Formulation and Evaluation of Herbal Floating Tablet

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Abstract **- The present study aimed at the formulation 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 annona squamosa and annona reticulata 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. Extracts of two 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 were 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.**

Index Terms **- Polyherbal, floating tablet, gastric ulcers.**

INTRODUCTION

Peptic ulcer disease represents a serious medical problem. Approximately 500,000 new cases are reported each year, with 5 million people affected in the United States alone. Interestingly, those at the highest risk of contracting peptic ulcer disease are those generations born around the middle of the 20th century. Ulcer disease has become a disease predominantly affecting the older population, with the peak incidence occurring between 55 and 65 years of age. In men, duodenal ulcers were more common than gastric ulcers; in women, the converse was found to be true. Thirty-five percent of patients diagnosed with gastric ulcers will suffer serious complications. Although mortality rates from peptic ulcer disease are low, the high prevalence and the resulting pain, suffering, and expense are very costly. Ulcers can develop in the esophagus, stomach or duodenum, at the margin of a gastroenterostomy, in the jejunum, in Zollinger Ellison syndrome, and in association with a Meckel's diverticulum containing ectopic gastric mucosa. Peptic ulcer disease is one of several disorders of the upper gastrointestinal tract that is caused, at least partially, by gastric acid. Patients with peptic ulcer disease may present with a range of symptoms, from mild abdominal discomfort to catastrophic perforation and bleeding.[1]

Literature review revealed the Antiulcer activity of A. reticulata leaves may be due to cytoprotective, antisecretory and antioxidant potential of phytoconstituents present in the extract.[2]Annona squamosa twigs contain active constituents as (+)-O-methylarmepavine, N-methylcorydaldine and isocorydine have antisecretory property which protect from peptic ulcer. It reduces gastric acidity, pepsin and gastrin level and inhibits H+-k+ ATPase pump. In the same manner, leaf extract was shown to be protective against aspirin plus pyloric ligation induced ulcer in mice.[3] Sankha bhashma neutralise the acid in stomach by reaction between acid present in the stomach and calcium carbonate present in the sankha bhashma.[4-7]

Therefore, in the present study the hydroalcoholic extract of these two ingredients (Annona squamosal, Annona reticulata) and sankha bhashma were combined together 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 fulfil 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.[8-9]

MATERIAL & METHODS

Material

Procurement of plant raw materials

Plant raw materials Annona squamosal leaves, Annona reticulata leaves part and mineral raw material Sankha bhashma were procured from local market in Latur, Maharashtra, 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 [10]

Plant raw materials were weighed as mentioned below and spread 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.

Sr.no	Plant part	Sample size
1	Annona squamosa leaves	500 gm
2	Annona reticulata leaves	500 gm

Microscopical evaluation[11]

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. Glycerine 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 annona squamosa, annona reticulata leaves and Sankha bhashma were carried out by determining size, shape, colour, order, and taste of raw materials.

Preparation of powder from plant raw materials[12]

Dried leaves of both the 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 both the 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[13]

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 measuring cylinder. 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)[14]

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[15]

The angle of repose of powder blend was determined by the funnel method. Accurately weight powder blend was 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.

$\tan \Theta = h/r$,

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 annona squamosa leaf extract,75mg of annona reticulata leaf extract and 25mg shankha bhashma as drug. Both the extracts 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 were 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 annona squamosa leaves	75	75	75
hydroalcoholic extract of annona reticulata leaves	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[16]

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 = $(Wt–W_0) \times 100/W_0$

Where,

W_0 is the initial weight of tablet, and Wt 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.

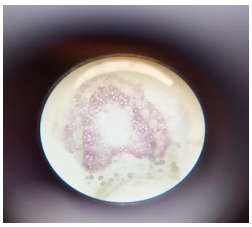
Thickness

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 (W_0) 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 = $(W_0XW)/W_0$ X100



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.

Determination of foreign matter of raw materials

Sr. No	Drug materials	Foreign matter (%)
1	annona squamosal	0.27 ±0.2
2	Annona reticulata	0.35±0.4

Morphological evaluation

Table no.3 morphology of A.squamosa and A. reticulata leaf.

