AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

Formulation and In-vitro Evaluation of Floating Tablets for Spray Dried Extract of Curcuma Longa, Piper Nigrum and Berberis Aristata

Patel Ritu D*[1], Patel Rakesh K[2]
1. Department of Pharmacognosy, Saraswati Institute of Pharmaceutical Sciences, Gandhinagar-382355, Gujarat, India.
2. Department of Pharmacognosy, Shree S K Patel college of Pharmaceutical Education and Research, Ganpat University, Kherva-382711, Gujarat, India.

ABSTRACT

Consumption of non-steroidal anti inflammatory drugs (NSAIDs) and Helicobacter pylori (*H.pylori*) infection are responsible factors for induction of peptic ulcer. Extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* is reported to be useful in stomach ailments and has been shown to possess antiulcer activity. Since, treatment for peptic ulceration includes a consumption of multiple herbs displays synergistic impacts compare to single herb against ulcer. The objective of this project work was defined with a view to retain the extracts of mention herbal drugs in stomach for better antiulcer activity. Hence, aim of the present work was to design and develop a floating tablet of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* for the treatment of peptic ulceration. The floating tablets were formulated using hydrophilic polymers as Hydroxy propyl methyl cellulose (HPMC K4M and HPMC E15), Sodium CMC and Sodium bicarbonate as a gas generating agent to reduce floating lag time. The formulated tablets were evaluated for the quality control tests such as weight variation, hardness, friability, swelling index, floating lag time, and total floating time. The *in vitro* release study of the tablets was performed in 0.1N HCl as a dissolution media. The results of the present study clearly indicate the HPMC K4M and HPMC E15 (Batch F-11) in appropriate concentration shown sustained release floating tablets. Such system can remain buoyant for 8 hours along with the sustained drug release for the same duration.

Keywords: Spray dried extract, *Curcuma longa, Piper nigrum, Berberis aristata*, Floating tablet.

*Corresponding Author Email: ritu301010@gmail.com
Received 20 September 2015, Accepted 03 October 2015

Please cite this article as: Patel RD *et al*., Formulation and In-vitro Evaluation of Floating Tablets for Spray Dried Extract of Curcuma Longa, Piper Nigrum and Berberis Aristata. American Journal of PharmTech Research 2015.

INTRODUCTION

Peptic ulcer disease (PUD) is an illness that affects a considerable number of people worldwide. It develops when there is an imbalance between the aggressive (*Helicobacter pylori*, HCl, pepsins, non-steroidal anti-inflammatory drugs (NSAIDs), bile acids, ischemia, hypoxia, smoking and alcohol) and protective factors(bicarbonate, mucus layer, mucosal blood flow, PGs and growth factors) at the luminal surface of the epithelial cells[1]. Both *H pylori* infection and consumption of NSAIDs significantly increase the risk of peptic ulcer and ulcer bleeding. Studies have demonstrated that the efficacy of herbal medicines is comparable or superior to that of drugs such as omeprazole or cimetidine in humans and animal models, and herbal medicines display fewer adverse effects. From the literatures, it is evident that curcumin (*Curcuma longa*), piperine (*Piper nigrum*) and berberine (*Berberis aristata*) were investigated as single drug for their antiulcer activity in various pharmacological studies. Single phytoconstituents is not sufficient to treat the symptoms associated with the ulcer. Thus the need of combination therapy or poly herbal formulations is essential[2]. The presence of both phenolic OH and CH_2 groups in β-diketone moiety of curcumin might protect patients from the adverse gastric side effects of many anti-inflammatory drugs, such as aspirin and exogenous substances such as cigarette, alcohol, and fast foods. However, it has also been recognized that the therapeutic effectiveness of curcumin is limited due to its lack of aqueous solubility, rapid systemic clearance, poor circulating bioavailability, and degradation in alkaline environment. To improve the bioavailability of curcumin, numerous approaches have been undertaken. These approaches involve, first, the use of adjuvant like piperine that interferes with glucuronidation. Also, piperine has been shown anti ulcer activity because of improved gastric mucosal integrity and muco-protective activity. Berberine is a natural iso quinoline quaternary alkaloid derived from *Berberis aristata*, exert inhibitory effects on the proliferation capacity of *H. pylori* and activities of H. pylori N-acetyltransferase[3-5]. Hence, effective delivery of curcumin, piperine and berberine to the stomach for treatment of peptic ulcers caused by *H pylori* infection and consumption of NSAIDs can be achieved by floating dosage forms. The floating drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of phytoconstituents that have an absorption window in a particular region of the gastrointestinal tract. The floating delivery system strategy allows local as well as systemic delivery of a curcumin, piperine and berberine to the stomach, which would efficiently reduced gastric acid secretion.[6,7] In the current work, floating tablets of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* were prepared by effervescent approach using

HPMC and Sodium CMC as the polymers. The aim of the study was to evaluate the effect of the polymers on floating and drug release behavior.

MATERIAL AND METHOD

Spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* were gifted from NJP Healthcare Private Ltd, Vapi.[8] HPMC K4M, HPMC E15 and Sodium CMC were purchased from Purvi Enterprise Ltd., Ahmedabad, India. Lactose, Di-basic calcium phosphate (DCP), Sodium bicarbonate, Citric acid, and Magnesium stearate were procured from S.D fine chemicals, Ahmedabad, India. All other reagents and chemicals used were of analytical grade.

