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FORMULATION AND EVALUATION OF FLOATING TABLET OF AMOXICILLIN TRIHYDRATE

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ABSTRACT

The study to investigation concerns the design and evaluation of floating tablets of Amoxicillin trihydrate, which after oral administration, are designed to prolonged the gastric residence time and to obtain site-specific drug delivery for the stomach and increased bioavailability. Amoxicillin is a Semi synthetic antibiotic, belonging Beta-lactum family, which is effective for bacterial treatment, especially for helicobacter pylori infection. The dosage form was designed by using HPMC K100M, HPMC K15M and Crosspovidine polymers as gelling agents, sodium bicarbonate as gas-generating agent and other excipients. The prepared floating tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content, swelling index, in-vitro floating studies, in-vitro drug release and short term stability studies. The floating properties and drug release characteristics were determined for the prepared tablets in 0.1 N HCl and water dissolution media. Dissolution Profile was compared with dissolution profile of marketed tablet. The data obtained from in-vitro dissolution studies were fitted in different models. Final optimized formulation batch AT-12 released 98.29% and 91.88% drug in 0.1N HCl and water respectively.

Key words: Amoxicillin trihydrate, Floating tablet, HPMC, Crosspovidine, in-vitro floating study

1. INTRODUCTION

The Floating that floats, in any sense, not fixed, fluctuating, circulating and not clearly committed to one side [1]. Drug release from new oral drug delivery systems can be sustained for up to 24 h for many drugs using current release technologies. However, the challenge in the development of oral controlled release dosage forms is to prolong the residence time of dosage forms in the stomach or upper gastrointestinal (GI) tract until drug is completely released. Rapid GI transit could result in incomplete drug release from the drug delivery system in the absorption zone leading to diminished efficacy of the administered dose. Several approaches are currently used to retain the dosage form in stomach. The principle of floating preparations offers a simple and practical approach to achieve increased residence time for the dosage form in stomach and sustained drug release [2]. The pathogenesis of peptic ulcer disease is not fully under stood three major causative factors are recognized: infection with gram-negative helicobacter pylori, increased hydrochloric acid secretion, and inadequate mucosal defense against gastric acid. Treatment approaches include 1) eradicating the H.pylori infection,2) reducing secretion of gastric acid or neutralizing the acid after it is released, 3)providing agent that protect the gastric mucosa from damage.[3] Amoxcillin trihydrate is a β-lactam antibiotic, semi synthetic penicillin of the amino penicillin group, has a broad in vitro spectrum against gram negative and gram positive bacterias. It acts through the inhibition of mucopeptide synthesis in bacterial cell and diffuses readily into most body tissues and fluids. Various hydrated forms of Amoxicillin, including monohydrate, dihydrate, trihydrate have been reported and amoxicillin which the trihydrate is the most stable form, Amoxicillin is not highly protein bound and its elimination half-life ranges from 0.7 to 1.4 hours in patients with normal renal function and these are partially metabolized to microbiologically inactive metabolites and both are rapidly excreted from the kidney [4] .The gastro retentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability. Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need for repeated dosages or with a low dosage frequency [5].

2.MATERIALS AND METHOD

Amoxicillin trihydrate, HPMC K100M, HPMC K15M, Crosspovidine, Citric acid, Sodium bicarbonate, microcrystalline cellulose, Magnesium Sterate, Talc taken and environment provided for study of stability test were from

Modern Laboratories, Pvt. Ltd., Indore. All other chemicals used were of analytical reagent grade. Double distilled water was used in entire study.

2.1.Method of Preparation of Amoxicillin Trihydrate Floating Tablets [6, 10, 11]

Effervescent floating tablets of amoxicillin trihydrate were prepared by direct compression technique. All the ingredients were accurately weighed and passed through different mesh sieves and in order to mixed the ingredients properly. Drug and different concentration of HPMC K100M Polymer were blend in mortar followed by the addition of Sodium bicarbonate, Microcrystalline cellulose, Crosspovidine, Citric acid, Talc and Magnesium stearate. After thoroughly mixing the ingredients tablets were compressed in rotary punching machine using 13 mm punch. Effervescent floating tablets of amoxicillin trihydrate were prepared by direct compression technique. All the ingredients were accurately weighed and passed through different mesh sieves and in order to mixed the ingredients properly. Drug, HPMC K100M, different concentration of Crosspovidine and HPMC K15M Polymer were blend in mortar (according to table) followed by the addition of Sodium bicarbonate, Citric acid, Talc and Magnesium stearate, After thoroughly mixing the ingredients tablets were compressed in rotary punching machine using 13 mm punch.

