ejpmr, 2021,8(6), 417-428

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION AND DESIGN OF CURCUMIN GASTRO RETENTIVE FLOATING TABLETS.

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Article Received on 08/04/2021 **Article Revised on 28/04/2021** **Article Accepted on 18/05/2021**

ABSTRACT

The purpose of the present study was to develop gastro retentive floating tablets of Curcumin using polymers such as HPMC K4M, Ethyl cellulose and xanthan gum. Formulations were prepared by direct compression method and evaluated for Hardness, Thickness, Weight variation, Friability, Drug content, Floating lag time, Total floating time, Swelling index, Invitro drug release. Among all the formulations FC7 formulation as got the higher percentage of drug release when compare to the other formulations. At the end of the result we can concluded that formulation FC7 containing the combination of three polymers HPMC K4M, Ethyl cellulose and Xanthan gum in the ratios of (3:1:1) got highest percentage of drug release that will enhances the bioavailability and absorption of drug.

KEYWORDS: Curcumin, floating lag time, floating drug delivery system.

INTRODUCTION

Oral route is one of the most extensively utilized routes for administration of dosage forms. Drugs that have an absorption window in stomach or upper small intestine, have low solubility and stability at alkaline pH were suitable to convert as Gastro Retentive Dosage Forms (GRDFs). GRDFs significantly extend the period of time over which the drugs may be released, they not only decrease dosing interval, but also increase patient's compliance.[1] For weakly-basic drugs, gastro-retentive floating dosage forms have presented a promising approach for the improvement of oral bioavailability of these drugs. Floating drug delivery systems (FDDS) are hydrodynamically- balanced systems (HBS) having a bulk density lower than gastric contents and thus; they remain buoyant in the stomach and retain the drug in the acidic medium favouring the drug release. Moreover, while the system is floating on the gastric contents, the drug is released at a controlled rate over prolonged period of time.[2] Drugs that are easily absorbed from the gastrointestinal tract (GIT) and have a short half-life are eliminated quickly from the blood circulation, require frequent dosing. To avoid this problem, the oral controlled release (CR) formulations have been developed in an attempt to release the drug slowly into the GIT and maintain a constant drug concentration in the serum for longer period of time. Such oral drug delivery devices have a restriction due to the gastric retention time (GRT), a physiological limitation. Therefore, prolonged gastric retention is important in achieving control over the GRT because this helps to retain the CR system in the stomach for a longer time in a predictable manner. The gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms that reside in the stomach for a longer period of time than conventional dosage forms.[3] Gastro retentive dosage forms can act as an alternative to parenteral therapy for all such drugs which have absorption window in the upper part of gastro intestinal tract. Gastric retention of the dosage form can be brought about by various approaches like floating, muco-adhesion, high density, etc. Floating drug delivery is suitable for the drugs having absorption from the upper part of gastrointestinal tract. Combination of controlled release systems with prolonged gastric retention provides a means to utilize the entire pharmacokinetic (PK) and pharmacodynamic (PD) advantages of controlled release dosage forms for such drugs.[4]

The oral controlled drug delivery system was developed to allow a controlled rate of drug release over an extended period of time. This system however, has a disadvantage of short gastric retention time, resulting in the incomplete release of drugs with narrow absorption window in the upper part of the gastrointestinal tract. To overcome this drawback, gastro retentive drug delivery systems (GRDDS) were introduced.[5] The gastro retentive drug delivery systems (GTDDS) can assist in improving the oral bioavailability of various pharmaceutical drugs that have an absorption window in a particular region of gastrointestinal (GI) tract.[6] Floating systems are low-density systems that have sufficiently buoyancy to float over the gastric content

and remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time, which results in increased gastric retention time and a better control of fluctuation in plasma drug concentration. After release of drug, the residual system is emptied from the stomach.[7] Many approaches have been worked out to improve the retention of an oral dosage form in the stomach (gastro retentive systems) e g. Floating system, swelling and expanding system, bio adhesive system, modified shape system, high density system and other delayed gastric emptying devices.[8] Prolonged gastric retention dosage form improves bioavailability, improves solubility for drugs that are less soluble in a high pH environment (e. g., cinnarizine and chlordiazepoxide), and reduces drug waste.[9] Floating systems are of two types: effervescent systems, depending on the generation of carbon dioxide gas upon contact with gastric fluids, and non-effervescent systems. The non-effervescent systems can be further divided into four sub types, including hydrodynamically balanced systems, microporous compartment systems, alginate beads and hollow microspheres/ microballons. In addition, super porous hydrogels and magnetic systems were also described. As suggested by Singh and Kim, floating drug delivery is of particular interest for the drugs which: (a) act locally in the stomach; (b) are primarily absorbed in the stomach; (c) are poorly soluble at an alkaline pH; (d) have a narrow window of absorption and (e) are unstable in the intestinal or colonic environment.[10]

MATERIALS AND METHODS

Materials

Curcumin obtained from Loba chemie Pvt Ltd, Mumbai. HPMC K4M, Ethyl cellulose, xanthan gum, Sodium bicarbonate, Citric acid, Lactose, Micro crystalline cellulose (MCC), Magnesium stearate and Talc, these all ingredients were obtained from SD fine chemicals Ltd, Mumbai.

Methods: The Gastro retentive floating tablets of curcumin were prepared by direct compression method using different ratios of polymers of HPMC K4M, Ethyl cellulose, Xanthan gum and other excipients like Sodium bicarbonate, Citric acid, Lactose, MCC, Magnesium stearate and Talc. All the ingredients are accurately weighed and passed through an 80mesh sieve. Then except magnesium stearate all the ingredients should be blended uniformly in a mortar. After sufficient mixing of drug as well as other components, add calculated amount of magnesium stearate as lubricant and further additionally mixed for the 2-3 minutes. The required amount of the blend of mixture was weighed and fed manually into the die of rotary tablet punching machine to produce tablets using concave faced punch of suitable diameter. The tablet hardness was maintained in the range of 4-6 kg/cm^2. The formulae of different floating tablets of curcumin are given in the Table-1.

TABLE-1: Formulae of different floating tablet formulations of curcumin.

