Research Article

Formulation and Evaluation of Floating Beads of Myrrh for Use in Ulcers

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ABSTRACT

Ulcers are lesions that are developed on the mucosal lining of stomach or small intestine causing gastric and duodenal ulcers. Antacids, histamine(H2) blockers, proton pump inhibitors (PPIs) and antibiotics are used for management and treatment of this condition. Long term use of PPI's is associated with gastric and renal impairments. Time tested herbal drugs provide a better alternative to antacids and PPIs in long term management of ulcers and other GI disorders. Liquorice, Brahmi, guggul, guava, myrrh, etc., have demonstrated usefulness in treatment and management of ulcers. Many research activities attempted in developing various herbal formulations of liquorice, curcuma, brahmi and others. Present work aims in the development of alginate beads of myrrh as a novel drug delivery system for sustained release. Alcoholic extract of myrrh was prepared by maceration method. The prepared extract was loaded in to floating beads by using sodium alginate and a copolymer of chitosan, sterculia or gelatin. All the formulated beads were evaluated for bead diameter, swelling percentage, buoyancy, entrapment efficiency, and in vitro drug release. The evaluation data obtained indicated F4 as the better candidate with 85.5%, 98%, and 90.08% entrapment efficiency, buoyancy, and % cumulative drug release in 10 hrs respectively. Animal studies need to be carried out in order to demonstrate therapeutic usefulness of myrrh beads for use in ulcer treatment.

Keywords: *Commiphora molmol*, myrrh, floating beads, buoyancy, sodium alginate, chitosan, sterculia, gelatin.

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INTRODUCTION

Ulcers are lesions that develop in the mouth, on arteries or veins and on the mucosal lining of the GIT. Ulcers of the GIT, the peptic ulcers are either gastric or duodenal ulcers depending on their location in the stomach or the small intestine[1]. The underlying causes for occurrence of ulcers include an infection with *Helicobacter pylori*, digestive disorders, eating junk food and wrong combination of foods and other lifestyle problems and prolonged stress etc. Treatment includes use of antacids (aluminium hydroxide, magnesium hydroxide) which act by neutralizing the excess acid in the stomach, antibiotics (amoxicillin, clarithromycin, metronidazole) for infection and proton pump inhibitors (omeprazole, pantoprazole, esomeprazole) that decrease acid release in the stomach and H2 blockers viz., ranitidine, famotidine, cimetidine etc[2]. Normally ulcers require long term treatment and are prone to recurrence. Therefore, long term treatment with PPI's and antacids might cause adverse effects such as difficult breathing, stomach pain, GI discomfort, kidney impairment and heart failure[3]. Complementary treatment with time tested herbal drugs may be a better alternative for long term management of ulcers[4]. Literature review indicated liquorice (*Glycyrrhiza gabra* is a better drug of choice[5]. Other herbs like *Commiphora molmol*[6], *Moringa oliefera*[7], *Psidium guajava*[8], *Aloe vera*[9], Piper nigrum[10], *Commiphora wightii*[11], *Plantago ovata*[12], *Curcuma longa*[13] are found to be useful as an alternative in ulcer management. Researchers have successfully developed formulations of liquorice such as tablets, mouth washes and gels for use in mouth ulcers, floating beads and floating tablets for peptic ulcers, tablets of brahmi, aloe vera, floating tablets of liquorice and isabgol, curcumin solid dispersion and floating tablets, piperine microspheres and floating beads[14-18] etc.

Myrrh is a gum resin extracted from the thorny tree of genus *Commiphora*. Traditionally the drug is useful as an antiseptic, local stimulant, used in incense and perfume making and is an astringent. Conventional topical formulations for application on wounds, gargles, rinses and mouth washes for inflammatory conditions of the mouth and throat are available. Researchers have demonstrated various pharmacological activities like anti-ulcer, anti-inflammatory, antibiotic through research works[19,20,21]. The anti-ulcer effect of myrrh extract was assessed in rats and the results demonstrated significant activity[22].

An attempt has been made to formulate sustained release dosage form of myrrh. Floating drug delivery system is the suitable for drugs which have narrow absorption window[23,24]. This approach if adopted, will reduce frequency of dosing, cause controlled or sustained release of drug and thereby increases therapeutic efficacy[25]. Therefore, the objective of this research work was to develop and evaluate floating beads of myrrh for use in ulcers.

MATERIALS AND METHODS

Materials

Myrrh, and Sterculia gum were purchased from Shyam sundar ayurvedics, Begumbazar, Hyderabad. Sodium alginate was obtained from Loba chemie Pvt Ltd., Mumbai. Gelatin, Chitosan, Calcium chloride from Ranbaxy fine chemicals Ltd., New Delhi. Calcium carbonate, sodium bicarbonate, Acetic acid were obtained from Sarabhai M chemicals, Baroda. All chemicals used were of analytical grade.

Preparation of myrrh extract

Commiphora molmol (myrrh) was extracted by maceration using 90% ethanol followed by refrigeration for three days, concentrated and dried in desiccator.