3. RESULTS AND DISCUSSION

3.1. Pre compression Properties of floating Tablet [6, 16,35]

a)Bulk density: The bulk density was found to be in the range 0.658-0.759 g/ml. The values obtained for Bulk density for all formulations were tabulated in Table 2.

b)Tapped Density: The value Tapped density was found to be in the range 0.775-0.890 g/ml. The values obtained for Tapped Density for all formulations were tabulated in Table 2.

c)Hausner's Ratio: The value Hausner's Ratio was found to be in the range 1.07 to 1.24. The values obtained for Hausner's Ratio for all formulations were tabulated in Table 2.

d)Angle of Repose (θ): The value Hausner's Ratio was found to be in the range 260.51'-320.33'. The values obtained for angle of repose for all formulations were tabulated in Table 2.

e)% Carr's Compressibility Index: The value Hausner's Ratio was found to be in the range 7.21-20.24. The values obtained for % Carr's for all formulations were tabulated in Table 2.

3.2. Post-compression Properties of floating Tablet [3, 7,16, 19, 20, and 21]

a)Shape of the tablet: Microscopic examination of tablets from each formulation batch showed circular shape with no cracks.

b)Tablet density: To provide good floating behavior in the stomach, the density of the device should be less than that of the gastric contents (1.097 g/cm3). The value Tablet density

was found to be in the range 0.61-1.74. The values were shown in Table 4.

c)Hardness test: The value Hardness test was found to be in the range 4.03±0.32±4.6±0.12 kg/cm2. The values obtained for Hardness for all formulations were tabulated in Table 3.

d)Friability test: The value Friability test was found to be in the range 0.59 -0.95 %. The values obtained for Friability for all formulations were tabulated in Table 3. [13, 16, 18]

e)Weight variation test: All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits of ±5% of the weight. The value Hausner's Ratio was found to be in the range 859±3.1-862±2.7. The values obtained for Weight variation for all formulations were tabulated in Table 3.

f)% Drug content in Water: Five tablets were weighed individually, and the drug was extracted in 0.1 N HCl, and the solution was filtered through 0.45µ membrane. The absorbance was measured at 274.6 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. The percentage Drug content in Water for all formulations was shown in Table 5. The value % Drug content in Water was found to be in the range 90.91±0.4 - 97.77±3.1. The values obtained for % Drug content for all formulations were tabulated in Table 3.

g)% Drug content in 0.1N HCL: The percentage Drug content in Water for all formulations was shown in Table 5. The value % Drug content in 0.1N HCL was found to be in the range 89.13±0.56 - 98.32±1.10. The values obtained for % Drug content for all formulations were tabulated in Table 3.

h)Buoyancy lag time: On immersion in water and 0.1N HCl solution pH (1.2) at 37oC, the tablets floated, and remained buoyant without disintegration. Table 4 showed the results of buoyancy study. The value Buoyancy lag time was found to be in the range of water to be 12-17 and HCL to be 12-16 hr. The values obtained for angle of repose for all formulations were tabulated in Table 4[22].

i)Floating Time: The lag time was carried out in beaker containing 100 ml of water and 0.1 N HCl as a testing medium maintained at 37 °C. The value floating time was found to be in the range of water to be 46-70 and HCL to be 30-65 sec. Table 4 showed the results of buoyancy study the time required for the tablet to raise to the surface and float was determined as floating lag time [17, 23, 24, and 25].

j)Swelling study: The plot of swelling index against time (h) of optimized formulation (AT1-AT12) is depicted in Fig. No. 1. The USP dissolution testing apparatus II, in 900 ml of 0.1 N HCl at 37±0.5 0C, rotated at 50 rpm. From the results it was concluded that swelling increases

as the time passes because the polymer gradually absorb water due to hydrophilicity of polymer [36].

k)In vitro Drug Release Study: The dissolution of drug from prepared floating tablet and marketed product at different time periods was plotted as cumulative % drug release v/s time curve as shown in table No.5, 6, 7, and 8[11, 26, 27, 28, 29].

