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Formulation and Evaluation of Floating Tablet of alfuzosin Hydrochloride

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ABSTRACT

The present study in the development of Hydrodynamically Balanced Systems (HBS) of Alfuzosin Hydrochloride (HCl), an antihypertensive drug which are designed to increase the gastric residence time, thus prolonging the drug release. Hydroxy propyl methyl cellulose (HPMC) of different viscosity grades at three different drug to polymer ratios were used to prepare HBS by direct compression technique. The prepared HBS tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content, swelling index , *invitro* floating studies, *invitro* drug release and short term stability studies. The drug polymer ratio, viscosity grades of HPMC, different diluents and gas generating agents were found to influence the drug release and floating properties of the prepared HBS. The floating properties and drug release characteristics were determined for the prepared HBS in 0.1 N HCl dissolution media. All the HBs formulations showed good *invitro* floating properties with an optimum concentration of gas generating agents sodium bicarbonate and citric acid. The rate of drug release decreased with increased polymer concentration. It was found that HPMC viscosity had significant impact on the drug release from the prepared HBS. Among the three viscosity grades of HPMC (K4M, K15M, K100M), HPMC K4M along with lactose as diluents was found to be beneficial in improving the drug release rate and floating properties . Regression analysis of drug dissolution profiles on the basis of Higuchi and Korsmeyer model indicated that diffusion is the predominant mechanism controlling the drug release. The short term stability study indicated that there was no much differences observed.

Keywords: Alfuzosin HCl, Hydrodynamically Balanced Systems, Hydroxy Propyl Methyl Cellulose, *Invitro* floating, Higuchi model , Korsmeyer model .

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INTRODUCTION

Oral route is the most convenient and extensively used route for drug administration. This route has high patient acceptability, primarily due to easy of administration [1].Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for other routes. Most of the oral controlled drug delivery systems rely on diffusion, dissolution or combination of both mechanisms, to release the drug in a controlled manner to the Gastrointestinal Tract (GIT) and the drug profile data, uch as dose, absorption properties and the quantity of drug needed, one can determine the desired release rate of the drug from controlled release dosage form [2]. Drugs that are easily absorbed from the G.I.T 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 [3].

More than 50% of drug delivery systems available in the market are oral drug delivery systems. These systems have the obvious advantages of case of administration and patient acceptance. One would always like to have ideal drug delivery systems that will possess two main properties

1. It will be a single dose for the whole duration of treatment, and
2. It will deliver the active drug directly at the site of action.

Unfortunately, such ideal systems are not available. Thus, scientists try to develop systems that can be as close to an ideal system as possible. There are certain situations in which gastric retention is not desirable. Aspirin and non-steroidal anti-inflammatory drugs are known to cause gastric lesions, and slow release of such drugs in the stomach is unwanted. Thus, drugs that may irritate the stomach lining or are unstable in its acidic environment should not be formulated in gtastroretentive systems. Further more, other drugs, such as Isosorbide dinitrate, that are absorbed equally well throughout the GI tract will not benefit from incorporation into a gastric retention system. Certain types of drugs can benefit from using gastroretentive devices. These include drugs that act locally in the stomach, are primarily absorbed in the stomach; are poorly soluble at an alkaline pH, have a narrow window of absorption, and degrade in the colon [4].

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site of the body, to achieve promptly and then maintain the desired therapeutic drug concentration that elicits the pharmacological action and to minimize the incidence and the severity of unwanted adverse effects. To achieve this goal, it would be advantageous and more convenient to maintain a dosing frequency to once, or at most, a twice-daily regimen. An appropriately designed extended release dosage form can be a major advance in this direction [5].

Many attempts have been made to develop sustained-release preparations with extended clinical effects and reduced dosing frequency. In order to develop oral drug delivery systems, it is necessary to optimize both the release rate of the drug from the system and the residence time of the system within the gastrointestinal tract [6].

The present investigation concerns the development of the floating tablet ,which after oral administration are designed to prolong the gastric residence time,Increase the drug bioavailability, diminish the side effects of irritating drugs [7].

MATERIALS AND METHODS

Alfuzosin HCl was obtaind as gift sample from Wockhardt, Research Centre, Aurangabad. Hydroxy propyl methyl cellulose K4M, K15M, K100M were gift sample from Wockhardt, Research Centre, Aurangabad. Microcrystalline cellulose, Lactose, Gift sample from Colorcon Asia Limited, Goa. sodium bicarbonate, citric acid, talc, magnesium stearate were procured from SD Fine chemical, Mumbai.

Procedure for preparation of HBS of Alfuzosin HCl

All the ingredients were accurately weighed and pass through sieve No. 60. In order to mix the ingredients thoroughly, drug and polymer were blended in a mortar for 15 minutes, then Microcrystalline Cellulose (MCC), sodium bicarbonate, lactose, citric acid, talc and magnesium stearate were mixed one by one. After thoroughly mixing these ingredients, the powder blend was passed through sieve no. 44.

Tablets were compressed on a rotatory punching machine (Clit pilot press) using flat surfaced, round shaped punches of 9mm diameter. Hardness of the tablet was maintained around 4.3 to 5.0kg/cm^2.

Evaluation of HBS of Alfuzosin HCl

Evaluation of Alfuzosin HCl granules

The flow properties of granules (before compression) were characterized in terms of angle of repose[8], tapped density, bulk density [9], Carr's index [10] and Hausner ratio.

Physical evaluation of Alfuzosin HCl floating tablets

Hardness test

The crushing strength (Kg/cm^2) of tablets was determined by using Monsanto hardness tester. In all the cases, means of six replicate determinations were taken. The results are given in table-4

Friability test

This was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated. The results are given in table-4.

Uniformity of weight

The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation. The results are summarized in table-4.

Uniformity of drug content

5 tablets were powdered in a glass mortar and 100 mg of powder was placed in a 100 ml stoppered conical flask. The drug was extracted with 0.1N HC1 with vigorous shaking on a mechanical gyratory shaker (100 rpm) for 5 hour and filtered into 50 ml volumetric flask through cotton wool and filtrate was made up to the mark by passing more 0.1 N HCI through filter, further appropriate dilution were made and absorbance was measured at 244.5 nm against blank. The results are given in table-4.

Determination of swelling index [11]

The swelling index of tablets was determined in 0.1N HCl (pH 1.2) at room temperature. The swollen weight of the tablet was determined at predefined time intervals over a period of 24 h. The swelling index (SI), expressed as a percentage, and was calculated from the following equation

$$SI = \frac{\text{Weight of tablet at time (t)} - \text{Initial weight of tablet} \times 100}{\text{Initial weight of tablet}}$$

In vitro floating studies

In vitro floating studies were performed for all the fifteen formulations as per the method described by Rosa *et al*[12]. The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT). The results are given in table-5.

In vitro dissolution studies

In vitro dissolution studies of HBS of Alfuzosin HCl were carried out using USP XXIII tablet dissolution test apparatus-II (Electrolab), employing a paddle stirrer at 50 rpm using 900m1 of 0.1N HC1 at 37±0.5°C as dissolution medium. One tablet was used in each test. At predetermined time intervals 5ml of the samples were withdrawn by means of a syringe fitted with a pre filter. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5°C. The samples were analyzed for drug release by measuring the absorbance at 244.5 nm using UV-Visible spectrophotometer after suitable dilutions. All the studies were conducted in triplicate.

