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Shaika Saadia Zubedi
Department of Pharmaceutics, Deccan School of Pharmacy, Hyderabad, Telangana, India

Shahid Mohammed
Department of Pharmaceutics, Deccan School of Pharmacy, Hyderabad, Telangana, India

Correspondence
Shaika Saadia Zubedi
Department of Pharmaceutics, Deccan School of Pharmacy, Hyderabad, Telangana, India

Formulation and *in-vitro* evaluation of Chlorzoxazone floating tablets

Shaika Saadia Zubedi and Shahid Mohammed

Abstract
Chlorzoxazone is a benzoxazinone derivative of BCS class II drug with mild sedative and centrally acting muscle relaxant activity. The oral delivery of muscle relaxant Chlorzoxazone tablets were facilitated by preparing floating dosage form which could increase its absorption by increasing the gastric residence time and to achieve sustainable drug release. Chlorzoxazone floating tablets were prepared by direct compression method in 8 different formulations (F1-F8) using HPMC K100 as rate retarding polymer, sodium bicarbonate and citric acid as gas generating agent. From the preformulation studies it was observed all the parameters were within limits. The prepared formulations were evaluated with pre-compression parameters like bulk density, compressibility index, hausner ratio, angle of repose and post-compression parameters like weight variation, thickness, hardness, friability, drug content, buoyancy lag time, total floating time, and *in-vitro* drug release. All the floating tablets possess good floating property with a total floating time for not less than 12hrs. *In vitro* dissolution studies of the formulations were done in pH 6.8 phosphate buffer using USP apparatus 2 (paddle method) at 50 rpm. Percent drug release of the formulations (F-1 to F-8) was from 65.34% to 99.12% after 12hrs. From the results, F-8 was selected as an optimized formulation. Kinetic studies of the optimized formulation (F8) showed that the drug release follows first order and Higuchi model which indicates drug release follows first order & diffusion mechanism. Optimized formulation (F8) was subjected to stability studies for 3 months at 25 ± 2 ºC / 60 ± 5% RH, 30±2 ^{0}C / 65±5% RH and 40 ± 2 ºC / 75 ± 5% RH and the results were found satisfactory within limits.

Keywords: Chlorzoxazone, floating tablets, HPMC k100, *in-vitro* drug release

1. Introduction
Oral delivery of drugs is by far the most preferred route of drug delivery due to ease of administration, patient compliance and flexibility in formulation [1]. The design of oral controlled drug delivery systems (DDS) is primarily aimed to achieve more predictable and increased bioavailability. Gastric emptying time in humans, which is normally 2-3 hours through the main absorption area (stomach or upper part of intestine), can result in incomplete drug release from DDS leading to diminished efficacy of administered dose [2]. Drug that are easily absorbed from the gastro-intestinal tract (GIT) and having a short half-life are eliminated quickly from the blood circulation. To avoid this problem, the oral controlled release formulations have been developed, as these will release the drug slowly into the GIT and maintain a constant drug concentration in the serum for a longer period of time, one of the feasible approaches to control the gastric residence time (GRT).
Several drug delivery systems with prolonged gastric retention time have been investigated [3, 4]. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion [5, 6], flotation [7], sedimentation [8, 9], expansion [10, 11], modified shape systems [12, 13], or by the simultaneous administration of pharmacological agents [14, 15]. The floating system in particular has been extensively researched, mainly because the floating system does not adversely affect the motility of the GI tract.
Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system is floating on gastric contents, drug is released slowly at a desired rate from the system. After the release of drug, the residual system is emptied from the stomach. This result is increase in GRT and a better control of fluctuations in plasma drug concentrations. Floating systems can be classified into two types, non-effervescent system and effervescent systems [1].
Chlorzoxazone (CLZ) is a centrally acting musculoskeletal relaxant with sedative properties.

Its IUPAC name is 5-chloro-3H-1, 3-benzoxazol-2-one. After oral administration, CLZ is completely absorbed and is rapidly metabolized in the liver to 6-hydroxychlorzoxazone which has little or no muscle relaxant activity when tested in mice and rats [16]. CLZ inhibits muscle spasm by exerting an effect primarily at the level of the spinal cord and subcortical areas of the brain. Its effect begins within an hour after an oral dose and lasts for 3–4 h. The usual initial oral dose is 500 mg three or four times daily; though the dose can often be reduced subsequently to 250 mg three or four times daily. CLZ is usually given with analgesics in compound preparations. The most common side effects of CLZ are drowsiness, dizziness and headache [17]. CLZ belongs to bio pharmaceutics classification (BCS) class II, i.e. low solubility and high permeability. Common skeletal muscle relaxants have been approved for either treatment of spasticity or for treatment of musculoskeletal conditions. Only baclofen, dantrolene and tizanidine are approved by FDA for the treatment of spasticity, but carisoprodol, Chlorzoxazone, cyclobenzaprine, metaxalone, methocarbamol and orphenadrine have been approved for treatment of musculoskeletal disorders [18].

Chlorzoxazone is a good choice for formulation as a gastroretentive dosage form as it comes under BCS II classification and its Pk_a value is 3.3. The increase in gastric time helps increase its solubility and hence its absorption. The present study aims in designing floating tablets of Chlorzoxazone using HPMC K100 and evaluating the prepared tablets for physicochemical properties, buoyancy lag time, total floating time, and *in-vitro* drug release.

