, 200 mL) saturated with Glycyrrhizin. The formed beads were left in the same solution for 45 min to improve their mechanical strength and finally dried at 50 °C in an oven (Choi et al., 2002)

Determination of mean diameter

The prepared beads (n > 100) were lined and the diameter was determined by Vernier caliper. Measurements for each sample were performed in triplicate. Mean diameter and its standard deviations were recorded (Patel, 2006).

Determination of drug loading and drug entrapment efficiency

The prepared beads were evaluated for percent Drug Loading (DL) and drug Entrapment Efficiency (EE). An accurately weighed sample of beads was crushed in a mortar and dissolved in pH 1.2 HCl solution (100 mL). This mixture was then centrifuged at 4,200 rpm for 30 min and filtered using 0.22 μ m microporous membrane before analysis with a UV spectrophotometer at 346 nm. The percent DL and EE were calculated (Kulkarni, 1999).

Ethical rules

Since in the present investigation there was no human or animals involved, there was no ethical rules to be considered.

RESULTS AND DISCUSSION

The glycyrrhizin alginate beads for stomach specific delivery was prepared and evaluated. The prepared glycyrrhizin alginate was evaluated for mean diameter, DL and EE. The mean diameter was found to be 1.16 ± 0.07

mm, DL was found to be 88.78% and EE was found to be 96.92%. The evaluation results are presented in table 1. In this study, the floating alginate beads of glycyrrhizin were formulated and the different parameters including diameter, drug loading and drug entrapment were evaluated. These parameters are applicable not only to the sustained release of drugs, but also to the targeting of the gastric mucosa (Madhavi et al., 2009). The formulation exhibited the optimum sustained release of glycyrrhizin, with excellent floating characteristics. Therefore, the alginate beads containing glycyrrhizin appear to be promising for drug delivery to the gastric mucosa in the therapy of *H. pylori* infection (Choi et al., 2002).

Table 1. Evaluation of parameters of glycyrrhizin alginate

 beads for stomach-specific delivery

CA: Glycyrrhizin	1:1
Mean Diameter (mm)	1.16 ± 0.07
Drug Loading (%)	88.78
Entrapped Efficiency (%)	96.92



Figure 1. Glycyrrhizin alginate beads for stomach-specific delivery

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Competing interests

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Authors' contribution

MR worked on the formulation aspect of the topic. SS worked on the design of formulation and evaluation aspects of the selected topic. SD worked on the selection of plant material and its extract to work for the selected topic. RD worked on the corrective measures adopted in formulation and evaluation parameters of the selected topic. All authors have read and approved the final manuscript

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