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DESIGN, DEVELOPMENT AND EVALUATION OF POLYHERBAL FLOATING FORMULATIONS FOR GASTRIC ULCER

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ABSTRACT

The present study aimed at the design, development and evaluation of polyherbal floating tablets for reducing gastric ulcer. Plants have always been an experimental source of drugs and many of the currently available drugs have been derived directly or indirectly from them. Following all data and knowledge floating tablets for gastric ulcers was prepared using Emblica officinalis (Gaertn), Glycyrrhiza glabra, Asparagus racemosus, and Sankha bhashma with sodium bicarbonate as floating agent. Development of floating herbal tablets for reducing gastric ulcers with no side effects and improve patient compliance. Floating tablet was prepared by direct compression technique. All extracts of three plant were dissolved in Isopropyl alcohol and this solution was mixed with other polymer,and Sodium bicarbonate by gentle mixing in mortar pastel in last Magnesium stearate and talk were added and mixed together. These blends was subjected to direct compression process for formulation of tablet. In conclusion, our data confirm that the selected formulation of poly herbal floating tablets has acceptable physicochemical features and may be considered as herbal medication for reducing gastric ulcers. Development of floating tablets can be advantageous, that can provide prolong gastric retention and increase efficacy of the dosage form.

KEY WORDS

Polyherbal, floating formulations, gastric ulcers.

INTRODUCTION

Ulcer results from a disrupted balance between formation of caustic gastric acid and maintenance of the protective mucosal barrier that depends on secretion of bicarbonate, prostaglandins, and mucosal growth factors. In general, gastritis and gastric ulcers are associated with insufficient mucosal protection, whereas duodenal ulcers are associated with excess acid secretion[1]. Helicobacter pylori infection may be responsible for up to 85% of gastric ulcers, worldwide. The bacteria disrupt the mucosal protective barrier, making it more vulnerable to acid damage and inciting an

inflammatory response. In the United States, *H pylori* is a less prevalent cause of ulcers; nonsteroidal anti-inflammatory drugs (NSAIDs) are the most common cause of gastric ulcers in the United States[2]. Other etiologies include irritants such as aspirin and steroids; severe physiologic stress, including burns, sepsis, trauma, and major

surgery; local trauma, such as nasogastric tube placement; and hypersensitivity and autoimmune reactions[3]. Various allopathic drugs like antibiotic, Proton pump inhibitors, Histamine H2-receptor antagonists, etc., are use for the treatment for ulcer.

In the most extents, these drugs have been helpful in the prevention of ulcer. But the involvement of side effects is major drawback of these drugs. As a result of problems in ulcer, there is high prevalence of usage of alternative traditional medicines for the treatment of ulcer[4]. Ayurveda offers a unique insight into comprehensive approach to ulcer management. Many medicinal plant species have been used ethnologically and traditionally to treat the symptoms

of ulcer worldwide. Literature review revealed the *Emblica officinalis (Gaertn)* decreases acid and pepsin secretion and increases mucin, *Glycyrrhiza glabra* increase the concentration of prostaglandins in the digestive system that promote mucus secretion in stomach stomach due to presence of flavonoid which, *Asparagus racemosus* has no effect on acid and pepsin, but increases mucin secretion, Sankha bhashma neutralise the acid in stomach by reaction between acid present in the stomach and calcium carbonate present in the sankha bhashma [5-8].

Therefore, in the present study the hydroalcoholic extract of these three ingredients (*Emblica officinalis Gaertn, Glycyrrhiza glabra, Asparagus racemosus)* and sankha bhashma were combined to gether and perform animal experiment for evaluation of anti-ulcer activity.here are not availability of such kind of anti-ulcer formulation in the market. Preparation of floating tablet which contain above four components will fulfill the market requirement for efficiently treat gastric ulcer problem acute or chronic. This herbal sustains release floating tablet formulation decrease dose, duration of dose and improve patient compliance [9-10].

MATERIAL & METHODS

Material

Procurement of plant raw materials

Plant raw materials *Glycyrrhiza glabra* (stolon), *Asparagus racemosus* (root), *Emblica officinalis* (fruit) part and mineral raw material Sankha bhashma were procured from local marcket in Warangal,Telengana, India. Raw materials were authentify by the reference books-WHO guideline, Ayurvedic pharmacopeia of India, Indian herbal pharmacopeia etc

Determination of foreign matter of raw materials [11]

Plant raw materials were weighed as mentioned below and spreaded it in a thin layer and sorted out of the foreign matter by visual inspection, using a magnifying lens (6x or 10x). The portions of these sorted foreign matters were weighed and value in the bulk was calculated per 100 gm of air-dried plant material.