2. Materials and Methods

2.1 Materials

Chlorzoxazone was received as a gift sample from Chiral Drugs Pvt. Ltd. (Gujarat). Hydroxyl propyl methyl cellulose (HPMC K100), microcrystalline cellulose (MCC), Sodium Bicarbonate, Citric acid, Magnesium stearate were procured from S.D. Fine chemicals, Mumbai, India.

2.2 Methodology

2.2.1 Preformulation Studies [19]

As per standard procedures, the preformulation studies including Compatibility study, Bulk density, tapped density, Hausner's ratio and Angle of repose was performed for the crude drug, Chlorzoxazone.

Bulk Density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. The loose bulk density is accurately weighted amount of sample (5gm) was transferred into a 50 ml measuring cylinder carefully to read the unsettled apparent volume to the nearest graduated unit.

Tapped Density: The tapped bulk density is accurately weighted amount of sample (5gm) transferred into a 50 ml measuring cylinder. The measuring cylinder was then tapped 100 times on a plane hard wooden surface and measures the tapped volume. Calculate the loose bulk density and tapped bulk density in gm/ ml by the following formula:

Loose bulk density (LBD) = Weight of granules/ Apparent volume
Tapped bulk density (TBD) = Weight of granules / Tapped volume

Compressibility Index: Percent compressibility of granules was determined by Carr's compressibility index. It was calculated by the following formula:

Carr's index: TBD-LBD/TBD X 100

Hausner's Ratio: This was calculated as the ratio of tapped density to bulk density of the sample.

HR: Tapped bulk density/ loose bulk density

Angle of Repose: The frictional forces in a loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

A funnel was kept vertically in a stand at a specified height above a paper placed on a horizontal surface. The funnel bottom is closed and sample powder is filled in funnel. Then funnel was opened to release the powder on the paper to form a smooth conical heap. The height of the heap was measured by using scale. The value of angle of repose are calculated by using the following formula,

$$\tan \theta = h/r$$
$$\theta = \tan^{-1} (h/r)$$

Where θ = Angle of repose, h = height of the heap and r = radius of the heap

2.2.2 Compatibility Studies

The drug excipient compatibility studies were performed by FT-IR spectroscopy.

2.2.3 Determination of Lambda Max

The sample solution containing 10µg/ml was prepared and scanned between 200-400nm in Double beam UV-Visible Spectrophotometer. The absorption maximum was found to be at 244nm.

Preparation of standard solution

Preparation of stock solution1: 100mg of Chlorzoxazone was weighed accurately and dissolved in 6.8 pH PO_4 buffer. The volume was made up to 100ml with 6.8 pH PO_4 buffer (1000µg/ml)

Preparation of stock solution2: From S.S1 10ml was pipette out in 100ml volumetric flask and made up to 100ml with 6.8 pH PO_4 buffer (100µg/ml).

Dilutions: From S.S2 0.2, 0.4, 0.6, 0.8, 1ml was pipette out in 10ml V.F and made up to 10ml with 6.8 pH PO_4 buffer which gives conc as 2, 4, 6, 8, 10µg/ml.

2.2.4 Preparation of Chlorzoxazone Floating Tablets

Tablets were fabricated by direct compression method. Accurately weighed quantities of polymer (HPMC K100) and MCC were taken in a mortar and mixed thoroughly, to this mixture required quantity of Chlorzoxazone (250mg) was added and mixed slightly with pestle. Accurately weighed quantity of Sodium bicarbonate and citric acid was taken separately in a mortar and powdered with pestle. The composition of each formulation is given in Table 1. The powder is passed through sieve #40 and mixed with the drug blend which is also passed through sieve #40. To this Magnesium stearate was added and mixed for additional 2 minutes. The mixture was then compressed into a tablet with 10mm round flat-faced punching machine. The weight of the tablets was kept constant for all the formulations.

Table 1: Composition of Chlorzoxazone Floating tablets

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8
Chlorzoxazone (Drug)	250	250	250	250	250	250	250	250
HPMC K100	170	175	150	160	120	110	100	90
Microcrystalline cellulose (MCC)	10	5	30	20	60	70	80	90
Sodium Bicarbonate ($NaHCO_3$)	15	15	15	15	15	15	15	15
Citric acid	10	10	10	10	10	10	10	10
Magnesium stearate	5	5	5	5	5	5	5	5
Total wt.	460	460	460	460	460	460	460	460

2.2.5 Post-Compression Evaluation of Tablets

Weight variation

Ten tablets were randomly selected from each formulation and weighed to determine the average weight and were compared with individual tablet weight. The average weight of the tablet is above 250 mg to percentage deviation is ± 5%.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm2. Tablets of each formulation were randomly picked and hardness was determined.

Thickness

The thickness of the tablets was measured using vernier caliper. It is expressed in mm. Three tablets of each formulation were picked randomly and its thickness was measured.