Drug Excipients Compatibility Study

DSC study

DSC scans of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* and mixture of spray dried extracts with excipients were recorded by DSC-Shimadzu-60, Japan. The temperature range was applied from 50-300°C at heating rate 20°C per minute. Thermograms were recorded by DSC 60 thermal analyzer.

FTIR study

FTIR spectroscopy was carried out for spray dried extracts and mixture of spray dried extracts with excipients used in the formulation. The IR spectra were recorded in between 500–4000 cm^{-1} in FTIR 8400S, Japan.

Preparation of Floating Tablets

Table 1 lists the composition of different floating formulations of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata*. All the ingredients, except magnesium stearate, were homogeneously blended for a suitable period and subjected to wet granulation using 5% PVP-K-30 in Isopropyl alcohol. The granules were dried in conventional hot air oven at 45°C. The dried granules of 16–20# fractions were mixed with magnesium stearate. This mixture was compressed into tablets having average weight 800 mg using 8 mm punches in a rotary tablet machine (Hardik engineering, Ahmedabad).

Table 1: Composition of Different Floating Tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Curcuma longa extract	250	250	250	250	250	250	250	250	250	250	250
Piper nigrum extract	125	125	125	125	125	125	125	125	125	125	125
Berberis aristata extract	125	125	125	125	125	125	125	125	125	125	125
HPMC K4 M	100		-	150	-	-	200	-	-	150	100
HPMC E 15	-	100	-	-	150	-	-	200	-	50	50
Sod.CMC			100	-	-	150	-	-	200	-	-

Lactose	115	115	115	65	65	65	15	15	15	-	-
DCP	-	-	-	-	-	-	-	-	-	15	65
Citric Acid	50	50	50	50	50	50	50	50	50	50	50
Sod. Bicarbonate	25	25	25	25	25	25	25	25	25	25	25
Mg. stearate	10	10	10	10	10	10	10	10	10	10	10
Total Tab Wt.	800	800	800	800	800	800	800	800	800	800	800

Evaluation of Tablet Properties

Determination of Pre-compression Parameters

The flow properties of granules (before compression) were characterized in terms of bulk density, tapped density, angle of repose and compressibility index.

Determination of post-compression Parameters

(A) Weight Variation:

Twenty tablets were selected randomly from the lot and weighed individually to check for weight variation.

(B) Hardness Test:

Monsanto hardness tester was used for the determination of hardness of tablets.

(C) Drug Content:

Ten tablets were finely powdered. Quantities of the powder equivalent to 500mg of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* were accurately weighed and transferred to a 100mL of volumetric flask. The flask was filled with methanol HPLC grade solution and mixed thoroughly. The solution was made up to volume 100mL and filtered. Dilute 1mL of the resulting solution to100mLwith Methanol HPLC grade. The peak area of the resulting solution was measured using HPLC (Spectra sytem, P-400, China) method adopted here (see in section 2.4.2(D))**.** The linearity equation obtained from calibration curve was used for estimation of curcumin, berberine and piperine.

(D) Estimation of curcumin, berberine and piperine in combined spray dried extract

The curcumin, berberine and piperine in spray dried extract were determined by HPLC method. 0.25, 0.50, 0.75, 1.00 and 1.25 ml of curcumin (190µg/ml), berberine (45 µg/ml),) and piperine (70 µg/ml) stock solution were transferred to 10ml volumetric flasks and volume was made upto the mark using methanol to obtain the final concentration 47.5, 95.0, 142.5, 190, 237.5 µg/ml of curcumin, 11.25, 22.5, 33.75, 45, 56.25 µg/ml of berberine and 17.5, 35, 52.5, 70, 87.5 µg/ml of piperine. The injection sample volume was 20 µL. The analyses were performed in triplicate and the drug content was calculated on the basis of the peak area against a calibration curve prepared by injecting standard solutions.

Chromatographic Condition

- Column: CurosilPFP 5µ
- Mobile phase: Methanol: 10mM Ammonium acetate with acetic acid (pH 3) (75:25)
- Flow rate: 1 ml/min
- Detection Wavelength: 254nm
- Injection Volume: 20µl

(E) Friability: Twenty tablets were accurately weighed and placed in the friabilator (Roche's Friabilator) and operated for 100 revolutions. The tablets were dedusted and reweighed. The tablets that loose less than 1% weight were considered to be compliant.

The % friability was then calculated by

$$\%\text{Friability} = \frac{(\text{Initial wt-Final wt})}{\text{Initial wt}} * 100$$

(F) Floating Lag Time, Total Floating Time Determination and Drug Release Studies:

Floating lag time and total floating time were determined in USP dissolution apparatus II (Electrolab, TDT-08L, Mumbai, India) simultaneously with drug release studies using 900 ml buffer pH 1.2 maintained at 37±0.5°C and at 50 rpm. The time required for the tablet to rise to the surface and float was determined as floating lag time. Total floating time is the total time for which the tablet floats in dissolution medium including floating lag time. The tablet did not stick to the dissolution vessel or the shaft. It was found to float freely in the vessel without being hindered by the shaft movement. For drug release studies, 5 mL of sample was withdrawn at 0.5,1, 2, 3, 4, 5, 6, 7 and 8 h and was replaced with equal volume of dissolution medium. The collected samples were filtered and analyzed at λmax 254 nm using a HPLC (Spectra sytem, P-400, China).

