

A REVIEW ON METHODOLOGY OF FLOATING TABLET: *GLYCYRRHIZA GLABRA* EXTRACT

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Abstract: Nature has forever been an incredible hotspot for the majority restorative mixtures giving us numerous therapeutic plants and microorganisms delivering useful synthetic substances. In this way, the interest for restorative plants, beauty care products, and wellbeing items is generally on the ascent. One such plant from the Leguminosae family is licorice and the logical name is *Glycyrrhiza glabra* Linn. Floating tablets delay the gastric home season of medications, further develop bioavailability, and work with neighborhood drug conveyance to the stomach. With this goal, floating tablets containing watery concentrate of liquorice as medication was ready for the treatment of *Helicobacter pylori* and gastric ulcers. The watery concentrate of liquorice was normalized by HPTLC. Tablets containing HPMC K100M (hydrophilic polymer), liquorice remove, sodium bicarbonate (gas creating specialist), powder, and magnesium stearate were arranged utilizing direct pressure technique. The details were assessed for actual boundaries like breadth, thickness, hardness, friability, consistency of weight, drug content, lightness time, disintegration, and medication discharge component. The definitions were streamlined based on lightness time and in vitro drug discharge. This review also throws light on different techniques used in developing floating dosage forms by *Glycyrrhiza glabra* extract along with study of *Glycyrrhiza glabra* current and novel advancements.

Keywords: *Glycyrrhiza glabra*, Floating tablets, *Helicobacter pylori*, gastric ulcers, bioavailability

INTRODUCTION

Plants have been used by humans for food, shelter, and treatment since the dawn of time. People relied entirely on certain medicinal plants prior to the invention of modern medicine and the unprecedented advancement of science and technology. The biochemical study of plants and their natural compounds has received a lot of attention. Only 6% of the 250000-400000 plant species have been studied and biological activities were investigated¹. Several compounds, including triterpenoids, saponins, tannins, phenols, flavonoids, and alkaloids, have been shown to improve a variety of physiochemical processes. Since then, humans have developed a number of medicines using natural products derived from medicinal plants². Ayurvedic medicine, which originated in India, is still widely practised in many developing countries. It became popular due to its ease of availability, low cost of production, satisfying efficacy, and fewer adverse effects³.

One such plant is *Glycyrrhiza glabra*, which is widely used in Ayurvedic medicine. This medicinal plant can be found in parts of Asia and southern Europe. It is thought that licorice originated in Iraq⁴. However, several *Glycyrrhiza* species are now commercially cultivated in Italy, France, Spain, Greece, Turkey, Turkmenistan, Uzbekistan, Syria, Afghanistan, Azerbaijan, and China⁵. *Glycyrrhiza glabra* has ability to fixed up nitrogen atom or gas from atmosphere through the symbiosis of nitrogen fixing bacteria.

TAXONOMICAL CLASSIFICATION OF *GLYCYRRHIZA GLABRA*

Kingdom	Plantae
Division	Angiospermae
Class	Dicotyledoneae
Order	Rosales
Family	Leguminosae
Genus	<i>Glycyrrhiza</i>
Species	<i>glabra</i> Linn ⁶

Glycyrrhiza genus contains around of about 30 species for ex. *G. glabra*, *G. uralensis*, *G. aspera*, etc.

SIMILAR NAMES

- Jaishbomodhu (Bengali),
- Mulaithi (Hindi),
- Licorice (English),
- Aslussiesa (Arab)⁷

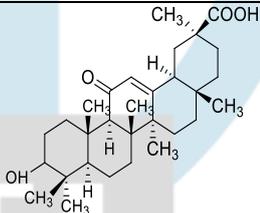
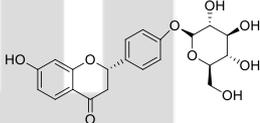
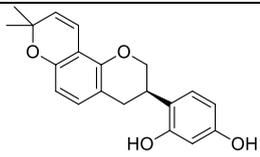
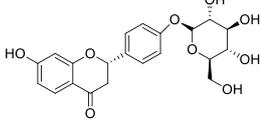
The *Glycyrrhiza* plant naturally inhabits nations like Bangladesh, India, China, Spain, Russia, Iran, Italy, and others where the soil is fertile, sandy, and has rivers or other sources of water nearby, making the area 70 accessible to enough water⁷. Typically, subtropical soils support the growth of the licorice shrub, a member of the pea family⁸. Its pinnate leaves range in height from 7 to 15 cm and have 9 to 17 leaflets each. The calyx is small and campanulate, while the flowers are thin and born in axillary spikes⁹.

