RESEARCH ARTICLE

Formulation and Evaluation of HPMC and Physillium Husk based floating tablets of Curcumin for Ulcer

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ABSTRACT

The purpose of the present study was to develop floating matrix tablets for Curcumin using psyllium husk as release controlling polymer and to compare the release pattern with synthetic polymers like HPMC K15M and HPMC K100M. Formulations were prepared by wet granulation method and evaluated for floating lag time, swelling index, erosion, drug content and *In-Vitro* drug release profile. It was found that floating duration of the formulation containing psyllium husk alone was less than that containing similar concentration of HPMC K15M and HPMC K100M. Release rate of the formulation containing psyllium husk in combination with HPMC K15M more than the formulation containing similar amount of HPMC K100M. The *In-Vitro* release data and drug release mechanism of the optimized formulation followed the higuchi kinetics and matrix type respectively. It can be concluded that psyllium husk can be a promising polymer for gastro retentive floating drug delivery systems in combination with synthetic polymers.

Keywords: Curcumin, psyllium husk, floating lag time, floating drug delivery system, HPMC K15M & HPMC K 100M.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost-effective manufacturing process.[1]

Pharmaceutical products designed for oral delivery are mainly conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:[2, 3]

1) Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2) A typical peak-valley plasma concentration-time profile is obtained which makes it difficult to attain steady state condition.
3) The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the CSS values fall or rise beyond the therapeutic range.
4) The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs.

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.[4]

Drug Delivery Systems:

Controlled Drug Delivery Systems:

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue[5].

Controlled drug delivery or modified drug delivery systems are conveniently divided into four categories.

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1) Delayed release
2) Sustained release
3) Site-specific targeting
4) Receptor targeting

Oral Controlled Drug Delivery Systems:

Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either local or systemic action.

Gastroretentive Dosage Form (GRDF):[9, 10]

It is evident from the recent scientific and patient literature that an increased interest in novel dosage forms that are retained in stomach for a prolonged and predictable period of time exists today in academic and industrial research groups. One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time (GRT), i.e. gastro retentive dosage form (GRDFs or GRDS).

GRDFs extend significantly the period of time over which the drugs may be released. They not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage form.

Need for gastroretentive drug delivery system: [11]

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need for repeated dosages or with a low dosage frequency. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, which is where absorption occurs and contact time is limited. Under normal or average conditions, for example, material passes through the small intestine in as little as 1-3 hours.5 In general, appropriate candidates for CRGRDF are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT.

Dosage form with prolonged GRT, i.e. gastro retentive dosage form (GRDF), will bring about new and important therapeutic options such as :

1. This application is especially effective in sparingly soluble and insoluble drugs. It is known that, as the solubility of a drug decreases, the time available for drug dissolution becomes less adequate and thus the transit time becomes a significant factor affecting drug absorption. To override this problem, erodible, gastroretentive dosage forms have been developed that provide continuous, controlled administration of sparingly soluble drugs at the absorption site.

2. GRDFs greatly improve the pharmacotherapy of the stomach through local drug release, leading to high drug concentration at the gastric mucosa. (For e.g. Eradicating Helicobacter pylori from the submucosal tissue of stomach) making it possible to treat stomach and duodenal ulcers, gastritis and oesophagitis, reduce the risk of gastric carcinoma and administer non-systemic controlled release antacid formulations (calcium carbonate).

3. GRDFs can be used as carriers for drugs with so-called absorption windows. These substances for e.g. antiviral, antifungal and antibiotic agents (Sulphonamides, Quinolones, Penicillins, Cephalosporins, Aminoglycosides, Tetracyclines etc.) are taken up only from very specific sites of the GI mucosa.

Approaches to Gastric Retention [17, 18]

Buoyant/ Floating Systems:

Floating Drug Delivery Systems [19] (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affecting the gastric emptying rate [Figure 1].

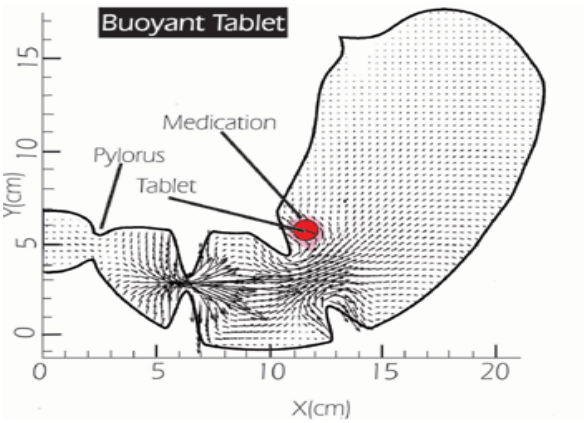


Fig 1. Graphic of Buoyant tablet, which is less dense than the stomach fluid and therefore remains in the fundus.

