To develop and evaluate floating tablets containing a model anti-ulcer herbal drug for the treatment of peptic ulcers

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Abstract:

Floating tablets containing Azadirachta indica bark extract were successfully formulated using HPMC K100M, Chitosan, sodium bicarbonate, talc, and magnesium stearate. All tablets exhibited favorable physical, chemical, and mechanical properties, with formulation F2 showing the most promising results in terms of floating behavior, swelling, and sustained drug release. In vitro dissolution testing in 0.1 N HCl (pH 1.2) at 37°C showed drug release between 93% and 96% within 12 hours. The formulation demonstrated significant gastroretentive potential, which may improve oral bioavailability and therapeutic efficacy. The safety profile and anti-ulcer activity of the A. indica bark extract-based floating tablets were validated in animal studies. Hence, these floating tablets could serve as a promising alternative dosage form for the treatment of peptic ulcer disease, combining the advantages of herbal medicine with modern controlled-release technology.

Keywords: Azadirachta indica, Peptic ulcer

Introduction:

Oral controlled release drug delivery have recently been of growing activity in pharmaceutical field to attain improved therapeutic advantages, such as convenience of dosing administration, patient compliance and flexibility in formulation. Drugs with short half-lives and drugs that conveniently absorbed from gastrointestinal tract advancement of oral sustained controlled release Formulations is an effort to release (GIT) are eliminated rapidly from the systemic circulation. For these kinds of drugs the drug gradually into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time.

Floating drug delivery system is a method to prolong gastric residence time, there by targeting site-specific drug release in the upper gastro intestinal tract (GIT) for local or systemic effects. This drug delivery system not just prolongs GI residence time but does so in a field of the GI tract that could maximize drug achieving its absorption site in solution and hence ready for absorption. Gastric emptying of pharmaceuticals is varying and is dependent on the dosage form and the fed/fasted state of the stomach. Normal gastric residence times generally range between 5 min and 2 h.

Material Methods:

1 Organoleptic Properties

The sensory organs of humans evaluated the organoleptic qualities. Color, smell, visual appeal, and other "organoleptic" factors were all taken into account.

1.1 Solubility study

Bark extract's solubility in several solvents was evaluated for quality using the USP National Formulary 2007 guidelines. An exact dose of the drug (1 mg) was measured out and placed in a 10 ml test tube, after which it was diluted with the appropriate solvents (methanol, ethanol, DMSO, chloroform, and acetone, each 1 ml).

1.1.2 UV spectroscopy analysis of neem bark extract

An exact and repeatable approach for estimating the extract's drug release is required. Therefore, the extract was estimated using UV spectroscopy.

1.1.2.1 λ Max determination by UV spectrum

Stock solutions of 1000 mcg/ml were prepared by diluting 100 mg of the dried extract into 100 ml of the solvent. The 10 mcg/ml solution was analyzed using UV spectroscopy, which scanned the spectrum from 200 to 400 nm.

1.2. UV spectroscopic calibration of drug extract

Determine how many milligrams per milliliter you need by correctly measuring the amount of dissolved substance you have left in your solvent. Absorbance at 207 nm was measured using solutions diluted to concentrations of 0, 25, 50, 100, 200, 300, and 400 micrograms per liter. To make the calibration curve, Excel was utilized. The absorbency of different solutions was measured using blank. Regression analysis was then applied to a scatter plot of absorbance against concentration.

1.3 Phytochemical Constituents of Neem bark extract

According to Ejikeme et al., 2014 the methods for determining phytochemicals used in this study were modified from those previously reported.

Drug-polymer interaction study

FTIR spectroscopy was used to investigate how medications interact with polymers, and the findings were surprising. These investigations gathered their spectra in a number of different ways, some of which involved the use of neem bark extract, polymers, or a mixture of active pharmaceutical ingredients and polymers. The drug-polymer interaction was studied using Fourier transform infrared spectroscopy. The spectra of both the polymer and the medicinal mixes including Neem bark extract were recorded using the FTIR - spectrophotometer (FTIR 8400S; SHIMADZU, Japan). Both the resolution and the range of the scanning are described to be between 400 and 4000cml (Devi VK, Jain N, Valli KS, et al., 2010).