The results of *in vitro* release profiles obtained for all the HBS formulations were fitted into four models of data treatment as follows

1. Cumulative percent drug released versus time (zero-order kinetic model) [13].
2. Log cumulative percent drug remaining versus time. (first-order kinetic model) [14].
3. Cumulative percent drug released versus square root of time (Higuchi's model) [15].
4. Log cumulative percent drug released versus log time (Korsmeyer-Peppas equation) [16].

Stability studies

Short-term stability studies were performed at a temperature of 45° ±1°C over a period of three weeks (21 days) on the promising HBS tablet formulation F10. Sufficient number of tablets (15) were packed in amber colored screw capped bottles and kept in hot air-oven maintained at 45°±1°C. Samples were taken at weekly intervals for drug content estimation. At the end of three weeks period, dissolution test and *in vitro* floating studies were performed to determine the drug release profiles, *in vitro* floating lag time and floating time. The data of dissolution and *in vitro* floating studies are shown in tables 11-13.

RESULTS AND DISCUSSION

In the present study, Hydrodynamically Balanced Systems of Alfuzosin HCl were prepared by using different viscosity grades of Hydroxy propyl methyl cellulose (HPMC), viz, K4M, K15M and K100M(4,000, 15,000 and 1,00,000cps respectively) at different drug to polymer ratio with or without gas generating agent like sodium bicarbonate and citric acid. Two different diluents used are lactose and MCC.

The weighed quantities of drug and polymers were mixed thoroughly in different ratios (1:9.5, 1:12 and 1:15.3) and HBS tablets were prepared by direct compression method. The prepared HBS tablets were evaluated The prepared tablets of all the formulations were evaluated for precompression parameters like angle of repose, bulk and tapped density and

compressibility index and physical characters like tablet hardness, friability, weight variation, buoyancy lag time, total floating time, Swelling index, *in-vitro* drug release.

Precompression parameters of Alfuzosin HCl granules

The formulations showed good flow property and compressibility index (Table 3). Angle of repose ranged from 23.13 to 35.13, Hausner ratio ranged from 0.012 to 0.154 and the compressibility index ranged from 17.32 to28.78. The LBD and TBD of the prepared granules ranged from 0.421 to 0.561 and 0.587 to 0.642 respectively. The results of angle of repose indicates good flow property of the granules and the value of compressibility index further showed support for the flow property. Given in table 3.

Post compression parameters of Alfuzosin HCl tablets

Hardness and friability: The hardness of the prepared HBS of Alfuzosin HCl was found to be in the range of 4.3 to 4.5 kg/cm^2 and is given in table 5. The friability of all the tablets was found to be less than 1% i.e. in the range of 0.37 to 0.65 given in table 4.

*Uniformity of weight***:** All the prepared HBS were evaluated for weight variation and the results are given in tables 4. The percent deviation from the average weight was found to be within the prescribed official limits.

Uniformity of drug content: The low value of standard deviation indicates uniform drug content in the tablets prepared as observed from the data given in table 4.

Invitro floating studies: Invitro floating studies were performed by placing tablet in USP XXIII dissolution apparatus-II containing 0.1N HCl, maintained at temperature of 37±0.5°C. The floating lag time and floating time was noted visually. The results are given in table 5.

In the initial HBS formulations of Alfuzosin HCl, formulation containing drug and different viscosity grades of HPMC with gas generating agent (F1 to F9), the floating lag time was found to be in between 2 seconds to 12 seconds and remained under floating conditions for 24hours.

Formulations containing lactose along with a gas generating agent sodium bicarbonate at varying concentrations (F10 containing 50mg per tablet has shown a floating lag time of 10 seconds remained floating for 24 hours. HBS formulations containing MCC along with sodium bicarbonate at varying concentrations (F11, F12, F13, F14, F15) the floating lag time was found to be in between 6 seconds to 24 seconds and remains under floating condition for 24 hours.

The floating lag time was found to be more in the formulations which contains less gas generating agent (sodium bicarbonate) in the HBS formulations which may be due to delayed swelling of the polymer.

It was observed that when an optimum concentration of sodium bicarbonate was used, there was a reduction in the floating lag time, where the dissolution medium was imbibed into the matrix, the interaction of acidic fluid with sodium bicarbonate resulted in the formation and entrapment of CO_2 gas within the swollen gel, thus causing floating as the matrix volume expanded and its density decreased.

Reduction in the floating lag time was observed by the addition of citric acid along with sodium bicarbonate. Formulations F13, F14 and F15 containing combinations of gas generating agents at varying concentrations exhibited a floating lag time of 24 seconds, 20 seconds and 15 seconds respectively which may be due to the immediate formation of CO_2 gas that provides buoyancy.
Hence it can be concluded that optimum concentration of sodium bicarbonate (80mg per tablet)

Swelling index studies: Tablets composed of polymeric matrices build a gel layer around the tablet core when they come in contact with water. This gel layer governs the drug release. Kinetics of swelling is important because the gel barrier is formed with water penetration. Swelling is also a vital factor to ensure floating and drug dissolution.To obtain floating , the balance between swelling and water acceptance must be restored [17-18].The swelling index of floating tablets of F1 to F15 is shown in Fig.1.

The HPMC grade also affects the swelling and hydration with considerably higher swelling index for HPMC K4M than HPMC K15M and K100M. HPMC K15M and K100M exhibited low swelling index, but there was no decrease in swelling rate. The reason for this appeared to be its high viscosity and high water retention property. Further, no significant effect of effervescents on swelling indices was observed. Swelling index values start decreasing when polymer erosion starts in the medium.

Invitro dissolution studies: Invitro dissolution studies were performed for all the batches of HBS of Alfuzosin HCl using USP XXIII dissolution test apparatus-II at 50rpm, 900ml of 0.1N HCl used as dissolution media. The *invitro* drug release data was given in tables 6 to 8 and drug release profiles are shown in figure-2 to 21.

Formulations F1, F2 and F3 containing drug : polymer ratio 1:9.5, 1:12 and 1:15.3 prepared with HPMC K4M exhibited 98.52, 94.36 and 92.36% of drug release in 10 hours respectively and the data is given in table 20 and drug release profiles are shown in figure-2, 7-9. Formulations F4, F5 and F6 containing drug : polymer ratio 1:9.5, 1:12 and 1:15.3prepared with HPMC K15M exhibited 90.31, 86.63 and 87.47% of drug release in 10 hours respectively and the data is given in table 21 and drug release profiles are shown in figure-3, 10-12. *Invitro* drug release data for formulations F7, F8 and F9 are given in table 7 and drug release profiles are shown in figure-4, 13-15. The formulations F7, F8 and F9 were prepared with HPMC K100M

in drug polymer ratios 1:9.5, 1:12 and 1:15.3 exhibited 95.78, 85.07 and 85.64% drug release rates in 10 hours respectively.