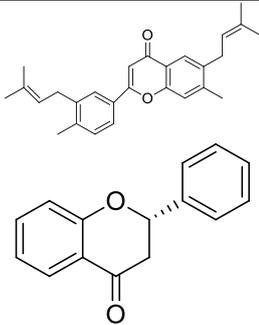
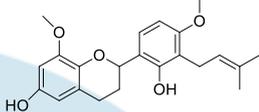
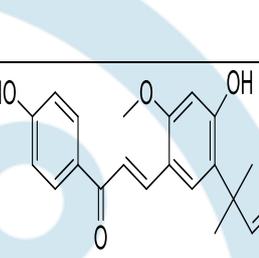
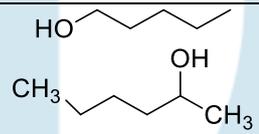
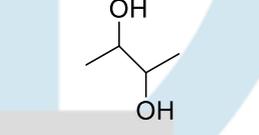
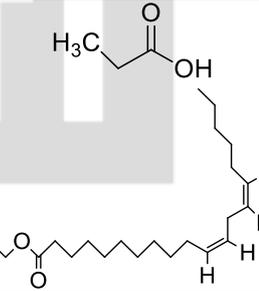
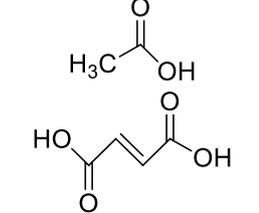
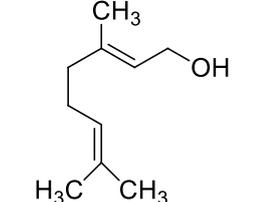
The flowers range in colour from purple to a light white blue and are around 1 cm long. The perennial herb itself has a maximum height of 2.5 cm. The fruit is a 1.5 cm long compressed legume that typically contains 3-5 brown reniform seeds. The root system has a fibrous, silky, and brightly coloured taproot¹⁰. The horizontal woody stolon arises from the taproot's three to five offshoot roots¹¹. The length of each subsidiary root is around 1.25 cm¹². The licorice root is thick and has numerous branches that are yellowish or pale yellow on the inside and reddish or lemon-colored on the outside¹³.

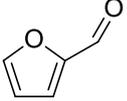
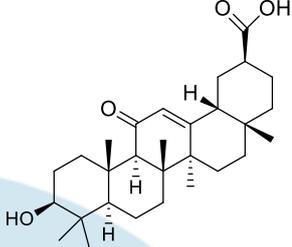
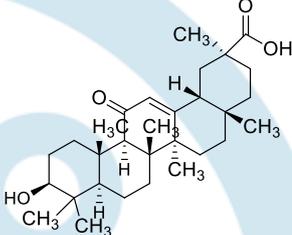


Many of roots and rhizomes were used as carminatives by the Indians, Egyptians, Chinese, Greeks, and Romans. Numerous respiratory tract illnesses, including tonsillitis, bronchitis, hoarseness, and cough, are treated with the roots, peeled or unpeeled roots, and rhizomes¹⁴. Additionally, licorice has been used to treat a variety of digestive system diseases, including colic, hyperdipsia, stomach ulcers, and flatulence¹⁵. Additionally, it is used to treat jaundice, psoriasis, paralysis, rheumatism, epilepsy, fever, and sexual dysfunction¹⁶. Furthermore, it helps with gout, edoema, acidity, leucorrhoea, bleeding, hiccough, and damaging vata dosha disorders like gastralgia, cephalalgia, ophthalmology, and pharyngodnia¹⁷. Glycyrrhiza root has been utilised in the culinary industry for more than 400 years as a flavouring and medicinal ingredient. Extracts of licorice are used as flavouring.