SL NO	INGREDIENTS	FC1	FC2	FC3	FC4	FC5	FC6	FC7
1	Curcumin	100	100	100	100	100	100	100
2	HPMC K4M	150	200	175	100	100	100	150
3	Ethyl cellulose				50	100	75	50
4	Xanthan gum	100	50	75	100	50	75	50
5	Sodium bicarbonate	50	50	50	50	50	50	50
6	Citric acid	40	40	40	40	40	40	40
7	Lactose	20	20	20	20	20	20	20
8	MCC	20	20	20	20	20	20	20
9	Magnesium stearate	10	10	10	10	10	10	10
10	Talc	10	10	10	10	10	10	10

Standard Calibration Curve[11]

100 mg of accurately weighed curcumin was dissolved in 100 ml of 0.1 N HCL in a volumetric flask that contains 1000 µg/ml concentration. From this 10 ml was taken and diluted up to 100ml using 0.1N HCL to produce 100µg/ml. From this stock solution 10, 20, 30,40, 50 and 60 µg/ml of different concentrations were prepared. The absorbance of these solutions was measured at ƛmax 424 nm by UV spectrophotometer. The standard calibration curve was plotted using the absorbance so obtained.

Fourier Transform Infra-Red (FTIR) Spectroscopy[11]

Interaction of drug with excipients was confirmed by carrying out IR interactions studies. Drug and excipients used in study were placed in air tight screw cap amber coloured vials, then vials were kept at room temperature as well as in hot air oven at 400C for one week to get them moisture free and FT-IR analysis was carried out with saturated potassium bromide using pellet making method. Standard and KBr were taken in the ratio of 1:300 to make a solid disc or pellet with the help of Hydraulic Pellet Machine.

Evaluation of Precompression parameters[12]

Angle of repose[12]

Fixed funnel method was used to measure the flow properties where the granules were poured from funnel walls to form conical heap in which its lower tip is 2-5 cm away from the hard surface. The static angle of repose was measured by using the formula,

$\theta = \text{Tan-1 } (h/r)/h$ - the height of the heap, r - radius of the heap

Bulk and tapped density[12]

The blend was sieved to ensure free from agglomeration free and was introduced into a calibrated measuring cylinder. The initial volume was observed and then the cylinder was allowed to tap onto a hard surface from 2.5 cm height. The tapping was continued to get saturated volume. From the above values, both poured bulk density and tapped density were determined.
Bulk density=weight of powder blend/Bulk volume
Tapped density=weight of powder blend/Tapped volume

Hausner's ratio and compressibility index[12]
Hausner's found that the ratio of tapped volume and poured volume was related to its interparticle friction and can be used as a direct tool for flow property evaluation. Compressibility index was determined by using the formula,
Compressebility index = Tapped density-Bulk density/Tapped density*100
Hausner's ratio=Tapped density/Bulk density

POST COMPRESSION PARAMETERS
The prepared curcumin floating tablets were evaluated for various quality control tests such as weight variation, hardness, thickness, friability and content uniformity.

Weight variation[13]
From each batch of the formulations, twenty tablets were selected randomly and weighed individually. The average weight was calculated out and it was then compared with the individual weight. From this percentage deviation was determined and then the result obtained was checked for IP specifications.

Hardness and friability[13]
The hardness of tablet was determined by Monsanto tablet hardness tester using randomly picked ten tablets from each batch. Friability test was performed by using Roche friabilator. Twenty tablets were weighed out and were placed into the plastic chamber of the friabilator that revolves at 25 rpm dropping the tablets at a distance of 6 inches height with each revolution for 4 mins. The tablets were dedusted, reweighed and the percentage friability was calculated after operating for 100 revolutions.

Thickness and diameter[14]
Ten tablets were selected randomly from each formulation. Thickness and diameter were measured by using digital vernier calipers.

DRUG CONTENT DETERMINATION[15]
The drug content of the prepared gastro retentive floating tablets was determined in triplicate. For each batch, 10 tablets were taken, weighed, and finely powdered. An accurately weighed powder equivalent to 100 mg of pure drug was taken and suitably dissolved under sonication for 30 minutes and shaking for 30 minutes in 0.1N HCl. The above solution was filtered through 0.4 µ p(Millipore) filter. The sample was analyzed after making appropriate dilutions using UV spectrophotometer at 424 nm against blank.

INVITRO BUOYANCY STUDIES[16]
In vitro buoyancy studies were done for all the formulations. The floating lag time (FLT) is the time engaged in the process of arising of tablet on medium surface. The total floating time (TFT) is the interval of time the dosage form takes to persistently stay on medium surface. 0.1 N HCl was prepared and in a 250-mL beaker and tablets were taken in it. The calculation of time interval needed for a tablet to rise and float on the surface was done.

SWELLING INDEX[17]
The swelling of tablet is three dimensional and the extent of swelling can be measured either by the % weight gain of swollen tablet or by the % volume increment calculated by × (diameter/2)2 × thickness with the assumption that the tablet swelled as a cylindrical form. The swelling studies of tablets were carried out in beaker containing 200 ml of 0.1N HCL. At selected regular intervals, the tablet is withdrawn and weighed. The swelling index (SI) was calculated according to the following equation:
Swelling index = St –Si/Si *100

where Si and St represent the initial diameter of the dry tablet and that of the swollen tablet at time t, respectively. The data represent mean ±SD from at least three samples per formulation (n=3).

INVITRO DISSOLUTION STUDIES[18]
In-vitro drug release of the samples was carried out using USP–type II (PADDLE TYPE) dissolution apparatus at 37±0.5ºc using 900 ml of 0.1N Hcl as the dissolution medium at 100 rpm speeds. One Curcumin tablet was placed in each VESSEL and was allowed to run for 12 hours. Aliquot of 5 ml was withdrawn at predetermined time interval and equivalent amount of fresh medium was replaced to maintain a constant volume. Collected samples were suitably diluted with 0.1N Hcl and analyzed at 424 nm using 0.1N Hcl as blank. The %cumulative drug release was calculated.

RESULTS AND DISCUSSION
TABLE-2: STANDARD CALIBRATION CURVE OF CURCUMIN.