In the above results, it was observed that as the concentration of the polymers increased, there is a decrease in the drug release rates. An increase in polymer concentration causes increase in viscosity of the gel as well as the gel layer with longer diffusional path. This could cause a decrease in effective diffusion coefficient of the drug and a reduction in drug release rate.

Formulations containing higher HPMC viscosity grades have slower drug release rates when compared to formulations with lower HPMC viscosity grades i.e. formulations F1, F2, F3 containing HPMC K4M have showed the fastest and formulations F7, F8, F9 containing HPMC K100M showed the slowest drug release rates. The amount of drug released for a particular drug polymer ratio was found to be in the order of K4M > K15M> K100M.

Among the three viscosity grades of HPMC studied, HPMC K4M with a drug-polymer ratio of 1:15.3 has been selected to study the influence of co-excipients lactose and MCC on drug release rates (F10, F11, F12 and F13). Formulation F10 containing lactose as diluent along with sodium bicarbonate exhibited 98.18% of drug release in 10 hours whereas formulation F11 and F12 containing MCC showed a drug release of 96.05 and 94.52% in 10 hours. It was observed that when Lactose was included along with HPMC K4M enhanced Alfuzosin HCl release from the HBS tablets when compared to same formulation with MCC. In the two excipients studied drug release was found to be faster in case of HBS containing MCC when compared to HBS with lactose (T_{90} for F10= 8.38hours and F11= 7.04 hours, T_{90} for F12=9.76 hours and F13= 7.38 hours).

Invitro release data of formulations F13, F14 and F15 are given in tables 8 and dissolution profiles are shown in figure-6, 19-21. These formulations containing drug and HPMC K4M along with MCC and a combination of gas generating agents sodium bicarbonate and citric acid exhibited a drug release of 95.21, 96.84 and 97.57% in 10 hours. The addition of citric acid in these formulations did not influence the drug release rates.

The dissolution T_{50} and T_{90} values for all the HBS formulations of Alfuzosin HCl is given in table 9. The comparative effect of two different diluents on the release profiles of Alfuzosin HCl from the HBS formulations in terms of dissolution T_{50} and T_{90} values is shown in figure-22. It was observed that HBS containing MCC (T_{90} for F11= 7.04 hours) exhibited shorter dissolution times when compared to formulations containing lactose (T_{90} for F10= 8.38hours).

Drug release kinetics: The *invitro d*rug release data was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equations, Higuchi and Korsmeyer models to ascertain the mechanism of drug release. The results of linear regression analysis of data including regression coefficient are summarized in table 10.

When the regression coefficient 'r' value of zero order and first order plots were compared, it was observed that the 'r' values of zero order were in the range of 0.90 to 0.99 whereas the 'r' values of first order plots were found to be in the range of 0.93 to 0.99 indicating drug release from all the formulations were found to follow 1st order kinetics. The good fit of the Higuchi model to the dissolution profiles of all the formulations suggested that diffusion is the predominant mechanism limiting drug release since the 'r' values of Higuchis plots were nearer to unity.

The *invitro* dissolution data as log cumulative percent drug release versus log time were fitted to Korsmeyer et al equation, values of the exponent 'n' was found to be in the range of 0.49 to 0.73 indicating that the drug release is by Non-Fickian diffusion mechanism.

Among the various formulations studied, HBS formulation F10 was considered as an ideal formulation which exhibited 90% of drug release in 8.38 hours (T_{90}) and floating lag time of 10 seconds with a floating time of 24 hours. Hence it is selected for further short term stability studies.

Stability studies: Short term stability study was performed for formulation F10 at 45±1^{0}C for 3 weeks (21 days). The samples were analysed for percent drug content, *invitro* floating ability and *invitro* drug release studies. The results are given in table 11 to 13. No appreciable difference was observed for the above parameters.

CONCLUSION

The following conclusions can be drawn from the results obtained in this study

- Hydrodynamically Balanced Systems offers a simple and practical approach to achieve increased gastric residence and to modify drug release profiles essential for sustained, site specific and localized drug action.
- The HBS of Alfuzosin HCl were developed by using different viscosity grades of HPMC by wet granulation technique. Lactose and MCC were used as diluents. Sodium bicarbonate and citric acid were used as gas generating agents either alone or in combination.
- All the prepared tablets prepared were found to be good without chipping, capping and sticking.
- The drug content was uniform and well within the accepted limits with low values of standard deviation indicating uniform distribution of drug within the HBS.
- The drug – polymer ratio, viscosity grades of HPMC, different diluents and gas generating agents were found to influence the release of drug and floating characteristics from the prepared HBS of Alfuzosin HCl.
- Polymer swelling is crucial in determining the drug release rate and is also important for flotation.
- The prepared HBS of Alfuzosin HCl showed excellent *invitro* floating properties. Addition of less quantity of gas generating agent sodium bicarbonate resulted in the reduction of

floating lag time. Addition of citric acid to the HBS with sodium bicarbonate has produced a marked reduction in the floating lag time upto less than 15 seconds. All the HBS system have showed a floating time of 24 hours. The floating lag time is dependent upon the concentration of gas generating agent sodium bicarbonate and citric acid was found to achieve an optimum *invitro* floating.

- The *invitro* dissolution profiles of all the prepared HBS formulations of Alfuzosin HCl were found to extend the drug release over a period of 10 hours and the drug release decreased with increase in viscosity of polymer.
- Release of Alfuzosin HCl from most of the HBS formulations was found to follow zero order kinetics (0.93 to 0.99) and derived correlation coefficient 'r' (0.98) indicated good fit of Higuchi model suggesting that diffusion is the predominant mechanism controlling the drug release. When drug release data fitted to Korsmeyer equation, the values of slope 'n' (0.49 to 0.73) indicated that the drug release was by Non-Fickian mechanism.
- Among the various HBS formulations studied, formulation F10 containing drug-polymer ratio (1:15.3) prepared with HPMC K4M showed promising results releasing ≈ 90% of the drug in 8.38 hours (T_{90}) with a floating lag time of 10sec and floating time of 24 hours has been considered as an ideal formulation and subjected to further short term stability studies.
- Optimized HBS of Alfuzosin HCl (F10) was found to be stable at 45^0C following a three week stability study.
- Finally, it may be concluded that this novel drug delivery system i.e HBS offers a valuable dosage form which delivers the drug at a controlled rate and at a specific site. The HBS of Alfuzosin HCl provides a better option for increasing the bio availability and reliability for hypertension and in benign prostatic hyperplasia to relieve symptoms of urinary obstruction by allowing a better control of fluctuations observed with conventional dosage forms.