(G) Drug Release Kinetics:

Different kinetic models such as zero order (cumulative amount of drug released vs. time), first order (log cumulative percentage of drug remaining vs. time) and Higuchi model (cumulative percentage of drug released vs. square root of time) were applied to interpret the drug release kinetics from the floating tablet.[9,10] Based on the highest regression values (r2) for correlation coefficients for formulations, the best-fit model was decided. In order to authenticate the release model, dissolution data can further be analyzed by Peppas and Korsmeyer's equation,

$Mt/M\infty = kt^nA$

Where, $Mt/M\infty$ is the fraction of drug released at time t. K is a constant and n characterizes the mechanism of drug release from the formulations during dissolution process. Value of n = 0.5

indicates case I (Fickian) diffusion or square root of time kinetics, 0.5 < n < 1 anomalous (non-Fickian) diffusion, n = 1 Case-II transport and n > 1 Super Case-II transport.

(H) Swelling index:

The tablets were weighed individually (W_0) and placed separately in petri dish filled with 5 ml 0.1N HCl at room temperature. The swollen weight of the tablets was determined at predefined time intervals until 8 h. The tablets were removed from petri dish, and the excess surface liquid was removed carefully using the tissue paper.[11] The swollen floating tablets were then reweighed (W_t) and % swelling index was calculated using the following formula:

$$\text{Swelling index} = \frac{W_t - W_0}{W_0}$$

Where, W_0 is the initial weight of tablet, and W_t is the weight of the tablet at time t.

Stability Studies

The optimized formulation of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* was packed in amber color bottle and aluminum foil laminated on the upper part of the bottle and these packed formulation was stored in stability chamber maintained at 40°C ± 2°Cand 75%± 5% RH for 3 months. The samples were withdrawn periodically and evaluated for their in drug content, *in vitro* buoyancy studies and for *in vitro* drug release.[12]

RESULTS AND DISCUSSION

Drug-Excipients Compatibility Studies

DSC thermograms of spray dried extract of *Curcuma longa, Berberis aristata and Piper nigrum* shown melting endotherm at 183°C, 130°C and 145°C respectively. While optimized batch (F11) showed the endothermic peak at 185°C and 110°C with the loss of its sharp appearance corresponding to peak of sprays dried extract of Curcuma longa and *Berberis aristata*. In the DSC thermogram of spray dried extract of *Piper nigrum in formulation* was shifted from 145°C to 150°C. The peak obtained in the DSC of *Curcuma longa, Berberis aristata and Piper nigrum* correlates with peak shown in formulation F-11. It does not show any well defined interaction between spray dried extract of *Curcuma longa, Berberis aristata and Piper nigrum* and its formulation (F-11) (Figure.1).

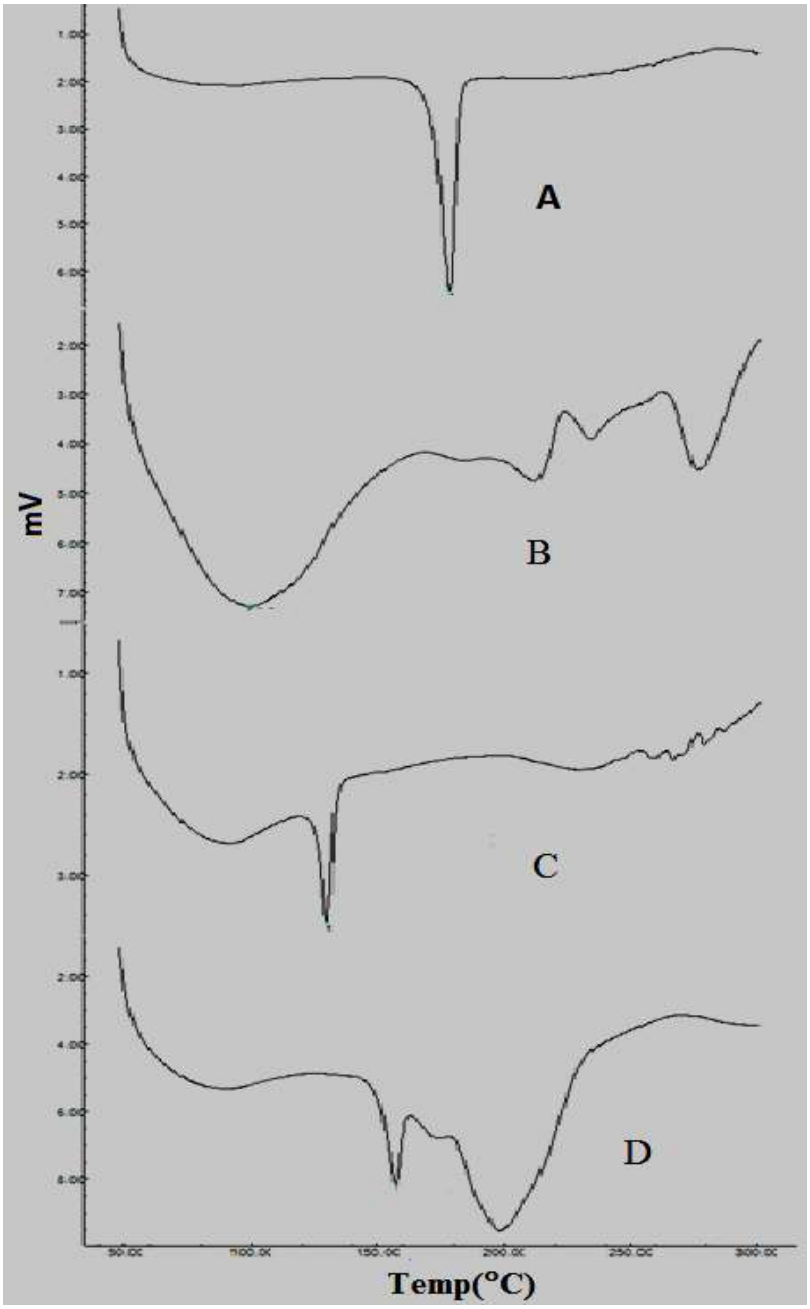

Figure1: DSC Spectra of Spray dried extract of (A) *Curcuma longa* (B) *Berberis aristata* (C) *Piper nigrum* and (D) Formulation F11.