Preparation of powder mixture and granules containing model drugs

The components of powder blends used in tablet production, including a binary mixture of HPMC K 100 M and sodium alginate gel-forming agents (1:1). The pills were made with three distinct concentrations of gas-forming sodium bicarbonate and citric acid: 0%, 10%, and 20% (by weight). Due to its high water solubility and low density, only 100 mg of Neem Bark Extract was used to evaluate the flotation and delayed release properties of six different tablet formulations (Fl-F6).

Neem bark extracts can be compressed more easily with the use of magnesium Stearate and Talc, which function as lubricants and gliders. It was mixed in a 180-micron sieve, then passed through a 350-micron sieve, which is adequate for compressing tablet- sized doses. Turbula mixer with a 250 ml glass bottle was used to combine the powders for 10 minutes at 60 rpm in a turbula mixer set to 60 RPM.

Flowability was improved by the wet granulation technique, making automatic powder compacting considerably easier. A Kenwood Chef Kneader was used to mix the powder mixes for 10 minutes before passing them through a 1,000 m sieve manually. Grains were dried overnight in an oven (SciQuio Ltd, UK) at 60°C and passed through an 853 m sieve to achieve the desired particle size, which was approximately 853 m long.

Table 1. Composition of prepared neem extract tablets

S. No	Ingredients	F1	F2	F3	F4	F5	F6
1	A. indica bark extract powder	240	240	240	240	240	240
2	Chitosan	200	--	--	---	100	100
3	HPMC K100 M	--	200	--	100	--	100
4	Carbopol 974 P	--	--	200	100	100	---
5	Sodium bicarbonate	20	20	20	20	20	20
6	Citric Acid	20	20	20	20	20	20
7	PVPK30	10	10	10	10	10	10
8	Magnesium Stearate	5	5	5	5	5	5
9	Talc	5	5	5	5	5	5

To compensate for weight, gassing agent content was increased from 10% to 20%.

1.4 Preparation of floating tablets

Neem extract tablets (granulated powders) were pressed using automated single-punch tableting machines with flat-faced punches and compression speeds of 85 revolutions per minute to determine how gassing agent concentration affected tablet porosity, floating capacity, swelling, erosion, and dissolution. Varying the compression force between punches between tablets produced tablets with crushing strengths of 49-54 N (group A), 54-59 N (group B), and 59-64 N (group C). It was possible to press tablets without the assistance of a human. Manually pressing the tablets was necessary because the F5 formulation's crushing strength could not be automatically pressed at 49-54 N, 54-59 N and 59-64 N; they were fed into a single-punch tableting machine and compacted.

This was done after a batch of hand-pressed tablets were made using the Fl-F6 formulations in order to assess the effects of granulation on the tablets' porosity, floating capacity, and dissolving behavior. The powder combinations were manually weighed into a single punch tableting machine, and then granulated into the desired tablet shapes. Automatic compacting was used for granulated powders, but manual pressing was required for the ungranulated powder mixtures.

1.4 Compressibility index

Powder Compressibility Scales Powder flow is hindered by the same interparticulate interactions that affect its bulking qualities, therefore comparing the bulk and tapped densities can provide insight into the relative importance of these interactions. Powders can be evaluated for their compressibility using the Compressibility Index. They are indicators of the powder's settling ability and allow for a determination of the relative weight of interparticle interactions. The bulk and tapped densities are more similar because the interactions between the particles are significantly weaker in a freely moving powder. For poorer flowing materials, the interparticle interactions will increase the difference between the bulk and tapped densities. In brief, 50 g samples of the powder combination and granules were tapped using the tapping instrument to determine their bulk and tapped volumes. Similar weight-to-volume ratios were observed between bulk density and tapped density.

1.4.1 Angle of repose

The angle of repose is frequently used when describing bulk solids. When calculating the angle of repose, it is assumed that the bulk solid heap is roughly conical in shape, which is generally the case for freely flowing materials.

1.4.2 Bulk density

Many pharmaceutical materials, including their performance and function, are affected by the density of their particles, powders, and compacts.

1.4.3 Moisture content

Before and after granulation, the moisture content of a sample of powder (weighing 1 gram) was measured using a Mettler Toledo Halogen Moisture Analyzer (Switzerland). Measurements were taken three times and the mean values minus the standard deviation (SD) are shown.