While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations. Floating systems can be classified into two distinct categories, non-effervescent and effervescent systems.

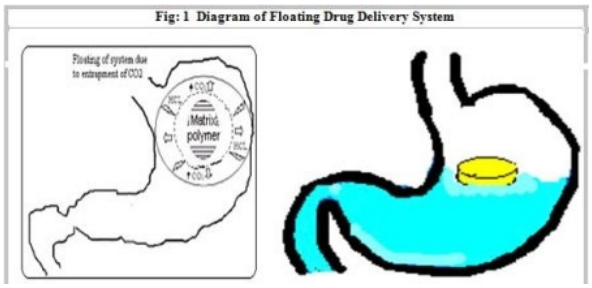


Fig 2: is showing the floating drug delivery in stomach

Mechanism of floating systems: [22]

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas generating systems and swelling or expanding systems), mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices and co-administration of gastric emptying delaying drugs. Among these, the floating dosage forms are the most commonly used. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is eliminated from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention effect, a minimal level of floating force (*F*) is also required to maintain the buoyance of the dosage form on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to *F* (as a function of time) that is required to maintain a submerged object [Figure 2].

$F = F_{buoyancy} - F_{gravity} = (D_f - D_s)\, gv$

Where,

F= total vertical force, D_f = fluid density,

D_s = object density, v = volume and

g = acceleration due to gravity.

Types of Floating Drug Delivery Systems (FDDS) [23, 24]

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are:

A. Effervescent System, and

B. Non- Effervescent System.

Advantages of FDDS: [28, 29]

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. These advantages include:

1. Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site.
2. Controlled delivery of drugs.
3. Delivery of drugs for local action in the stomach.
4. Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate.

5. Treatment of gastrointestinal disorders such as gastro-esophageal reflux.
6. Simple and conventional equipment for manufacture.
7. Ease of administration and better patient compliance.
8. Site-specific drug delivery.

Disadvantages of FDDS:

1. Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
2. Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
3. High variability in gastric emptying time due to its all or non-emptying process. Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diametral size. Therefore patients should not be dosed with floating forms just before going to bed.

MATERIALS AND METHODS

Materials: Curcumin, HPMC K15M, HPMC K100M, Psyllium husk, Sodium bicarbonate, Citric acid, Magnesium stearate, Talc, Polyvinyl pyrrolidone K-30, Hydrochloric acid, Potassium chloride, Potassium Dihydrogen Phosphate and Disodium Hydrogen Phosphate.

The equipments used in this study were Dissolution Apparatus, Disintegration Apparatus, UV Spectrophotometer, Digital Balance, Hardness Tester, Friability Tester, Punching Machine, Vernier Callipers and FT-IR.

Methods:

- **Formulation of Floating Tablets:**

Different batches of floating matrix tablets were prepared by wet granulation method using different ratios of drug, psyllium husk, HPMC K 15 M and HPMC K 100 M. The respective powders (drug & polymers) were blended thoroughly and a dump mass was prepared by adding the granulating agent (5 % PVP K-30 in isopropyl alcohol). Dump mass was passed through sieve number 10 and dried in hot air oven at 600C for 20mins. After drying, granules were further passed through sieve number 22 to attain the uniformity in granules. Finally, optional additives like magnesium stearate and talc were added and finely blended. The required amount of the blend was weighed and fed manually into the die of single punch tableting machine to produce tablets using concave faced punch of suitable diameter. The tablet hardness was maintained in the range of 2-5 kg/cm^2. The compositions for polymeric solutions were mentioned in Table1.

Table 1: Compositions for Different Formulations

S. No	Ingredients	Formulations (in mg/tablet)				
		F1	F2	F3	F4	F5
1	Curcumin	100	100	100	100	100
2	HPMC K15M	200	-	-	100	-
3	HPMC K100M	-	200	-	-	100
4	Psyllium husk	-	-	200	100	100
5	Sodium bicarbonate	50	50	50	50	50
6	Citric acid	25	25	25	25	25
7	Magnesium stearate	20	20	20	20	20
8	Talc	5	5	5	5	5

- **Evaluation of Prepared Tablets:** Floating tablets of curcumin extract were evaluated for following physicochemical parameters:

Preformulation Studies: It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included solubility and compatibility studies.