l)Dissolution Data Treatment: The dissolution data so obtained was fitted to various kinetic models like Zero Order, First order, Higuchi, Hixson-crowell models. Results were shown in table 9 and 10. Zero-order rate describes the systems where the drug release rate is independent of its concentration. The first order which describes the release from release rate is concentration dependent. Higuchi's model describes the release of drugs from an insoluble matrix as a square root of a time-dependent process based on Fickian diffusion. It illustrates the Higuchi square root kinetics, showing the cumulative percent drug release v/s the square root of time. The dissolution data were also plotted in accordance with the Hixson-Crowell cube root law, the applicability of the formulation to the equation indicated a change in surface area and diameter of the tablets with the progressive dissolution of the matrix as a function of time show in table No. 9,10[30, 34].

m)Stability Study: The selected Formulation AT-12 was evaluated for stability studies which were stored at 25ºC±2ºC and RH±5%RH (relative humidity) and 45ºC±2ºC and RH±5%RH tested at 30 day, and were analyzed for their drug content at that interval. The residual drug contents of formulations were found to be within the permissible limits and the results of 30 day duration are shown in the table No. 11[29, 31, 32, 33].

4.CONCLUSION

This study aimed to evaluate the floating and release behavior of directly compressed hydrophilic matrices (HPMC K100M, HPMC K15M) and Crosspovidine to develop floating single unit drug delivery systems. Despite the floating ability of HPMC matrices, as a result of swelling and gel formation of the hydrophilic matrix, the addition of NaHCO3 to the matrix was essential to ensure rapid floating. Preliminary formulations with various polymers, either alone or in combination, yielded a wide variety of release profiles to obtain an idea of the range and type of polymers to be used in the final formulation design. Based on such studies, HPMC K100M, crosspovidine were selected as release modifier polymeric fillers and sodium bicarbonate as the float accelerator. Flow property of all the powder evaluated by Bulk density, tapped density, Angle of repose, Hausner ratio and Carr's index.

Floating tablets evaluated by hardness, Friability, weight variation, Drug content and In-vitro drug release study. All formulation has good hardness, Friability, Weight uniformity, Content uniformity and complies the Standard of

pharmacopoeia and tablets Evaluated for swelling index, floating time and floating lag time. In-Vitro drug release studies were performed in water and 0.1N HCl for 12 hour. Optimized formulation batch AT-12 released 98.29% and 97.88% drug in 0.1N HCl and water respectively. The data obtained from in-vitro dissolution studies were fitted in different models. Dissolution Profile was compared with dissolution profile of marketed tablet Comparison study with marketed product of Amoxicillin trihydrate showed optimized formulation has better sustain released rate in comparison to the commercial product. The marketed product released the drug 82.23% and 91.94 % for 1 hour in 0.1N HCl and Water respectively. Stability of Optimized formulation (AT-12) was performed for 1 month at 25ºC±2ºC/59% RH±5%RH (relative humidity) and 45ºC±2ºC/ 65%RH±5%RH. It showed that there was no change in the formulation after 1month. In-vitro drug release study show that after 1 month, the drug release for 12 hours obtained within range of targeted release profile and there was no drastic change in drug content and . There was no change in the formulation after 1 month accelerated stability stud. It indicates that prepared formulation of was stable.

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Table 1: Composition of all the formulations (Formulations AT-1 – AT-12)

Ingredients (Mg per tablet)	AT-1	AT-2	AT-3	AT-4	AT-5	AT-6	AT-7	AT-8	AT-9	AT-10	AT-11	AT-12
Amoxicillin Trihydrate	500	500	500	500	500	500	500	500	500	500	500	500
HPMC K100M	10	20	30	40	50	60	70	80	90	100	110	120
HPMC K15M	120	110	100	90	80	70	60	50	40	30	20	10
Crosspovidine	50	50	50	50	50	50	50	50	50	50	50	50
Citric acid	20	20	20	20	20	20	20	20	20	20	20	20
Sodium bicarbonate	60	60	60	60	60	60	60	60	60	60	60	60
MCC	90	90	90	90	90	90	90	90	90	90	90	90
Magnesium Sterate	5	5	5	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Total Weight	860	860	860	860	860	860	860	860	860	860	860	860

Table 2: Evaluation Result of Powder blend

Batch	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Hausner's ratio	Angle of Repose (θ)	% Carr's index
AT-1	0.723	0.823	1.13	26.51	12.15
AT-2	0.713	0.890	1.24	31.20	19.88
AT-3	0.658	0.798	1.21	33.09	17.54
AT-4	0.744	0.812	1.09	32.33	8.00
AT-5	0.701	0.813	1.15	28.12	13.77
AT-6	0.699	0.790	1.13	30.05	11.51
AT-7	0.691	0.775	1.12	28.32	10.83
AT-8	0.722	0.810	1.12	31.09	10.86