Table-1: Preliminary Trial Formulation (for 1 tablet)

Ingredient (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Alfuzosin HCl	10	10	10	10	10	10	10	10	10
HPMC K4M	95	120	153	-	-	-	-	-	-
HPMC K15M	-	-	-	95	120	153	-	-	-
HPMC K100M	-	-	-	-	-	-	95	120	153
MCC	50	50	-	50	50	-	50	50	-
Sodium bicarbonate	48	53	60	48	53	60	48	53	60
Lactose	-	-	50	-	-	50	-	-	50
Citric acid	-	-	-	-	-	-	-	-	-
Magnesium sterate	4	4	4	4	4	4	4	4	4
Talc	3	3	3	3	3	3	3	3	3

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Table-2: Final Formulation (for 1 tablet)

Ingredient (mg)	F10	F11	F12	F13	F14	F15
Alfuzosin HCl	10	10	10	10	10	10
HPMC K4M	153	153	153	153	153	153
HPMC K15M	-	-	-	-	-	-
HPMC K100M	-	-	-	-	-	-
MCC	-	50	50	50	50	50
Sodium Bicarbonate	80	60	80	60	80	60
Lactose	50	-	-	-	-	-
Citric acid	-	-	-	10	20	30
Magnesium sterate	4	4	4	4	4	4
Talc	2	2	2	2	2	2

Table 3: Precompression flow properties of granules of Alfuzosin HCl

Formulation code	Angle of repose (θ) in degrees	Bulk density (gm/cm3)	Tapped density (gm/cm3)	Carr's index (%)	Hausner ratio (HR)
F1	28.13	0.486	0.614	18.12	0.154
F2	25.45	0.468	0.623	19.43	0.142
F3	28.67	0.431	0.591	22.10	0.065
F4	30.89	0.463	0.591	24.67	0.110
F5	24.34	0.521	0.632	17.32	0.146
F6	23.13	0.541	0.642	18.45	0.098
F7	28.15	0.561	0.632	21.78	0.141
F8	29.67	0.421	0.621	28.68	0.056
F9	30.90	0.458	0.581	25.90	0.078
F10	31.23	0.437	0.623	28.78	0.012
F11	25.41	0.483	0.587	26.53	0.088
F12	24.58	0.510	0.610	21.32	0.112
F13	34.15	0.486	0.614	21.49	0.139
F14	30.96	0.483	0.606	20.44	0.128
F15	35.13	0.488	0.614	20.52	0.124

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Table–4: Physical properties of HBS formulations F1 to F15

Formulation code	Diameter (mm)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation*(mg)	Percent drug content* ± SD
F1	9	2.65	4.6±0.5	0.59	204.95	98.49±0.001
F2	9	2.73	4.3±0.9	0.65	235.65	99.2±0.002
F3	9	2.87	4.9±0.3	0.70	274.70	99.36±0.01
F4	9	2.67	4.5±0.6	0.55	205.60	99.78±0.006
F5	9	2.77	4.5±0.8	0.71	236.55	99.92±0.017
F6	9	2.89	4.7±0.7	0.72	275.20	100.10±0.022
F7	9	2.64	4.6±0.3	0.58	205.25	100±0.46
F8	9	2.71	4.5±0.5	0.69	235.15	98.82±0.65
F9	9	2.86	4.8±0.9	0.57	275.25	99.68±0.75
F10	9	3.55	4.5±0.5	0.85	294.85	100±0.65
F11	9	3.68	4.5±0.2	0.75	274.70	99.28±0.53
F12	9	3.60	4.5±0.4	0.77	295.15	99.31±1.15
F13	9	3.70	4.6±0.3	0.91	286.40	99.78±0.77
F14	9	3.65	4.5±0.1	0.93	315.50	100±1.03
F15	9	3.76	4.5±0.4	0.86	306.65	100.17±0.83

Table-5: *In vitro* floating of HBS of Alfuzosin HCl

Formulation code	Floating lag time (Seconds)	Floating time (hrs)
F1	12	24
F2	4.5	24
F3	2	24
F4	9	24
F5	6	24
F6	4	24
F7	8	24
F8	7	24
F9	5	24
F10	10	24
F11	11	24
F12	6	24
F13	24	24
F14	20	24
F15	15	24

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Table-6:*In Vitro* release data of HBS of Alfuzosin HCl F1 to F5

Sl. No.	Time (Hrs)	F1	F2	F3	F4	F5
		Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD
1.	01	25.789±0.33	22.21±0.88	20.10±0.11	15.68±0.45	17.37±0.35
2.	02	45.052±0.96	36.31±0.41	42.73±0.35	17.89±0.33	31.36±0.22
3.	03	62±0.95	52.73±0.53	55.57±0.89	47.15±0.31	52.73±0.65
4.	04	78.42±0.42	54.21±0.98	58.84±0.51	51.36±0.85	62.10±0.95
5.	05	85.47±0.48	67.68±0.21	61.68±0.45	54.21±0.49	64.73±0.42
6.	06	86.526±0.55	71.15±0.35	67.26±0.49	60.0±0.53	70.21±0.48
7.	07	88.42±0.22	75.84±0.45	75.68±0.83	70.68±0.82	74.94±0.55
8.	08	91.26±0.53	80.31±0.59	80.0±0.77	76.89±0.73	79.68±0.22
9.	09	96.52±0.29	85.68±0.85	84.84±0.65	85.63±0.45	84.0±0.35
10.	10	98.52±0.46	94.36±0.18	92.36±0.81	90.31±0.78	86.63±95

Table-7:*In Vitro* release data of HBS of Alfuzosin HCl F6 to F10

Sl. No.	Time (Hrs)	F6	F7	F8	F9	F10
		Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD
1.	1	22.10±0.96	38.94±0.40	35.05±0.71	31.54±1.15	28.21±0.86
2.	2	43.57±0.33	58.63±0.80	54.21±0.42	51.15±0.64	41.84±0.16
3.	3	62.63±0.59	73.78±0.75	63.47±0.67	65.36±0.38	55.21±0.18
4.	4	65.68±0.54	76.63±0.48	67.26±0.80	67.26±0.76	62.68±1.19
5.	5	69.26±0.97	80.73±1.33	71.0±0.66	71.71±0.33	66.31±0.51
6.	6	72.31±0.62	84.0±1.30	74.84±0.65	73.42±0.73	71.94±0.60
7.	7	74.73±0.60	85.36±0.80	76.64±0.71	76.26±0.65	78.42±0.53
8.	8	77.26±0.51	87.89±0.68	78.15±0.96	77.77±0.82	85.84±0.45
9.	9	83.26±0.33	93.57±0.71	82.42±0.63	83.17±0.33	93.36±0.71
10.	10	87.47±0.76	95.78±0.42	85.07±0.51	85.64±0.82	98.18±0.14

Table-8:*In Vitro* release data of HBS of Alfuzosin HCl F10 to F15

Sl. No.	Time (Hrs)	F11	F12	F13	F14	F15
		Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD	Cumulative* percent drug released ±SD
1.	1	28.52±0.63	29.36±0.32	30.63±0.33	31.36±0.55	31.68±0.91
2.	2	48.31±1.20	33.57±0.83	39.15±0.39	35.05±0.48	45.63±0.85
3.	3	58.73±0.93	39.89±0.57	45.94±0.70	47.47±0.66	61.73±0.95
4.	4	70.52±0.94	46.63±0.34	60.26±0.40	55.26±0.70	69.15±0.67
5.	5	77.05±0.26	53.78±0.69	75.84±0.84	69.15±0.56	77.21±0.96
6.	6	83.42±0.80	60.42±0.69	80.36±0.74	78.68±0.58	83.16±0.18
7.	7	89.94±0.83	66.63±0.34	85.31±0.42	83.73±0.54	88.94±0.17
8.	8	92.52±0.58	73.47±0.93	90.52±0.69	87.84±0.31	93.89±0.20
9.	9	94.21±0.44	82.94±0.62	93.89±0.67	91.15±0.78	95.15±0.31
10.	10	96.05±0.32	94.52±0.59	95.21±0.53	96.84±0.34	97.57±0.33