A. Description

Curcumin was physically examined for colour and odour etc.

B. Solubility

Solubility of curcumin was determined in water, phosphate buffer 7.4, ethanol, DMSO, tetra hydro furan etc.

C. Interaction Studies

Drug-polymer interaction study

Interaction of drug with polymers was confirmed by IR interaction studies. The pure drug along with polymer was subjected to IR studies. Combinations studied were pure drug, drug with HPMC K15M, drug with HPMC K100M and drug with psyllium husk.

Pre and Post Compression parameters:

Primary stock solution: 100 mg of curcumin was accurately weighed and dissolved in 30 ml ethanol and diluted to 100 ml with distilled water.

Secondary stock solution: 1 ml of primary solution was diluted to 100 ml distilled water to get a concentration of 10 µg /ml. From these 1 ml was pipette out diluted to 10 ml to get a concentration of 1 µg/ml.Aliquots of 1 ml, 2 ml, 4 ml, 6 ml, 8 ml, and 10 ml were pipette out and diluted to 10 ml with distilled water to get a 1 µg, 2 µg, 4 µg, 6 µg, 8 µg, and 10µg concentration of curcumin. Standard graph was plotted by keeping the known concentration on X-axis and obtained absorbance on Y-axis. The results are presented in table and represented graphically.

Construction of Standard Plot of Curcumin:

Drug Content Determination (Assay): USP defines content uniformity test for tablets containing100 mg or less of drug substance in case of uncoated tablets and for all sugar coated tablets regardless to the drug content.

Ten tablets are individually assayed for their content (according to the method described in the individual monograph) the requirements for content uniformity are met if the amount of the active ingredient in each tablet lies within the range of 85-115 % of the label claim.

Thickness [47- 49]: The dimensions of the tablet like thickness, diameter were measured using vernier calipers. Ten tablets were selected randomly for this test and the average value was reported.

Size and Shape [54-58]: The particle size and shape plays a major role in determining solubility rate of the drugs and thus potentially its bio availability. The particle size of the formulations was determined using sieve analysis.

Weight Variation: If the drug forms greater part of the tablet, any variation in the tablet weight obviously indicates a variation in the active ingredient. Weigh 20 tablets individually (i.e. determine the weight of each tablet alone; X1, X2, X3… X20)

The average weight of tablets=**Total weight of tablets/ Number of tablets**

Average weight of tablets **(X) = (X1+X2 +X3+…+ X20)/20**

Hardness: Tablets require a certain amount of strength, or hardness and resistance to friability, to is withstand mechanical shocks of handling in manufacture, packaging and shipping .Special hardness testers are used for this purpose (manually or motor driven testers). The test measures crushing strength property defined as the compressional force applied diametrically to a tablet which just fracture or break it. A force of about 4 Kg is considered the minimum requirement for a satisfactory tablet. Certain tablets such as lozenges and buccal tablets that are intended to dissolve slowly intentionally are made hard; others such as immediate-release tablets are made soft.

Friability Test: Friability test was done by Roche friabilator. Ten tablets were weighed and were subjected to the combined effect of attrition and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 in. with each revolution. Operated for 100 revolutions, the tablets were de dusted and reweighed. The percentage friability was calculated.

Disintegration Test [54-58]: This test determines whether tablets disintegrate within a prescribed time when placed in a liquid medium under prescribed experimental conditions. The U.S.P. device to test disintegration uses 6 glass tubes that are open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1L beaker of water. Simulated gastric fluid at 370C ± 20C was used. The tablet should remain 2.5 cm below the surface of liquid on their upward movement and not closer than

2.5 cm from the bottom of the beaker in their downward movement. The basket containing the tablets was moved up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet.

***In-Vitro* Drug Release Studies**[54-58]: The *In-Vitro* drug release studies of the 7 batches of curcumin floating drug delivery formulations were performed using USP dissolution rate test apparatus.