ACTIVE CONSTITUENTS OF *GLYCYRRHIZA GLABRA*

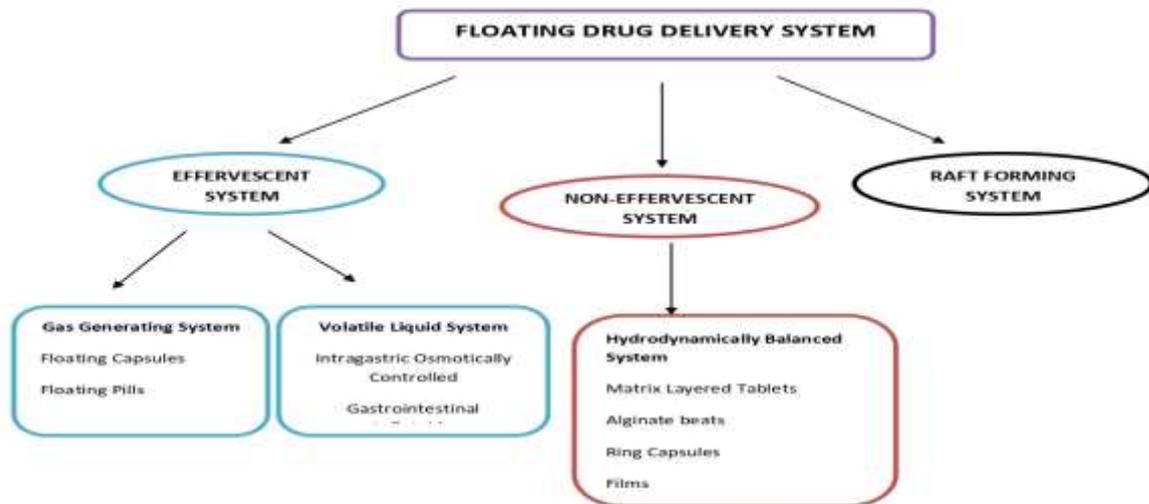
Class of the constituents	Name of constituents	Structures	References
Triterpenoid	Glycyrrhizin		18
Flavonoid	Liquiritin, isoliquiritin, liquiritigenin		19,20
	Glabrene, glabridin		21
	Rhamnoliquiritin		22

	Glucoliquiritinapioside, prenyllicoflavone A, shrinflavone, hrinterocarpin, 1-methoxy-phaseolin		23 24
	Glisoflavone, kanzonol R,		25
	licochalcone A		26
Alcohol	Pentanol, hexanol		27
	2,3 Butanediol		28
Acid (Volatile)	Propionic acid, benzoic acid, ethyl linoleate		29
	Acetic acid, malic acid, butyric acid, fumaric acid, citric acid		30
Terpenoid	Alpha terpineol, geraniol		31 32

Aldehyde	Furfuraldehyde		33
Saponin	Glycyrrhizic acid,		34
	18-β-glycyrrhetic acid		35

Over the past three decades, due to their significant advantages, oral controlled release dosage formulations have been created. Therapeutic benefits like simplicity of administration, patient compliance and formulation flexibility. However, this strategy has a number of physiological issues like being unable to stop and find the controlled drug distribution system inside the targeted gastric area due to inconsistent stomach emptying and motility³⁶. Ingestion of gastroretentive dose forms is possible area for several hours, considerably extending the duration of medicines' gastrointestinal residency long-term gastric. Retention boosts bioavailability, cuts down on wasted medication, furthermore increases the solubility of less soluble in water medicines a pH level above 7³⁷. The many forms of gastroretentive effervescent and oral dosage forms are floating medication delivery techniques. systems without effervescence.