1.4.4 Post compression evaluation

Testing was performed on tablets made from granules to determine their strength and friability in the tablet crushing process as well as their weight uniformity and the uniformity of their drug content, as well as their apparent density and porosity.

Table 2. Weight variation table

USP standards	Max % difference allowed	BP/IP standards
130 mg or less	10%	84 mg or less
130 mg - 324 mg	7.5%	84 mg - 250 mg
More than 325 mg	5%	More than 250 mg

1.5. Drug content uniformity

Pharmaceutical analytical parameter for controlling the quality of tablets and capsules, "Uniformity of Content." Each capsule or tablet's active ingredient content is determined using a suitable analytical method applied to a random sample of capsules or tablets.

1.6 Tablet apparent density and porosity

Vernier callipers (m) were used to measure the d and h dimensions of the tablets. Equation (5) (Ali et al., 2007) was used to calculate the apparent density (D) of tablets using their weight (w) and the circular constant.

1.7 Tablet floating capacity

In vitro investigations to measure the floatation capacity were conducted under the same circumstances and with the same equipment. Tablets' emergence from and persistence on the dissolution media's surface (floating lag time) and duration (floating duration) were determined using visual analysis techniques (Yin et al., 2013). The three measures' average and standard deviation are displayed.

1.8 Swelling and erosion studies

The masses of three randomly selected pills were recorded. The percentages of tablet dissolution medium uptake (DMU) and tablet mass loss (ML) were calculated using the USP Dissolution Apparatus under conditions identical to the drug release research. According to the drug release experiment, tablets containing either Neem extract or cefalexin monohydrate were withdrawn from the medium at 0, 5, 1, 2, 4, 6, 8, 12, and 24 hours. The pills were dried to a uniform weight in a drying oven set to 60 degrees Celsius, after which the excess liquid was filtered away.

1.9 Stability studies

A drug substance's quality, safety, and/or degradation behavior can be identified by stress testing, Q1A(R2), the ICH's industry guidance for assessing novel drug substance stability (ICH, 2003). In a packaging duplicate, the medicine can be stored at 40°C ± 2°c and 75% ± 5% RH for six months.

1.10 Acute toxicity study

OECD guideline 425 was used to perform acute toxicity study on animals for neem bark extract. The different doses (50 mg/kg, 150 mg/kg, 300 mg/kg, 500 mg/kg, 1000 mg/kg and 2000 mg/kg) of bark extract were given to animals. The animals were intensively observed for first 4 h of drug administration then every 24 h of interval for 14 days for any change in fur color, behavior, feeding, lacrimation, and urination.

1.12 Anti-ulcer activity of neem extracts floating tablets

Institute supplied twelve 150 ±20 g male albino rats. The animals were maintained in the animal home at 25±1°C for a 12-hour dark/light cycle. They ate pellets and drank freely. The experimental protocol was authorized by CPCSEA. Neem extract tablets (weighing 30 ± 1 mg corresponding to 5.73 mg medication) were manually pressed using a single- punch tableting machine with concave-faced punches (4.00 mm) for granulated powders 20±1 N and a crushing strength tester. This study used neem extract (2.88 mg/ml) as a control. Before the experiment, the rats were randomly divided into two groups and given free water for 12 hours. It was divided into two groups: GI (tablets) and G2 (reference solution). A single dose of the preparations (tablet and solution) was administered via intra-gastric gavage directly into the stomach. 5.75 ±0.15 mg. The CPCSEA approved the experimental protocol for 0.5, 1, 2, 4, 6, 8, 12 and 24 hours. tail-bleeding procedure.

1.13 Grouping of animals

Each of the five groups consisted of seven albino rats, and randomization was carried out. Group 1 animals received nothing but distilled water (the normal control). The rats in group 2 of the experiment received a single dosage of indomethacin (as a negative control). A ranitidine dose of 20 milligrams per kilogram of body weight was given to individuals in Group 3. Animals in Group 4 (F2) were given a pill containing 20 milligrams of an indica bark extract per kilogram of body weight. Prior to receiving indomethacin, subjects were given ranitidine and Formulation (F2) for a combined 21 days. Oral infusions of these were administered once a day throughout the experiment using an oral incubator. Food and water were available at any time.