The dissolution medium was 900 ml 0.1N HCl. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37±0.50C. The tablet was placed into the vessel and a suitable device such as a wire or glass helix was used and the speed of rotation was kept at 50 rpm. At predetermined time intervals 5 ml of samples were withdrawn and replaced by an equal volume of fresh medium to maintain the sink conditions. Samples collected at 0.5,1,2,3,4,5,6,7,8,9,10,12and 24hrs were filtered and analyzed at each interval for curcumin content released at λ_{max} of 420 nm using UV-Visible Spectrophotometer. The results were tabulated in table 9.6 and represented graphically in graph 9.3.

Release Kinetics:

The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and it is particularly evident in the case of Floating drug delivery. As a model dependent approach, the dissolution data are fitted to five popular release models such as zero-order, first-order, diffusion, erosion and power law equations, which have been described in the literature. The order of release from matrix systems was described by using zero- order kinetics or first- order kinetics. The mechanism of drug release from floating drug delivery systems was studied by Higuchi equation and erosion equation.

Floating Lag Time[50-51]: Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as floating time. The test for floating time measurement is usually performed in simulated gastric fluid or 0.1M Hcl maintained at 370ºc. It is determined by using dissolution apparatus containing 900 ml of 0.1mole/lit as a dissolution medium at 370ºc. Floating properties of FDDS that enable them to be retained in stomach for prolonged period of time is usually acquired due to low density of the HBS dosage forms.

Swelling Studies[54-58]: Swelling of hydrophilic polymer such as Hydroxy Propyl Methylcellulose greatly depends upon the contents of the stomach and the osmolality of the medium. For each formulation, one tablet was weighed and placed in a beaker containing 200 ml of distilled water. After each hour the tablet was removed from beaker and weighed again up to 8hours. The percentage weight gain by the tablet was calculated by using the formula:

Swelling index (S.I) = {(Wt-Wo)/Wo} x 100

Where,

S.I. = swelling index

Wt = Weight of tablet at time t

Wo = Weight of tablet before immersion

Erosion Studies[54,-58]: Erosion studies were performed by a method dissolution test apparatus was used for this purpose. The dry matrices were weighed, placed in dissolution basket containing 900 ml of 0.1 N HCl (pH 1.2) maintained at 37 ± 0.5°C, and the basket was rotated at 100 rpm. At regular intervals, the whole basket-matrix assembly was removed from the dissolution vessels and dried to a constant weight in a hot air oven at 50°C.

Matrix erosion (%) =$W_d t/W_0 \times 100$

$W_d t$- weights of dried tablet at time t

W_0 -initial weight of dry tablet

Results and Discussion:

Floating drug delivery tablets were being formulated and the present study focused on the

formulation of FDDS by using different polymes like phyllium husk, HPMC K 100 and HPMC K15 and to evaluate its efficacy in reducing ulcers caused by H.pylori. The Floating drug delivery tablets were characterized for their weight variation, hardness, friability, drug content determination, disintegration, in-vitro dissolution studies, IR, floating lag time, swelling studies and erosion studies.

Evaluation of Floating Tablets:

➢ Preformulation Studies:

1. Description: Curcumin was physically examined for colour and odour etc. It is an orange yellow powder, with characteristic odour.

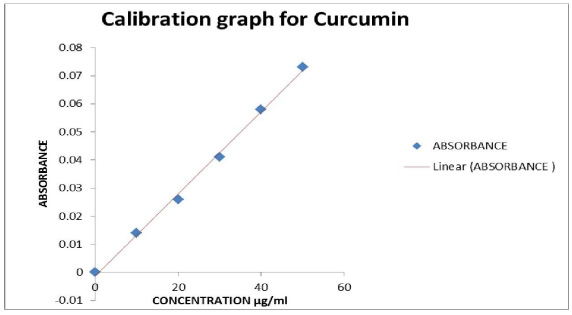
2. Solubility: Curcumin was insoluble in water, poorly soluble in buffer solution pH 7.4, and soluble in ethanol, DMSO, and Tetra hydro furan (THF).

➢ Pre and Post Compression Parameters:

Calibration Curve for Curcumin: The standard plot as per dilutions 10, 20, 30, 40, and 50 µg/ml mentioned in the experimental procedure for curcumin was done and the results are tabulated in Table9.1 and plotted in Graph 9.1.