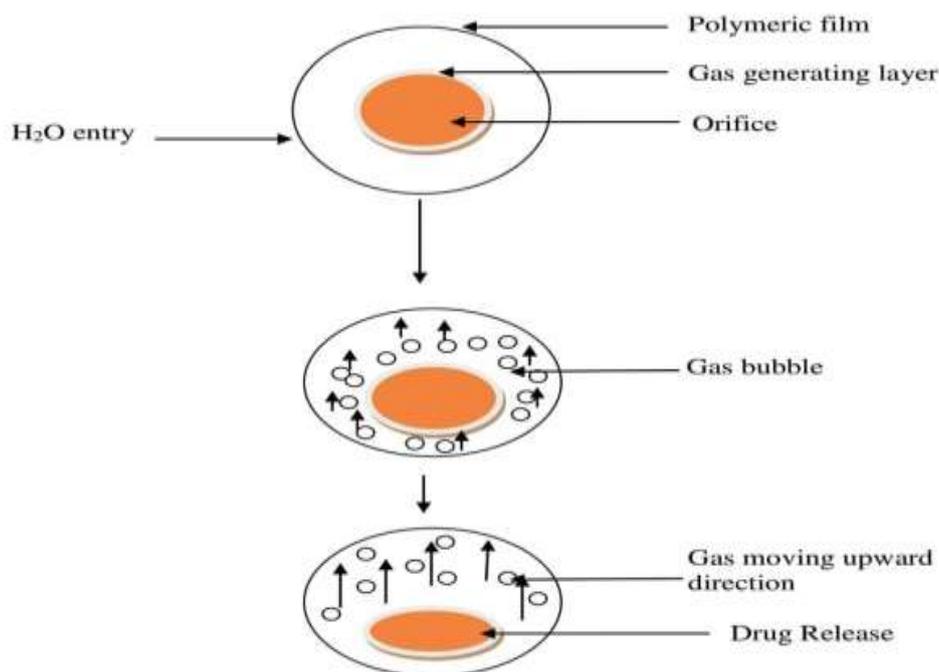
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Diagrammatically shown: Types or Subtypes of Floating Drug Delivery System

Floating drug delivery systems, low density systems, raft systems using alginate gel, bioadhesive or mucoadhesive systems, high density systems, superporous hydrogel, and magnetic systems are now used to create successful gastroretentive drug delivery systems. The floating dose formulations have been the most widely employed of these³⁸.

Because they float in the stomach without slowing down the gastric emptying rate, floating medication delivery devices have a lower bulk density than gastric fluids. The medicine is slowly withdrawn from the system at the desired rate while the body is floating on the contents of the stomach³⁹. The stomach's residual system is emptied after the medication has been released. This prolongs the stomach retention period and stabilises the variation in plasma medication concentration⁴⁰.



Mechanism of floating drug delivery system (FDDS)

FLOATING MEDICATION DELIVERY SYSTEM BENEFITS:

- Floating dose systems are gastric retention-behaving medication delivery methods that have a number of benefits⁴¹.
- Simple and traditional formulation method localised medication delivery.
- Controlled delivery of medicines delivery of medication to a specific stomach location for residual effect.
- Enhanced medication absorption by increased GRT and prolonged interaction with the dosing regimen's target site.
- In treating gastroesophageal reflux disorders (GERD).
- Ease of administration with higher patient compliance⁴².

The floating drug delivery system also carries certain disadvantages which limit its applicability

- Drugs that have a significant first-pass metabolism and are significantly absorbed throughout the gastrointestinal system are the preferred candidates.
- Some medications in the floating system can irritate the mucosal linings of the stomach.
- Gastric emptying in floating systems can happen at random and is greatly influenced by its size. As a result, patients shouldn't take their medication before bed⁴³.

METHODS TO EVALUATE AND FORMULATE TABLET FROM *GLYCYRRHIZA GLABRA*

Glycyrrhiza consists of peeled or unpeeled dried roots and stolons of *Glycyrrhiza glabra* Linn belonging to the family Fabaceae⁴⁴. Licorice has been reported to be effective in the treatment of gastric and glycyrrhetic acid, the glycyrrhizin aglycone, has an anti-inflammatory effect and anti-ulcer effect⁴⁵. *Glycyrrhiza* can increase the concentration of prostaglandins in the digestive system that they promote mucus secretion from the stomach; also reported that licorice prolongs the life of surface cells in the stomach and has an antipepsin effect⁴⁶. It has also been reported that *Helicobacter pylori* shows susceptibility to licorice extract⁴⁷.