1.14 Isolation of stomach and collection of gastric juice

After inducing ulcers, the animals were humanely put down by cervical dislocation on day 23. It was then necessary to open the abdomen to remove the stomach and extract it. After the stomach's larger curvature was opened, the contents were extracted and deposited in a centrifuge tube. After centrifuging for 10 minutes at 3000 rpm with 5 milliliters of water, it was added to the mixture. The obtained supernatant was employed in the subsequent biochemical studies that were carried out on it. After being homogenized and stored in an acidic pH 7.4 solution (1:4 (w/v)), the stomachs were prepared for the process under the microscope.

1.15 Determination of gastric secretion parameters

Toepfer's indicator (2 ml) could be used to measure the amount of stomach acid output in the supernatant. We utilized a pH meter to check the acidity of the stomach liquid. We measured the sample's specific pepsin activity and mucin concentrations using procedures developed by Sanyal et al. and Cornell et al.

1.15.1 Methods for the measure of gastric acid secretion

The aspiration test is the most accurate way to measure gastric acid secretion, but it is invasive and requires putting a tube (endoscopic or nasogastric tube) in the lowest of the stomach. Typically, a radiologic examination or a recovery test involving the aspiration of 100 mL of water through the gastric tube is used to determine the optimal placement of the tube. Subatmospheric pressure of 30 to 50 mmHg was then used to measure the basal acid output (B.A.O.), and either a pump with continuous suction or a syringe was used to take readings every 15 minutes. Maximum acid output (M.A.O.) was collected by stimulating the stomach with pentagastrin, histamine, or tetragastrin and then aspirating the contents over the course of an hour at four separate 15-minute intervals. After collecting samples, acid concentration is determined by titrating them with alkaline solution and chemical indicators to assess volume and titratable acid.

1.15.2 lntragastric pH measurement

Transnasally placed in the gastric corpus, the combination pH electrode (often composed of glass or antimony) is connected to a recording equipment. Since intragastric pH varies significantly between regions and is also correlated with postprandial states, it is important to verify fluoroscopically that the intragastric electrode is kept in a relatively stable position. Although initially designed for esophageal pH studies, this technique has gained widespread acceptance due to its potential application in the diagnosis and management of patients suffering from acid-related disorders, including the ability to gauge the efficacy of drugs that reduce stomach acid.

1.15.3 Quantification of ulceration Szabo and Hollander's method for determining the extent of ulceration in animals given indomethacin was used in this study. Using a dissecting microscope equipped with a square-grid lens, vascular congestion and lesions/hemorrhagic erosions were rated on a scale from 0 to 5. Damage to the mucosa was calculated by dividing the glandular stomach's total surface area by 1,000. The ulcer index (U.I.) was shown to be the most accurate technique to measure the average ulcer score for each animal, enabling the computation of the percentage of inhibition against ulceration

1.16 Statistical Analysis The mean minus the standard deviation is used to get the standard error of the mean (SEM). One-way ANOVA and numerous Tukey's comparison tests were employed for our statistical analysis in GraphPad Prism version 5.0. An outcome with a $*p<0.05$ significance threshold was significant.

Results:

2. Pre-formulations studies

2.1 Organoleptic properties

An evaluation of the API's organoleptic qualities, including color, odor, appearance and state, was conducted. Neem bark extract was discovered to have a white color to it when tested. Neem bark extract have a characteristic odor and has a white powder appearance, according to research conducted on it. Neem bark extract exhibited the same color, appearance, and odor as the LP. requirements for these characteristics. The bark extract was brown in color with characteristic odor. The appearance was dried powder in a solid state

Table 1 Organoleptic properties of neem bark extract

Drug	Organoleptic properties	Observation
Neem bark extract	Color	Brown
	Odor	Characteristic odor
	Appearance	Dry powder
	State	Solid

2.2 Solubility study

Neem bark extract solubility was tested in a wide range of volatile and non-volatile liquids, including methanol, ethanol, chloroform, and water. It was observed that the extract was readily soluble in water, Dimethyl sulfoxide, ethanol, and chloroform; however, very slightly soluble in n-Hexane .