Sl No	Concentration(µg/ml)	Absorbance at 424 nm
0	0	0
1	10	0.115
2	20	0.21
3	30	0.319

4	40	0.415
5	50	0.513
6	60	0.63

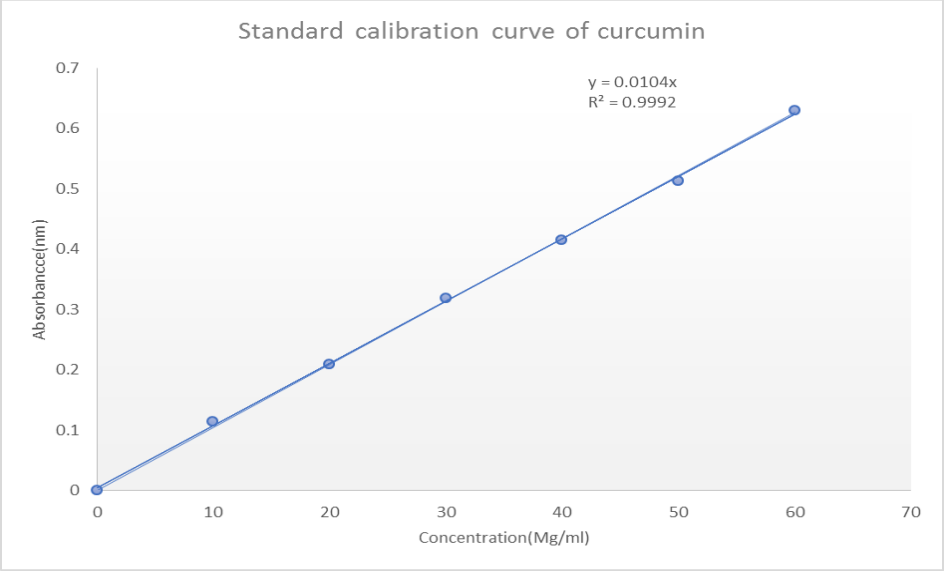

FIGURE-1: STANDARD CALIBRATION CURVE OF CURCUMIN.

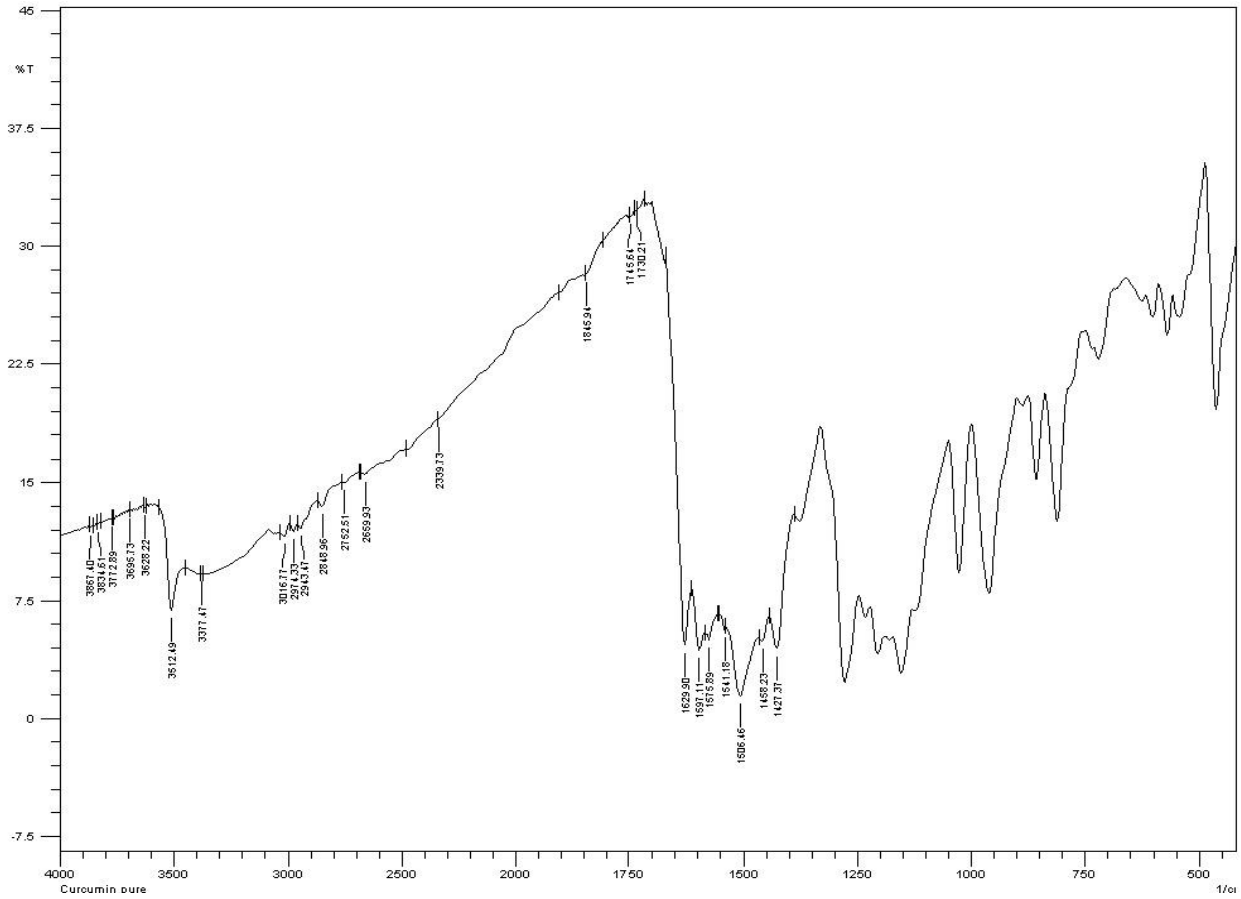

FIGURE-2: FTIR SPECTRA OF PURE CURCUMIN.

TABLE-3.1: FTIR Spectrum values of pure drug Curcumin.