Table 9.1: Standard values for calibration curve of curcumin

S. No	CONCENTRATION (µg/ml)	ABSORBANCE
1	10	0.014
2	20	0.025
3	30	0.039
4	40	0.058
5	50	0.073



Graph 9.1: Calibration graph for curcumin

Drug Content Determination: The assay of the different formulations F_1, F_2, F_3, F_4, F_5 were determined as given in the experimental methods and the results were tabulated in Table 9.2.

Table 9.2: Drug content determination

S. NO	FORMULATIONS	ASSAY
1	F1	99.6±0.85%
2	F2	98.21±0.41%
3	F3	92.32±0.47%
4	F4	105.15±0.35%
5	F5	100.48±0.72%

The assay or drug content in the formulations ranged between 92-106%. The assay value of F4 was found to be higher compared to the other formulations.

Weight Variation Test: Weight variation test results were plotted in Table 9.3.

Table 9.3: Weight variation

S. NO	FORMULATION	% WEIGHT
1	F1	100.2 % ± 1.58%
2	F2	99.8 % ± 2.87%
3	F3	101.3 % ± 1.93%
4	F4	103.6 % ± 2.33%
5	F5	98.3 % ± 1.85%

No of tablets taken= 20

Limit of % weight = 90%-110%

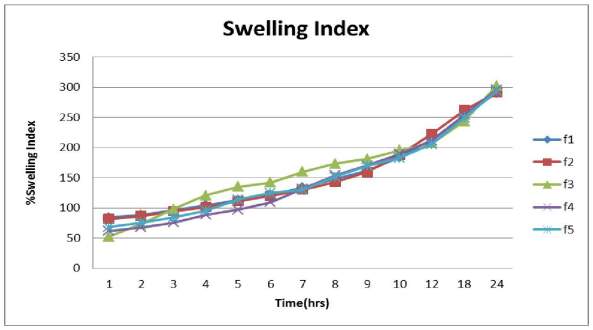
Swelling Index: Swelling is a vital factor to ensure floating. To obtain floating, the balance between the swelling and water must be reported. The formulation containing psyllium husk took about 5-8hrs to swell completely as compared to the formulation prepared with HPMC K100M that took 3-5 hrs.to swell completely. In the first hour of study, the swelling index for formulation prepared with psyllium husk alone was 52.2% (batch F3) and 81.73% (batch F2) for the formulation prepared with HPMC K100M. The swelling index after complete swelling was 302.45% for formulation prepared with psyllium alone (F3) and 291.62% for formulation prepared with HPMC K100M alone (F2). The difference in the swelling index was because, psyllium husk is a natural agent that took more time to hydrate when compared to synthetic polymer HPMC K100M. Addition of HPMC K15M in

formulation containing psyllium enhanced the swelling index at initial stage (F4= 61.8%) but swelling index after complete swelling was decreased (F4 = 295.21%). Finally the swelling index optimised formulation after complete swelling was for 295.21% formulation containing psyllium husk in combination with HPMC K15M.

Table 9.4: Swelling index

Time (hr)	F1	F2	F3	F4	F5
1	83.94	81.73	52.2	61.8	68.24
2	88.23	86.71	73.29	67.84	75.79
3	96.07	94.27	97.73	75.55	84.29
4	104.12	101.22	120.66	88.74	95.43
5	112.56	111.37	135.29	97.09	113.67
6	121.34	119.9	142.11	109.18	124.41
7	133.69	130.18	159.91	131.72	130.11
8	147.42	143.21	173.4	153.63	151.3
9	161.76	159.35	181.21	170.28	169.77
10	183.89	187.87	195.51	189.33	182.83
12	212.66	222.48	207.43	211.94	205.61
18	252.17	261.64	243.59	253.67	249.44
24	291.15	291.62	302.45	295.21	293.46

Graph 9.2: Swelling index



Floating Capacity: Floating duration & dimensional stability are important in case of once daily formulation to obtain the continuous and constant drug release up to the 24 hrs. If physical integrity of the formulation is not maintained, the tablet could break down in to the small fragments and escape from the upper part of GIT. The floating lag time and duration of floating of formulation F3 containing 200 mg of psyllium husk (drug: polymer ratio of 1:2) was 12 minutes & 8 hrs respectively and the dimensional stability was maintained up to 24 hrs. Incorporation of HPMC K15M enhanced the floating duration (F4= 24 hrs.) This might be due the synthetics nature of HPMC K15M, which hydrated at a faster rate than that of psyllium husk. HPMC K15M also helps to maintain dimensional stability at initial stage. There was no measurable effect of HPMC K15M on FLT. Formulation prepared with HPMC K100M in similar amount as that of psyllium and HPMC K15M combination (F5) showed the floating duration 24 hrs. (Table 9.5)

Erosion Studies: The percentage of matrix eroded was more for the formulations prepared with psyllium husk alone (F3 = 9.35%) than that of HPMC K100M (F2=3.56%) and HPMC K15M (F1=2.32%) after 12 hours study. Addition of HPMC K15M in formulation containing psyllium husk reduced the erosion (F4=5.35 %).