*Average of three determinations

ISSN: 0975-8585

Table–9: Dissolution t_{50} and t_{90} values of HBS of Alfuzosin HCl

Sl. No.	Formulation Code	t_{50}(hours)	t_{90}(hours)
1	F1	2.25	7.12
2	F2	2.75	10.67
3	F3	2.34	11.63
4	F4	3.18	11.79
5	F5	3.18	10.38
6	F6	2.29	10.28
7	F7	1.28	8.19
8	F8	1.42	10.58
9	F9	1.58	10.50
10	F10	2.39	8.38
11	F11	2.06	7.00
12	F12	4.28	9.76
13	F13	3.26	7.38
14	F14	3.15	8.19
15	F15	1.57	7.08

Table–10: Regression analysis data of trial formulations of Alfuzosin HCl

Batch		Zero order	First order	Higuchi's equation	Peppas equation
F1	r	0.91082	0.9718	0.9588	0.966
	A	24.58	2.0774	2.7308	1.48
	B	8.867	0.168	32.52	0.5634
F2	r	0.9518	0.9902	0.9829	0.9827
	A	26.818	1.9345	1.6071	1.3917
	B	6.422	0.0749	28.37	0.5634
F3	r	0.9103	0.96716	0.9524	0.942
	A	31.29	1.8682	7.9356	1.4124
	B	5.028	0.0519	22.7748	0.51
F4	r	0.9302	0.9812	0.9671	0.9494
	A	18.336	1.9665	1.179	1.1918
	B	6.3805	0.0595	28.6948	0.7341
F5	r	0.9392	0.9936	0.9792	0.9711
	A	23.756	1.9728	8.2982	1.3102
	B	7.076	0.0848	31.4552	0.6727
F6	r	0.9088	0.973	0.9539	0.9493
	A	33.451	1.8883	6.6566	1.4432
	B	5.89	0.07495	26.3757	0.5316
F7	r	0.9116	0.9348	0.9579	0.9666
	A	48.99	1.7507	25.2	1.6425
	B	5.1887	0.0987	28.2386	0.3572
F8	r	0.9216	0.975	0.9735	0.9707
	A	43.117	1.7732	19.6238	1.5963
	B	4.56	-0.059	21.48	0.3494

ISSN: 0975-8585

Batch		Zero order	First order	Higuchi's equation	Peppas equation
F9	r	0.907	0.9728	0.9537	0.9593
	A	41.6	1.8141	19.269	15641
	B	4.859	0.0651	21.8348	0.3894
F10	r	0.9863	0.9198	0.9961	0.9963
	A	28.32	2.15	2.1096	1.4630
	B	7.250	0.1478	31.2929	0.5257
F11	r	0.9474	0.9977	0.9836	0.9854
	A	35.172	2.020	3.6875	1.5032
	B	7.046	0.1407	31.2621	0.5194
F12	r	0.9947	0.8963	0.9720	0.9704
	A	19.235	2.08837	8.2107	1.3982
	B	7.07	0.100	29.522	0.5144
F13	r	0.9692	0.888	0.9854	0.9859
	A	27.48	2.0785	5.2458	1.4563
	B	7.6786	0.1303	33.36	0.5458
F14	r	0.9823	0.9681	0.9890	0.9825
	A	25.0286	2.1163	7.2609	1.4420
	B	7.7500	0.1378	33.343	0.5467
F15	r	0.9583	0.9894	0.9889	0.9872
	A	35.55	2.074	4.4062	1.5495
	B	7.0652	0.1566	31.1576	0.4844

Table-11: Stability data of HBS formulation (F10) at 45±1°C

Sl. No.	Time in days	Physical changes	Mean ± SD (45 ±1°C)
1.	01	--	98.18±1.35
2.	07	No change	97.68±1.30
3.	14	No change	97.55±1.31
4.	21	No change	97.6±1.50

Table-12: *Invitro* floating studied of formulation (F10)

Sl. No.	Formulation code	Floating lag time (seconds)	Floating lag time (hrs)
1.	F10	10	24
2.	F10	12	24
3.	F10	10	24

ISSN: 0975-8585

Table-13: *In vitro* Release Data of the Formulation (F10)

Sl. No.	Time (Hrs)	Cumulative * Percent Drug Released ± SD at 45±1°C	
		1st Day	21st Day
1.	01	28.21 ± 0.73	27.95 ± 0.07
2.	02	41.84 ± 0.90	40.84 ± 0.54
3.	03	55.21 ± 0.68	54.98 ± 1.20
4.	04	62.68 ± 0.64	61.95 ± 1.60
5.	05	66.31 ± 0.71	65.88 ± 1.02
6.	06	71.94 ± 0.27	70.82 ± 0.99
7.	07	78.94 ± 1.48	77.63 ± 0.81
8.	08	85.84 ± 0.76	85.10 ± 1.12
9.	09	93.36 ± 0.94	92.79 ± 1.24
10.	10	98.18 ± 0.57	97.60 ± 0.42

*Average of three determinations.

Figure-1: Swelling index studies of Alfuzosin HCL (F1 to F15)

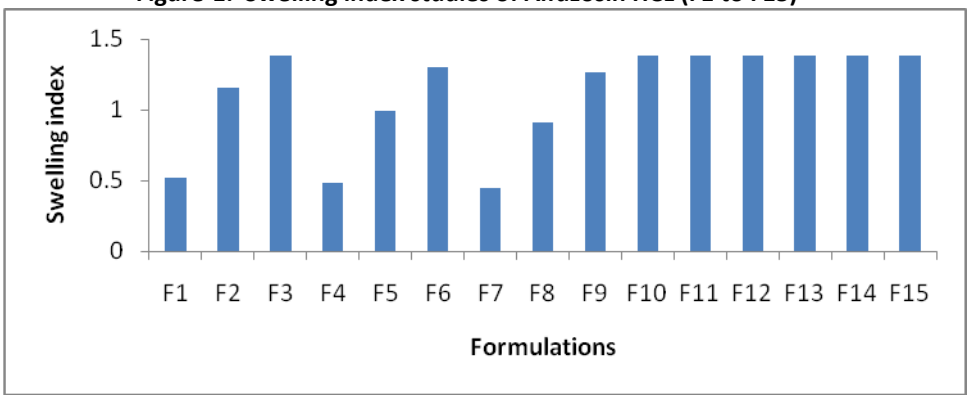

Figure-2: Cumulative Percent Drug Released Vs Time Plots (Zero Order) of formulation F1, F2 and F3