Functional group	Frequency(cm^{-1})
O-H Stretching	3695.73
O-H Stretching	3512.49
C-H Stretching	3016.77
C-H Stretching	2943.47
C-H Bending	1845.94
C=O Stretching	1730.21
C=C Stretching	1575.89
C-H Bending	1458.23
O-H Bending	1427.37

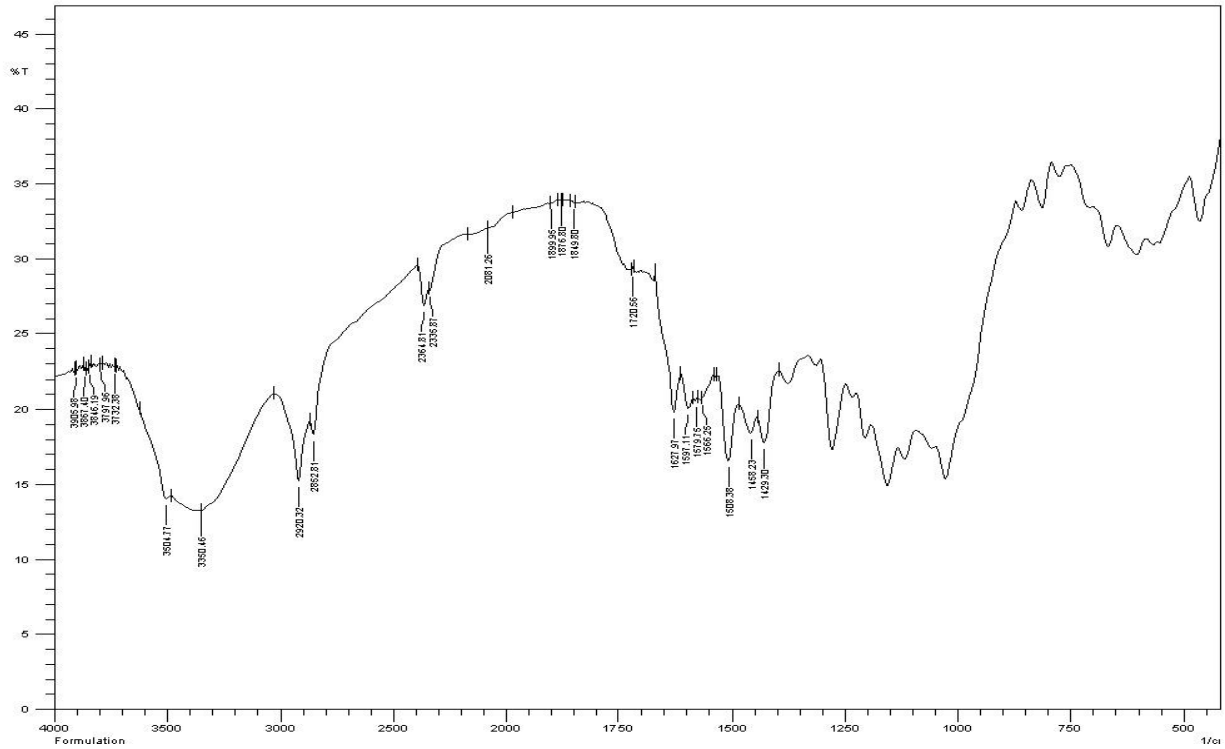

FIGURE-3: FTIR SPECTRA OF OPTIMISED FORMULATION.

TABLE 3.2: FTIR Spectrum values of optimised formulation.

Functional group	Frequency(cm^{-1})
O-H Stretching	3504.77
C-H Stretching	2920.32
C-H Stretching	2852.81
O=C=O Stretching	2335.87
C=C=C Stretching	2081.26
C-H Bending	1899.45
C=O Stretching	1720.56
C=C Stretching	1627.97
C=C Stretching	1579.75
C=C Stretching	1566.25
C-H Bending	1458.23
O-H Bending	1429.3

TABLE-4.1: PRE- COMPRESSION PARAMETERS.

Formulation code	Angle of repose(Ɵ)±SD	Bulk density(gm/cm3) ±SD	Tapped density(gm/cm3) ±SD
FC1	35.11±0.351	0.49±0.005	0.76±0.002
FC2	44.98±0.019	0.46±0.005	0.67±0.003
FC3	44.82±0.249	0.47±0.004	0.71±0.004

FC4	35.4±0.288	0.54±0.003	0.76±0.003
FC5	43.21±0.282	0.47±0.004	0.76±0.003
FC6	40.4±0.288	0.54±0.003	0.71±0.004
FC7	43.04±0.052	0.47±0.004	0.76±0.003

TABLE-4.2: PRE-COMPRESSION PARAMETERS.

Formulation code	Carr's index ±SD	Hausner's ratio ±SD
FC1	34.7±0.012	1.53±0.001
FC2	31.97±0.012	1.47±0.0001
FC3	33.31±0.012	1.5±0.0002
FC4	28.57±0.014	1.39±0.004
FC5	37.4±0.081	1.59±0.005
FC6	23.8±0.081	1.31±0.001
FC7	37.6±0.081	1.59±0.014

TABLE-5.1: POST COMPRESSION PARAMETERS.

Formulation code	Hardness (Kg/cm2) ±SD	Thickness(mm)±SD	Diameter(mm)±SD
FC1	4.4±0.057	3.5±0.05	12.5±0.081
FC2	4±0.05	3.4±0.05	12.4±0.125
FC3	5.4±0.057	3.4±0.05	12.5±0.081
FC4	5.1±0.189	3.4±0.05	12.4±0.125
FC5	5.9±0.057	3.4±0.05	12.5±0.081
FC6	4.4±0.057	3.5±0.05	12.5±0.095
FC7	4.9±0.057	3.5±0.05	12.4±0.129

TABLE-5.2: POST COMPRESSION PARAMETERS.

Formulation code	Friability (%) ±SD	Weight variation(mg)±SD	Drug content (%) ±SD
FC1	0.8±0.008	498.6±0.472	96.46±0.008
FC2	0.6±0.008	500.4±0.081	94.75±0.008
FC3	0.21±0.008	501.4±0.081	93.48±0.008
FC4	0.78±0.008	501.3±0.125	95.94±0.012
FC5	0.8±0.015	498.6±0.472	98.36±0.005
FC6	0.7±0.048	498.4±0.057	97.65±0.008
FC7	0.8±0.009	500.4±0.081	99.33±0.009

TABLE-6: INVITRO BUOYANCY TEST.

Formulation code	Floating lag time (Minutes)(FLT)	Total floating time(hrs)(TFT)
FC1	28	>24
FC2	3	>24
FC3	3	>24
FC4	30	>24
FC5	33	>24
FC6	1	>24
FC7	3	>24

TABLE-7.1: SWELLING INDEX.