Table 2 Solubility study of neem bark extract

Drug	Solvents	Observation/Inference
Neem bark extract	n-Hexane	Very slightly soluble
	Ethanol	Soluble
	DMSO	Soluble
	Chloroform	soluble
	Water	Soluble

2.3 Melting point study

The melting point of a substance can be calculated using the capillary method. The melting point of the Neem bark extract was found to be 141°C, which is well within the limits of the drug specification.

Table 3 Melting point study of Neem bark extract

Drugs	Observed	Reference
Neem bark extract	141°C	138-141°C

2.4 Determination of Partition coefficient

It was determined what the drug's partition coefficient was in the n-Octanol:water mixture. It's the ratio of how much of the unionized medication is in the water to how much is in the organic solvent when the two are in equilibrium. Drugs can be classified as lipophilic or hydrophilic based on their partition coefficient. Drugs with P values significantly over 1 are considered lipophilic, while drugs with P values significantly below 1 are considered hydrophilic. The partition coefficients of the Neem bark extract were found to be 3.47 shown in Table 6.4.

Table 4 Partition coefficient:

S. No.	Drug	Solvent	Partition coefficient
1	Neem bark extract	n-Octanol: water	3.47

2.6 UV Spectroscopy (Determination of A.max)

Nimbin concentrations in the mobile phase were recorded using UV spectrophotometer UV spectra. At a wavelength of 214 nm, the highest absorption was seen. Nimbin detection at this specific wavelength was used.

2.7 Preparation of Standard Curve of Nimbin

100 mg medication was dissolved in 100 cc acid buffer pH 1.2. Dilution yielded 10 ml of pH 1.2 acid buffer. 5-25 µg/ml stock solution was serially diluted. The UV absorbance of 214 nm was used to measure the solution's absorbance value (Table 6.5).

Figure 6.1 shows the calibration curve of nimbin. The calibration curve of nimbin and absorbance were like our study as result found by Kuravadi *et al.,* 2015.

Table 5 Calibration curve of nimbin based on UV absorbance

S. No.	Concentration (µg/mL)	Absorbance (nm)
1	5	0.033
2	10	0.065
3	15	0.097
4	20	0.128
5	25	0.154

2.8 Phytochemical analysis of neem bark extract

Qualitative chemical test are performed to analyze the presence of chemical constituents present in the bark extract of neem. The extract shows the presence of alkaloid, glycosides, carbohydrates, phytosterol, proteins and amino acids, gum and mucilage, steroids, fats and tannin. However, extract showed absence of saponins and flavonoids (Table 6.7).

Table 7 Phytochemical test for neem bark extract

S. No	Test	Neem bark extract
	Alkaloids	
a.	*Dragendorjf 'stest*	+
b.	Wagner's test	+
	Glycosides	
a.	Legal test	+
b.	Keller- kiliani test	+
	Steroids	
a.	Salkowski test	+
	Carbohydrates	
a.	Molisch's test	+
b.	Fehling test	-
	Flavonoids	
a.	Lead acetate test	-
	Protein & Amino acid	
a.	Ninhydrin test	+
b.	Biuret test	-
	Tannin & Phenolic compound	
a.	Lead acetate test	+
b.	Ferric chloride test	-
	Gum & mucilage	
a.	Test with ruthenium red	+
	Saponin	

a.	Foam test	-
	Oils & Fats	
a.	Spot test	+

2.9 Pre-compression evaluation

Flow properties of the prepared granules were characterized by measuring the angle of repose. All the formulations showed improved flow properties, as compared to the pure drug. The values of angle of repose was found between 22°18' – 27°75'and it showed good flowability. However, bulk density was in the range of 0.416 – 0.525 gm/ml. Tapped density was in the range 0.489-0.608 gm/ml, Carr's index ranging from 10.35-17.62% and it showed excellent to good flow rate. Hausner's ratio ranging from 0.055- 0.095, it indicated reasonable flow and all batches of granules were found to fit in respect of flowability.

