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Formulation and Evaluation of Caffeine Loaded Floating Tablets

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ABSTRACT

The aim of the present work was to fabricate and characterize caffeine loaded floating tablets loaded as sustained release dosage forms. Several formulations were prepared by varying the concentrations of sodium bicarbonate and citric acid. Floating tablets were prepared using HPMC as a binder and sodium bicarbonate as gas generating agents. The prepared floating tablets were evaluated for tablet properties such as hardness, thickness, friability, weight variation and floating property. *In vitro* dissolution was conceded out for about 16 hrs in 0.1N HCl at 37±0.5 °C using USP paddle type dissolution apparatus. It was noted that, all the prepared formulations had desired floating lag time and constantly floated on dissolution medium. The drug release from floating tablets was found that the varying concentration of the polymer affected the drug release. In the present surveillance that floating drug delivery system can be prepared and evaluated.

Keyword: Floating Tablets, Caffeine, Hydrodynamically balance system, Effervescence, Sustain Release, Sodium bicarbonate.

INTRODUCTION

Floating drug delivery system (FDDS), also called hydrodynamically balanced system, is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. This technology is suitable for drugs with an absorption window in the stomach or in the upper part of the small intestine, drugs acting locally in the stomach and for drugs that are poorly soluble or unstable in the intestinal fluid [1,2]. Effervescent floating drug delivery systems generate gas (CO_2), thus reduce the density of the system and

remain buoyant in the stomach for a prolonged period of time and released the drug slowly at a desired rate. The effervescent system utilizes matrices prepared with swellable polymers and effervescent components, e.g. sodium bicarbonate and citric acid. This produces an upward motion of the dosage form and maintains its buoyancy. [3,4] Floating systems having low density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach without affecting the gastric emptying rate for a prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased gastric retentive time and reduces fluctuation in the plasma drug concentration.[5]

Gastric retention systems are important for drugs that are degraded in the intestine, drugs with local action in the stomach, drugs with poor solubility in intestine due to alkaline pH, drugs with rapid absorption from gastrointestinal tract to produce transient peaks in serum drug levels. [6] Caffeine acts as a central nervous system stimulant, temporarily warding off drowsiness and restoring alertness. It produces increased wakefulness, faster and clearer flow of thought, increased focus, and better general body coordination. Effervescent floating tablet of Caffeine retain in stomach improves solubility, bioavailability, reduces drug waste.

Floating dosage delivery systems (FDDS) is important technological drug delivery systems which offer several advantages in the drug delivery as they improved drug absorption, because of increased GRT so that dosage form spent more time at its absorption site. FDDS have mechanism of Controlled release drug delivery system. They have the local action such as drug deliver in the stomach. They minimize the mucosal irritation due to drugs, by drug releasing slowly at controlled rate. FDDS may be used in the treatment of gastrointestinal disorders such as gastro-esophageal reflux. There is better patient compliance and ease of administration. This is site-specific drug delivery system [7].

MATERIALS AND METHODS

Materials

Caffeine was purchased from Merck Lab Mumbai, India. HPMC, Carbapol, Sodium bicarbonate, Citric acid, poly vinyl pyrrolidine, tartaric acid and Talc tablets were purchased CDH, New Delhi.

Methodology

Formulation of Floating Tablet

The matrix floating tablets of Caffeine were prepared by wet granulation technique. All the powders were passed through 80 mesh sieve. The required quantity of drug, polymer and filler were mixed thoroughly, and granules were prepared by using starch solution. The granules were dried at 60 ºC in a oven. Talc and magnesium stearate were finally added and the granules were compressed on single punch tablet compression machine to formulate the floating tablets Table 1 [8].

Table 1: Formulation of Caffeine Loaded Floating tablets

Formulation ingredients (mg/tablet)	Formulations				
	F1	F2	F3	F4	F5
Drug (Caffeine)	100	100	100	100	100
HPMC	50	50	50	50	50
Carbopol	50	50	50	50	50
Citric acid	10	20	30	40	50
Sodium bicarbonate	20	40	60	80	100
Micro crystalline cellulose	260	230	200	170	140
Magnesium Stearate	5	5	5	5	5
Talc	5	5	5	5	5
Total	500	500	500	500	500

Characterization of floating tablet

Shape of Tablets

Compressed tablets were examined by using the magnifying lens for the shape of the tablet [7].