Analytical method

Absorption maxima of myrrh extract was determined by scanning 10µg/ml solution of myrrh in 0.1N HCl (2ml methanol was used to increase solubility) between 200-400nm using Double beam UV-visible spectrophotometer. Absorption maxima was found to be 220nm.

Standard graph was prepared using dilutions of 150, 200, 250, 300, 350, 400 µg/ml and absorbance measured at 220nm using 0.1N HCl as blank and linear equation Y=0.0022x + 0.05265 and R = 0.9935 were obtained.

Preparation of myrrh floating alginate beads

The extracted myrrh was formulated as floating beads using ionotropic gelation method. The drug, polymers and gas forming agent were added to distilled water and stirred to get a homogenous solution. The mixture was withdrawn in to 50ml syringe (needle size of 30mm length, 0.9mm width) and added drop wise into a 10% acetic acid solution containing 3% calcium chloride. The beads produced were washed with water and dried for 24 hours and % yield calculated. Table 1 indicates the composition of the formulated beads.

Table 1: Composition of myrrh floating beads

Formulation code	Myrrh (mg)	Sodium alginate (g)	Sterculia (mg)	Gelatin (mg)	chitosan (mg)	Calcium carbonate (mg)
F1	100	1.5	100	-	-	90
F2	100	1.5	200	-	-	90
F3	100	1.5	-	200	-	90
F4	100	1.5	-	-	200	90

Evaluation[26]

- All evaluation tests were carried out in triplicate

% Yield

The percentage yield of floating alginate beads was calculated using formula.

$$\text{Yield percentage} = \frac{\text{weight of the product obtained}}{\text{drug and polymers total weight}} \times 100$$

Bead diameter

Bead size measurement was carried out by using vernier calipers. Fifteen beads were taken and the size was measured and average diameter noted.

% Swelling

50 beads were taken and immersed in distilled water maintained at 37^{0}C for 15mins. They were then removed and weighed immediately.

$$\%\ \text{swelling} = \frac{[\text{swollen beads weight} - \text{dried beads weight}]}{\text{dried beads weight}} \times 100$$

FTIR studies

To observe the modification after the cross linking, the FTIR spectra of the myrrh extract and the myrrh floating beads were taken on the KBr pellets on Nicolet 5700 FTIR.

Drug entrapment efficiency

100 mg of beads were triturated and transferred to tubes containing 2 ml of methanol and 0.1N HCl. This mixture was centrifuged for 15min and the supernatant was made up to volume in a 10ml volumetric flask using 0.1N HCl. Absorbance was measured at 220nm. The percentage drug entrapment was calculated.

In-vitro buoyancy

In- vitro buoyancy studies were carried out using USP type 2 (rotating paddle) dissolution test apparatus. 100 mg of beads were added to dissolution medium containing 900 ml of 0.1N HCl. The temperature was maintained at 37^{0}C (±0.5) and paddle rotating speed was adjusted to 50 rpm. The floating beads were recovered from the dissolution medium after 10hrs. The buoyancy percentage was calculated using the formula:

$$\% \text{ buoyancy} = \frac{\text{Number of beads floating}}{\text{Total number of beads}} \times 100$$

In-vitro drug release

In-vitro drug release studies were carried out using USP type 2 (rotating paddle) dissolution apparatus. 100 mg of beads were filled into capsules and placed in the dissolution medium containing 900 ml of 0.1N HCl, maintained at 37^{0}C (±0.5) and paddle rotating speed was adjusted to 50 rpm. Aliquot of 5ml was withdrawn at 1hour intervals for 10 hrs and the sink condition was maintained by replacing with equal volume of fresh dissolution medium. The samples were diluted with distilled water and were analyzed spectrophotometrically at 220nm.

RESULTS AND DISCUSSION

Percentage yield, diameter and percentage swelling of the prepared beads are presented in table 2.

Table 2: Indicative of %yield, diameter and %swelling of prepared beads.

Formulation code	Yield (g)	Bead diameter (mm)	Swelling (%)
F1	1.52	0.56±0.31	266±51
F2	1.68	0.43±0.66	278±12
F3	1.80	0.62±0.45	300±35
F4	1.85	0.53±0.72	330±28

Percentage yield and swelling is found to be higher in F3 and F4. F3 and F4 alginate beads were formulated using gelatin and chitosan as copolymers respectively. F2 and F1 contains sterculia as the copolymer. Chitosan is a natural cationic copolymer. Higher swellability of F4 formulation may be due to the hard coat on the outer surface provided by chitosan which attributes mechanical strength to withstand the swelling.

FTIR studies of the pure myrrh extract and myrrh floating beads is presented in fig., 1 and 2 respectively. Through FTIR spectrums it is interpreted that there is no chemical interaction with excipients as characteristic absorbance peaks of myrrh were retained.