Characters	*A.squamosa* leaf	*A.reticulata* leaf
Size	10-15 cm long and 3-5 cm wide	10-22 cm long,4-7 cm width
Shape	Alternate, Bilateral, Petiolate, Ovate – lanceolate	Alternate, Bilateral, Petiolate, Oblong-lanceolate,
Venation	Reticulate	Reticulate
Apex	Obtuse	Acute
Base	Asymmetric	Asymmetric
Margin	Simple, Empirical	Simple, Empirical
Colour	Dark Green above Light Green below	Light Green both the surface
Odour	Aromatic	Unpleasant
Taste	Bitter	Bitter, Mucilaginous

MICROSCOPICAL EVALUATION

T.S. of leaf *A.squamosa*

Transverse section through midrib shows the upper and lower single layered compactly arranged barrel shaped epidermis with thick cuticle and rarely simple trichomeson lower surfaces. Lamina upper 1-2 layered palisade parenchyma and lowers 5-6 layers of spongy parenchyma throughout the lamina lysogenous cavities are very common, prismatic crystals, oil globules and tannin content material spread throughout the lamina and also even in midrib. Through midrib shows vascular bundle radially arranged. Vascular bundle surrounded by pericyclic fibres on both the side, rest of consist parenchyma cells.

T.S. of leaf *A.reticulata*

Transverse section through midrib shows the upper and lower single layered compactly arranged rectangular to barrel shaped epidermis with thick cuticle and multicellular trichomes filled with tannin on lower surfaces. Lamina upper single layered palisade parenchyma and lowers 6-7 layers of spongy parenchyma lysogenous cavities are very common, prismatic crystals, oil globules and tannin content material spread throughout the lamina and also even in midrib. Through midrib shows vascular bundle radially arranged. Vascular bundle surrounded by pericyclic fibres on both the side, rest of consist parenchyma cells, in center a group of stone cells in observed.

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

Table no 4: Moisture content of raw materials

Sr. No	Drug materials	Loss on drying (%)
1	Annona squamosa	13.06± 0.054
2	Annona reticulata	14.03 ± 0.057

Values are in *Mean ± SD (n=3)

Table no.5: Evaluation of the ready to compress material to check flow properties.

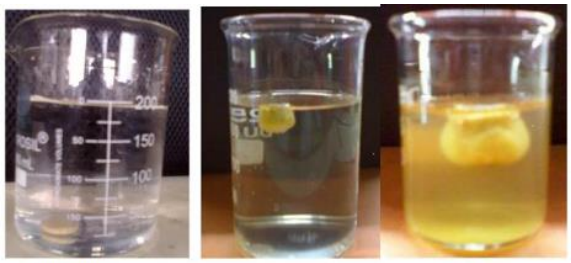
Batch	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose (Φ)	Carr's index (%)	Hausner' ratio
F1	0.44±0.12	0.57±0.3	21±0.3	14±0.2	1.01±0.2
F2	0.47±0.156	0.52±0.1	27±0.5	12±0.1	1.54±0.5
F3	0.46±0.23	0.51±0.23	25±0.25	13±0.2	1.52±0.2

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 behaviour of the tablets (In Vitro buoyancy studies)

Floating 7 lag time and duration of floating of tablets are as shown in Table 5 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



In vitro buoyancy study

Swelling index

Swelling index of all floating matrix tablets are as shown in Table 5. Concentration of HPMCK100M polymer increased, swelling index was increased.