Table 8 Characterization of granules of prepared tablets

Formulation	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (0)
Fi	0.502	0.597	15.91	0.095	22°18'
F2	0.476	0.531	10.35	0.055	25° 34'
F3	0.468	0.545	14.25	0.077	24° 69'
F4	0.416	0.505	17.62	0.089	22° 51'
Fs	0.525	0.608	13.65	0.083	27° 75'
F6	0.419	0.489	14.31	0.070	23° 66'

2.5 Post-compression evaluation

2.6 Weight Variation

At the beginning of several trials, weight variation was noted, but in the final trial tablet, the weight variation was found to range between 500 ± 1.24 and 500 ± 4.61 mg (Target weight – 500 mg/Tablet), indicating that it is within standard official limits (Figure 6.8 and Table 6.9).

2.6.1 Thickness Evaluation

When determining the thickness of the tablets, a Vernier Caliper was utilised. There is no noticeable difference in the thickness of the tablet between the two different strengths (Figure 6.9 and Table 6.9).

2.6.2 Hardness Test

With the help of a Monsanto hardness tester, we were able to determine the tablet's hardness in kglcm^2 . Within a range of 5.2 ± 0.27 *kglcm*^{2} to 7.0 ± 0.51 kglcm2, tablets' hardness was determined to be consistent (Figure 6.10 and Table 6.9).

2.6.3 Friability Test

Roche Friabilator was used to test the material's capacity to break down into friable pieces. Tablet friability ranged from 55.25% to 0.89% for a sample of 20 tablets tested. This means the manufactured pills are mechanically stable because they are fewer than the standard limit of 1 per cent (Figure 6.11 and Table 6.9).

2.7 Evaluation of formulated tablets

All formulations had a diameter between 11.04 and 11.86 millimetres and a thickness between 3.21 and 3.43 millimetres. 5.2 to 7.0 kglcm2 of hardness were measured. The USP standards for friability and weight homogeneity were met by all formulations (Table 6.9). Figure 6.12 showing diameter of tablets. Zwitterions and precipitation of the active chemical occur at pH values in the small intestine, which inhibits absorption in the lower portion of the gut (Mathiowitz *et al.,* 1999).

2.8 Drug content uniformity

Fl to F6 included 97.4 ± 1.54 percent to 99.91 ± 1.98 percent of Nimbin, according to the results. The findings are summarised in the Table 6.9 and Figure 6.13.

2.8.1 Tablet density

The density of the tablets ranging from 0.82 *glee* to 0.99 *glee.* For floating of tablets, the density of tablets should be less than the gastric fluid density (1.004). So, it gives the successive result (Figure 6.14 and Table 6.9).

2.8.2 Buoyancy lag time studies

The floatability of all tablet formulations was good and lasted for roughly 10 hours. Table shows how the floating lag time varies among all formulations. It was found that Formulation F2 had the lowest latency time, whereas F3 had the highest latency time. Figure 6.15 showing prepared tablets. Table 7.4 displays the buoyancy time for various formulations. Floatability of all formulations was determined to be less than 5 minutes. Swollen polymer gellifies sodium bicarbonate produced by carbon dioxide in acidic solution (hydrocolloids). So, the dose form floats. Floatability can be explained by the time needed for dissolving media to infiltrate tablet matrix and develop swelling layer for C02 trapping. Tablet mass drops as C02 and medicine are released from the matrix. As the solvent front entered HPMC K IOO polymer layer, tablet volume increased. Reduced tablet density extends flotation time past 8 hours. The latest study enhanced floating pills' 8-hour stability and 99% drug release. The chemicals utilised in formulation development were chosen to ensure that the medicine would be released for 12 hours. Polymers' swelling and density, as well as a gas-generating agent, all play a role in floating medicine delivery (Arora *et al.,* 2005). Carbon dioxide is formed when sodium bicarbonate

combines with stomach juices and creates gas. An inflated matrix holds the gas in place and gives the formulation buoyancy (Arora *et al.,* 2005). HPMC KIOOM was utilised because of its high viscosity and swelling properties.