Table 9.5

S. No	F.C	DRUG	P	HPMC 15M	HPMC 100M	$NaHCo_3$	FLT(min)	FD (hrs.)	DS (hrs.)	Drug released (24hrs)
1	F1	100	-	200	-	50	1	24	24	70.28±1.62%
2	F2	100	-	-	200	50	1	24	24	66.47±1.36%
3	F3	100	200	-	-	50	12	8	24	56.23±2.12%
4	F4	100	100	100	-	50	5	24	24	89.86±1.08%
5	F5	100	100	-	100	50	5	24	24	74.77±1.41%

F.C = Formulation Code, P = Psyllium Husk Powder,

$NaHCo_3$ =Sodium Bi Carbonate, FLT = Floating Lag Time,

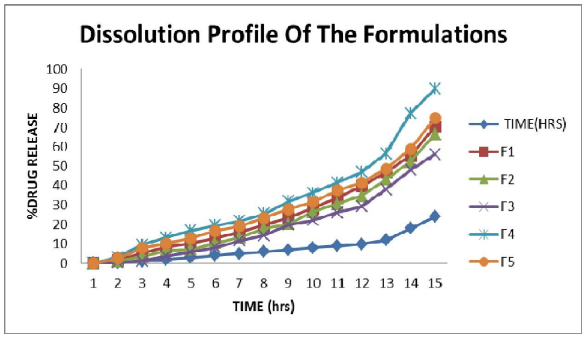
FD = Floating Duration

***In-Vitro* Studies:** The *In-Vitro* release studies were performed as mentioned in the experimental methods and the results were tabulated below in the table 9.6 and represented graphically in Graph 9.3. Two different polymers (Psyllium husk and HPMC) were used to prepare the floating tablets. It was observed that type of polymer influences the release pattern. The formulation prepared with psyllium husk alone showed more sustained release (F3 =56.23%) than those prepared with HPMC K100M (F2 =66.47%) and HPMC K15M (F1 =70.28%) after 24hrs study. But formulations prepared with psyllium husk alone were not able to float up to 24 hrs. To enhance floating duration HPMC K15M was added. The formulation containing HPMC K15M and psyllium (F4) was able to float up to 24hrs and release rate was enhanced (F4=89.86%).Finally, the cumulative percent release from optimized formulation prepared with psyllium in combination with HPMC K15M (F4=89.86%) was more than that of formulation prepared with HPMC K100M (F5=74.77%).

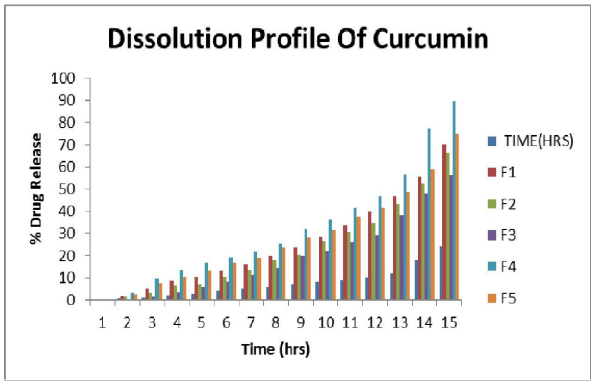
Release Kinetics: The *In-Vitro* release data of optimized formulations were treated with different kinetics models to explain the release kinetics curcumin from floating matrix tablets. These models were zero order, first order, higuchi model. Higuchi model was considered as the best fitted model.