		Swelling index (%)		
Time(hrs)	FC1	FC2	FC3	FC4
1	61.66±0.471	92±0.816	111±0.816	73.66±0.471
2	85.66±0.471	134.33±0.471	153±0.816	120.33±0.471
3	105.66±0.471	152±0.816	178.33±0.471	133.66±0.471
4	133.66±0.471	182.33±0.471	193±0.816	155.66±0.471
5	145±0.816	205.66±0.471	203±0.816	171.66±0.471
6	160.33±0.471	233.66±0.471	241±0.816	198.33±0.471

TABLE-7.2: SWELLING INDEX.

		Swelling index (%)	
Time(hrs)	**FC5**	**FC6**	**FC7**
1	66.33±0.471	58±0.816	61±0.816
2	118.33±0.471	73.66±0.471	86.33±0.471
3	130.33±0.471	91±0.816	101±0.816
4	151.66±0.471	101.66±0.471	113.66±0.471
5	177.66±0.471	121.66±0.471	125±0.816
6	201.66±0.471	131.66±0.471	141.66±0.471

TABLE-8: INVITRO DRUG RELEASE STUDY.

	Percentage drug release (%CR)						
Time(hrs)	**FC1**	**FC2**	**FC3**	**FC4**	**FC5**	**FC6**	**FC7**
0	0	0	0	0	0	0	0
0.5	13.84	14.71	11.25	16.44	40.67	48.46	8.65
1	17.3	16.44	15.57	20.76	43.26	51.05	23.36
2	19.9	18.17	17.3	22.5	48.46	54.51	28.55
3	22.5	20.76	21.63	24.23	53.65	57.11	36.34
4	25.09	25.09	23.36	25.96	57.98	60.57	42.4
5	26.82	28.55	27.69	29.42	61.44	64.03	48.46
6	32.01	38.94	45.66	40.67	65.76	68.36	59.71
7	38.07	46.73	55.38	46.73	74.42	76.15	70.09
8	42.4	51.05	61.44	53.65	80.48	82.21	80.48
9	47.59	57.98	68.36	60.57	83.94	87.4	89.13
10	56.25	63.17	80.48	70.09	90	91.73	92.59
12	64.03	77.88	91.73	81.34	95.19	96.92	97.78

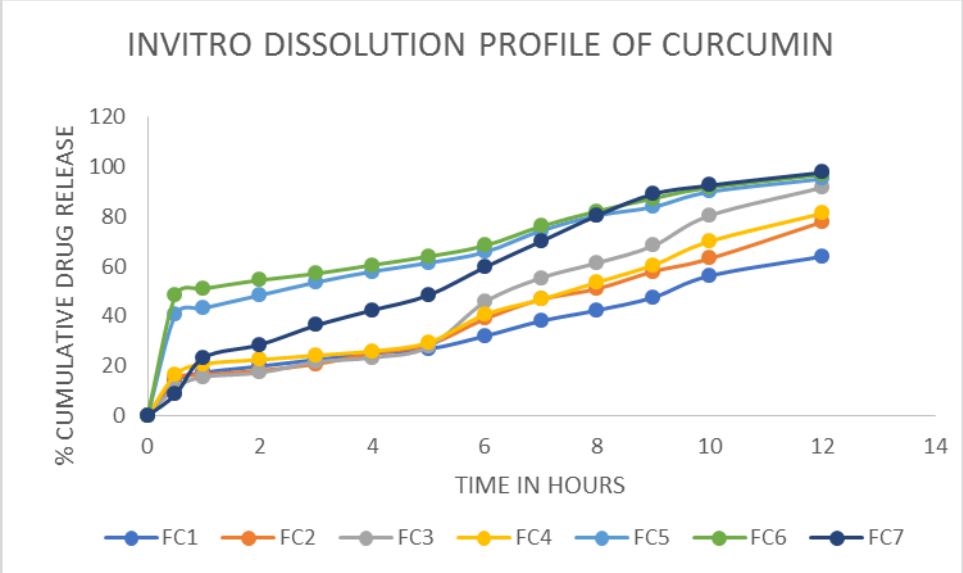

FIGURE 4: INVITRO DISSOLUTION PROFILE OF CURCUMIN.

RELEASE KINETICS PROFILE OF FORMULATIONS FC1 – FC7.

TABLE-9.1: Comparative Invitro release profile formulations FC1-FC7 according to Zero order kinetics.

		% Cumulative drug release					
Time(hrs)	**FC1**	**FC2**	**FC3**	**FC4**	**FC5**	**FC6**	**FC7**
0	0	0	0	0	0	0	0
0.5	13.84	14.71	11.25	16.44	40.67	48.46	8.65
1	17.3	16.44	15.57	20.76	43.26	51.05	23.36
2	19.9	18.17	17.3	22.5	48.46	54.51	28.55
3	22.5	20.76	21.63	24.23	53.65	57.11	36.34
4	25.09	25.09	23.36	25.96	57.98	60.57	42.4
5	26.82	28.55	27.69	29.42	61.44	64.03	48.46

6	32.01	38.94	45.66	40.67	65.76	68.36	59.71
7	38.07	46.73	55.38	46.73	74.42	76.15	70.09
8	42.4	51.05	61.44	53.65	80.48	82.21	80.48
9	47.59	57.98	68.36	60.57	83.94	87.4	89.13
10	56.25	63.17	80.48	70.09	90	91.73	92.59
12	64.03	77.88	91.73	81.34	95.19	96.92	97.78

TABLE-9.2: Comparative Invitro release profile formulations FC1-FC7 according to First order kinetics.

	Log % cumulative drug retained						
Time(hrs)	**FC1**	**FC2**	**FC3**	**FC4**	**FC5**	**FC6**	**FC7**
0	2	2	2	2	2	2	2
0.5	1.9353	1.9308	1.9481	1.9219	1.7732	1.7121	1.9607
1	1.9175	1.9219	1.9264	1.8989	1.7538	1.6897	1.8844
2	1.9036	1.9129	1.9175	1.8893	1.7121	1.6579	1.854
3	1.8893	1.8989	1.8941	1.8794	1.666	1.6323	1.8038
4	1.8745	1.8745	1.8844	1.8694	1.6234	1.5958	1.7604
5	1.8643	1.854	1.8591	1.8486	1.5861	1.5559	1.7121
6	1.8324	1.7857	1.7351	1.7732	1.5345	1.5002	1.6051
7	1.7919	1.7264	1.6495	1.7264	1.4079	1.3774	1.4758
8	1.7604	1.6897	1.5861	1.666	1.2904	1.2501	1.2904
9	1.7194	1.6234	1.5002	1.5958	1.2057	1.1003	1.0362
10	1.6409	1.5662	1.2904	1.4758	1	0.9175	0.8698
12	1.5559	1.3447	0.9175	1.2709	0.6821	0.4885	0.3463

TABLE-9.3: Comparative Invitro release profile formulations FC1-FC7 according to Higuchi release kinetics.