Preparation of aqueous extract from *Glycyrrhiza glabra* root

The powdered liquorice root was once extracted with distilled water containing ammonia. The extraction temperature used to be maintained at 90°C with steady shaking. The extract used to be filtered and focused to get a thick paste. The quantity of glycyrrhetic acid in the extract used to be determined with the aid of HPTLC⁴⁸.

Sample and standard preparation

200 and 50mg of the extract was refluxed with 50 ml 1N HCL for 4 h. It became cooled to room temperature and it became extracted with (20 ×5) ml chloroform. The blended chloroform extract was washed with water and filtered⁴⁹. It changed into evaporated at temperature of 30°C and the residue changed into dissolved in chloroform: methanol (1:1) and the quantity changed into made up to 25 ml. 10 mg of 18-β-glycyrrhetic corrosive was broken down in 25 mL of chloroform: methanol (1:1).

Versatile stage . First run chloroform-CH₃)₂CO (9:1)

Second run chloroform-diethyl etherformic corrosive (80:15:1)

Technique. 2, 3 and 4 μL of standard and test were applied in groups on precoated silica gel HPTLC plates by Linomat V utensil. Band length was 6 mm and distance between the groups was kept at 4 mm. The plate was dried and checked at 254 nm in absorbance mode. How much glycyrrhetic corrosive was found by examination of pinnacle region of standard and concentrate⁵⁰.

Tablet Formulation

Each of the tablets were planned by direct pressure method utilizing polymer like HPMC K100M and different fixings like psyllium husk, magnesium stearate, powder, and sodium bicarbonate. All fixings were gone through strainer no # 80 and weighed precisely on electronic equilibrium. The concentrate, HPMC K100M, sodium bicarbonate, and psyllium husk were blended appropriately in a mortar and pestle to get a uniform tablet mix. At last powder and magnesium stearate were blended in with the mix. The tablet mix was then gauged exclusively as per the recipe and packed into tablets utilizing single punch tableting machine⁵¹.

Evaluation of Tablet

The pre-arranged drifting tablets were assessed for distance across and thickness utilizing Vernier calipers. The hardness of the tablets was assessed utilizing a Monsanto hardness analyzer. The not entirely set in stone in a Roche friabilitor. 20 tablets from every plan were gauged and determined⁵².

The diameter across of all plans was in the range 11.166-11.933 mm; thickness was in the reach 4.02-4.086 mm. The hardness went from 3.1 to 3.5 kg/cm². All plans passed the USP necessities for friability and consistency of weight.

Buoyancy time

FLT of all plans was found to be under 5 min. The carbon dioxide produced from sodium bicarbonate upon contact with the acidic medium will remain captured in the gellified layer of the enlarged polymer (hydrocolloids). This creates a vertical movement of the dose structure and keeps up with its buoyancy⁵³. The FLT might be made sense of because of the time expected for disintegration medium to enter the tablet lattice and foster the enlarged layer for capture of CO₂ produced in situ. The tablet mass diminished dynamically due to freedom of CO₂ what's more, arrival of medication from the lattice. Then again, as dissolvable front infiltrated the polished polymer layer, the expanding of HPMC K100 M caused an expansion in volume of the tablet. The joined impact is a net decrease in thickness of the tablets, which drags out the term of floatation past 8 h⁵⁴.

During detailing improvement, the fixings utilized were chosen in view of the methodology of accomplishing drug discharge for 8 h. Drifting medication conveyance depends on the expanding property and thickness of the polymers as well as the gas creating agent⁵⁵. The work was begun utilizing psyllium husk which grows upto multiple times of its unique volume and the thickness of psyllium husk is lower than the gastric fluids⁵⁶. Sodium bicarbonate was utilized as a gas generating specialist, which responds with the gastric liquids and produces carbon dioxide. This gas is ensnared into enlarged network and gives lightness to the formulation⁵⁷. HPMCK100M having high thickness and capacity to grow was utilized.