Table no.6 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	1.8	12	2.32
F3	1.9	12	1.89

Weight variation

Weight variation data of the prepared tablets indicated no significant difference in the weight of individual tabletfrom the average value. (Table 7)

Hardness

Hardness of the prepared tablets was observed within the range of 3.9 to 4.3 kg/cm2. (Table 7)

Thickness

Thickness of floating matrix tablets was found in the range of between 3.2-3.6 mm. (Table 7)

Friability

Friability of tablets was within range. (Table 7)

Table 7: Evaluation of physical parameters for batch F1-F3

Batch code	Weight Variation a (mg)	Hardness*(kg/cm2)	Thickness*(mm)	Friability b (%)
F1	576 ± 0.875	4.4 ± 0.1	3.7 ± 0.1	0.8%
F2	576 ± 0.476	4.2 ± 0.1	3.5 ± 0.15	07%
F3	576± 0.934	3.8 ± 0.43	3.3± 0.16	09%

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

CONCLUSION

Present investigation was evaluation of polyherbal formulation (floating tablet) of annona squamosal leaves extract, annona reticulata leaves 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 drugs was done using pharmacognostic, physicochemical parameters, preliminary photochemical investigation, quantification of active constituents, and pharmacological investigation. Hydro alcoholic extract of both the leaves and Shankha bhashma showed good in vivo anti-ulcer activity A. reticulata leaves may be due to cytoprotective, antisecretory and antioxidant potential of phytoconstituents present in the extract. Annona squamosa reduces gastric acidity, pepsin and gastrin level and inhibits H+-k+ ATPase pump. by decreases acid and pepsin secretion and increases mucin. 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.

REFERENCES

[1] Kashikant Yadav*, Nagarathna P. K; Research On Evaluation Of Anti-Ulcer And Analgesic Activity Of Methanolic Extract Of Leaves Of Annona Reticulata Linn.World Journal of Pharmaceutical Research; 2019; Volume 8, Issue 6, 981-1004.

[2] Narwade DA, Aher AN; A Review On: Phytochemical and Pharmacological Study of Annona Squamosa; PharmaTutor; 2019; 7(1); 5-10; http://dx.doi.org/10.29161/PT.v7.i1.2019.5

[3] Annonyms, “Indian Herbal Pharmacopoeia”, Regional research Laboratory and Indian drug manufacturers Association, 1998, 1, pp.89.

[4] Quality Standards of Indian Medicinal Plants”,Published by Indian Council of Medicinal Research, New Delhi, 2003, vol 1, pp.30-31.

[5] Quality Standards of Indian Medicinal Plants”,Published by Indian Council of Medicinal Research, New Delhi, 2003, vol 8, pp.30-31.

[6] Anonymous, “Official method of analysis of the association of official analytical chemist”, 11th ed., AOAC international, Virginia, USA, 1970, pp.513.

[7] Malu S. P., Obochi G. O., Edem C. A. and Nyong B. E., “Effect of methods of extraction on phytochemical constituents and antibacterial

properties of tetracarpidium conophorum seeds", Global journal of pure and applied sciences, 2009, 15(3), pg. 373-376.

[8] Chia-chi chang Ming-hoa yang, Hwei-mei wen, "Estimation of total flavanoid content in Proolis by two colorimetric method", Journal of food and drug analysis ,2002, 10(3), pp.175-182.

[9] lalla J.K., hamrapurkar PD.palit P.G, "Preparation, characterization and analysis of Shankha Bhasma", Indian Drugs, 2002, 39(3), pp.152 –157.

[10] S.K. Gupta, "Drug screening method", Medical publication, New Delhi, pp.178.

[11] Anonyms, Indian Pharmacopoeia, Ministry of Health and Family Welfare, Govt. of India, The controller of publications, New Delhi, 1996, A-54.

[12] Lachman.L, Lieberman.A, Kinig.J.L., "The Theory and Practice of Industrial Pharmacy", Varghese Publishing House, Bombay, 4thedition, 1991, pp.67-68.

[13] PatelD. M., PatelN. M., PandyaN. N., JoganiP. D., "Formulation and optimization of carbamazepinefloating tablets", Indian journal of Pharmaceutical sciences, 2007, 69(6), pp.763-767

[14] Huang, L.L., Schwartz,J.B.,"Studies on drug release from a carbomer tabletmatrix"Drug Dev Ind Pharm.,1995; 21(13):1487–1501.

[15] Luessen, H.L., Verhoef,J.C., Borchard,G, "Mucoadhesive polymers in peroral peptide drug delivery"Pharm Res.,1995;12:1293–1298.