FTIR spectroscopy was used to assess the interaction between excipients and spray dried extract of *Curcuma longa, Berberis aristata and Piper nigrum* in the floating tablets. In FTIR study, complexation, shifts or changes in the absorption spectrum may occur. FTIR spectrum of spray dried extract of *Curcuma longa* showed a stretching vibration at 3418 cm^{-1} indicating presence of OH group and at 1630 cm^{-1} indicating presence of C=O group. The IR spectrum of spray dried extract of *Berberis aristata* exhibited C-H stretching at 2820 cm^{-1} while C=C and C=N stretching was observed at 1597 cm^{-1}. Also, IR spectrum of spray dried extract of *Piper nigrum* found at 3008

cm^{-1} for alkenes, 2933 cm^{-1} for CH_2-CH_2-CH_3, 1630 cm-^{1} form NH_2 and 1528 cm^{-1} for ketonic group. The FTIR spectra of spray dried extract of *Curcuma longa, Berberis aristata, Piper nigrum* and formulation (F-11) were found to be similar to i.e. no shifting or change in the spectrum was observed (Fig ure2).

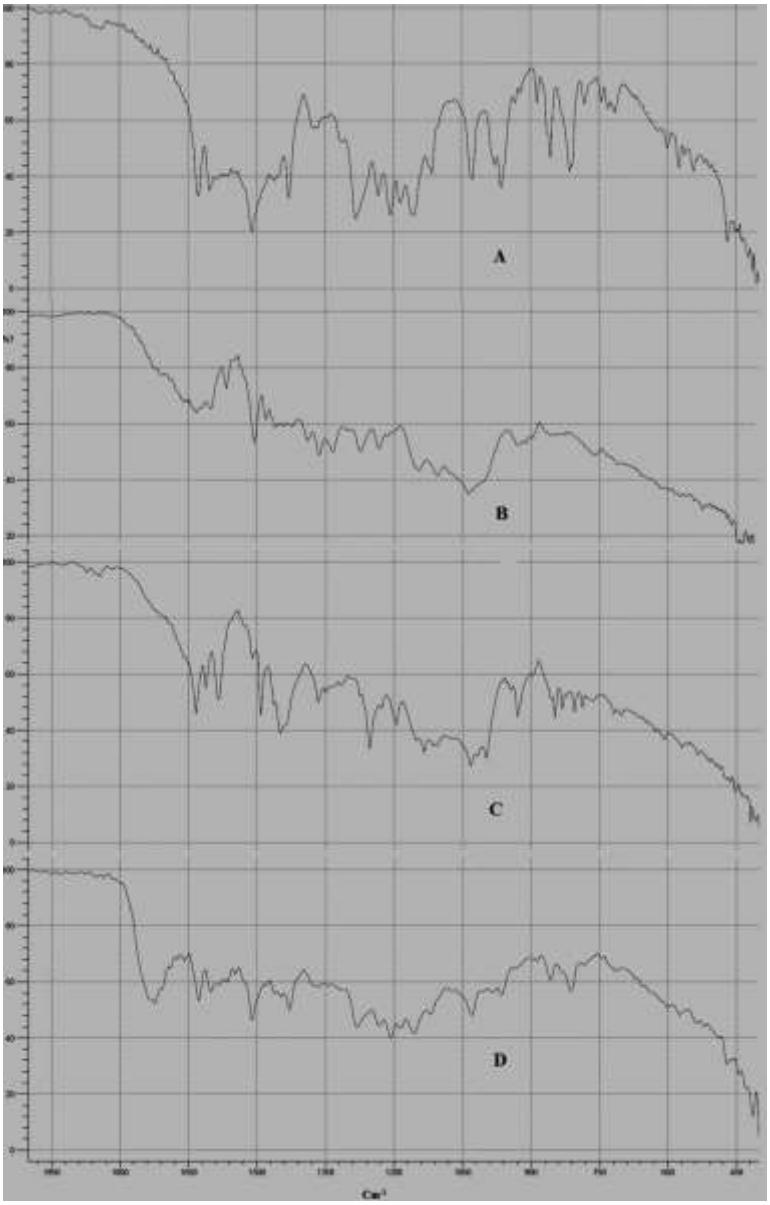

Figure 2: FTIR Spectra of Spray dried extract of of (A) *Curcuma longa* (B) *Berberis aristata* (C) *Piper nigrum* and (D) Formulation F11.

Pre-compression Parameters

Results of the pre-compression parameters performed on the blend for batch F1 to F11 were tabulated in Table 2. The bulk density and the tapped density for all the formulations varied from 0.333 to 0.477 g/cm^3 and 0.400 to 0.572 g/ cm^3 respectively. Carr's index lies within the range of 11.2 to 23.08%. All formulations show good compressibility. Angle of repose of all the

formulations was found to be less than 30°, which indicates a good flow property of the powders. Hausner ratio was found to be in the range of 1.17 to 1.22.