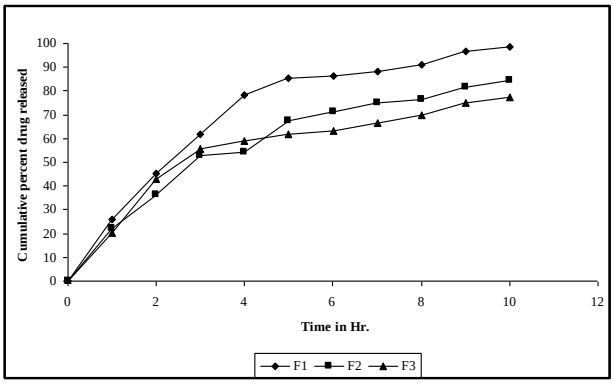

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Figure-3: Cumulative Percent Drug Released Vs Time Plots (Zero Order) of formulation F4, F5 and F6

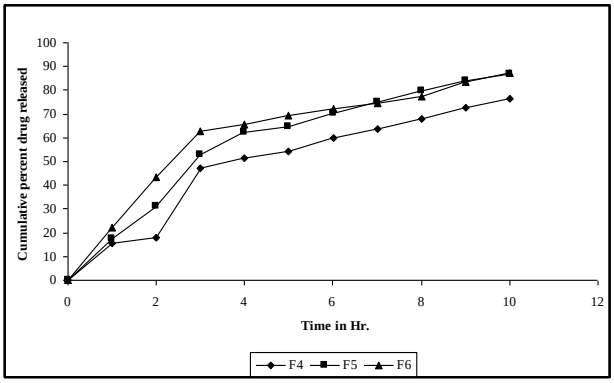


Figure-4: Cumulative Percent Drug Released Vs Time Plots (Zero Order) of formulation F7, F8 and F9

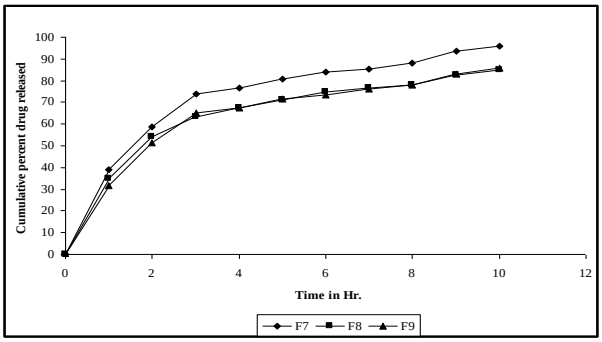


Figure-5: Cumulative Percent Drug Released Vs Time Plots (Zero Order) of formulation F10, F11 and F12

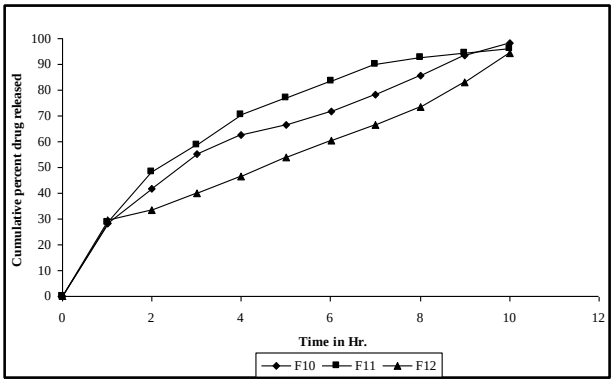
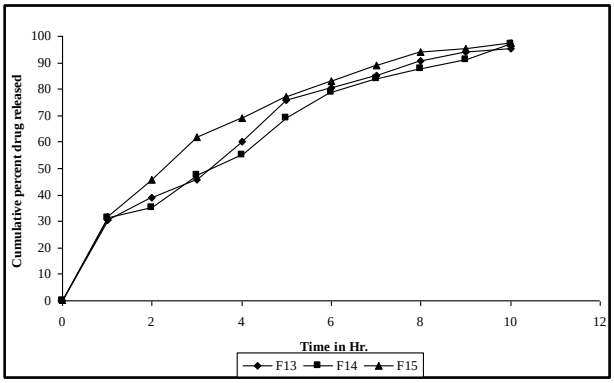


Figure-6: Cumulative Percent Drug Released Vs Time Plots (Zero Order) of formulation F13, F14 and F15



ISSN: 0975-8585

Figure-7: Log Cumulative Percent Drug Remaining Vs Time Plots (First Order) of formulation F1, F2 and F3

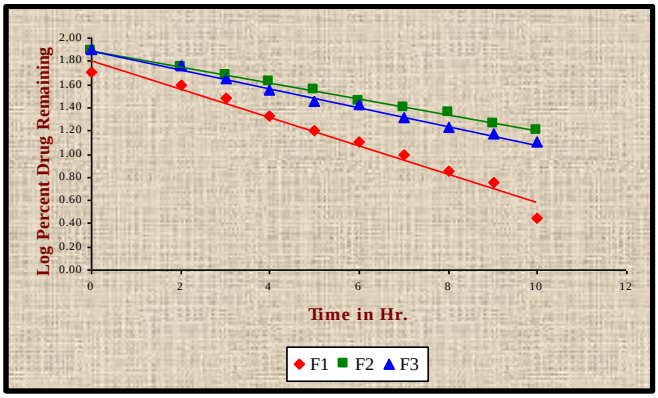


Figure-8: Cumulative Percent Drug Released Vs Square Root of Time (Higuchi's Plots) of formulation F1, F2 and F3

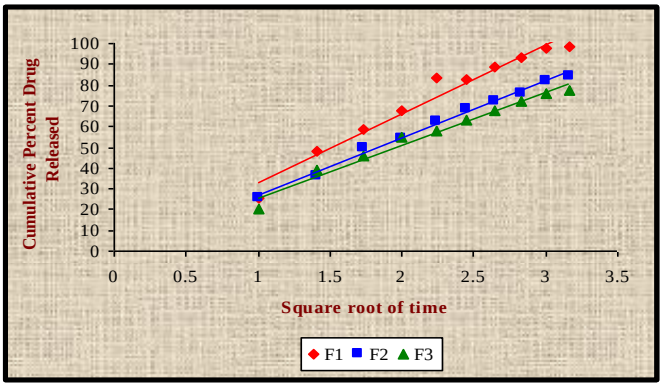


Figure-9: Log Cumulative Percent Drug Released Vs Log Time (Korsmeyer Plots) of formulation F1, F2 and F3

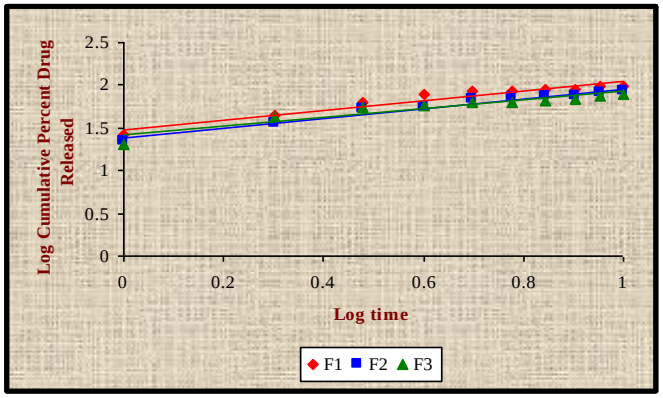


Figure-10: Log Cumulative Percent Drug Remaining Vs Time Plots (First Order) of formulation F4, F5 and F6