Table 9.6: *In-Vitro* release profiles of the formulations

TIME (hrs)	F1	F2	F3	F4	F5
0.5	1.74±0.36	1.23±0.27	0.24±0.4	3.08±0.21	2.52±0.19
1	5.11±0.93	3.27±0.73	1.33±0.90	9.46±0.21	7.89±0.91
2	8.37±0.42	6.65±0.84	3.70±0.78	13.27±0.93	10.21±1.34
3	10.34±1.55	7.11±1.24	5.73±1.99	16.96±1.20	12.9±1.81
4	12.92±0.83	10.54±1.25	8.26±0.96	19.49±1.94	16.76±1.13
5	16.01±0.82	13.52±0.72	11.63±0.95	21.7±2.0	19.14±1.36
6	19.72±0.85	17.95±1.14	14.34±0.62	25.58±1.14	23.51±0.25
7	23.38±0.39	20.26±0.67	19.88±0.34	31.95±0.98	27.88±1.16
8	28.38±0.29	26.49±0.72	22.11±0.47	36.19±1.34	31.50±0.16
9	33.61±0.86	30.69±1.16	26.17±0.59	41.45±1.69	37.62±0.58
10	39.74±0.86	34.75±0.93	29.23±0.67	46.87±0.66	41.42±1.26
12	46.82±0.59	43.11±0.81	38.14±1.13	51.79±0.16	48.61±0.94
18	55.48±0.67	52.34±1.19	47.99±2.19	61.80±1.52	58.73±1.98
24	70.28±1.62	66.47±1.36	56.23±2.12	89.86±1.08	74.77±1.41



Graph 9.3: Dissolution profiles of curcumin formulations



Graph 9.3.1: Dissolution profiles of curcumin formulations

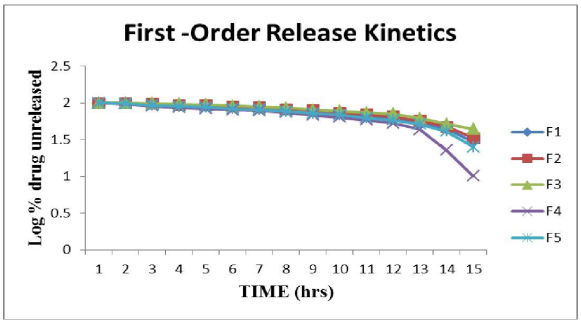
Table 9.9.1: Zero-order plot

TIME(HRS)	F1	F2	F3	F4	F5
0.5	1.74	1.23	0.24	3.08	2.52
1	5.11	3.27	1.33	9.46	7.89
2	8.37	6.65	3.7	13.27	10.21
3	10.34	7.11	5.73	16.96	12.9
4	12.92	10.54	8.26	19.49	16.76
5	16.01	13.52	11.63	21.7	19.14
6	19.72	17.95	14.34	25.58	23.51
7	23.38	20.26	19.88	31.95	27.88
8	28.38	26.49	22.11	36.19	31.5
9	33.61	30.69	26.17	41.45	37.62
10	39.74	34.75	29.23	46.87	41.42
12	46.82	43.11	38.14	56.45	48.61
18	55.48	52.34	47.99	77.25	58.73
24	70.28	66.47	56.23	89.86	74.77

Graph 9.4: Zero-order plot

Table 9.9.2: First-order plot

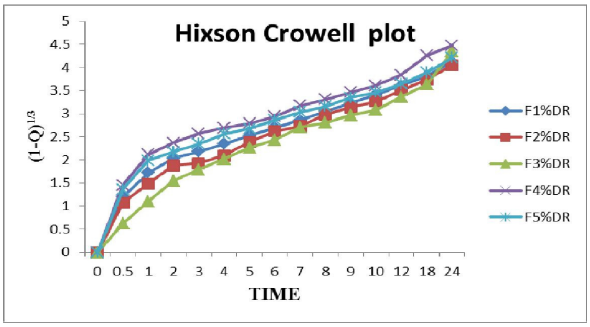
TIME(HRS)	F1	F2	F3	F4	F5
0	2	2	2	2	2
0.5	1.9924	1.9946	1.9989	1.986	1.9889
1	1.9772	1.9856	1.9942	1.9568	1.964
2	1.962	1.9701	1.9836	1.9382	1.953
3	1.9526	1.9679	1.9747	1.9193	1.94
4	1.9399	1.9516	1.9625	1.9058	1.92
5	1.9242	1.9369	1.9463	1.8938	1.9077
6	1.9046	1.9141	1.9328	1.8717	1.8836
7	1.8843	1.9017	1.9037	1.8328	1.858
8	1.855	1.866	1.8915	1.8049	1.8357
9	1.822	1.8408	1.8682	1.767	1.795
10	1.78	1.8146	1.8498	1.7253	1.7677
12	1.7257	1.755	1.7914	1.6389	1.7109
18	1.6485	1.678	1.7161	1.3569	1.6156
24	1.473	1.525	1.6412	1.006	1.4019



