

Formulation and Evaluation of Anti-Diabetic Floating Tablet of Piper Betel Leaves

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ABSTRACT: Floating herbal tablets prolong the gastric residence time of drugs, improve bioavailability, and facilitate local drug delivery to the stomach. In this study, floating tablets containing ethanolic extract of piper betel as main active ingredient were prepared for the treatment of gastric ulcers. The tablets containing ethanolic extract of piper betel, carbopol, HPMC K100M, Sodium Bicarbonate, Talc and magnesium stearate were prepared by direct compression method. Tablets were further evaluated for physical parameters like diameter, thickness, hardness, uniformity of weight and buoyancy time. Formulation was optimized on basis of buoyancy time. All of these tablets were evaluated and was found within the range. The buoyancy time of all tablet formulations was less than 3min and remained in floating condition throughout the study, maximum till 24 hours. The optimized formulation was found to be F4 which was having buoyancy time of 0.20min. Formulation containing carbopol, sodium bicarbonate and HPMC K100M in combination can be promising for gastro retentive drug delivery systems.

KEYWORDS: floating tablets, Piper betel, Herbal product.

INTRODUCTION

The best and most common way to distribute drugs to the systemic circulation is via the oral route (1). Due to its greater flexibility in dosage form formulation than other routes, the oral route of administration has garnered more attention and success than other ones despite having significant benefits in drug delivery (2). Therefore, research is constantly looking for new ways to deliver drugs with a well-controlled release profile over a long period of time. A floating drug delivery system (FDDS) is a novel drug delivery method developed to increase the bioavailability and therapeutic effectiveness of specific medications by increasing their time spent in the gastrointestinal tract (3). For drugs that need prolonged release to maintain therapeutic levels or have low solubility or stability in the stomach's acidic environment, this method is highly effective. An oral sustained control release drug delivery system's primary objectives are to increase product safety and prolong its half-life in the stomach (4). Currently, a variety of techniques are employed to create a successful stomach-specific or gastro-retentive drug delivery system, including hydrodynamically balanced systems (HBS) / floating drug delivery systems (5), low density systems, raft systems incorporating alginate gels (6), bio adhesive or mucoadhesive systems (7), high density systems, super porous hydrogels (8), and magnetic systems (9). Developing a gastro retentive drugs delivery system is made more simpler and more logical by using floating drug delivery systems. Piper betel Linn. (Paan, the local name) A dioecious annual creeper with many tiny adventitious roots, Piperaceae reaches a height of around one metre, typically cultivated in the country's hotter, wetter regions (12), (13). Blood sugar levels and serum fat levels are significantly lowered as a result of Piper betel water extract treatments. Additionally, it exhibits insulinomimetic activity (14). One of the most common gastrointestinal problems is an ulcer, which develops as a result of an imbalance between elements that are defensive (mucus, prostaglandins, and blood flow) and offensive (gastric acid, pepsin, bile, and oxidative stress). When an ulcer develops in the first portion of the intestine, it is referred to as a duodenal ulcer rather than a gastric ulcer. Peptic ulcers are frequently caused by *Helicobacter pylori* [16], NSAIDs [17], tobacco usage [18], Crohn's disease [19], and others. With some consequences, such as bleeding, perforation, and stomach blockage, it exhibits a variety of symptoms, including upper abdominal pain, belching, and vomiting. (20). Hence piper betel is selected because it has potent therapeutic effect, even in small quantities.

MATERIALS AND METHODS

Standard graph:

Preparation of standard graph of piper betel 0.1N HCl

Preparation of primary stock solution: 100 mg of ethanolic extract were precisely weighed and then added to a 100 ml volumetric flask. When 0.1 N HCl is added in little amounts, it dissolves the ethanolic extract and increases its content to 100 ml.