	% Cumulative drug release						
Square root of time	**FC1**	**FC2**	**FC3**	**FC4**	**FC5**	**FC6**	**FC7**
0	0	0	0	0	0	0	0
0.7071	13.84	14.71	11.25	16.44	40.67	48.46	8.65
1	17.3	16.44	15.57	20.76	43.26	51.05	23.36
1.4142	19.9	18.17	17.3	22.5	48.46	54.51	28.55
1.732	22.5	20.76	21.63	24.23	53.65	57.11	36.34
2	25.09	25.09	23.36	25.96	57.98	60.57	42.4
2.236	26.82	28.55	27.69	29.42	61.44	64.03	48.46
2.4494	32.01	38.94	45.66	40.67	65.76	68.36	59.71
2.6457	38.07	46.73	55.38	46.73	74.42	76.15	70.09
2.8284	42.4	51.05	61.44	53.65	80.48	82.21	80.48
3	47.59	57.98	68.36	60.57	83.94	87.4	89.13
3.1622	56.25	63.17	80.48	70.09	90	91.73	92.59
3.4641	64.03	77.88	91.73	81.34	95.19	96.92	97.78

TABLE-9.4: Comparative Invitro release profile formulations FC1-FC7 according to Peppas release kinetics.

	Log % cumulative drug release						
Log time	**FC1**	**FC2**	**FC3**	**FC4**	**FC5**	**FC6**	**FC7**
0	0	0	0	0	0	0	0
0	1.238	1.2159	1.1922	1.3172	1.636	1.7079	1.3684
0.301	1.2988	1.2593	1.238	1.3521	1.6853	1.7364	1.4556
0.4771	1.3521	1.3172	1.335	1.3843	1.7295	1.7567	1.5603
0.602	1.3995	1.3995	1.3684	1.4143	1.7632	1.7822	1.6273
0.6989	1.4284	1.4556	1.4423	1.4686	1.7884	1.8063	1.6853
0.7781	1.5052	1.5903	1.6595	1.6092	1.8179	1.8348	1.776
0.845	1.5805	1.6695	1.7433	1.6695	1.8716	1.8816	1.8456
0.903	1.6273	1.7079	1.7884	1.7295	1.9056	1.9149	1.9056
0.9542	1.6775	1.7632	1.8348	1.7822	1.9239	1.9415	1.95
1	1.7501	1.8005	1.9056	1.8456	1.9542	1.9625	1.9665
1.0791	1.8063	1.8914	1.9625	1.9103	1.9785	1.9864	1.9902

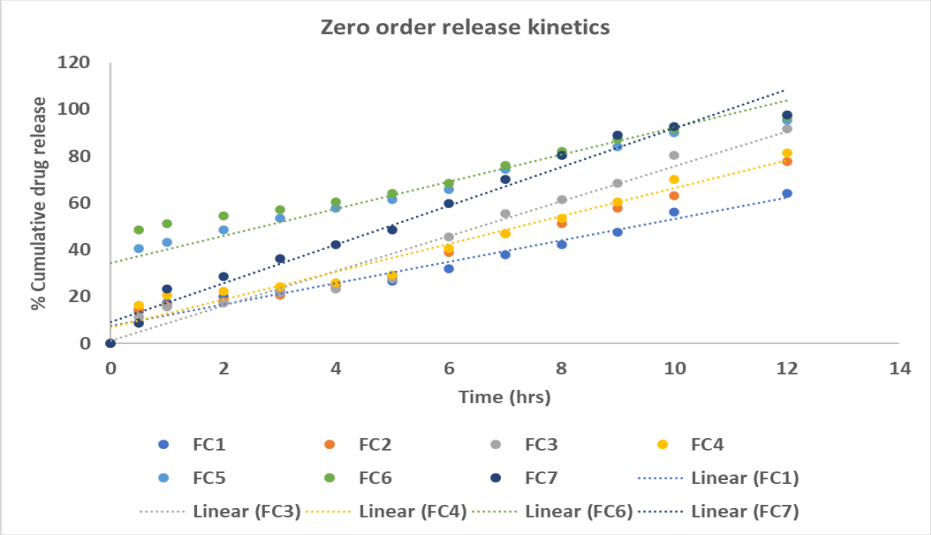

FIGURE-5: Comparative Invitro release profile formulations FC1-FC7 according to Zero order kinetics.

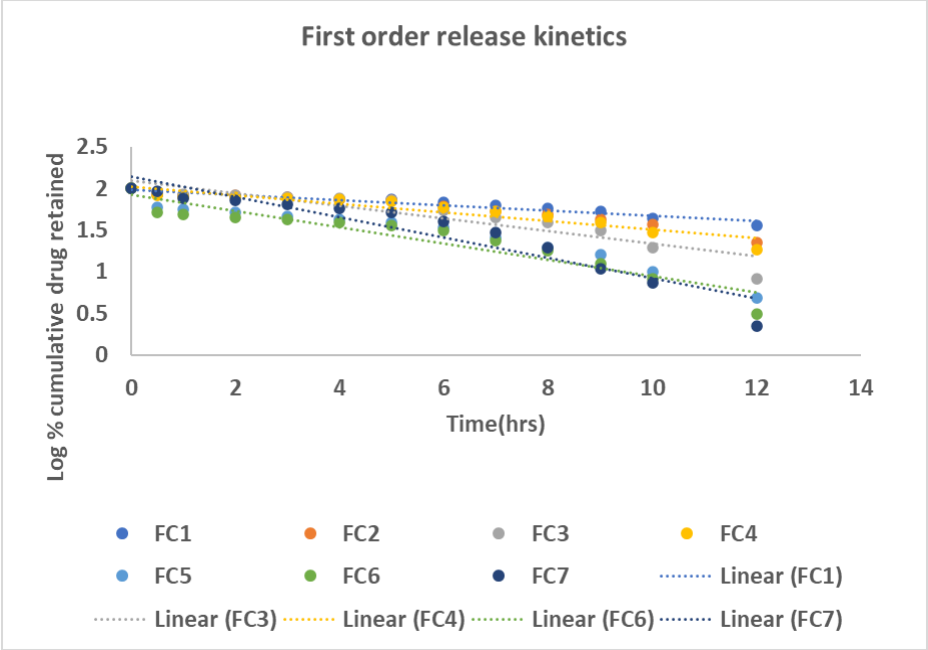

FIGURE-6: Comparative Invitro release profile formulations FC1-FC7 according to First order kinetics.