Table 2: Pre-Compression Parameters of Designed Formulations (F1–F11)

	Pre-compression evaluation parameters				
Granules	**Bulk density (gm/cm^3) (n=3) Mean±SD**	**Tapped density (gm/cm^3) (n=3) Mean±SD**	**Angle of repose (n=3) Mean±SD**	**Carr's Index(CI)**	**Hausners ratio(HR)**
F1	0.384±0.02	0.454±0.05	28.40±1.02	15.42	1.18
F2	0.333±0.05	0.400±0.03	26.47±1.2	16.75	1.20
F3	0.357±0.06	0.434±0.04	29.35±0.09	17.74	1.22
F4	0.408±0.04	0.487±0.07	29.40±1.25	16.22	1.19
F5	0.449±0.01	0.527±0.06	29.56±1.10	14.80	1.17
F6	0.410±0.02	0.490±0.04	28.54±0.08	16.33	1.20
F7	0.363±0.08	0.444±0.03	26.34±1.26	18.24	1.22
F8	0.477±0.02	0.572±0.02	28.76±1.31	16.61	1.20
F9	0.417±0.03	0.496±0.01	27.35±1.29	15.93	1.19
F10	0.463±0.01	0.541±0.04	21.94±1.10	14.42	1.17
F11	0.443±0.04	0.517±0.05	21.54±1.26	14.31	1.17

Post compression Parameters

The formulated tablets were subjected for post compression evaluation such as thickness, weight variation, hardness, friability and drug content. Tablet thickness was uniform in all the formulations and values for tablets ranged from 4.8 to 5.2 mm. The hardness of all formulations was in the range of 4.3 to 6 kg/cm^2, indicating satisfactory mechanical strength. The average weight of the tablets for all the formulations was found to 800 mg with a standard deviation of 0.57 to 3.51. The friability values ranged from 0.61 to 0.84%. All the values are below 1% indicating that tablets having enough mechanical strength[11]. The percent content of curcumin, piperine and berberine in the tablets was found to be in between 95.02 to 99.71%. Table 3 shows the results of physicochemical characters of floating tablets.

Table 3: Post-Compression Parameters of Developed Formulations (F1–F11)

Post compression parameters of formulations (F1–F11)							
Batch	**Thickness (mm) (n=3) Mean±SD**	**Weight variation (mg) (n=20) Mean±SD**	**Drug content (%) (n=3) Mean±SD**			**Hardness(kg/cm^2) (n=3) Mean±SD**	**Friability (%) (n=10) Mean±SD**
			Curcumin	**Piperine**	**Berberine**		
F1	4.9±0.04	800±1.20	96.02±0.9	95.02±0.5	97.02±0.8	4.8±0.03	0.61±0.04
F2	5.0±0.02	800±2.30	97.60±0.8	95.40±0.5	96.32±0.4	4.5±0.04	0.62±0.03
F3	5.0±0.03	800±3.51	96.80±0.7	98.48±0.6	97.29±0.3	4.3±0.02	0.77±0.05
F4	5.1±0.06	800±3.21	98.05±1.0	96.12±0.5	95.33±0.6	4.9±0.05	0.82±0.06
F5	4.8±0.08	800±2.58	97.80±1.1	95.62±0.7	95.51±0.9	5.0±0.04	0.73±0.04
F6	5.2±0.02	800±3.26	96.08±0.8	96.08±0.8	96.08±0.8	5.5±0.03	0.61±0.02

F7	5.0±0.01	800±3.06	96.10±0.7	98.50±0.5	97.43±0.1	6.0±0.04	0.73±0.07
F8	5.0±0.03	800±1.28	96.81±0.9	95.41±0.5	98.81±0.7	5.2±0.06	0.84±0.06
F9	4.9±0.02	800±0.98	95.80±0.8	98.80±0.9	97.80±0.4	5.0±0.07	0.78±0.05
F10	5.0±0.04	800±0.57	99.54±1.1	98.34±0.9	97.24±0.8	4.5±0.08	0.54±0.03
F11	5.1±0.07	800±1.06	98.71±0.7	99.71±0.6	98.61±0.4	5.3±0.05	0.71±0.05

Floating lag time, total floating time determination and drug release studies

Floating tablets were prepared with the aim of having maximum drug release in 8h and with minimum floating lag time and good matrix integrity. Table 4 shows results for floating lag time, total floating time and matrix integrity. Effects of various polymers and their concentration on floating behavior and were studied. HPMC K4M, HPMC E5 and sodium carboxymethyl cellulose (Sod.CMC) were tried at different concentrations to study their influence on floating behavior and *in vitro* release of release of curcumin, piperine and berberine from floating tablets. In case of formulations F1, F2 and F3, only batch F1 containing HPMC K4M exhibited floating lag time and total floating time of 360 Sec and 6 hr respectively. It was found that formulation F1 showed release of 99.86%, 90.84% and 93.85% for curcumin, piperine and berberine at end of 6^{th} hr respectively. It was also noticed that F2 and F3 had not satisfactory matrix integrity and floating behavior (Fig 3-5). It was found that formulation F4 floated for almost 8h, whereas formulation F5 and F6 remained buoyant for approximately 3h and 4h respectively (table 4). From the results of drug release studies, it was found that formulations F4–F6 did not give the desired release. F4 showed a release of curcumin, piperine and berberine of 84.74%, 88.78% and 94.96% at the 8 h. It was not satisfactory drug release especially for curcumin and piperine at end of 8hr. Also, formulation F5 and F6 were showed complete release of curcumin, piperine and berberine within 4 h. Thus, the formulations F4–F6 were not considered for further studies. In order to further increase in polymer concentration, sustain release of curcumin, piperine and berberine from tablets was observed (F7, F8 and F9). Also, increasing the HPMC K4M concentration to 200 mg in formulation F7 increased the buoyancy to 840 sec and reduced the rate of release of curcumin piperine and berberine to 75.13%, 79.35% and 85.93% at end of 8h consequently. Because of poor matrix integrity of formulation F8 and F9, were shown incomplete drug release from floating tablets. It was found from literatures that increase in the polymer concentration, the viscosity of the gel layer around the tablet increases, thereby limiting the release of active ingredient[10,12,13]. However, all the above formulations (F1-F9) prepared with lactose, which leads to rapid uptake of medium into the core by diffusion, resulting in immediate generation of carbon dioxide causing poor matrix integrity. Therefore, formulation F10 and F11 were formulated using DCP as filler of