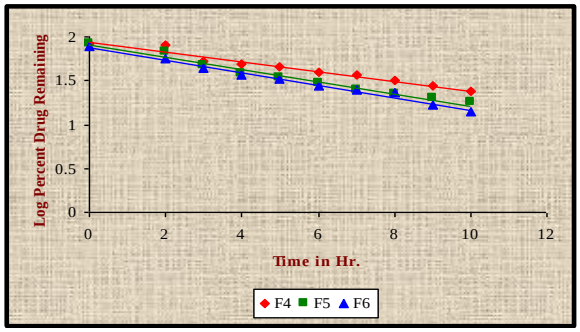


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Figure-11: Cumulative Percent Drug Released Vs Square Root of Time (Higuchi's Plots) of formulation F4, F5 and F6

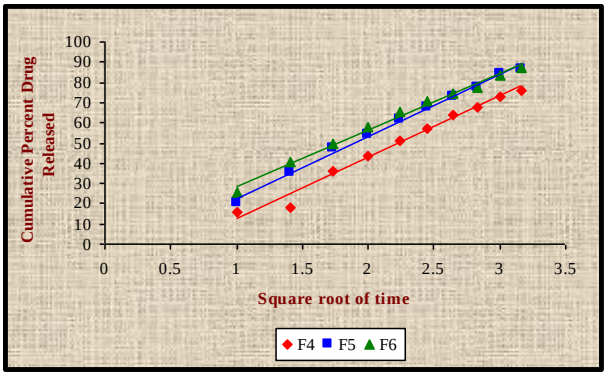

Figure-12: Log Cumulative Percent Drug Released Vs Log Time (Korsmeyer Plots) of formulation F4, F5 and F6

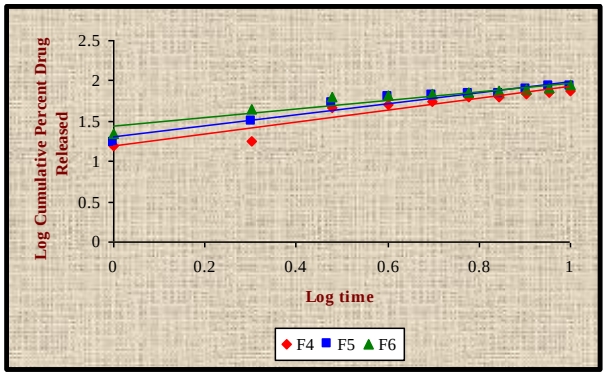

Figure-13: Log Cumulative Percent Drug Remaining Vs Time Plots (First Order) of formulation F7, F8 and F9

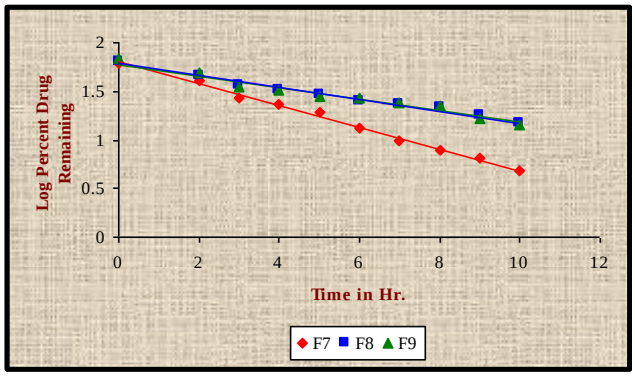

Figure-14: Cumulative Percent Drug Released Vs Square Root of Time (Higuchi's Plots) of formulation F7, F8 and F9

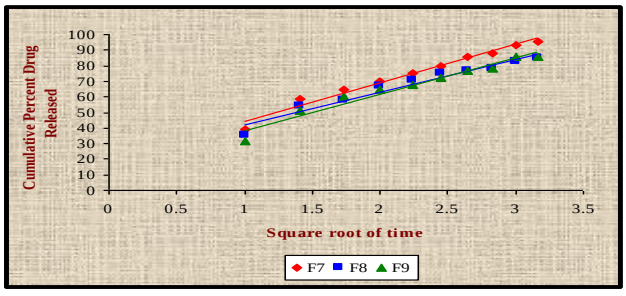

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Figure-15: Log Cumulative Percent Drug Released Vs Log Time (Korsmeyer Plots) of formulation F7, F8 and F9

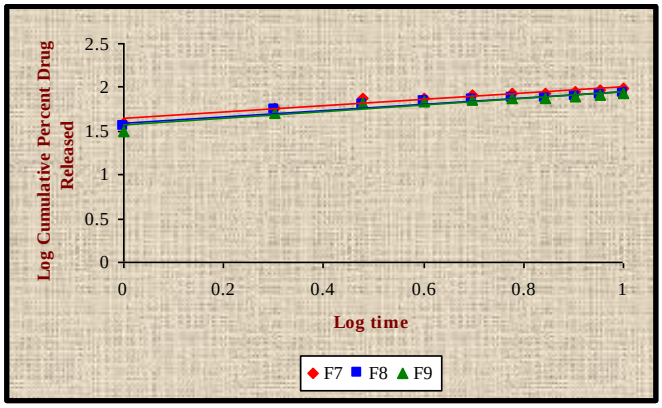

Figure-16: Log Cumulative Percent Drug Remaining Vs Time Plots (First Order) of formulation F10, F11 and F12

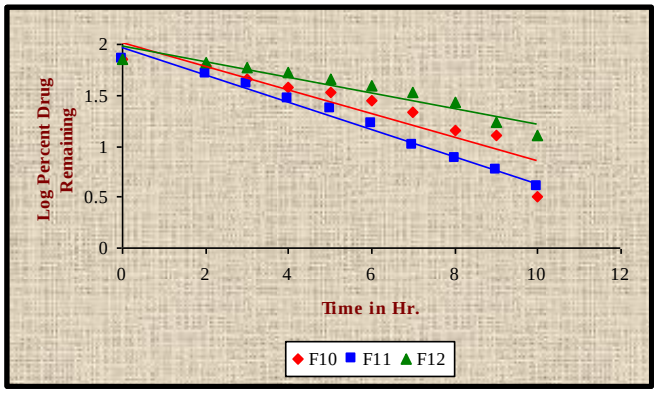

Figure-17: Cumulative Percent Drug Released Vs Square Root of Time (Higuchi's Plots) of formulation F10, F11 and F12