Table 9 Evaluation of *A. indica* bark extract floating tablets

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Diameter (mm)	Drug contents (%)	Buoyancy (min)	Density (glee)
Fl	500 ± 1.24	3.25 ± 0.12	6.3 ± 0.19	0.79	11.04 ± 0.31	99.52 ± 1.51	2.51 ± 0.35	0.97
F2	500 ± 2.17	3.43 ± 0.46	5.2 ± 0.27	0.89	11.13 ± 0.21	98.69 ± 1.62	1.80 ± 0.12	0.89
F3	500 ± 1.61	3.21 ± 0.23	7.0 ± 0.51	0.85	11.33 ± 0.26	99.91 ± 1.48	3.91 ± 0.56	0.93
F4	500 ± 1.45	3.37 ± 0.25	6.1 ± 0.37	0.52	11.40 ± 0.32	99.48 ± 1.73	2.31 ± 0.74	0.99
F5	500 ± 2.36	3.28 ± 0.59	6.5 ± 0.65	0.67	11.86 ± 0.48	97.40 ±1.54	2.70 ± 0.48	0.82
F6	500 ± 1.52	3.41 ± 0.36	5.5 ± 0.24	0.71	11.52 ± 0.24	99.94 ± 1.98	2.00 ±0.31	0.94

2.8.3 Swelling Study of Tablets

Results show that formulation containing HPMC Kl OOM in higher concentration had higher % swelling than formulations containing Carbapol and Chitosan Formulation F2 had the maximum swelling of 144.25 after 12 hours and formulation F3 had the lower swelling capacity of 133.83 after 12 hours (Table 6.10 and Figure 6.16). Figure 6.17 showing swelling characteristics of floating tables. It is important to note that the swelling agents utilised in this investigation are super dissolving agents. As these agents are swelled, they disintegrate very quickly (Chanvanpatil *et al.,* 2006).

Table 10 Percentage swelling of formulation Fl - F6

Time (hr)	F1	F2	F3	F4	Fs	F6
1	79.28 ±.25	115.37 ±1.5	73.66 ± 1.34	85.36 ± 1.85	95.28 ± 1.91	92.81 ± 1.2
2	95.42 ±1.2	124.42 ±1.4	92.57 ± 1.2	99.35 ±1.4	105.32 ± 1.5	102.38 ± 1.8
3	103.59 ±1.4	130.43 ±	99.72 ± 1.5	105.25 ±	112.54 ±	108.36 ± 1.41
4	106.72 ±.85	134.73 ± 2.10	104.69 ± 1.8	111.52 ±	120.31 ± 1.8	114.31 ± 4.25
5	112.48 ±1.3	139.23 ± 1.2	110.39 ±	116.21 ±	126.63 ±	121.56 ± 1.4
6	117.39 ± 2.1	141.1 ± 1.57	115.19 ± 1.5	119.28 ± 1.4	131.54 ± 1.5	127.56 ± 3.89
8	123.24 ±	142.36 ±	121.91 ±	126.36 ± 1.2	137.87 ± 1.2	133.39 ± 1.5
10	128.69 ±1.8	142.89 ±	125.73 ± 2.25	131.8 ± 1.47	139.26 ± 1.2	137.52 ± 1.19
12	134.74 ±1.4	144.25 ±	133.83 ± 1.2	137.38 ± 1.5	140.17 ±	139.61 ± 1.85

Data are represented as mean ± SD (n=3)

2.9 *In vitro* drug release studies

The dissolution medium used to test the release of the tablet formulations was O. IN HCl for *in vitro* drug release. Floating tablet batches Fl through F6 were tested for *in vitro A. indica* release. Using the dissolution profiles, one can compare the release profile of a medicine with varied polymer concentrations from batches. An *A. indica* bark extract's gelling capabilities may have been responsible for the drug's long-lasting effects.

In vitro release of HPMC KIOOM at various doses. The drug release raised from 82.13 ± 1.25 percent to 95.58 ± 1.20 percent when HPMC KIOOM concentration was increased from 100 (F5) to 200 mg (F2), respectively. Gases are created in these systems by using sodium bicarbonate. After coming into touch with stomach acid, it produces gas. It is trapped in the water-soluble polymer matrix, which floats in the stomach's acidic environment. Release is slowed because sodium bicarbonate, which is alkaline, creates an alkaline microenvironment.