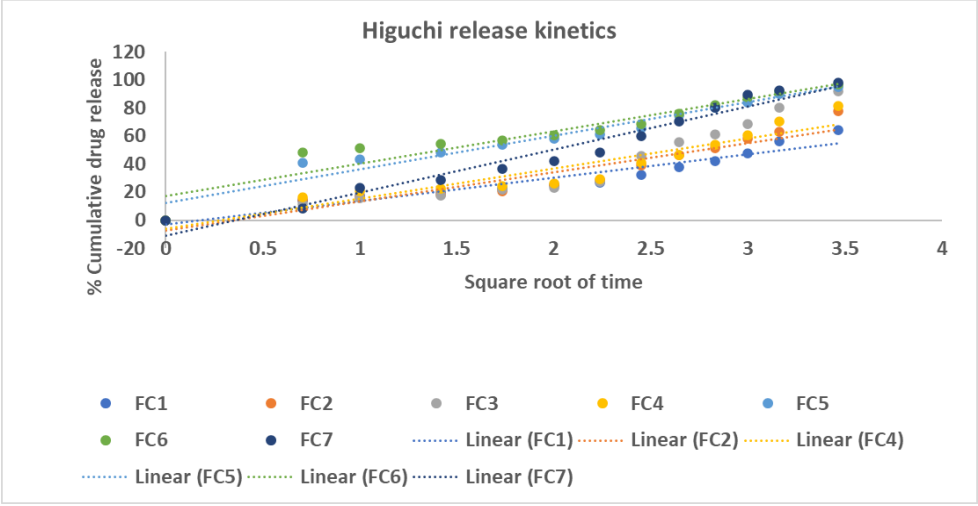

FIGURE-7: Comparative Invitro release profile formulations FC1-FC7 according to Higuchi release kinetics.

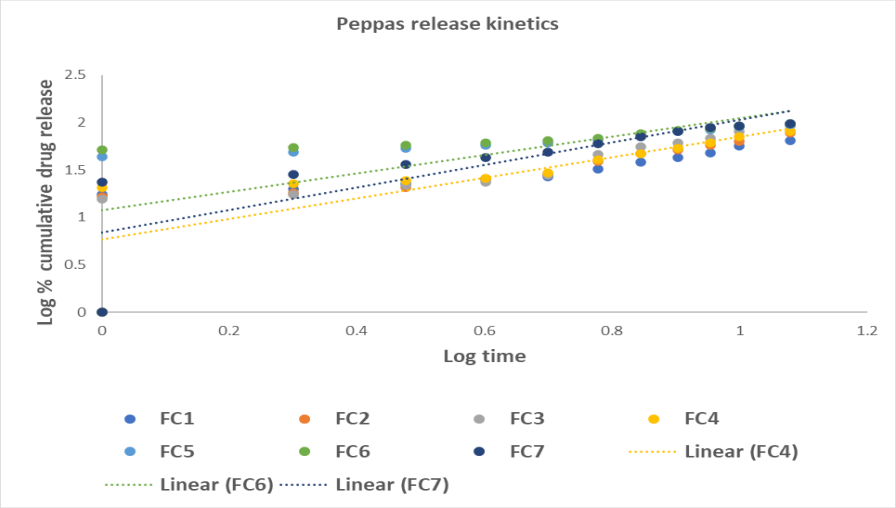

FIGURE-8: Comparative Invitro release profile formulations FC1-FC7 according to Peppas release kinetics.

Table-10: Result of model fitting for formulations FC1-FC7.

Formulation code	% Cumulative	Zero order	First order	Higuchi	Peppas	
					r^2	'n' values
FC1	64.03	0.9608	0.9405	0.918	0.641	0.7399
FC2	77.88	0.974	0.9191	0.8998	0.7045	0.7025
FC3	91.73	0.9707	0.8587	0.8732	0.7482	0.6692
FC4	81.34	0.9587	0.8962	0.8879	0.6483	0.7649
FC5	95.19	0.851	0.9272	0.9495	0.48	1.0331
FC6	96.92	0.7893	0.8928	0.9041	0.4442	1.0746
FC7	97.78	0.9731	0.8976	0.9612	0.6595	0.839

DISCUSSION

Standard calibration curve of Curcumin: Figure 1 shows the standard calibration curve for Curcumin with slope, regression co-efficient.

Compatibility Studies: Compatibility studies of pure drug Curcumin with all excipients were carried out prior to the preparation of floating tablets. The FTIR spectra of pure curcumin and the drug and physical mixtures of the optimised formulation was shown in the Figure 2 and Figure 3. The I.R spectrum of pure drug Curcumin and physical mixture of drug, polymer and excipients of optimized formulation were studied. The characteristic absorption peaks of curcumin were obtained at 3695.73 cm^{-1}, 3512.49 cm^{-1}, 3016.77 cm^{-1}, 2943.47 cm^{-1},1845.94 cm^{-1}, 1730.21 cm^{-1}, 1575.89 cm^{-1}, 1458.23 cm^{-1}, 1427.37 cm^{-1}. The peaks also obtained in the spectrum of physical mixture of drug, polymer and excipients of the optimized formulation. By correlating the I.R spectrum of pure drug curcumin with the physical mixtures of the optimized formulation, it was found that the drug is compatible with the formulation components. From the above studies it can be concluded that there was no interaction between the pure drug curcumin and polymers and excipients. The FTIR Spectrum values of the pure drug curcumin and optimized formulation were shown in the Table-3.1 and Table 3.2.