choice. Formulation F10 containing HPMC K4M and HPMC E15 (150 and 50 mg) showed curcumin, piperine and berberine release of 80.87%, 83.21% and 88.36% at end of 8th hr. While F11 with HPMC K4M and HPMC E15 (100 and 50 mg) showed complete release of curcumin, piperine and berberine. In the case of formulation F11, it was observed that 98.38%, 99.13% and 98.58% released at end of 8 h and 51.87%, 52.98% and 53.44% released within 3h for curcumin, piperine and berberine as is the criteria for controlled release matrix (Figure 3-5). F11 also showed optimum floating lag time, total floating time and excellent matrix integrity. The dissolution data of optimized formulation (F-11) was fitted to zero order, first order, Higuchi model and Korsmeyer-Peppas model to study release kinetics of curcumin, piperine and berberine. The mechanism of release of curcumin, piperine and berberine from F-11 was determined by finding the r^2 value for each kinetic model. For Formulation (F-11), r^2 value of zero-order and Korsmeyer–Peppas model is very near to 1 than the r^2 values of other kinetic models (Table 5). Thus it can be said that the drug release follows zero-order and Korsmeyer–Peppas model mechanism. Also, Korsmeyer–Peppas equation's 'n' values for curcumin, piperine and berberine in batch F11 were above 0.5. It was concluded that the optimized formulation followed mixed mechanism of diffusion and erosion, so called anomalous/Non-Fickian diffusion mechanism for curcumin, piperine and berberine release[14].

Table 4: *In vitro* buoyancy data for designed formulations (F1-F11)

Floating lag time, total floating time and matrix integrity			
Batch	**Floating lag time (Sec)**	**Total floating time (h)**	**Tablet integrity at pH 1.2**
F1	360	6	Accepted
F2	---	---	---
F3	---	---	---
F4	720	>8	Good
F5	300	3	Erode
F6	600	4	Erode
F7	840	>8	Good
F8	480	4	Erode
F9	900	4.5	Erode
F10	1140	>8	Good
F11	330	>8	Good

Table 5: Release Kinetics Data of the Formulations F11

Batch code		**Zero order**	**First order**	**Higuchi model**	**Korsmeyer-Peppas**	
F11		r^2	r^2	r^2	η	r^2
	Curcumin	0.9976	0.9835	0.9931	0.561	0.9914
	Piperine	0.9977	0.9820	0.9947	0.555	0.9944
	Berberine	0.9958	0.9813	0.9930	0.502	0.9935

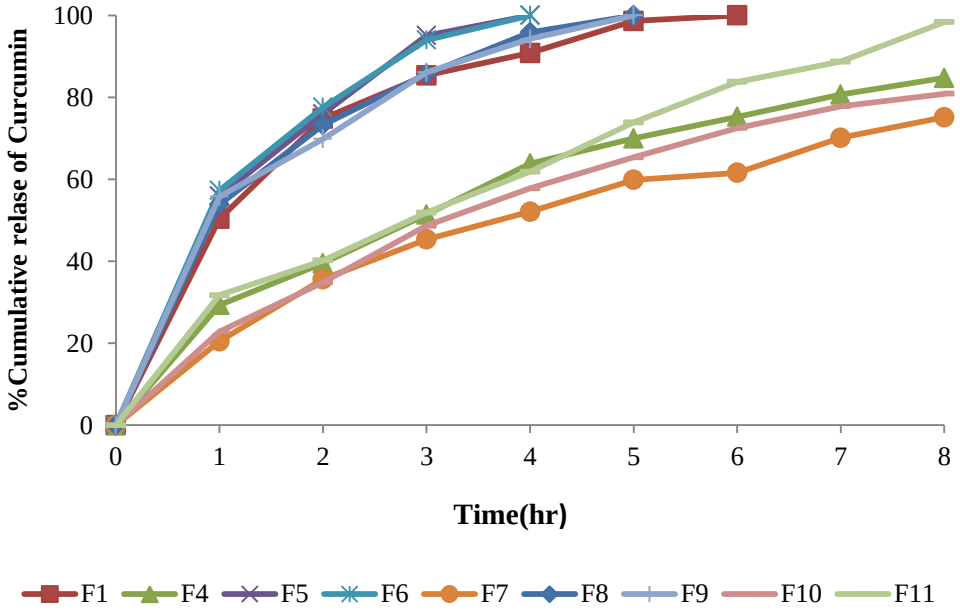

Figure 3: *In vitro* Drug Released Profile of Curcumin in Formulations F1 to F11.