Stability studies of prepared floating tablets

After centrifugation (3000 rpm for 15 minutes) at room temperature, the tablets showed no evidence of drug precipitation, creaming, phase separation or flocculation when viewed visually. After six months of storage, no significant changes in the characteristics of tablets were found during the stability tests, proving that formulation is stable for at least six months (Table 6.19). Table 6.20 showing stability studies of dissolution profile of formulation F2. Figure 6.31 showing dissolution profile of formulation F2 after six months of storage. Visual inspection of tablets during stability testing revealed that it did not cream or precipitate the medication and did not exhibit phase separation or flocculation. After centrifugation at room temperature, the emulsion formed was found to be stable. According to the results of stability investigations, there were no notable changes in tablets properties after six months of storage. Weight variation, hardness, thickness, diameter and drug release of the optimized formulation did not significantly.

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Diameter (mm)	Drug release (%)
Fl	500 ± 0.23	3.20 ± 0.11	6.1 ± 0.19	11.04 ± 0.30	80.35 ± 1.40
F2	498 ± 1.34	3.35 ± 0.41	5.1 ± 0.24	11.11 ± 0.20	94.69 ± 1.78
F3	500 ± 1.29	3.01 ± 0.23	7.0 ± 0.67	11.33 ± 0.26	77.45 ± 1.45
F4	499 ± 0.34	3.37 ± 0.24	6.0 ± 0.35	11.39 ± 0.34	79.39 ± 1.43
F5	498 ± 1.24	3.18 ± 0.59	6.1 ± 0.64	11.83 ± 0.44	73.29 ± 1.88
F6	500 ± 1.24	3.40 ± 0.36	5.4 ± 0.22	11.52 ± 0.24	78.93 ± 1.23

Values are represented as mean ± SD, n = 3

Table 11. Stability studies of dissolution profile of formulation F2

Time (Hours)	Storage condition (For 6 months)	
	45°C	75°C
1	6.23±1.5	7.95±1.5
2	21.24±1.4	25.88±1.4
3	35.93±1.34	38.47±1.34
4	48.43±2.10	52.49±2.10
5	61.12±1.2	64.39±1.2
6	69.25±1.57	72.45±1.57
8	82.45±1.83	86.59±1.83
10	92.49±1.59	94.56±1.59
12	96.05±1.20	99.45±1.20

2.9 Acute toxicity of the test drug

A. indica bark extract was found safe at the dose of 2000 mg/kg body weight, no behavioural change was seen in rats. There was no mortality among the animals, and they were all active.

2.10 Effect of *A. indica* bark extract floating tablet on Ulcer Index and Percentage Protection

The word "peptic ulcer" refers to both gastric ulcers and duodenal ulcers, which are both frequent. It's possible that the aggressive and defensive aspects are out of balance. Many efficient antiulcer treatments have long been used in the treatment of peptic ulcers; however, these medications are not without side effects. A constant demand for safe anti- ulcer medications exists due to the significant morbidity associated with this condition, prompting researchers to investigate into safer herbal remedies (Rao *et al.,* 2002).

With regular Ranitidine and *A. indica* bark extract floating tablet, ulcer index decreased significantly ($p<0.05$) from the positive control compared to both groups (Group 2). ,showing ulcer index and percentage of ulcer inhibition in rats. *A. indica* bark extract floating tablet pre-treated group had a similar percentage of ulcers inhibited compared to the standard group.

There are a variety of ways an ulcer can be triggered. Pyloric ligation was the most often utilised method of inducing an ulcer. Pyloric ligation causes stomach acid to accumulate and pepsin to be activated. Ulcers can arise because of any of these factors (Adinortey *et al.,* 2013). The synthesis of prostaglandin E2 and l2 in the gastric epithelial cells is also decreased by mucosal digestion, which is critical for inhibiting gastric acid secretion and stimulating the secretion of mucus, bicarbonate, and phospholipids (Hisam *et al.,* 2012). Pyloric ligated ulcers are also thought to be caused in part by histamine (Goswami *et al.,* 2011).

Table 8. Efficacy of *A. indica* bark extract floating tablet against peptic ulcer

Groups	Drug	Ulcer index	Percentage inhibition
Group - 1	Distilled water	0	0
Group - 2	Indomethacin	5.48±2.66	0
Group - 3	Ranitidine	2.06±1.43 *	55.71±2.10
Group - 4	F2	2.28±0.85 *	49.48±1.32

Data are represented as mean ± SEM (n=7), significantly different at *p value < 0.05 as compared to positive control.

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