Friability test

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed and transferred into Friabilator. The Friabilator was operated at 25rpm for 4min. The tablets were weighed again and% friability was then calculated by:

$$\%F = W \text{ (initial wt)} - W_o \text{ (final wt)} / W \times 100$$

***In-vitro* buoyancy studies**

The *in vitro* buoyancy was determined by floating lag time method. The tablets were placed in 250 ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface was determined as floating lag time (FLT). The total duration of time by which the tablets remain buoyant is called total floating time (TFT).

Drug Content

Ten tablets from each formulation were weighed and powdered. Powder equivalent to the average weight of the tablet was accurately weighed in a 100 ml volumetric flask and dissolved in a suitable quantity of 6.8 pH phosphate buffer and made upto 100ml with 6.8 pH phosphate buffer and filtered. 2 ml of filtrate was transferred to a 100 ml volumetric flask & volume made upto 100ml with 6.8 pH phosphate buffer. The absorbance of the resulting solution is measured by Uv-visible Spectrophotometer, Elico, PG Instrument at 244nm.

***In vitro* Dissolution studies** [20]

In-vitro drug release profile of the prepared floating tablets were evaluated using USP Type II dissolution apparatus (paddle, 900 ml 6.8 pH PO_4 buffer, 37 ± 0.5 ^oC, 50 rpm). One tablet was placed in each dissolution vessels and the system was run. Aliquots of samples were withdrawn till 12thhr at 1hr interval. Fresh dissolution medium was replaced to maintain the original volume. The withdrawn aliquots were filtered, suitably diluted with 6.8 pH PO_4 buffer to obtain concentration of 10µg/ml. Absorbance was measured spectrophotometrically at 244nm to determine%drug release.

Analysis of Release Mechanism

In order to examine the release mechanism of Chlorzoxazone from the prepared floating tablets of the optimized formulation (F8), the results of the dissolution study was examined in accordance to the kinetic models. The dissolution profiles of formulations were analyzed according to zero-order, first order, Higuchi's square root and Korsmeyer-Peppas equations. The regression coefficient R2 value nearer to 1 indicates the model fitting of the release mechanism. The results are shown in Table 7 and Figure 6 to 9.

Stability studies

The optimized formulation was selected and were placed in plastic tubes containing desiccants and stored at ambient humidity conditions, at room temperature 25 ± 2 ^oC / 60 ± 5% RH, 30±2 ^0C / 65±5% RH and accelerated temperature 40 ± 2 ^oC / 75 ± 5% RH. The samples kept for stability were evaluated for the hardness, thickness, friability, floating test, drug content and in-vitro dissolution after 30, 60 and 90 days.

3. Results and Discussion

The floating tablets of Chlorzoxazone were formulated in eight different batches F1 to F8. All formulations were prepared by using HPMC K100 as rate retarding polymer, MCC as hydrophilic diluent, Sodium bicarbonate and citric acid as a gas-generating agent and Magnesium stearate as lubricant.

Drug-Excipients Compatibility

The FTIR spectrum of formulation was compared with that of drug spectrum and the results showed that the peaks and functional group are similar to that of drug spectrum. This shows that the drug is compatible with the excipients (Figure 1 & 2).