AT-9	0.721	0.856	1.18	32.11	15.77
AT-10	0.751	0.813	1.08	33.23	7.62
AT-11	0.710	0.855	1.20	32.01	20.24
AT-12	0.759	0.818	1.07	28.61	7.21

Table 3: Evaluation Result of floating tablet

Batch	Tablet density (g/cm^3)	Hardness (kg/cm^2)	Friability (%)	Weight variation	% Drug content in Water	% Drug content in 0.1N HCL
AT-1	1.74	4.51±0.10	0.86	860±4.15	90.91±0.4	95.21±3.20
AT-2	1.69	4.03±0.32	0.93	860±2.13	93.12±0.52	98.1±0.22
AT-3	0.83	4.30±0.42	0.90	859±3.1	96.54±0.69	97.52±.55
AT-4	1.13	4.6±0.12	0.91	860±2.43	97.77±3.1.	89.13±0.56
AT-5	0.99	4.4±0.99	0.79	861±1.99	94.25±4.1	98.12±1.02
AT-6	1.55	4.1±0.30	0.76	862±2.7	91.79±5.1	97.81±2.1
AT-7	1.20	4.3±0.30	0.85	861±4.3	95.30±0.1	93.54±1.62
AT-8	1.22	4.5±0.20	0.93	860±3.1	91.27±2.0	98.32±1.89
AT-9	0.61	4.4±0.85	0.95	861±2.9	95.67±1.3	96.47±1.20
AT-10	1.27	4.3±0.22	0.59	860±1.8	95.85±0.52	97.92±2.01
AT-11	0.87	4.1±0.77	0.78	861±2.2	97.33±2.1	97.83±1.30
AT-12	0.95	4.6±0.12	0.94	860±3.7	96.39±2.7	99.32±1.10

Table 4: Buoyancy study of formulation AT-1-AT-12

Batch	Buoyancy lag time in water (sec)	Floating time in water (hr)	Buoyancy lag time in HCl (sec)	Floating time in HCl (hr)
AT-1	62±0.22	>12	35±2.0	>14
AT-2	70±0.09	>12	45±0.5	>13
AT-3	68±2.20	>12	30±1.7	>12
AT-4	48±1.80	>17	50±1.3	>13

AT-5	53±2.23	>12	63±1.12	>12
AT-6	47±1.15	>12	42±1.45	>15
AT-7	57±0.97	>16	55±1.32	>15
AT-8	46±2.10	>12	60±1.82	>14
AT-9	58±1.54	>12	65±0.48	>12
AT-10	65±0.72	>15	48±1.22	>14
AT-11	67±1.54	>12	58±1.36	>15
AT-12	68±1.21	>12	48±1.85	>16

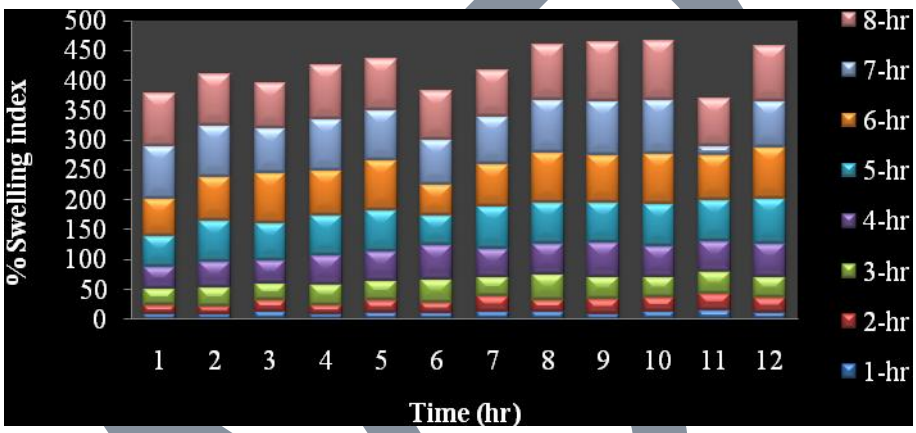

Figure 1: swelling index of floating tablets AT-1-AT-12

Table 5: Dissolution parameter

Medium:	**Water, 0.1N HCl**
Volume	900ml
Apparatus	USP – type II
RPM	50 rpm
Time point	0.5, 1 , 2 , 3 , 4 , 5 , 6 , 7 , 8 , 9 , 10 , 11 and 12 hour
Volume withdrawn	5ml of solution
Temperature	37°C ± 0.5°C
λ maxima	274.6 nm