Preparation of standard solutions: Pipetted 1, 2, 3, 4, 5, and 6 ml of the secondary stock

Formulation and Evaluation of Anti-Diabetic Floating Tablet of Piper Betel Leaves

Solution into separate 10 ml volumetric flasks, where 10, 20, 30, 40, 50, and 30 g/ml of the ethanolic extract of piper betel, respectively, were added.

At a wavelength of 266 nm, the standard solutions were scanned, and the associated absorbances were recorded. Then, using concentration on the X-axis and absorbance on the Y-axis, a standard graph was created.

PREPARATION OF ETHANOLIC EXTRACT OF PIPER BETEL

Initially, 2 litres of the extraction solvent were poured into a flask (Round Bottom) together with 100 gms of the material crammed into a thimble. The soxhlet extraction was carried out for 18 to 24 hours until the liquid that was collected in the siphon tube appeared clear. To obtain dry extract powder, the extracted solvent was afterwards evaporated under decreased pressure. The dried extracts' percentage yields were then calculated.

MATERIALS

Piper betel extract was used as the active ingredient. HPMC (HPMC K100MCR) and carbopol were used as the polymers. Sodium bicarbonate was used as an effervescent agent. The other ingredients used were magnesium stearate, talc. All the materials used in experimental works were obtained from CMR College of pharmacy, Hyderabad, India. All reagents used were of analytical grade.

METHODS

Preparation of floating tablets of piper betel (By direct compression method)

The composition of different formulation of ethanolic extract of piper betel leaf floating tablets is shown in Table 1. ethanolic extract of piper betel leaf (200 mg) and all other ingredients were weighed separately and passed through sieve no. 25. All the material were collected in mortar and pestle and triturated, to prepare a homogeneous mass and pressed in a direct compression machine, four different formulations (F1 to F4) of tablet were prepared by varying concentration of ingredients shown in Table I.

COMPOSITION OF PIPER BETEL FLOATING TABLETS

Table 1. Composition of piper betel floating tablets

S.No.	Ingredients	F1 (mg)	F2(mg)	F3(mg)	F4(mg)
1	Ethanolic extract	200	200	200	200
2	Carbopol	80	90	100	110
3	HPMC K100M	100	90	80	70
4	Sodium bicarbonate	40	40	40	40
5	Talc	15	15	15	15
6	Magnesium stearate	5	5	5	5
7	Total weight (mg)	500	500	500	500

POST-COMPRESSION EVALUATION PARAMETER FOR FORMULATED TABLETS OF PIPER BETEL:

1. Weight variation test: The average weight of each formulation's twenty tablets was calculated by weighing them all. The following formula was used to determine the percent deviation.

INDIVIDUAL WEIGHT – AVERAGE WEIGHT

$$\% \text{ Deviation} = \frac{\text{Individual Weight} - \text{Average Weight}}{\text{Average Weight}} \times 100$$

AVERAGE WEIGHT

In accordance with the Indian Pharmacopoeia's guidelines, the weight variation's percentage difference must not exceed 10%.

- Diameter and Thickness-** Using Vernier Calipers diameter and thickness of each tablet were measured and noted.
- Hardness-** A Monsanto hardness tester was used to assess the tablets. Tablets of each formulation's hardness were examined and recorded.
- Friability** The friability was determined using the Roche friabilator, which is given as a percentage. 20 tablets were taken after being weighed (W initial). Selected tablets that had been preweighed were placed in the friabilator, which rotated for 4 minutes at a speed of 25 rpm (100 revolutions). The tablets were then taken out of the chamber, cleaned, and weighed once more (W final). Next, the % friability was determined using

$$F = \frac{(W \text{ initial}) - (W \text{ final})}{(W \text{ initial})} \times 100$$

4. In vitro buoyancy/ floating study

All of the formulations were subjected to in-vitro buoyancy tests. In a 100 ml beaker with 0.1N HCL pH 1.2, the tablets from each

Formulation and Evaluation of Anti-Diabetic Floating Tablet of Piper Betel Leaves

formulation that were randomly chosen were retained. Total floating time (TFT) is the amount of time the dosage form spends continuously resting on the surface of the medium. Floating lag time is the amount of time it takes for the tablet to rise to the surface and float.