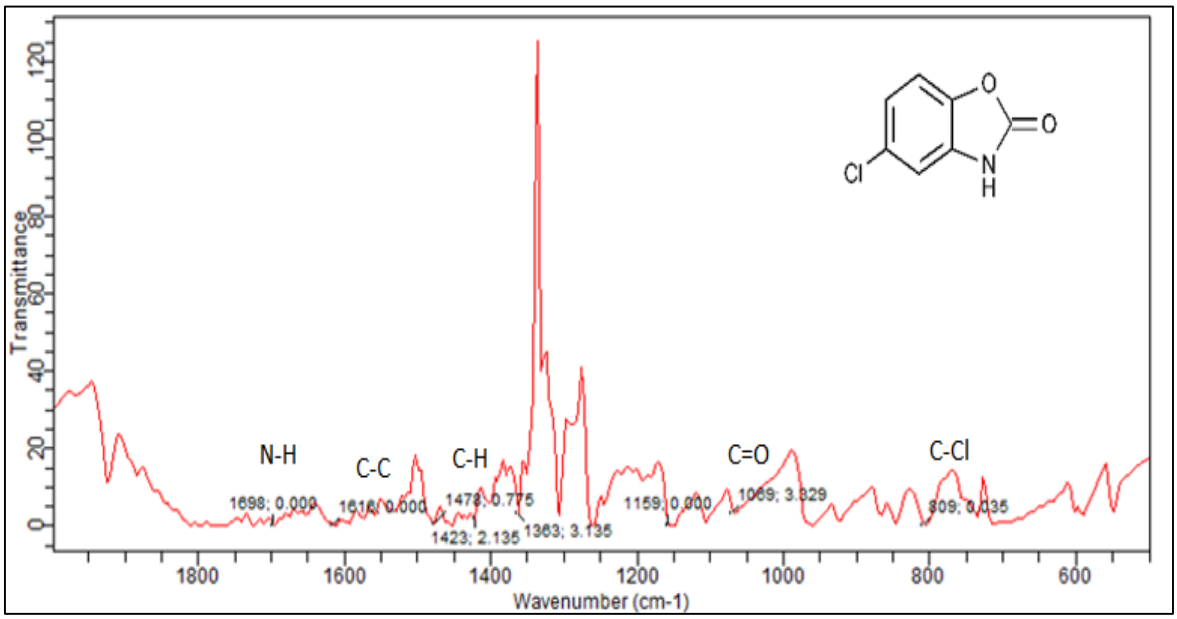

Fig 1: FTIR Spectrum of Chlorzoxazone

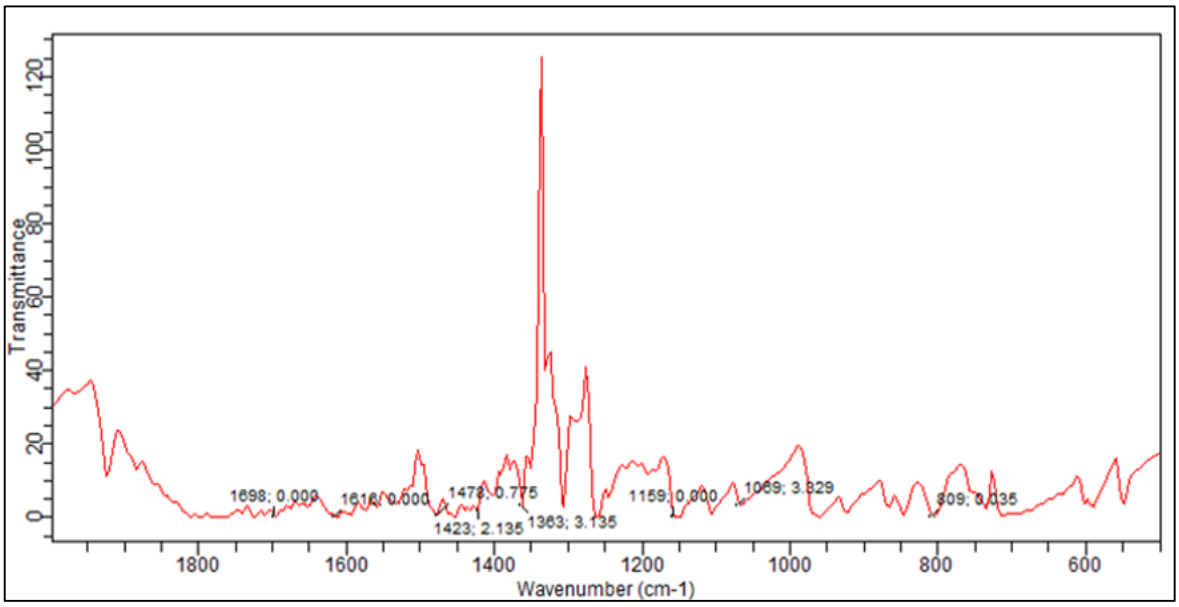

Fig 2: FTIR Spectrum of Drug and Excipients

Determination of lambda max

The lambda max of Chlorzoxazone was found to be at 244nm. The standard graph of Chlorzoxazone in 6.8 pH phosphate buffer showed a good linearity with R^2 of 0.9997 (Table 2, Figure 3).

Table 2: Standard graph of Chlorzoxazone

S.NO	CONC(µg/ml)	ABS (244nm)
1	2	0.221±0.02
2	4	0.45±0.05
3	6	0.68±0.06
4	8	0.901±0.031
5	10	1.12±0.024
6	12	1.325±0.012

All values are expressed as mean ± SD, n=3

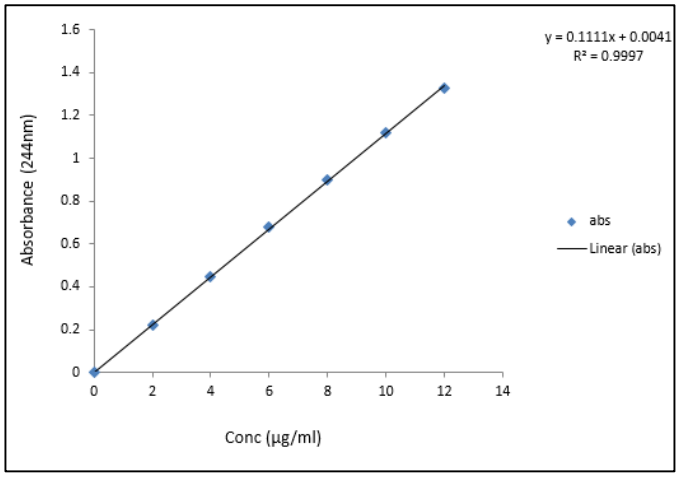

Fig 3: Standard Graph of Chlorzoxazone

Pre-Compression Evaluation

The result of all eight formulations of bulk density, tapped

density, compressibility index, hausner ratio and angle of repose indicates reasonably good flow property of granules. Results were calculated and the values ranged as follows, Cars index: 10.43-15.43, Hausner ratio: 1.10-1.19, Angle of repose: <30° for all formulations (Table 3). The results of the physical tests of many of the blends were in the limits and comply with the standards.