Tablet Dimensions

Thickness and diameter can be measured by using a calibrated varniear caliper. Three tablets of each formulation were selected randomly and average thickness was measured [7].

Friability

Friability of tablets was determined in Roche friabilator. It was expressed in percentage (%). Ten tablets were initially weighed (W initial) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. Tablets were dusted and re-weighed. % Friability of tablets less than 1% was considered acceptable [7]. The % friability was then calculated by –

$$\%F = 100\ (1\text{-}W0/W)$$

Hardness

Hardness indicates the ability of a tablet during handling to withstand with the mechanical shocks. The hardness of the tablets was tested using a Monosanto hardness tester. It was expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined [9].

Weight variation Test

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation from electronic precision balance (CTG 302B-300). A little variation is allowed in the weight of tablet by U.S. Pharmacopoeia. In all formulations, the tablet weight is 500mg. hence 5% maximum difference allowed (Table 2) [10].

Table 2: Standard limit value in weight variation test

Average Weight of a tablet	Percentage Deviation
130mg or less	±10
>130mg and <324mg	±7.5
324mg or more	±5

Floating Test

The time between introduction of dosage form and its buoyancy on simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken

for dosage form to emerge on surface of medium called floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time (TFT) [10].

Swelling Characteristics (Water Uptake Study) :

The swelling properties of tablet containing drug were determined by placing the tablet matrices in the dissolution test apparatus, in 900 ml of 0.1 N HCl at 37± 0.5 C. The tablets were removed periodically from dissolution medium. After draining free from water tissue paper, these were measured for weight gain [11].

Swelling characteristics were expressed in terms of percentage water uptake (WU %)

$$WU\ \% = \frac{\text{Weight of swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}} \times 100$$

***In vitro* dissolution study**

In vitro dissolution of caffeine loaded fast dissolving tablets was studied in USP type-II dissolution test apparatus (LABINDIA, DS 8000) employing a paddle stirrer at 50 RPM using 900 ml of pH 6.8 phosphate buffer as dissolution medium at 37±0.5˚C. One tablet was used in each test. Aliquots of dissolution medium (5 ml) were withdrawn at specified intervals of time and analyzed for drug content by measuring the absorbance. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of caffeine released was calculated and plotted against time [8].

Drug content

For the drug content twenty tablets were weighed, crushed and powdered. An amount of the powder equivalent to 100 mg of caffeine was taken and dissolved in 100 ml of pH 6.8 buffer, filtered, diluted suitably and analyzed for drug content at 271 nm using UV-Visible double beam spectrophotometer (UV 2201 SYSTRONICS) [12] .

Accelerated stability studies

The promising formulation was tested for a period of 3 months at different temperature of 40ºC with 75% RH, for their drug content [13].

Table 3: Evaluation Parameters

Evaluation Parameter	Formulation batch				
	F1	F2	F3	F4	F5
Thickness (mm)	2.9±0.09	3.0±0.12	3.2±0.15	2.9±0.13	3.1±0.18
Diameter(mm)	10.8±0.02	10.9±0.14	11.1±0.15	10.9±0.16	11.2±0.23
Shape	Circular	Circular	Circular	Circular	Circular
Hardness (kg/cm²)	5.4±0.15	5.6±0.13	5.8±0.09	4.1±0.05	4.2±0.02
Friability (%)	0.52±0.10	0.60±0.10	0.71±0.09	0.50±0.07	0.66±0.06
Weight variation	503±1.51	503±1.18	502±1.45	501±1.59	499±0.58
Total Floating Time (h)	>8	>10	>11	>9	>14
Buoya-ncy lag time (s)	68	58	52	48	40
Drug content (%)	94.62±0.51	92.68±0.25	96.71±0.28	97±0.35	99.12±0.28

n =3

Table 4: *In vitro* cumulative percent drug release of caffeine loaded Floating Tablets