Plant part	Sample size
Glycyrrhiza glabra(Stolon)	500 gm
Asparagus racemosus (root)	500 gm
Emblica officinalis fruit.	250 gm.

Microscopical evaluation[12]

Coarse powder of individual plant raw materials was boiled with chloral hydrate for 5 minutes separately. Materials were mounted on glass slide then stained with phloroglucinol followed by concentrated HCL. After staining slide was wash with distilled water. Glycerin was added on slide and materials were covered with cover slip. Microscopic features were observed under low power (10 x) and high power (40 x).

Morphological evaluation of plant raw materials

Morphological evaluation of Glycyrrhiza glabra(stolon), Asparagus racemosus (root), Emblica officinalis (fruit) part and Sankha bhashma were carried out by determining size, shape, colour, order and taste of raw materials.

Preparation of powder from plant raw materials[13]

Plant materials of Liquorice stolon, Shatavari root and Amla fruit parts were powdered separately (60 #) using mechanical pulverizer. Powdered plant materials were stored in dry and cool place

FORMULATION AND EVALUATION OF HERBAL FLOATING TABLET:

Preparation of Plant extract

Hydroalcoholic extract [ethanol: water (70:30)] of all three plants parts powder were extract by soxhlet apparatus at the temperature 100 C till sufficient extraction was done. The liquid extract was concentrated at reduce temperature (50± 5C) on Rotary evaporator (Equitron rotevar, Medica instrument mfg. co.). Then semisolid extract was dried in dessicator. This dried extract and Shankha bhashma equal proportion was used for preparation for floating tablets.

Preformulation study:

Bulk and Tap density[14]

Both bulk density (BD) and tapped density (TD) was determined as per USP. A quantity of 10 gm of powder blend was introduced in to 25 ml measuringcylinder. After that the initial volume was

noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. BD and TD were calculated using the following equations.

BD= Weight of the powder blend/Untapped Volume of the packing

TD=Weight of the powder blend/Tapped Volume of the packing

Carr's Index (Compressibility index)[15]

The Compressibility Index of the powder blendwas determined by Carr'scompressibility index. The formula for Carr's Index is as below:

Carr's Index (%) = [(TD-BD) x100]/BD

Housner's ratio

The formula for Housner's ratio is as below:

Housner's ratio = Tape density/Bulk density

Angle of repose[16]

The angle of repose of powder blend was determined by the funnel method. Accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured, and angle of repose was calculated using the following equation.

Tan Θ= h/r,

Where, h and r are the height and radius of the powder cone.

Preparation of floating tablets

Floating tablet was prepared by direct compression technique. All the powders were passed through80 mesh sieve. Required quantity of drug, HPMC K 100m as polymer, Carbopol 934 as polymer, sodium bicarbonate as floating agent, DCP in each formulation were mixed thoroughly. Talc and magnesium stearate were finally added as glidant and lubricant respectively. The blend was compressed (12 mm diameter, flat punches) using multi-punch tablet compression machine. Each tablet of all three batches contains 75mg of Emblica officinalis fruit extract (75mg of Emblica officinalis extract equivalent to 19.45mg of gallic acid),75mg of Glycyrrhiza glabra stolon extract (75mg of Glycyrrhiza glabra extract equivalent to 4.81mg of glycyrrhizinic acid), 75 mg of Asparagus recemosus root extract and 25mg shankha bhashmaas drug. All extracts of three plant were dissolved in Isopropyl alcohol and this solution was mixed with other polymer, DCP and Sodium bicarbonate by gentle mixing in mortar pastel in last Magnesium stearate and talk were added and mixed together. These blends was subjected to direct compression process for formulation of tablet.

Table 1: Formulation of floating tablets with different amount of polymer

Ingredients (mg)	F1	F2	F3
hydroalcoholic extract of Liquorice stolon	75	75	75
hydroalcoholic extract of Shatavari root	75	75	75
Hydroalcoholic extract of Amla fruit	75	75	75
Shankha bhashma	25	25	25
HPMC K100M	57.5 (10%	86.25 (15%)	28.75 (5%)
Carbopol 934	57.5 (10%)	28.75 (5%	86.25 (15%)
DCP	80.70	80.70	80.70
NaHCO3	115 (20%)	115 (20%)	115 (20%)
Magnesium Stearate	5.70	5.70	5.70
Talc	8.60	8.60	8.60
Total weight of tablet in mg	575	575	575

Evaluation of floating tablets:

Floating behavior of the tablets (In Vitro buoyancy studies)

The time that tablets took to emerge on the water surface (floating lag time) and the time the tablets constantly float on the water surface (duration of floating) were evaluated in 250 ml beaker.