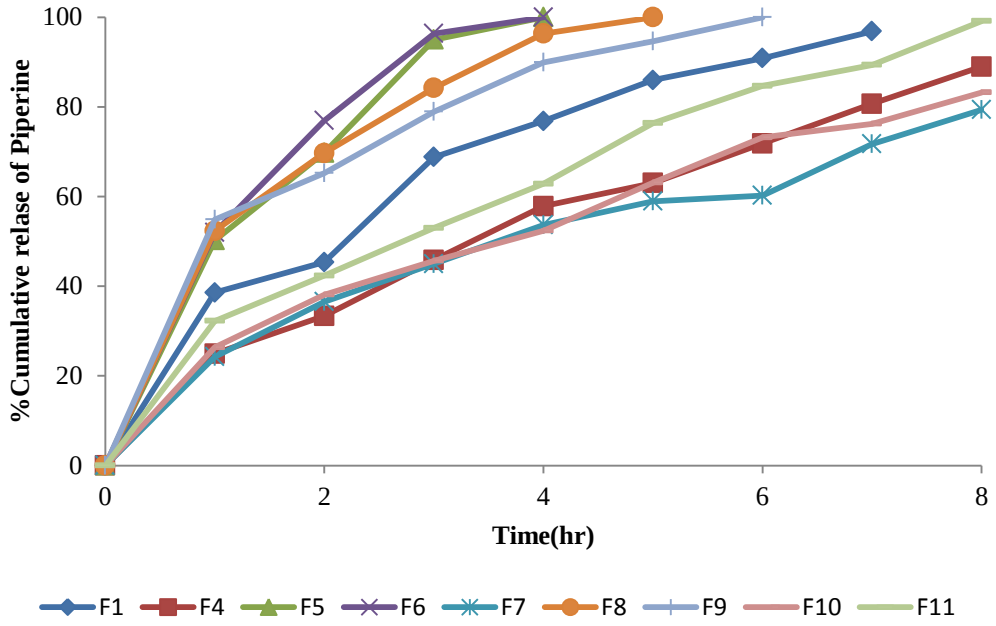

Figure 4: *In vitro* Drug Released Profile of Piperine in Formulations F1 to F11

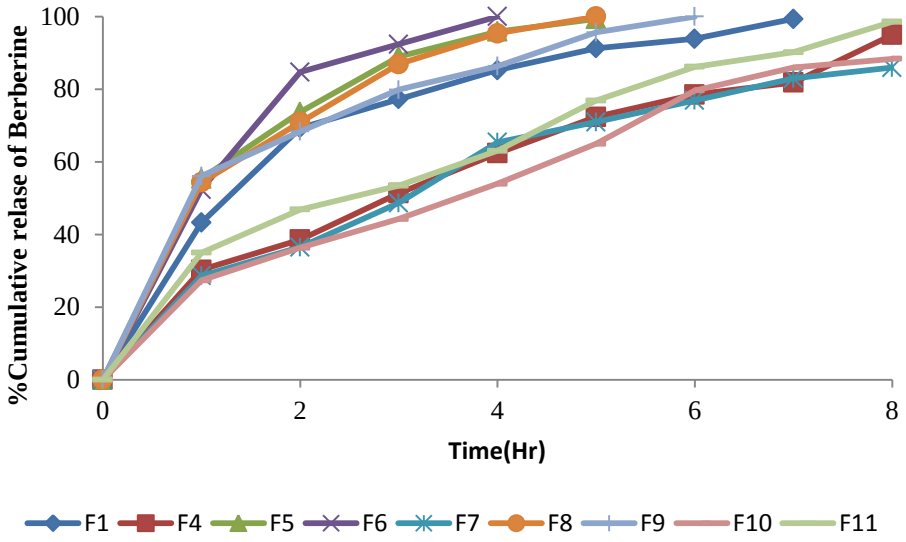

Figure 5: *In Vitro* Drug Released Profile of Berberine in Formulations F1 to F11

Swelling Index

The swelling index of the tablets formulation F1, F4, F7, F10 and F11 was evaluated and plot of % swelling index versus time (h) was depicted in Figure 6, where the highest and lowest swelling was observed with the formulation F1 and F11 after 8 hrs, respectively. As time increase, the swelling index was increased, because weight gain by tablet was increased proportionally with rate of hydration[9, 11]. Later on, it decreased gradually due to dissolution of outermost gelled layer of tablet into dissolution medium. The swelling index was increased with concentration of HPMC since this polymer gradually absorbs buffer due to hydrophilic nature.