Time (h)	Percent (%) drug release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
0.5	17.5	16.9	20.2	15.3	18.5
1.0	30.8	27.5	32.5	26.3	28.8
2.0	42.0	39.6	45.5	37.1	39.9
3.0	55.6	51.6	57.9	49.9	51.2
4.0	62.3	69.8	69.9	67.8	70.8
6.0	75.1	76.9	75.8	72.4	73.7
8.0	78.1	80.9	83.5	89.5	88.7
12.0	87.5	89.56	92.12	93.5	94.7
16.0	94.7	95.4	96.7	97.9	98.3

n =3

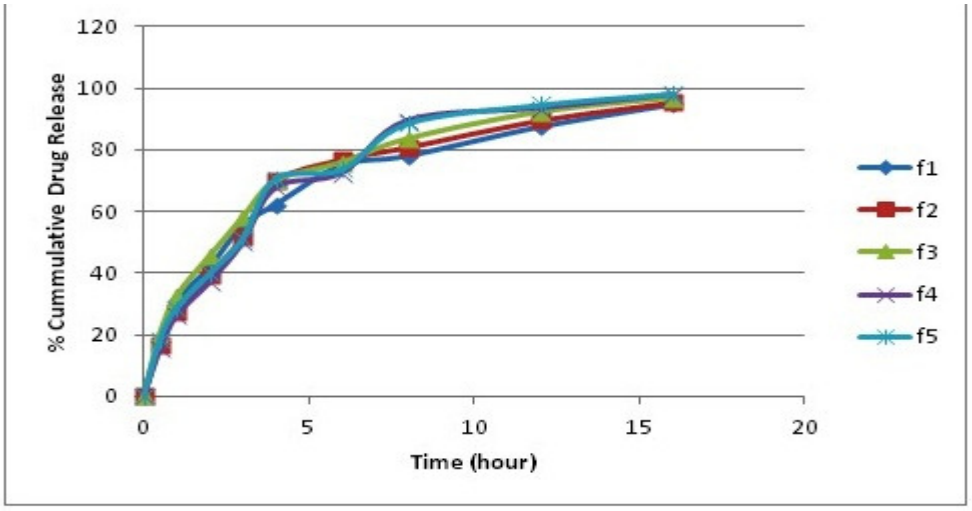

Fig 1: *In-vitro* cumulative percent drug release of caffeine loaded floating tablets

RESULT AND DISCUSSION

Caffeine loaded Floating Drug Delivery system based tablets were prepared by effervescent method and evaluated for the treatment of improving muscle coordinations, warding off drowsiness etc as use as gastro retentive drug delivery system to increase its local action and bioavailability. All the tablet confirmed to the requirement of assay as per I.P. Hardness, % Friability, Thickness, Weight Variation and content uniformity were within acceptable limit The main aim was to optimize the formulation for more than 16 h. The weight variation of the tablet varied between 503 to 499 mg. The percent deviation was within the range such as within 5% which is stated in the pharmacopoeial specifications i.e. according to pharmacopoeia limits these were acceptable. In all the formulations the hardness values specifies good mechanical strength and the hardness of the tablets decrease with increase in the amount of effervescent components as the hardness range of different formulations was found to be between 4.2 to 5.4 kg/cm^2. The friability was ranged from 0.50 to 0.71 % which indicates the formulated tablets have good mechanical strength. The drug content was ranged from 94.62 to 99.12%. The buoyancy floating time was ranged from 68 to 40 s and total floating time was ranged from 8 to 14 h for various formulations Figure 1. Optimized formulation F5 was subjected to curve fitting analysis, zero order, and first order, Higuhi Kinetics, Korsmeyer and Peppas model. Formulation F5 is considered as promising formulation and the drug release followed the controlled mechanism of Higuchi kinetics (r2

= 0.9531).The optimized formulation was subjected to accelerated stability studies as per ICH guidelines Table 3 and Table 4.

CONCLUSION

Floating drug delivery system is a delivery system which provide a potential approach for gastric retention, so that the drug float on the gastric media for more than 16 hours i,e. controlled release. The effervescent-based floating drug delivery was a promising approach to achieve *in-vitro* buoyancy. All the batches of tablets were found due to presence of sodium bicarbonate and citric acid as decrease in the citric acid level increased the floating lag time and tablets were found to float for longer duration. It is concluded from the in-vitro dissolution data that increase in the concentration of citric acid and sodium bicarbonate there is increased in the % Cumulative drug release rate but reduced the floating time.

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