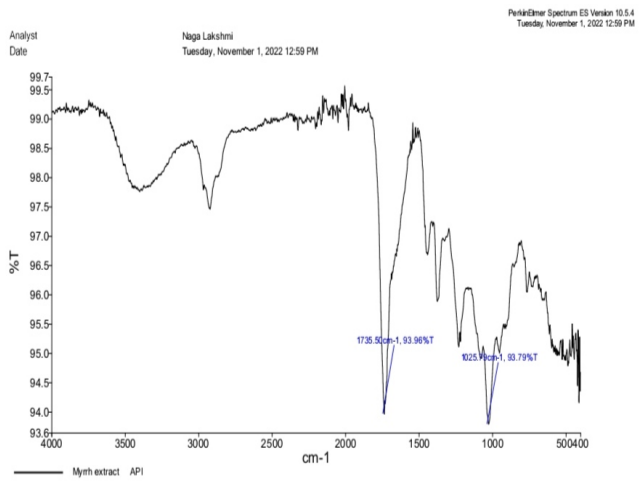

Figure 1: FTIR of the myrrh extract.

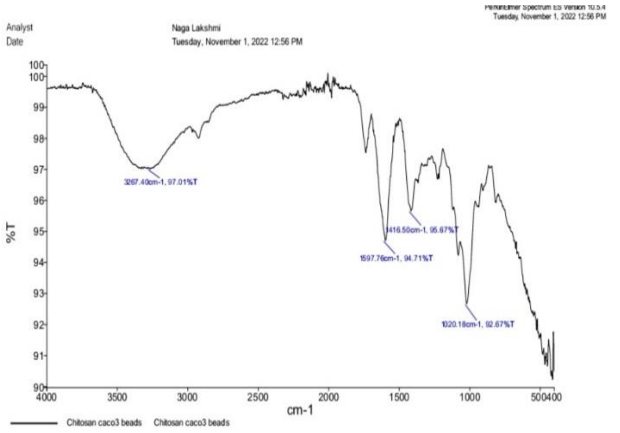

Figure 2: FTIR of the myrrh floating beads of chitosan.

Drug entrapment, percentage buoyancy and drug release percentages are presented in table 3.

Table 3: Data of drug entrapment and invitro buoyancy of prepared beads.

Formulation code	% drug entrapment	*% in-vitro* buoyancy	*% in-vitro* drug release in 10 hrs.
F1	80.2	93	72.77
F2	81.2	95	81.25
F3	84.6	96	86.73
F4	85.5	98	90.08

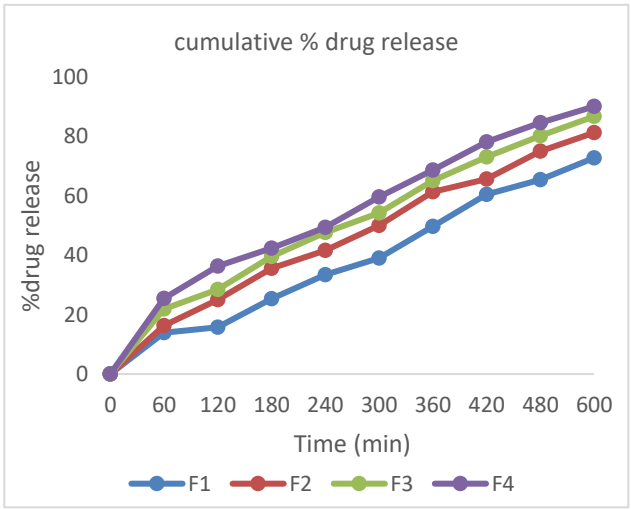

Figure 3: Graphical representation of cumulative % drug release plotted against the time (min) and the % drug release

The entrapment efficiency was higher in F4 and is 85.5%. It contains chitosan as a copolymer. The % buoyancy was higher in F3 and F4. F4 has highest buoyancy and determined to be 98%. The difference in the buoyancies observed in various formulations may be due to the varying molecular properties of the copolymers used. Chitosan has similar density as that of the dissolution media. Sterculia and gelatin possess higher densities which explains the better buoyancy property of F4. The % cumulative *in vitro* drug release was higher in F4 and is found to be 90.08% in

10 hours and a graphical representation is presented in fig.3. Drug release depends on the molecular weight and drug polymer ratio and therefore favors chitosan as a better copolymer for formulation of beads.

CONCLUSION

Alginate beads of myrrh were formulated using copolymers such as chitosan, sterculia, or gelatin. Calcium carbonate was used in the formulation for buoyancy and calcium chloride as a source of divalent cation for ionic gelation. The formulated beads were evaluated for bead diameter, swelling percentage, in-vitro buoyancy, entrapment efficiency, and % drug release. F4 emerged out to be a better formulation with entrapment efficiency, buoyancy, and % cumulative *in vitro* drug release of 85.5%, 98%, and 90.08% respectively. The molecular attributes of chitosan are responsible for better buoyancy and higher drug release in 10 hrs. Therefore, floating beads of myrrh appears to be a promising formulation for use in ulcers. However, further studies need to be conducted for optimisation and study in animals to demonstrate the formulation efficacy in treatment of ulcers. Safety studies are needed to demonstrate its suitability as an alternative drug for use in long term management of ulcers.

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AUTHORS CONTRIBUTION

All the authors have contributed in designing and successful execution of this research project.

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