Table 6: *In-vitro* dissolution profile of Amoxicillin trihydrate floating tablet in 0.1N HCl AT-1-AT-12

Time (Hour)	% Drug release in 0.1N HCl											
	AT-1	AT-2	AT-3	AT-4	AT-5	AT-6	AT-7	AT-8	AT-9	AT-10	AT-11	AT-12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	13.26	26.7	21.94	17.51	20.86	14.64	22.05	13.26	24.85	21.42	16.31	19.29
2	26.72	42.77	39.26	30.66	34.01	31.96	38.12	26.72	41.43	29.06	22.46	34.01
3	40.06	27.54	27.54	47.86	51.21	49.16	55.32	40.06	64.5	53.81	39.66	49.67
4	51.95	63.75	61.1	57.64	60.99	53.8	59.1	51.95	72.69	64.26	55.72	64.39
5	64.12	72.81	67.12	63.92	67.27	59.82	68.16	64	84.53	74.4	63.86	71.96
6	66.33	84.68	79.23	76.13	79.48	68.7	80.03	66.33	93.11	82.14	77.7	79.7
7	78.35	90.71	86.84	80.67	84.02	79.54	86.06	78.35	95.65	85.08	77.77	84.6
8	83.94	97.64	94.11	91.92	95.27	87.41	92.99	83.94	98.84	88.31	82.53	92.05
9	85.97	98.92	96.21	93.85	97.2	89.51	94.27	85.97	99.64	93.14	88.16	93.93
10	90.01	102.87	96.57	94.46	97.81	89.81	98.22	90.01	97.84	94.67	95.71	95.75
11	96.43	104.62	98.35	96.32	99.67	91.59	100.22	96.43	96.35	95.98	96.18	97.2
12	99.3	106.58	101.95	97.59	100.94	95.19	101.09	99.3	98.71	98.04	97.38	98.29

Table 7: *In-vitro* dissolution profile of Amoxicillin trihydrate floating tablet in water AT-1-AT-12

Time (Hour)	% Drug release in water											
	AT-1	AT-2	AT-3	AT-4	AT-5	AT-6	AT-7	AT-8	AT-9	AT-10	AT-11	AT-12
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	22.25	17.90	22.39	16.01	17.88	23.66	20.27	23.02	15.8	19.14	21.75	22.67
2	30.25	31.03	30.12	21.01	30.11	32.14	27.34	32.54	28.1	28.14	30.89	32.31
3	40.40	40.1	35.07	26.28	38.61	41.99	36.21	43.85	39.8	42.29	40.08	43.5
4	51.51	31.03	38.11	30.4	44.68	54.02	44.04	52.39	47.2	49.68	52.01	52.54
5	66.57	39.08	42.79	48.08	53.5	61.98	53.84	60.26	59.3	76.51	59.79	59.61
6	64.13	43.84	53.6	54.77	62.98	70.17	63.19	70.58	66.7	62.19	68.19	69.32

7	64.13	49.86	66.4	65.52	72.8	80.87	74.63	80.49	76.6	74.07	78.78	79.91
8	65.08	51.71	70.02	70.54	78.11	90.99	85.93	91.63	88.1	85.05	88.9	90.98
9	68.53	53.61	75.83	74.32	80.97	95.08	86.69	95.01	91.8	86.35	92.08	94.36
10	66.15	65.93	81.43	78.43	86.73	95.01	89.99	97.36	95.2	87.58	96.05	92.53
11	68.37	71.63	85.07	81.34	88.2	93.06	91.96	96.06	93.1	89.4	96.76	95.16
12	72.47	74.45	86.31	87.23	90.12	89.12	94.26	93.92	92.4	93.55	97.17	97.88

Table 8: *In-vitro* dissolution profile of market Amoxicillin trihydrate tablet in water and 0.1N HCL

Time (minute)	**% Drug release**	
	(Water)	(0.1N HCl)
0	0	0
10	34.25	63.79
20	52.44	65.57
30	61.05	67.22
40	65.13	71.10
50	73.13	79.83
60	82.23	91.94

Table 9: Data Analysis by Model Dependent methods (HCl)