Table 3: Pre-Compression Parameters

Formulation	Bulk density (gm/mL) ±SD	Tapped density (gm/mL) ±SD	Carr's index ±SD	Hausner's ratio (HR) ±SD	Angle of repose (θ) ±SD
F1	0.408 ± 0.004	0.456 ± 0.001	10.43 ± 1.166	1.11 ± 0.014	26.24 ± 0.571
F2	0.410 ± 0.005	0.474 ± 0.007	15.43 ± 0.174	1.15 ± 0.002	27.73 ± 0.453
F3	0.439 ± 0.005	0.484 ± 0.007	12.23 ± 0.122	1.10 ± 0.001	28.26 ± 0.439
F4	0.566 ± 0.010	0.640 ± 0.002	11.55 ± 1.629	1.13 ± 0.020	25.67 ± 1.111
F5	0.565 ± 0.009	0.649 ± 0.003	12.98 ± 1.492	1.14 ± 0.019	26.01 ± 0.771
F6	0.578 ± 0.10	0.675 ± 0.026	14.30 ± 2.059	1.16 ± 0.028	27.55 ± 1.054
F7	0.425 ± 0.008	0.057 ± 0.013	11.12 ± 1.306	1.19 ± 0.018	28.01 ± 0.553
F8	0.419 ± 0.005	0.495 ± 0.014	13.33 ± 1.518	1.18 ± 0.021	28.08 ± 0.985

All values are expressed as mean ± SD, n=3

Post-Compression Evaluation of tablets

Weight variation, Hardness, Thickness and Friability

The weight variation was within range of ±5% complying with pharmaceutical specifications. The hardness for formulations was found to be between 4.0-4.25 kg/cm^2 indicating satisfactory mechanical strength. The friability was below 1% for formulations (Table 4).

Drug content

The drug content uniformity was examined as per I. P specification. All the batches of tablets were found to comply with uniformity of content test (Table 4). Drug content was in the range of 96.59±0.57% to 99.47±0.57% in the prepared formulation.

Table 4: Post Compression Parameters of Chlorzoxazone floating tablet

Formulation	% Weight variation Mean±SD	Hardness (kg/cm^2) Mean±SD	Thickness (mm) Mean±SD	Friability (%)±SD Mean±SD	Drug content (%)
F1	0.21 ± 0.002	4.0 ± 0.3	4.62 ± 0.024	0.508 ± 0.002	98.84
F2	0.36 ± 0.010	4.5 ± 0.3	4.69 ± 0.023	0.459 ± 0.026	96.59
F3	0.32 ± 0.002	4.2 ± 0.4	4.30 ± 0.032	0.368 ± 0.001	98.88
F4	0.06 ± 0.022	4.5 ± 0.4	4.00 ± 0.034	0.274 ± 0.002	97.71
F5	0.45 ± 0.002	4.5 ± 0.2	4.52 ± 0.019	0.459 ± 0.001	98.88
F6	0.19 ± 0.007	4.6 ± 0.2	4.34 ± 0.019	0.438 ± 0.005	98.67
F7	0.42 ± 0.034	4.5 ± 0.2	4.58 ± 0.014	0.431 ± 0.007	99.38
F8	0.19 ± 0.004	4.5 ± 0.2	4.89 ±0.012	0.263 ± 0.002	99.47

All values are expressed as mean ± SD, n=3

***In-vitro* Buoyancy studies**

From the results, it was observed that the buoyancy lag time for F1, F2, F3, F4, F5, F6, F7 and F8 was 56 sec, 50 sec, 55 sec, 57 sec, 55 sec, 50 sec, 49 sec and 45 secs respectively (Table 5). The total floating time for all the formulations showed sustained release of drug for 12hrs.

Table 5: Floating characteristics of Floating tablets of Chlorzoxazone

Formulation	Lag time (sec)	Floating Duration (hrs)
F1	56	≥ 12
F2	50	≥12
F3	55	≥12
F4	57	≥12
F5	55	≥12
F6	50	≥12
F7	49	≥12
F8	45	≥12

***In vitro* Dissolution study**

From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling, and drug diffusion. It was observed that all the tablets ascended to the upper one third of the dissolution vessels within a short time, and remained floated until the complete of release studies. The drug release study was carried out up to 12 hrs. The percentage drug release from batch F1 to F6 vary from 70.65% to 89.54% because of increase in concentration of polymer (HPMC K100). The% drug release was 90.65% in formulation F7. High drug release is observed in formulation F8 i.e. 99.12% because of low concentration of polymer (HPMC K100) (Table 6, Figure 4). Formulation F8 was selected as an optimized formulation as it showed high percentage drug release and was compared with the sustained release tablets (Figure 5).