In vitro drug release

In vitro drug concentrates in 0.1N HCl as the disintegration medium to concentrate on the medication arrival of the tablet details. As the centralization of psyllium husk expanded from 75 (F1) to 125 mg (F3) per tablet, the percent aggregate medication discharge diminished from $98.29 \pm 0.86\%$ (F1) to $96.1 \pm 0.634\%$ (F2). The percent aggregate medication discharge for (F3) was $99.8 \pm 0.965\%$ later 8 h. The sluggish arrival of the medication might have credited to the gelling properties of psyllium husk⁵⁸.

As the focus of HPMC K100M was expanded from 40 (F4) to 60 mg (F5), drug discharge diminished from $97.5 \pm 0.696\%$ to $97.3 \pm 0.408\%$. This may be because of the expanded polymer fixation which might have expanded the dissemination way length for the medication, which might have hindered the drug discharge⁵⁹.

The impact of sodium bicarbonate on in vitro drug was done. In such frameworks, sodium bicarbonate goes about as a gas-producing specialist. It produces gas when it comes into contact with an acidic climate of the stomach. This gas captures into the network of watersoluble polymers and the definition floats in an acidic climate of the stomach⁶⁰. As the fixation was expanded from 90 (F6) to 110 mg (F7) per tablet, the drug discharge was diminished from $98.3 \pm 0.935\%$ to $93.6 \pm 0.706\%$. Sodium bicarbonate being soluble in nature makes a soluble microenvironment around the tablet, which diminished the medication discharge from the tablet⁶¹.

Optimization of tablet formulation

In light of the lightness time and % aggregate medication discharge definitions were advanced. The lightness season of all definitions was in the reach 3.5-5 min. The % aggregate medication discharge was in the reach 93.34-99.8%. The advanced definition was viewed as F6. The lightness time was 3.5 min and % aggregate medication discharge was 98.3%⁶².

Analysis of release kinetics

To concentrate on the delivery rate energy what's more, the delivery instrument of the medication from the tablet definitions, the in vitro drug discharge information were dealt with with the numerical condition like first request energy condition, zero-request energy condition, Higuchi's condition, and Korsmeyer's condition⁶³.

At the point when information were treated with Higuchi's condition to find out about the instrument of medication discharge, it was seen that the qualities didn't give a decent fit for the Higuchi condition. None of the plans followed first-request energy, which was affirmed by the unfortunate relationship coefficient values. All details best fitted both zero-request ($R^2=0.945-0.9912$) and Korsmeyer also, Peppas condition ($R^2=0.9817-0.9982$)⁶⁴. At the point when n takes esteem 0.5, it demonstrates Fickian dissemination controlled drug discharge and for the worth 1.0 shows case II vehicle (expanding controlled drug discharge). Upsides of n between 0.5 what's more, 1.0 can be viewed as a marker for the non-Fickian (atypical vehicle) dissemination. For all plans, the worth of n was in the reach 0.6242-0.8408 showing strange vehicle wherein the medication discharge instrument is constrained by both dissemination and polymer unwinding^{65,66}.

CONCLUSION

Floating tablets of liquorice remove utilizing psyllium husk, HPMC K100M, powder, sodium bicarbonate, and magnesium stearate were ready. Formed tablets were inside satisfactory cutoff points for different physicochemical assessments for tablets like tablet aspects, hardness, consistency of weight, friability, lightness time, and in vitro drug discharge. In vitro disintegration reads up for the drifting tablets were done in 0.1N HCl at 37 °C. Around 93-the vast majority of the drug was delivered in 8 h. Definition F6 showed great floating way of behaving alongside better-controlled drug discharge in contrast with other arranged plans. Planned floating tablets best fitted to Korsmeyer-Peppas model and zero-request energy. All definitions for the worth of n was in the reach 0.624-0.84 showing bizarre vehicle where in the medication discharge instrument is constrained by both dispersion and polymer

unwinding. We can reason that psyllium husk, sodium bicarbonate and HPMC K100M in blend can be promising polymers for gastroretentive drug conveyance frameworks. Floating tablets of watery concentrate of liquorice can be formed as a way to deal with increment gastric home time, in this way working on its bioavailability. The reviewing data demonstrate a promising capability of fluid concentrate of liquorice floating tablets as an option to the traditional measurements structure.

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