Formulation code	**R / K**	**Zero Order**	**First Order**	**Higuchi Model**	**Krosmeyer -Peppas Model**	**Hixon Model**	**n value**
AT-1	R	0.9474	0.9914	0.9366	0.9500	0.9123	0.629
	K	6.177	0.221	25.817	19.296	0.039	
AT-2	R	0.9812	0.99.19	0.9403	0.9527	0.9851	0.289
	K	7.094	0.382	29.457	34.296	0.201	
AT-3	R	0.9456	0.91202	0.9479	0.9412	0.9606	0.648

	K	5.237	0.460	23.306	16.838	0.058	
AT-4	R	0.9304	0.9779	0.9805	0.9517	0.9882	0.216
	K	4.952	0.454	22.53	17.983	0.006	
AT-5	R	0.9468	0.9819	0.9476	0.9768	0.9948	0.023
	K	7.253	0.539	29.642	29.456	0.099	
AT-6	R	0.9106	0.9107	0.9602	0.9669	0.9982	0.106
	K	7.071	0.601	30.044	26.785	0.016	
AT-7	R	0.9134	0.9612	0.9191	0.9075	0.9531	0.149
	K	6.953	0.624	28.555	23.757	0.073	
AT-8	R	0.9323	0.9408	0.9154	0.9502	0.9286	0.201
	K	7.525	0.623	27.853	22.027	0.053	
AT-9	R	0.9581	0.9305	0.9570	0.9378	0.9576	0.221
	K	8.038	0.645	29.548	23.757	0.033	
AT-10	R	0.9543	0.9805	0.9698	0.9443	0.9847	0.028
	K	7.3307	0.680	32.538	19.697	0.098	
AT-11	R	0.9351	0.9904	0.9120	0.9259	0.9968	0.129
	K	7.148	0.637	30.882	12.297	0.086	
AT-12	R	0.9110	0.9673	0.9414	0.9517	0.9965	0.086
	K	8.0156	0.0642	28.485	15.754	0.097	

R- Regression coefficient, **K-** Release constant, **n -**Diffusional coefficient for the drug release

Table 10: Data Analysis by Model Dependent methods (Water)

Formulation code	R / K	Zero Order	First Order	Higuchi Model	Krosmeyer -Peppas Model	Hixon Model	n value
AT-1	R	0.9952	0.9407	0.9734	0.9131	0.9447	0.619
	K	7.77	0.221	22.391	15.139	0.023	
AT-2	R	0.9113	0.9415	0.9860	0.9111	0.9229	0.633
	K	8.769	0.382	26.024	30.229	0.044	

AT-3	R	0.9854	0.9739	0.9819	0.9844	0.9835	0.612
	K	6.912	0.460	19.873	27.861	0.043	
AT-4	R	0.9787	0.9691	0.9944	0.9115	0.9103	0.611
	K	6.607	0.454	19.097	26.716	0.064	
AT-5	R	0.9103	0.9419	0.9935	0.9724	0.9800	0.632
	K	8.920	0.539	26.204	38.189	0.063	
AT-6	R	0.9991	0.9167	0.9114	0.9947	0.9405	0.631
	K	7.100	0.601	26.567	40.860	0.053	
AT-7	R	0.9114	0.9098	0.9113	0.9120	0.9325	0.625
	K	6.982	0.624	25.074	40.503	0.055	
AT-8	R	0.9338	0.9130	0.9847	0.9307	0.9152	0.623
	K	6.778	0.623	24.372	25.745	0.050	
AT-9	R	0.9235	0.9193	0.9976	0.9844	0.9067	0.628
	K	7.350	0.645	26.065	27.475	0.044	
AT-10	R	0.9183	0.9495	0.9330	0.9374	0.9059	0.634
	K	8.196	0.680	29.058	38.601	0.037	
AT-11	R	0.9214	0.9841	0.9197	0.91.41	0.9063	0.643
	K	7.683	0.637	30.392	34.537	0.036	
AT-12	R	0.9123	0.9658	0.9123	0.93.04	0.9130	0.642
	K	6.949	0.699	27.023	27.137	0.045	

R- Regression coefficient, **K-** Release constant, **n** -Diffusional coefficient for the drug release

Table 11: Stability study AT-12

Time	**Initial drug content of Formulation AT-12**	**Formulation AT-12 stored at** 25ºC±2ºC and %RH±5%RH		**Formulation AT-12 stored at** 40ºC±2ºC and RH±5%RH	
		Physical appearance*	**Drug content**	**Physical appearance***	**Drug content**
30 day	99.32%	+++	98.91%	+++	96.74%

***+++ = same as initial time, +++ = Slight change in color