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FORMULATION AND EVALUATION OF TOLTERODINE EXTENDEDRELEASE TABLETS

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ABSTRACT

The objective of this study was to develop and evaluate Tolterodine Extended Release matrix tablet by using various grades and ratios of hydroxy propyl methyl cellulose (HPMC), Xanthan gum, Ethyl cellulose as rate controlling hydrophilic polymers and bioequivalent testing with the innovator Detrol. The drug was compatible with the formulation components. Hence Lactose Anhydrous, Di calcium Phosphate (DC grade), Xanthan gum, Ethyl cellulose, HPMCK4M, HPMCK100M, Opadry orange were selected as excipients for the lab scale development. Blends were evaluated for various parameters such as bulk density, tapped density, Carr's index, Hausner's ratio and the parameters evaluated for the matrix tablet are Drug content, hardness, Friability, weight variation and Thickness and all physicochemical properties are within the limits. Drug release from tablets complies with the prescribed limits. Formulation development from F1 to F13 was executed to optimize the composition. At the final, the dissolution profile of the batches F11 was closer with the reference product. The results were indicated that all results were in limits aftertwo months period. Hence the optimized formulation F11 was stable.

KEYWORDS: Tolterodine Extended, hydroxy propyl methyl cellulose (HPMC), Opadry orange.

INTRODUCTION

Over past 30 year as the expanse and complication involved in marketing new drug entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on development of sustained or controlled release drug delivery systems. There are severalreasons for the attractiveness of these dosage forms. Oral drug delivery has been knownfor decades as the most widely utilized route of administration among all the routes thathas been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage form. Nowadays most of the pharmaceutical scientists are involved in developing an ideal DDS. This ideal system should have advantage of single dose for whole duration of the treatment and it should deliver the drug directly at specific site. The design of oral sustain drug delivery system (OSDDS) should be primarily aimed to achieve the more predictability and reproducibility to control the drug release, drug concentration in the target tissue and

optimization of the therapeutic effect of a drug by controlling its release in the body with lower and less frequent dose. Conventional drug therapy typically involves the periodic dosing of a therapeutic agent that has been formulated in a manner to ensure its stability, activity and bioavailability. For most of the drugs, conventional methods of formulation are quite effective. However some drugs are unstable and toxic and have a narrow therapeutic range, exhibit extreme solubility problems, require localization to a particular site in the body or require strict compliance or long-term use. The need in designing sustained or sustained delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, sustained release dosage form is a dosage form that release one or more drugs continuously in a predetermined pattern for a fixed period of time, either systemically or to a specified target organ. The goal of many of the original controlled-release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. The term "controlled release," implies a system that provides continuous delivery of the drug or a predetermined period with predictable and reproducible kinetics and known mechanism of release. This means reproducible kinetics and known mechanism of release. This means that the release of drug ingredient(s) from a controlled-release drug delivery system proceeds at a rate that is not only predictable kinetically, but also reproducible from one unit to another. On the other hand, the term "sustained release" is usually used to describe a pharmaceutical dosage form formulated such that the liberation of the drug in the systemic circulation is prolonged over time resulting in a plasma profile which is sustained in duration. During the last two decades there has been remarkable increase in interest in controlled release drug delivery system. This has been due to various factor viz. the prohibitive cost of developing new drug entities, expiration of existing international patents, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems.

Modified release dosage forms are dosage forms that use time course and location to achieve therapeutic objectives not offered by conventional dosage forms. Two types are recognized: extended release dosage forms, which allow a twofold reduction in dosing frequency, and delayed release dosage forms, which release the drug at a later time than immediately after administration. The terms controlled release, prolonged release, and sustained release are interchangeable with extended release. Extended release (ER) releases the drug slowly, maintaining plasma concentrations at a therapeutic level for a prolonged period, while controlled release (CR) releases the drug at a constant rate. The pharmaceutical industry has been successful in developing controlled-release formulations, which aim to achieve steady-state blood concentration levels within the therapeutic effective and non-toxic range for extended periods. The oral route of administration has gained more attention due to its flexibility in dosage design. The evolution of controlled-release technology began with matrix technology, with the introduction of the Spansule in 1952. Extended release oral drug formulations have been used since the 1960s to enhance performance and patient compliance. These formulations prevent side effects associated with high concentration and low plasma concentrations, improving overall therapy. The design of oral drug delivery depends on factors such as delivery system type, disease, patient, therapy length, and drug properties. By considering conventional dosage forms and drug profile data, the desired release rate can be determined from controlled-release dosage forms. Over the years, there has been significant effort in designing drug delivery systems that can reduce cyclical plasma concentrations. The first commercially available controlled release system was Dexedrine Spansules in 1952. The design of oral sustain drug delivery systems (DDS) aims to achieve predictability, reproducibility, and optimization of therapeutic effect by controlling drug release with lower and less frequent doses. Conventional drug therapy typically involves periodic dosing, but continuous administration is

desirable for unstable, toxic, narrow therapeutic range, or long-term use.