5. In vitro dissolution studies

In vitro dissolution studies of ethanolic extract of piper betel floating tablets were carried out by using USP type II apparatus (paddle type). Dissolution vessel was filled with 900ml 0.1 N HCL pH 1.2 and then temperature of the medium was adjusted to $37 \pm 0.50^\circ\text{C}$. Rotational speed of paddle was set at 50 rpm and then one tablet was introduced in each dissolution vessel. 10ml solution were withdrawn from the dissolution vessels at every hour for 8 hrs and the samples were replaced with 10ml fresh dissolution medium. Absorbance of this solution was measured at 218 nm using a UV spectrophotometer.

6. Drug release kinetics

The results of an in-vitro dissolution research of a formulation that showed good parameters were investigated using different kinetics equations (zero order, first order, Higuchi model, and Korsmeyer Peppas) in order to determine the precise mechanism of drug release from the dosage form.

RESULTS AND DISCUSSION:

Standard graph of piper betel

The standard plot of piper betel in 0.1N HCl was shown in figure. The data of absorbance was shown in table. The correlation coefficient obtained was 0.997

Evaluation of formulated tablets:

The thickness of all formulations was in the range 3.95-4.11 mm. The hardness ranged from 4.30-5.21 kg/cm². All formulations passed the USP requirements for friability and uniformity of weight Table No.2

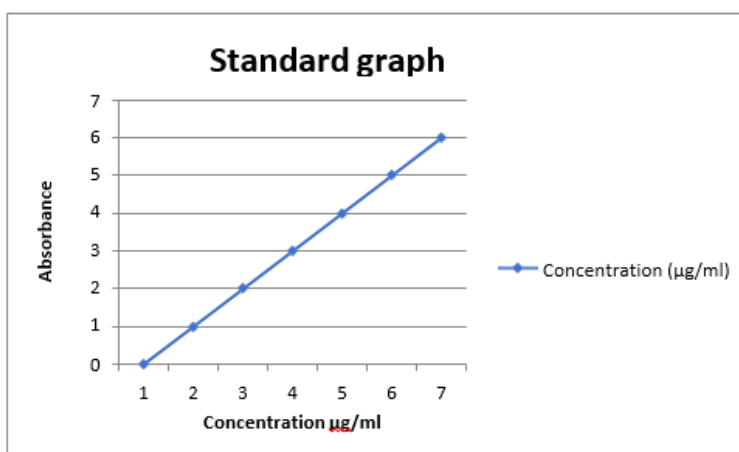
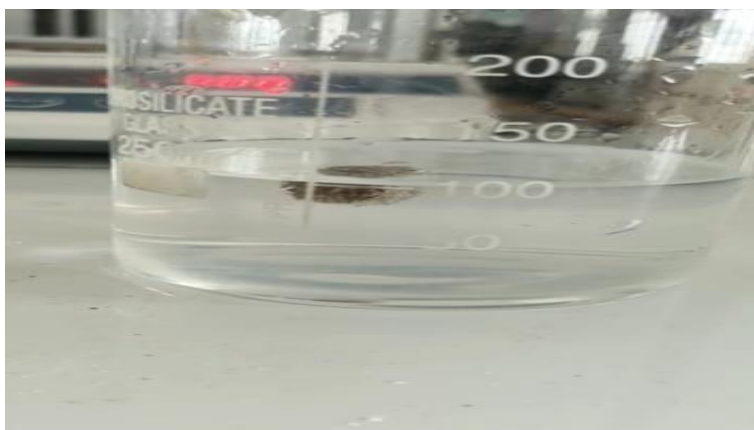