Determination of swelling index[17]

The swelling index of tablets was determined in 0.1 N HCl (pH 1.2) at room temperature. The swollen

weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

Swelling index = $(W_t – W_0) \times 100/W_0$

Where,

W_0 is the initial weight of tablet, and W_t is the weight of the tablet at time t

Weight variation test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method.

Hardness

The hardness of five tablets was determined using the Pfizer hardness tester and the average values were calculated.

Thickness

The thickness of the tables was determined by using vernier calipers. Five tablets were used, and average values were calculated.

Friability

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W0) or a sample of 10 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below.

% Friability = $(W_0 – W)/W_0 \times 100$

RESULTS AND DISCUSSION

This chapter includes various results obtained from the investigations performed. An attempt has also been made to discuss these results in order to provide convincing reasons for the studies performed

STANDARDIZATION OF RAWMATERIALS

Procurement of plant raw materials

Plant raw materials were procured, and it is authentified by morphological and microscopical identification and results were match with authentic reference books

Determination of foreign matter of raw materials

Table 2: Foreign matter of raw materials

Sr. No	Drug materials	Foreign matter (%)	Inference
1	Liquorice	0.35 ± 0.1	Within limit
2	Amla	0.79 ± 0.02	Within limit

Morphological evaluation of plant raw materials:

Liquorice

Shape: Cylindrical,

Size: 10 to 15 cm long, 2 cm wide,

Color: Yellowish –brown or dark brown externally, and yellowish internally,

Odor: Faint and characteristic,

Taste: Sweet.

Shatavari

Shape: Finger like

Size: About 1m

Color: Creamish white

Odor: Indistinct

Taste: Sweet

Amla

Shape: Depressed

Size: 2 cm long, 1 cm wide

Color: Brown

Odor: Characteristic

Taste: Astringent

Sankha bhashma

Sankha bhashma is white in color with very fine powder characteristic.

Microscopical evaluation

Liquorice

Powder microscopy of Liquoriceshowed presence of xylem vessel, oval and globular shape starch grain and prismatic calcium oxalate crystalsVessel Starch grain Calcium oxalatecrystal

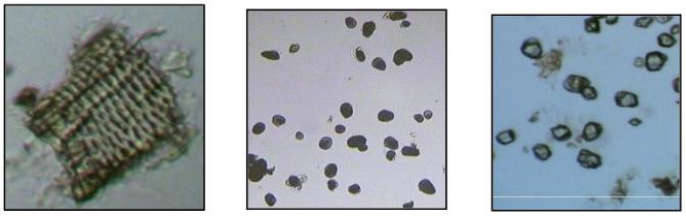

Figure1: Powder microscopy of Liquoric

Shatavari

Powder microscopy of Shatavari root shows presence of pitted vessel, starch grain.

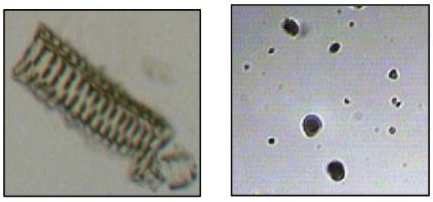

Figure2: Powder microscopy of Shatavari

Amla

Powder microscopy of Amla showed presence of pitted vessel attached with paranchyma, stone cells and epidermal cells.

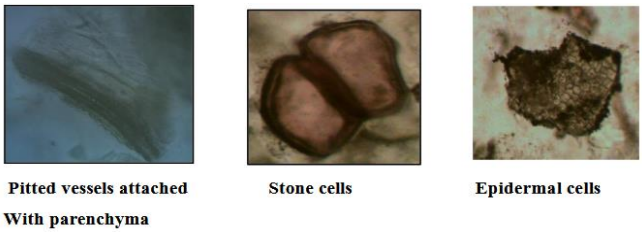

Figure3: Powder microscopy of Amla

Determination of moisture content of raw materials by loss on drying method.

Table3: Moisture content of raw materials

Sr. No	Drug materials	Loss on drying (%)
1	Liquorice	6.7 ± 0.03
2	Shatavari	7.8 ± 0.01
3	Amla	4.0 ± 0.05

Values are in *Mean ± SD (n=3)

Preformulation study:

Table4: Evaluation of the ready to compress material to check flow properties

Batch	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose (Φ)	Carr's index (%)	Hausner' ratio
F1	**0.44±0.12**	**0.57±0.3**	**21±0.3**	**14±0.2**	**1.01±0.2**
F2	**0.47±0.156**	**0.52±0.1**	**27±0.5**	**12±0.1**	**1.54±0.5**
F3	**0.46±0.23**	**0.51±0.23**	**25±0.25**	**13±0.2**	**1.52±0.2**

Values are in Mean ± SD (n=3)

The evaluation results of powder blends were found to be within range for each parameter. The results of angle of repose showed that the good flow ability. Hausner's ratio and carr's index of all three batches is good which indicates that all three batches powder granules have good compressibility.