Table 6: *In-vitro* dissolution study of Chlorzoxazone floating tablets

Time (hrs)	Cumulative% Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	Sustained Release tablet
1	14.43	8.88	13.42	12.59	13.42	14.00	19.62	15.76	29.40
2	14.96	9.79	15.98	14.67	20.08	22.03	24.43	24.33	40.85
3	16.68	10.52	22.40	19.55	24.71	26.00	31.99	35.12	54.62
4	17.05	11.72	25.32	23.53	36.88	36.57	40.87	43.12	61.73
5	18.51	12.48	32.18	25.36	45.23	45.52	48.09	49.15	74.43
6	22.51	15.98	41.63	32.18	51.19	54.43	55.94	60.23	80.17
7	34.09	20.44	47.56	42.56	59.23	60.89	61.09	68.41	85.10
8	43.51	28.65	53.89	50.56	63.23	65.12	66.45	74.32	91.48
9	50.56	39.41	59.88	56.12	72.34	70.12	70.12	80.65	93.71
10	57.09	47.90	63.90	66.90	76.33	78.66	76.90	85.56	95.10
11	64.32	55.09	69.87	78.34	80.45	81.45	83.23	93.78	96.49
12	70.65	65.34	71.23	80.12	85.99	89.54	90.65	99.12	98.23

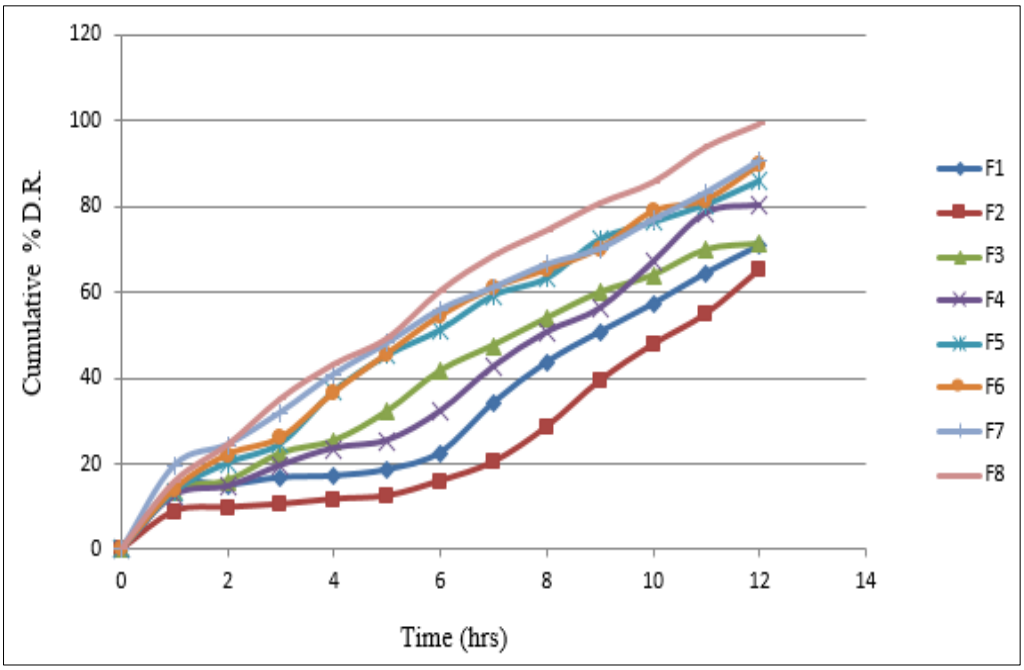

Fig 4: Cumulative percentage drug release of all formulations

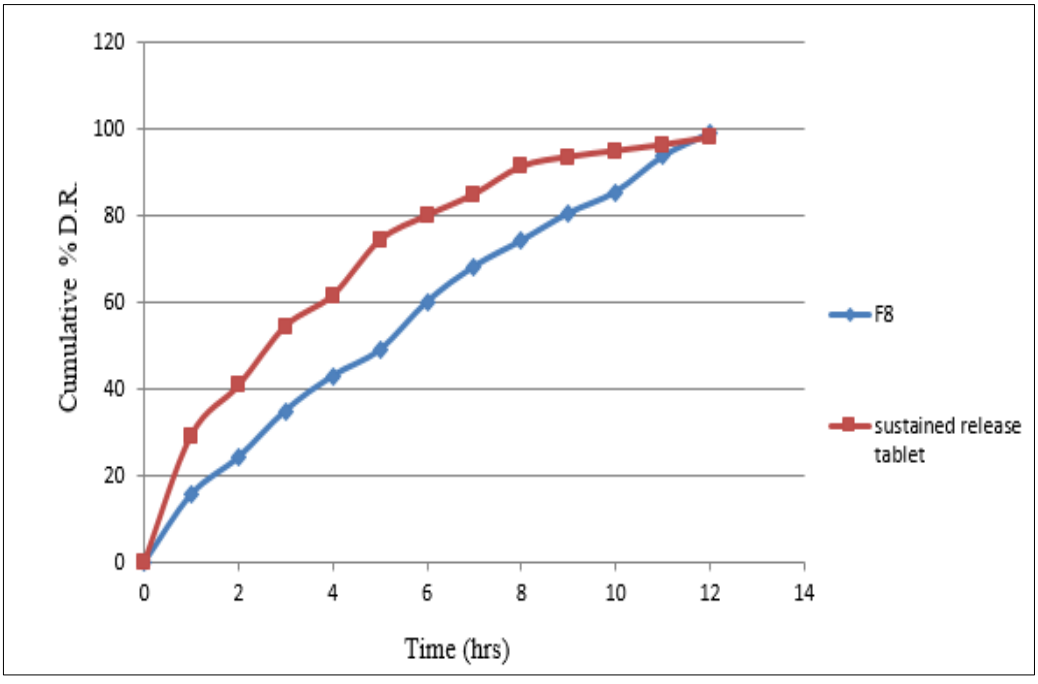

Fig 5: Cumulative percentage drug release of optimized formulation (F8) & Sustained Release Tablet

Analysis of drug release mechanism

The data obtained from *in-vitro* dissolution studies of optimized formulation F8 was fitted in different models viz. Zero order, First order, Higuchi model and Peppas model. The R^2 values of optimized formulation were obtained in all models i.e. Zero order, First order, Higuchi model and Korsmeyer-peppas model (Figure 6, 7, 8, 9). It was observed that the formulation follows first order and drug release mechanism follows Higuchi model (Table 7).