Table 2. Standard graph of piper betel

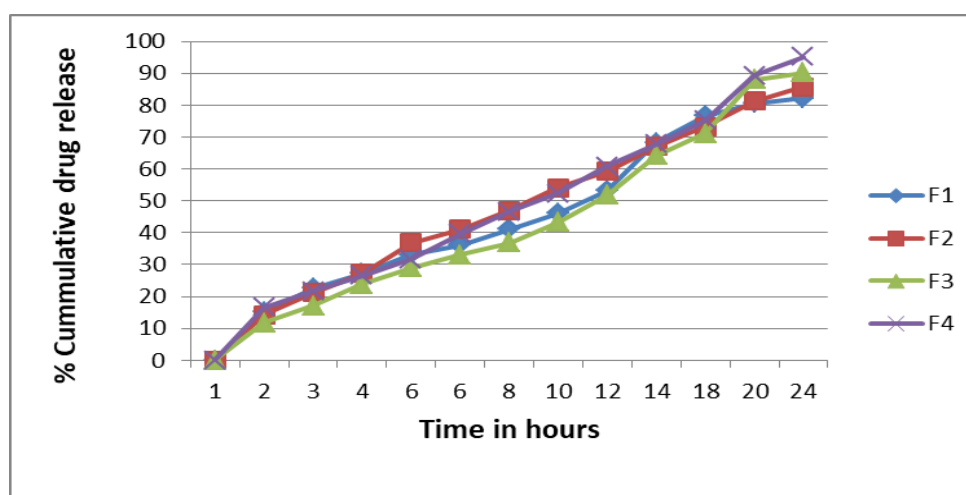
Formulation	Uniformity Of weight(mg)	Hardness (kg/cm ²)	Friability (%)	Drug content(mg)	Buoyancy time(sec)
F1	472.1±0.25	4.25±0.11	0.57±0.06	39.26±0.15	180
F2	5.00±0.07	0.51±0.09	39.61±0.35	30.02±2.40	114
F3	487.6±0.29	4.25±0.19	0.70 ±0.05	39.80±0.12	90
F4	483.2±0.45	5.25±0.08	0.68±0.07	39.42±0.20	20

The formulation were developed, initially F1 was prepared with a relatively low concentration of carbopol resulting in a tablet with high rigidity. However in subsequent formulation (F2 to F4) the amount of carbopol is increased gradually to achieve the desired level of buoyancy. This increase in carbopol concentration resulted in a more porous and swollen tablet, which exhibited reduced floating time and more controlled release of the active ingredient, allowing for sustained release over an extended period.

F4 buoyancy test

**Table 3. Invitro dissolution studies**

Time	F1	F2	F3	F4
0	0	0	0	0
1	15.12	14.18	11.81	16.56
2	22.62	21.26	17.14	21.67
3	27.2	27.17	23.88	26.56
4	33.15	36.92	29.1	31.76
6	36.19	41.1	33.14	39.77
8	41.1	46.92	36.91	46.54
10	46.15	54.02	43.22	52.23
12	53.15	59.2	51.84	60.84
14	68.3	67.15	64.23	67.78
18	76.66	73.3	71.11	75.22
20	80.56	81.23	87.98	89.23
24	82.11	85.76	90.11	95.18



CONCLUSION

Floating tablets of piper betel extract, HPMC, carbopol, talc, sodium bicarbonate, and magnesium stearate were prepared. Formulated tablets were within acceptable limits for various physicochemical evaluations for tablets like tablet dimensions, hardness, uniformity of weight, friability, buoyancy time, and in vitro drug release. In vitro dissolution studies for the floating tablets were carried out in 0.1N HCl at 37 °C. About 80-95% of the drug was released in 24h. Formulation F4 showed good floating behavior along with better--controlled drug release in comparison to other prepared formulations. We can conclude that carbopol, sodium bicarbonate and HPMC in combination can be promising polymers for gastroretentive drug delivery systems. Floating tablets of ethanolic extract of piper betel can be formulated as an approach to increase gastric residence time, thereby improving its bioavailability. The results indicate a promising potential of ethanolic extract of piper betel floating tablets as an alternative to the conventional dosage form.

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