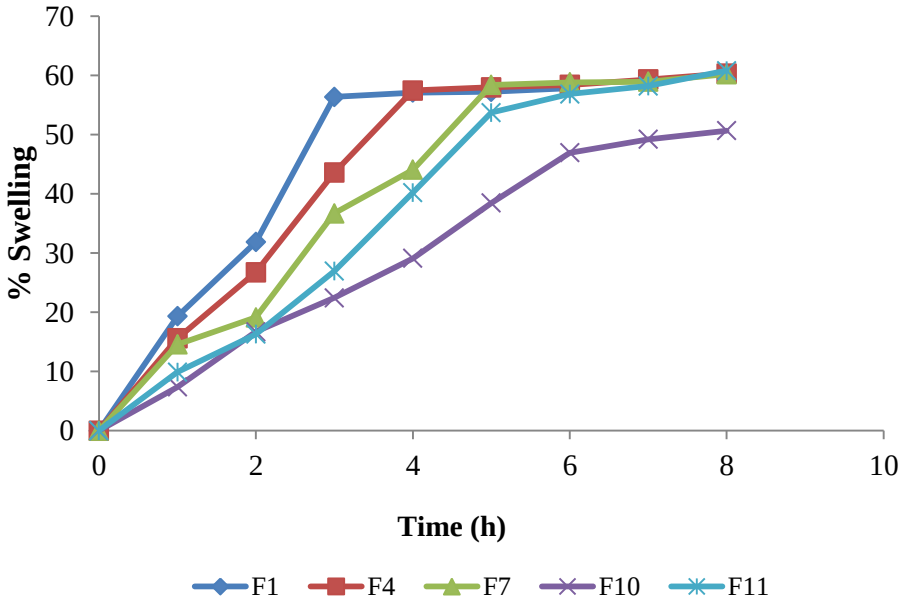

Figure 6: Swelling Index of Formulations

Stability study

The results of stability studies did not show any significant change in the drug content, *in vitro* buoyancy studies, and *in vitro* dissolution studies of formulation (F-11).

Table 6: Stability study of Batch F11

Time (months)	Drug content			Floating behavior		*In vitro* drug release at 8h		
	Curcumin	Piperine	Berberine	Floating lag time (Sec)	Total floating time(h)	Curcumin	Piperine	Berberine
Zero	98.71±0.7	99.71±0.6	98.61±0.4	335	>8	98.38±0.5	99.13±0.7	98.58±0.6
First	95.41±0.8	98.61±0.5	96.31±0.3	341	>8	97.28±0.2	98.53±0.2	97.48±0.5
Second	97.61±0.7	99.41±0.4	98.41±0.5	330	>8	98.48±0.4	97.13±0.4	96.58±0.4

CONCLUSION

In the present work, batch F-11 containing HPMC K4M and HPMC E15 in a weight of 100 and 50 mg along with ratio of 2:1 for sod bicarbonate and citric acid as effervescent agents gave better controlled drug release and floating properties in comparison to the other formulations. The most promising mechanism that the release patterns of the optimized formulation was followed by non-Fickian diffusion or anomalous diffusion. Finally, it was concluded that synthetic polymers such as HPMC can be successfully used for the sustained release of spray dried extract of *Curcuma longa*, *Piper nigrum* and *Berberis aristata* through floating drug delivery.

REFERENCES

1. Awaad AS., Elmeligy RM, Soliman GA. Natural products in treatment of ulcerative colitis and peptic ulcer. J Saudi Chem Society. 2013; 17:101–124.
2. Vimala G. Shoba FG. A review on antiulcer activity of few Indian medicinal plants. Int J Micro. 2014, 14.
3. Yadav SK, Sah AK, Jha RK, Sah P, Shah DK. Turmeric (curcumin) remedies gastroprotective action. Pharmacog Rev. 2013; 7(13): 42-46.
4. Chiung HC, Shu FP, Chih HL, Yihsing Y, Tingyu C, Jing-YW et al. Development of novel nanoparticles shelled with heparin for berberine delivery to treat helicobacter pylori. Acta Biomaterialia. 2011; 7:593-603.
5. Weiping B, Huibin Man, Maoqiang Man. Efficacy and safety of herbal medicines in treating gastric ulcer: a review. World J Gastroenterol. 2014; 20(45): 17020–28.
6. Balaji G, Ramesh B, Mahendranath G, Jagadeesh kumar D Babu, V.V. Protective effects of a poly herbal formulation against aspirin induced ulcers in wistar rats. Int J Pharm and Pharm Sci. 2012; 4, 5.

7. Zhen HZ, Yong SS, Hui P, Were LL. Munyendo, Hui XL, Sheng-LZ. Preparation and evaluation of Berberine Alginate Beads for Stomach-Specific Delivery. Molecules. 2011; 16, 10347-56.
8. Juliana SC, Fernando BD, Luís Alexandre PF. Development of enteric coated tablets from spray dried extract of Feverfew (Tanacetum parthenium L.) Braz J Pharm Sci. 2009; 45(3), 574-584.
9. Kadam AM, Upadhye S, Honmane S, Patil S, Patil S. Formulation and Evaluation Of Anti-Ulcer Floating Tablet Using Swellable Polymers. Inte J Drug Deliv. 2014; 6, 244-253.
10. Pawar H A, Gharat PR, Dhavale RV, Joshi PR, Rakshit PP. Development and Evaluation of Gastroretentive Floating Tablets of an Antihypertensive Drug Using Hydrogenated Cottonseed Oil. ISRN Pharmaceutics. 2013, Article ID 137238, 1-9.
11. Ranade AN., Wankhede SS., Ranpise NS., and Mundada MS. Development of Bilayer Floating Tablet of Amoxicillin and Aloe Vera Gel Powder for Treatment of Gastric Ulcers. AAPS PharmSciTech. 2012; 13, 4, 1518-23.
12. Kumavat SD, Chaudhari YS, Borole P, Mishra P, Shenghani K, Duvvuri P. Degradation Studies of Curcumin. Int J Pharm Rev Res. 2013; 3(2); 50-55.
13. Shishu, Gupta N, Aggarwal N. A Gastro-retentive Floating Delivery System for 5-Fluorouracil. Asian J Pharm Sci. 2007; 2(4):143-149.
14. Emara LH, Abdou AR, Elashmawy AA, Badr RM, Mursi NM. In Vitro Evaluation of Floating Matrix Tablets of Amoxicillin and Metronidazole for the Eradication of Helicobacter Pylori. Inte J Pharm Pharma Sci. 2013; 4 (3): 671-681.