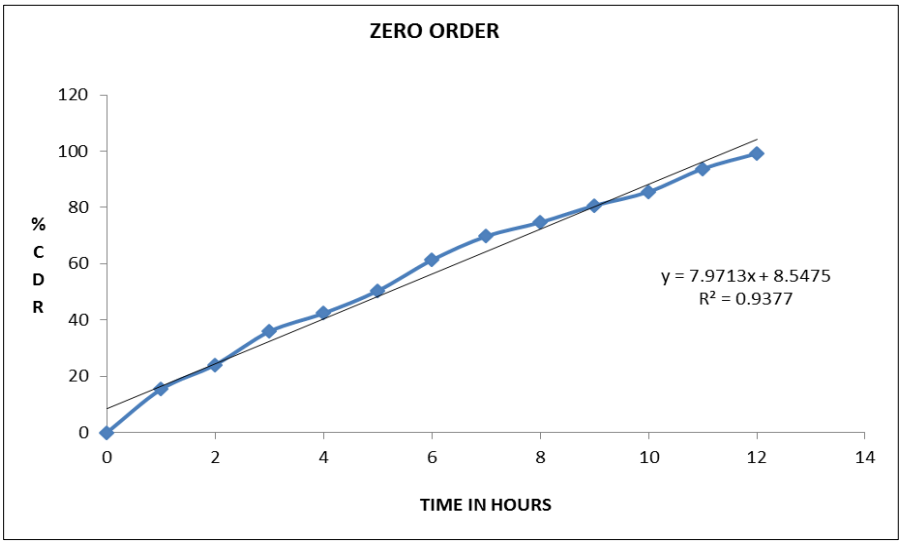

Fig 6: Zero order plot of Cumulative% drug release vs. time of optimized formulation

Fig 7: First order plot of Log Cumulative% drug remaining vs. time of optimized formulation