Graph 9.5: First-order plot

Table 9.9.3: Hixon Crowell plot

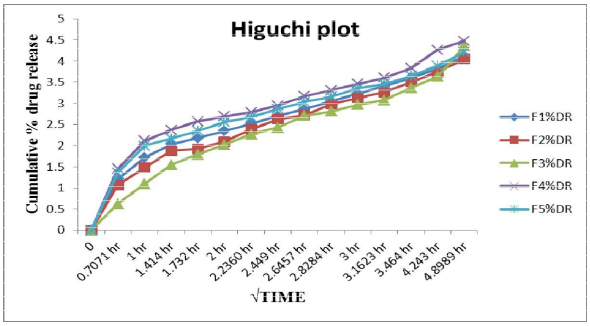
TIME	F1	F2	F3	F4	F5
0.5	1.2027	1.0714	0.6214	1.4549	1.3608
1	1.7224	1.484	1.099	2.1149	1.99
2	2.0304	1.88	1.5467	2.3675	2.169
3	2.1786	1.9229	1.7894	2.5693	2.345
4	2.3465	2.0925	2.0214	2.691	2.559
5	2.52	2.3823	2.2656	2.789	2.6749
6	2.7017	2.6183	2.4295	2.946	2.8647
7	2.8594	2.7261	2.7089	3.173	3.0322
8	3.05	2.9809	2.8067	3.3077	3.158
9	3.227	3.1308	2.9689	3.4608	3.3507
10	3.4125	3.263	3.08	3.605	3.4599
12	3.6042	3.506	3.366	3.836	3.6495
18	3.8139	3.74	3.6339	4.2589	3.887
24	4.1268	4.051	4.352	4.479	4.2128



Graph 9.6: Hixon Crowell plot

Table 9.9.4: Higuchi plot

√TIME	F1	F2	F3	F4	F5
0	1.74	1.23	0.24	3.08	2.52
0.7071 hr.	5.11	3.27	1.33	9.46	7.89
1 hr.	8.37	6.65	3.7	13.27	10.21
1.414 hrs.	10.34	7.11	5.73	16.96	12.9
1.732 hrs.	12.92	10.54	8.26	19.49	16.76
2 hrs.	16.01	13.52	11.63	21.7	19.14
2.2360 hrs.	19.72	17.95	14.34	25.58	23.51
2.449 hrs.	23.38	20.26	19.88	31.95	27.88
2.6457 hrs.	28.38	26.49	22.11	36.19	31.5
2.8284 s.hr	33.61	30.69	26.17	41.45	37.62
3 hrs.	39.74	34.75	29.23	46.87	41.42
3.1623 hrs.	46.82	43.11	38.14	56.45	48.61
3.464 hrs.	55.48	52.34	47.99	77.25	58.73
4.243 hrs.	70.28	66.47	56.23	89.86	74.77



Graph 9.7: Higuchi plot

Interaction Studies:

Drug-polymer interaction study FTIR: Interaction of drug with polymers was confirmed by carrying out IR interactions studies. The IR overlay spectrum of drug alone and drug with polymer were seen. It shows that there are no interactions found between the drug and polymers.

CONCLUSION

From the above work it can be concluded that the objective of the proposed project has been fulfilled and hydro dynamically balanced systems for curcumin using psyllium husk, HPMC K15M and HPMC K 100M have been successfully formulated and evaluated. The conclusion of the studies can be summarized as: Psyllium husk might be a promising polymer for gastro retentive floating drug delivery systems in combination with synthetic polymer like HPMC K 15M. Use of HPMC K 15M with psyllium husk enhanced the floating duration and helped to maintain the dimensional stability at initial stage, which is necessary in case of once daily formulations. The F4 (HPMC K15M + Psyllium husk) formulation was the optimized formulations for hydro dynamically balanced systems From FT-IR studies it was concluded that no interactions exists between drug and polymers. Optimized formulation followed the Higuchi kinetics while the drug release mechanism was found to be diffusion type through swollen matrix.

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