Formulation development of floating tablets: The floating tablets of Curcumin were prepared using direct compression method. The composition of different formulations was shown in Table-1.

PRE -COMPRESSION PARAMETERS.

Angle of repose: The values are found to be in the range of 35°11' to 44°98'. All the formulation showed angle of repose below 45° which indicates a good flow property of the granules. The results are shown in Table-4.1.

Bulk density: The values are found to be in the range of 0.46 to 0.54. The results are shown in the Table-4.1.

Tapped density: The values are found to be in the range of 0.67 to 0.76. The results are shown in the Table-4.1.

Compressibility index: Carr's index lies within the range of 23.8 % to 37.6 %. All formulations show good compressibility. The results are shown in Table-4.2.

Hausner ratio: Hausner ratio was found to be in the range of 1.31 to 1.59 as shown in Table 4.2.

POST COMPRESSION PARAMETERS.

Weight variation test: The values of tablets ranged from 498.4 ± 0.057 to 501.4 ± 0.081mg. All the tablets passed weight variation test as the % weight variation

was within the Pharmacopeial limits of ±10 % of the weight and is shown in table 5.2.

Hardness test: The hardness of all formulations was in the range of 4.0±0.05 to 5.9 ±0.057 kg/cm2. The Hardness values are shown in the Table-5.1.

Thickness test: The thickness of all formulations in the range of 3.4 ±0.05 to 3.5 ±0.05. Thickness values are shown in the Table-5.1.

Friability test: The friability values of prepared tablets are given in Table-5.2. The values ranged from 0.2% to 0.8%.

Content uniformity test: The percent drug content of tablets was found to be in between 93.48% to 99.33% of Curcumin and all results are shown in table 5.2.

In vitro Buoyancy Studies: The Gastro retentive floating tablets of curcumin of different formulations like FC1, FC2, FC3, FC4, FC5, FC6 and FC7 containing HPMC K4M, Ethyl cellulose and Xanthan gum. These seven formulations exhibited floating lag time (FLT) of 28, 3, 3, 30, 33, 1 and 3 minutes respectively and Total floating time (TFT) of more than 24 hours for all the formulations respectively. The results of Invitro buoyancy studies are shown in the Table-6.

Swelling Study: The percentage of swelling obtained from the water uptake studies of all the formulations is shown in Figure 7.1 and 7.2. It was observed that the swelling indices were increased with increase in polymer concentration. Formulation FC3 containing a high percentage of polymer shows the maximum swelling i.e., 241 % at 6 hrs compared to that of the other formulations containing lower polymer concentration FC6. The swelling was strong enough to maintain the matrix integrity without disintegrating the tablets as well as to avoid burst effect and retarded the release of drug for a prolonged period of time. Generally swelling is essential to ensure the floating of the tablets. Therefore, an appropriate balance between swelling and water uptake is necessary. Swelling study was performed on all the formulations for 6 hrs.

In vitro Dissolution Studies: In vitro studies were performed to study the drug release from dosage form in the physiological condition. The in vitro drug release profiles of FC1-FC7 are shown in Figure 4. Diffusion and swelling are the most important rate-controlling mechanisms of controlled drug delivery. The low viscosity grade HPMC K4M has been used in this study rather than higher viscosity grades. Hydroxypropyl methylcellulose is the most important hydrophilic carrier material used for the preparation of oral controlled drug delivery systems. HPMC swells by absorbing water and forms a swollen layer barrier for drug to diffuse through this layer. As proportion of HPMC in tablet is increased, thickness of the diffusion barrier layer increases. This results in reduced drug release initially. This may be attributed to high level of sodium bicarbonate used in these formulations. As the concentration of sodium bicarbonate increases, water uptake capacity of the formulation increases. This increases the porosity of the matrix and results in increased driving force for drug release, which results in increased drug release from the matrix system. Hence, amount of drug released increases with increasing concentration of sodium bicarbonate. The Gastro retentive floating tablets of Curcumin of different formulations like FC1, FC2, FC3, FC4, FC5, FC6 and FC7 showed the release of 64.03%, 77.88%, 91.73%, 81.34%, 95.19%, 96.92% and 97.78% at the end of 12 hours respectively. Among this seven different formulations FC7 was considered as optimised formulation because it shows more percentage of drug release compared to other formulations. The Invitro drug release results of all the formulations are shown in the table-7.

Drug release kinetics data of Curcumin floating tablets

The Drug release values obtained for formulations FC1 to FC7 were shown in Table-8. The values of invitro release were attempted to fit into the various mathematical models. Plots of Zero order, first order, Higuchi model and Peppas model were depicted in the Figure 5, 6, 7 and 8 respectively. The drug release data were explored for the type of release mechanisms followed. The best fit with the highest determination r^2 coefficients was shown by both the zero order and Higuchi models. Zero order release describes the release rate independent of drug concentration. Higuchi square root kinetics model describes, release drug from the insoluble matrix as square root of time dependent process. It describes the release of drug by simple diffusion mechanism. The value of n with regression coefficient for all the formulations is shown in Table-10. However as indicated by the values of r^2 both the models i.e., Higuchi and Peppas were found to be efficient in describe the release of Curcumin from the floating tablets.

CONCLUSION

The present study was aimed to develop Gastro retentive floating tablet of curcumin. The tablets prepared by the combination of HPMC K4M, Ethyl cellulose and Xanthan gum in order to develop a sustained release tablets that could retain in the stomach for longer periods of time delivering the drug to the site of action., i.e., stomach. Tablets were developed using sodium bicarbonate as gas generating agents and HPMC K4M as polymer by direct compression technique. The polymers in combination with NaCO3 can increase the retention time of formulation in stomach thereby increasing drug absorption and reducing the dose frequency. The FTIR studies indicated the absence of the drug-polymer interactions. From the drug content and in-vitro dissolution studies of the formulations, it was concluded that the formulation FC7 is the best formulation with

good floating property with sustained drug release were obtained in our study FC7. As a result of this study it may be concluded that the floating tablets using a combination of polymers in optimized concentrations can be used to increase the GRT of the dissolution fluid in the stomach to deliver the drug in a sustained manner and offers a suitable and practical approach in serving desired objectives of gastro retentive floating tablets.

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