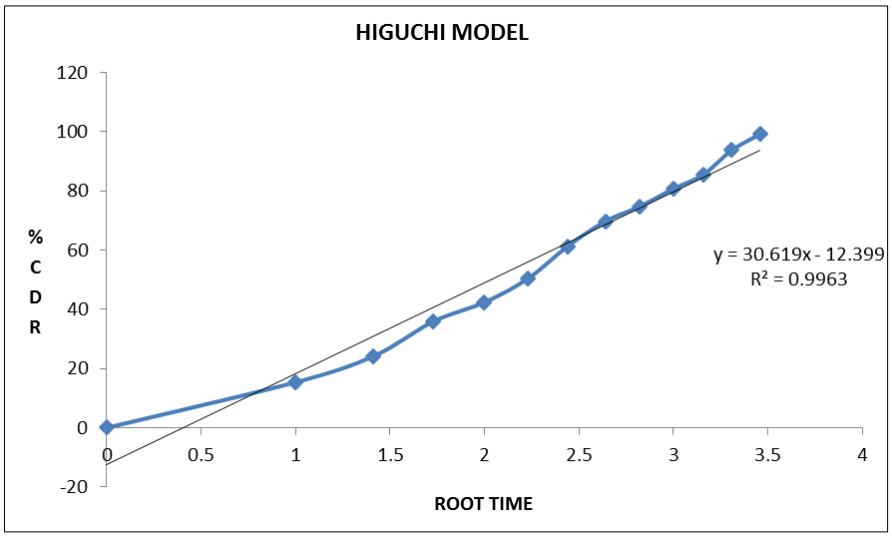

Fig 8: Plot of Cumulative% drug release vs. Root time of optimized formulation

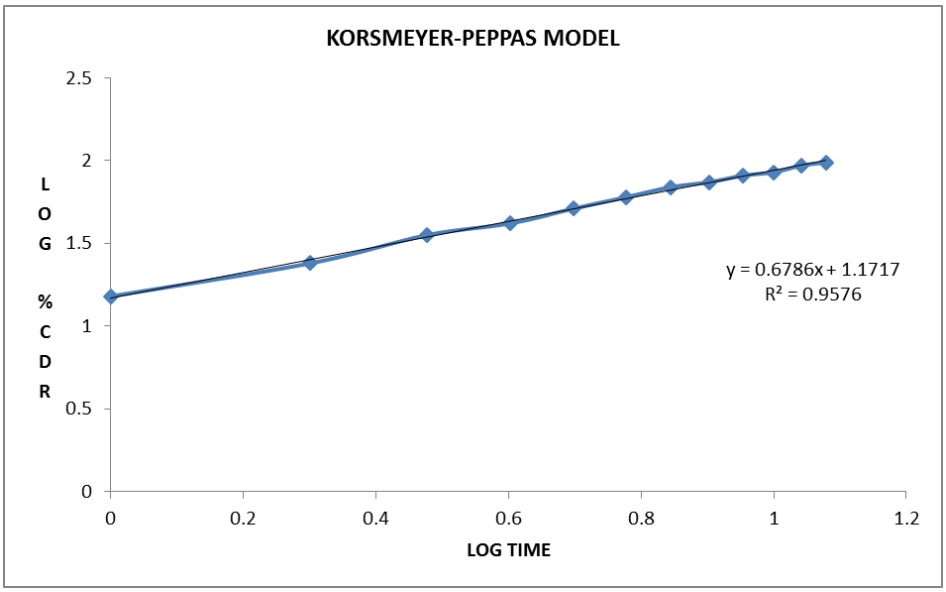

Fig 9: Plot of Log Cumulative% drug release vs. Log time of optimized formulation

Table 7: Kinetic Release Data of Different Model for Optimized Formulation (F8)

Formulation Code	Zero order (R^2)	First order (R^2)	Higuchi (R^2)	Korsmeyer-peppas (R^2)	Korsmeyer-peppas Model (n Value)
F8	0.937	0.995	0.996	0.957	0.678

Stability Studies

During and at the end of the accelerated stability, the tested tablets showed non-significantly different drug content from that observed at the beginning of the study. They also showed satisfactory hardness and buoyancy properties during and at the end of the accelerated study period. The selected formulation of Chlorzoxazone floating tablets were carried out for stability studies for 3 months in different temperatures such as short term stability at 25 ± 2 ºC / 60 ± 5% R.H, 30±2 ^{0}C / 65±5% RH and accelerated stability at 40 ± 2 ºC / 75 ± 5% R.H for a period of 3 months and the samples were tested for hardness, thickness, friability, *in vitro* buoyancy, drug content and *in vitro* drug release for every month (Table 8). There was no significant change in the tested parameters, *in-vitro* buoyancy, drug content and *in-vitro* drug release of the Chlorzoxazone floating tablets.

Table 8: Stability Studies of Optimized Formulation (F8)

Days	Temperature	Parameters						
		Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Floating lag Time (sec)	Total Floating time (hrs)	Drug Content (%)	% Drug Release
1st Day	25 ± 2ºC / 60 ± 5%	4.03 ± 0.2	3.89 ± 0.012	0.263 ± 0.002	45	12	98.89	98.97
	30±2 ^{0}C / 65±5%	4.03 ± 0.2	3.86 ± 0.011	0.260 ± 0.003	45	12	98.84	98.96
	40 ± 2ºC / 75 ± 5%	4.02 ± 0.2	3.59 ± 0.013	0.259 ± 0.021	46	12	98.87	98.12
After 30 days	25 ± 2 ºC / 60 ± 5%	4.01 ± 0.3	3.74 ± 0.011	0.250 ± 0.025	46	12	98.77	98.86
	30±2 ^{0}C / 65±5%	4.01 ± 0.2	3.71 ± 0.003	0.251 ± 0.025	45	12	98.76	98.82
	40 ± 2 ºC / 75 ± 5%	4.00 ± 0.2	3.51 ± 0.089	0.248 ± 0.055	47	12	98.80	98.97
After 60 days	25 ± 2 ºC / 60 ± 5%	4.00 ± 0.2	3.70 ± 0.012	0.245 ± 0.022	46	12	98.74	98.80
	30±2 ^{0}C / 65±5%	4.00 ± 0.1	3.60 ± 0.006	0.242 ± 0.007	46	12	98.71	98.77
	40 ± 2 ºC / 75 ± 5%	4.01 ± 0.1	3.40 ± 0.033	0.239 ± 0.052	47	12	98.74	98.74
After 90 days	25 ± 2 ºC / 60 ± 5%	4.01 ± 0.1	3.65 ± 0.011	0.230 ± 0.012	47	12	98.60	98.75
	30±2 ^{0}C / 65±5%	4.01 ± 0.2	3.63 ± 0.004	0.228 ± 0.004	47	12	98.59	98.73
	40 ± 2 ºC / 75 ± 5%	4.00 ± 0.2	3.29 ± 0.006	0.220 ± 0.016	48	12	98.69	98.62

4. Conclusion

Chlorzoxazone is a skeletal muscle relaxant belonging to BCS class II. An attempt was made to formulate floating tablets of Chlorzoxazone so as to increase the Gastric Residence Time (GRT) to improve the absorption. Different formulations were formulated using HPMC K100 as retarding agent and sodium bicarbonate and citric acid as gas generating agent by direct compression method. Increasing the concentration of HPMC K100 decreases the drug release. The formulation was optimized based on *in-vitro* drug release.

Thus, formulation F8 was selected as an optimized formulation because it gave best results in terms of drug release in a sustained manner. Data obtained from kinetic study of optimized formulation (F8) showed that the drug follows first order and drug release mechanism is by Higuchi model. The results of the stability study of F8 formulation indicated that the drug was stable throughout the stability test for a period of 3 months.

From the present study, it is evident that a promising controlled release floating tablets of Chlorzoxazone can be developed. Further detailed investigations are required to establish efficacy of these formulations.

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