Floating behavior of the tablets (In Vitro buoyancy studies)

Floating lag time and duration of floating of tablets are as shown in Table 4 Sodium bicarbonate was used as a gas-generating agent in order to float the tablet. The sodium bicarbonate induces CO2generation in the presence of dissolution medium (0.1 N HCl). The gas generated is trapped and protected within the gel formed by hydration of the polymer, thus decreasing the density of the tablet below 1 gm/mL, and the tablet becomes buoyant. Duration of floating for all batches was up to 12 hr.

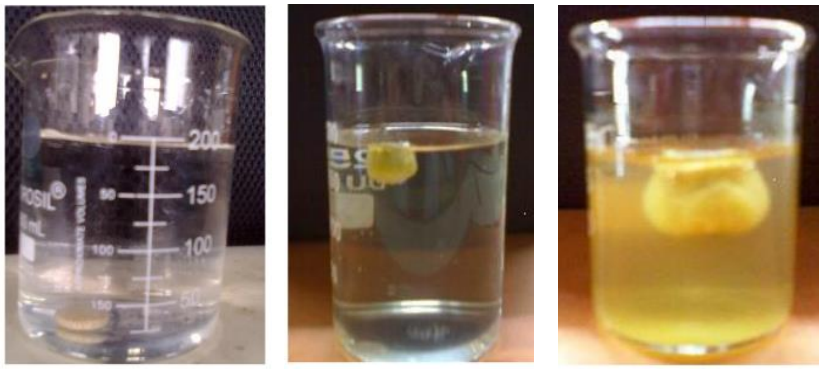

Figure 4: In vitro buoyancy study

Swelling index

Swelling index of all floating matrix tablets are as shown in Table 4. Concentration of HPMCK100M polymer increased, swelling index was increased.

Table 5: Evaluation parameter for batch F1-F3

Batch code	Floating lag time (min)	Duration of floating (hr)	Swelling index
F1	2.5	12	2.13
F2	1.9	12	1.89
F3	1.8	12	2.32

Weight variation

Weight variation data of the prepared tablets indicated no significant difference in the weight of individual tablet from the average value. (Table6)

Hardness

Hardness of the prepared tablets was observed within the range of 3.9 to 4.3 kg/cm2. (Table6)

Thickness

Thickness of floating matrix tablets was found in the range of between 3.2-3.6 mm. (Table6)

Friability

Friability of tablets was within range. (Table6)

Table 6: Evaluation of physical parameters for batch F1-F3

Batch code	Weight Variation [a](mg)	Hardness* (kg/cm^2)	Thickness*(mm)	Friability [b] (%)
F1	575 ± 0.875	4.3 ± 0.1	3.6 ± 0.1	0.7%
F2	575 ± 0.476	4.1 ± 0.1	3.4 ± 0.17	06%
F3	575 ± 0.934	3.9 ± 0.43	3.2 ± 0.17	08%

All Values are in [a] Mean ± SD (n=20), *Mean ± SD (n=5), [b] Mean ± SD (n=10)

CONCLUSION

Present investigation was design, development and evaluation of polyherbal formulation (floating tablet) of Glycyrrhiza glabra Stolon extract, Asparagus racemosus root extract, Emblica officinalisfruit extract and shankha bhashma. This all are traditional ayurvedik herbal drugs. The popularity of this drug is related to several beneficial properties, including, proven efficacy in controlling gastric and abdominal disorders. Standardization of this all drugs was done using pharmacognostic, physicochemical parameters, preliminary photochemical investigation, quantification of active constituents, and pharmacological investigation.Hydro alcoholic extract of stolon part of Glycyrrhiza glabra, Asparagus racemosus and fruit part of Emblica officinalis and Shankha bhashma showed good in vivo anti-ulcer activity by decreases acid and pepsin secretion and increases mucin, Increase the concentration of prostaglandins in the digestive system that promote mucus secretion from the stomach. Developed floating tablet were prepared by using hydroalcoholic extract of specific part of plant and Shankha bhashma. Floating tablets was prepared by direct compression method using HPMC K100M and Carbopol as polymer, Sodium bicarbonate as a gas generating agent. The floating tablet remains up to12 hr. By selecting a suitable composition of polymer, the desire drug dissolution profile can be achieved. Development of sustained release formulation of can be advantageous, that can provide prolong gastric retention and increase efficacy of the dosage form.

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