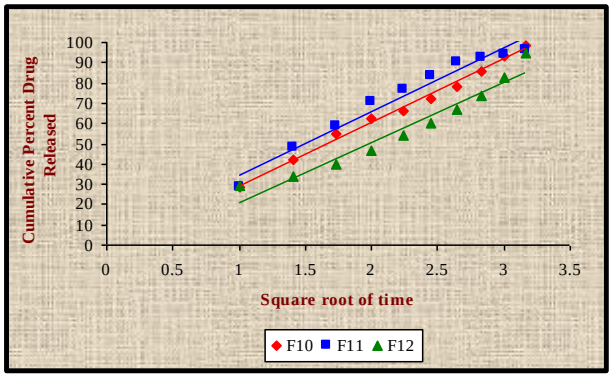

Figure-18: Log Cumulative Percent Drug Released Vs Log Time (Korsmeyer Plots) of formulation F10, F11 and F12

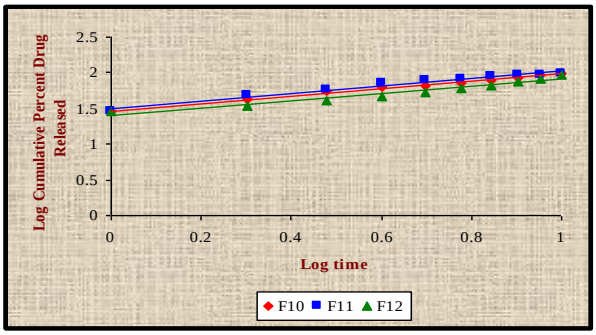

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Figure-19: Log Cumulative Percent Drug Remaining Vs Time Plots (First Order) of formulation F13, F14 and F15

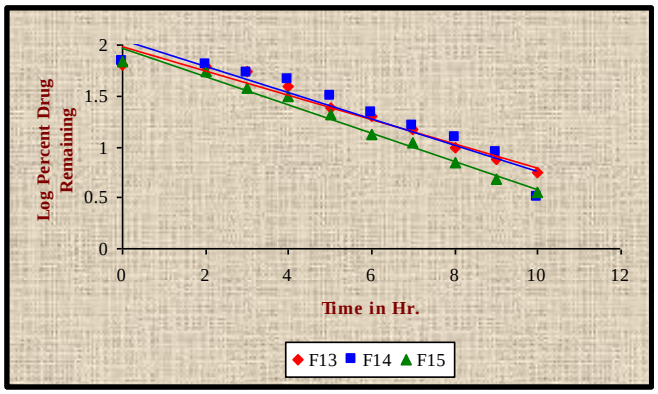

Figure-20: Cumulative Percent Drug Released Vs Square Root of Time (Higuchi's Plots) of formulation F13, F14 and F15

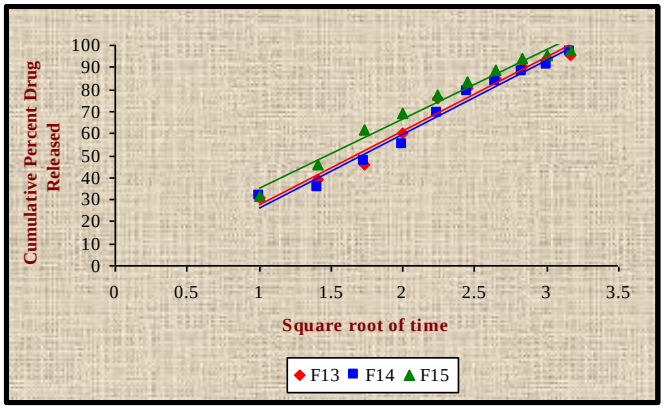

Figure-21: Log Cumulative Percent Drug Released Vs Log Time (Korsmeyer Plots) of formulation F13, F14 and F15

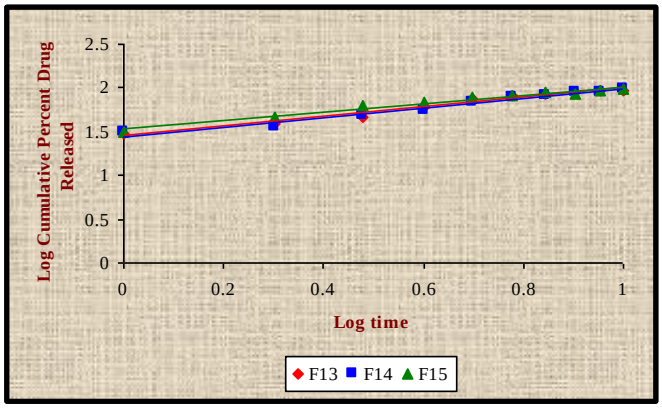

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Figure-22: Dissolution t_{50} and t_{90} values of HBS of Alfuzosin HCL

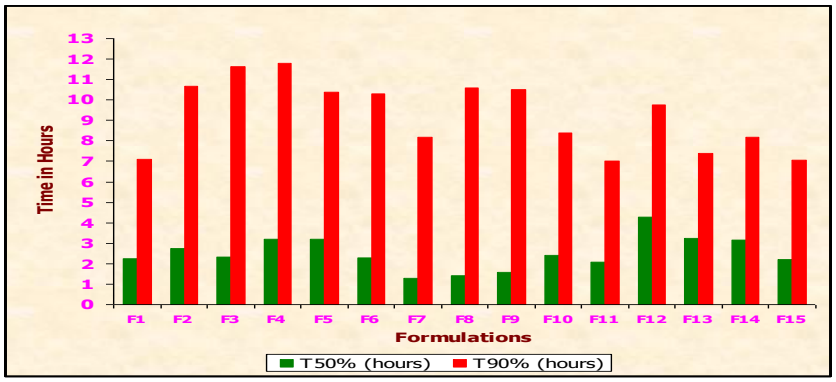
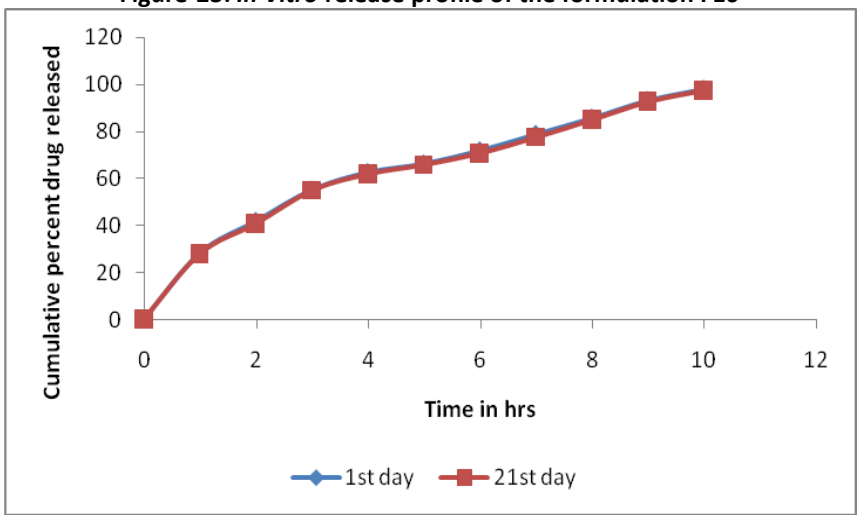


Figure-23: *In Vitro* release profile of the formulation F10



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