Oral controlled-release drug delivery systems (CRDDS) offer numerous advantages over traditional, immediate-release products, including reduced fluctuations, reduced side effects, patient comfort and compliance, reduced healthcare costs, reduced total dose, and improved treatment efficiency. However, oral CRDDS also have limitations such as poor in vitro-in vivo correlation, possible dose dumping, less flexibility in accurate dose adjustment, patient variation, high cost, and need for additional patient education.

Criteria for oral CRDDS include desirable half-life, high therapeutic index, small dose, undesirable absorption and solubility characteristics, a desirable absorption window, and first past clearance. A short half-life may result in a large dosage form, while a high therapeutic index may lead to fatalities. Small doses may be unsuitable for sustained release formulations due to the size of the unit dose. Poor absorption and solubility characteristics may also reduce overall absorption efficiency. The absorption window, which refers to the specific part of the gastrointestinal tract, is another important factor in determining the suitability of a drug for sustained release.

METHODOLOGY

This study focuses on the compatibility of potassium bromide and drug excipients using Differential Scanning Calorimetry (DSC). The study involves preparing a standard and sample, grinding it, and placing it in an IR pellet die. Differential scanning calorimetry is used to measure the specific heat and enthalpies of transition. Thermograms are obtained using a differential scanning colorimeter at a heating rate of 15ºC/min over a temperature range of 0 to 1000°C. The calibration curve is constructed using UV methods, using 0.1M HCl and pH 6.8 media for dissolution. The maximum wavelength is determined by scanning concentrations 5-30 µg/ml between 200nm to 400nm. Various concentrations of Tolterodine are prepared using these media, and the absorbance is noted at λ max. The equation for the calibration curve is determined and used for calculating the concentration of unknown samples. A linear regression analysis is performed on absorbance data points, generating a straight-line equation for the calculation of drug amount.

S. No	Name of the Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
1	Tolterodine	2.84	2.84	2.84	2.84	2.84	2.84
2	Lactose anhydrous (DCGrade)	100.16	90.16	60.16	100.16	90.16	100.16
3	DCP (DC Grade)	65	65	75	65	65	75
4	Xanthan gum	30 (15%)	40 (20%)	60 (30%)	-	-	-
5	Ethyl cellulose	-	-	-	30 (15%)	40 (20%)	-
6	Methocel K4M	-	-	-	-	-	20 (10%)
7	Magnesiumstearate	2	2	2	2	2	2
	Total Weight	200	200	200	200	200	200
	Film coating (%)	3.0	3.0	3.0	3.0	3.0	3.0

S. No	Name of the Ingredient	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)	F11 (mg)	F12 (mg)	F13 (mg)
1	Tolterodine	2.84	2.84	2.84	2.84	2.84	2.84	2.84
2	Lactose anhydrous (DC Grade)	80.16	60.16	40.16	40.16	40.16	40.16	40.16
3	DCP (DC Grade)	75	75	55	55	65	55	55
4	Xanthangum	-	-	60 (30%)	50 (25%)	-	-	-
5	MethocelK4M	40 (20%)	60 (30%)	40 (20%)	50 (25%)	70 (35%)	80 (40%)	90 (45%)
6	MethocelK100M	-	-	-	-	10 (5%)	10 (5%)	10 (5%)
7	Magnesimstearate	2	2	2	2	2	2	2
	Total Weight	200	200	200	200	200	200	200
	Film coating(%)	3.0	3.0	3.0	3.0	3.0	3.0	3.0

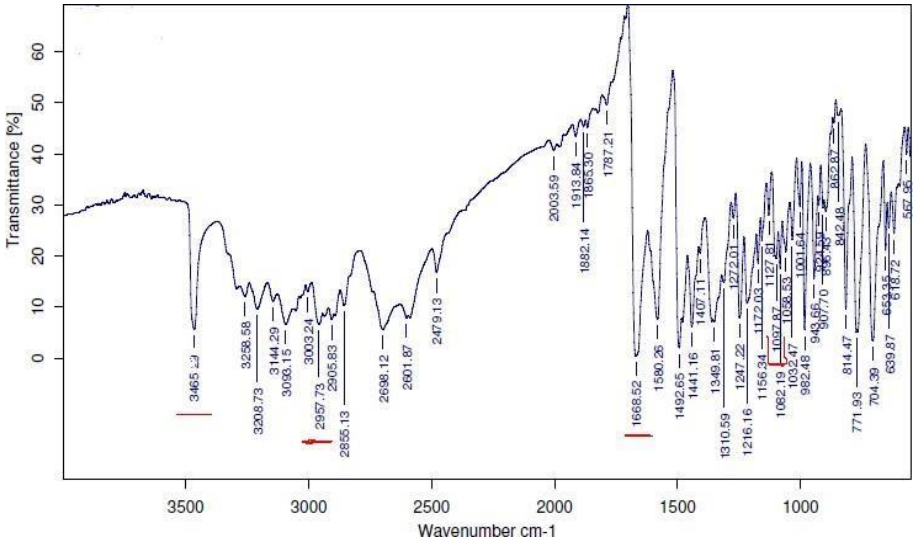
RESULTS AND DISCUSSION

Pre formulation studies

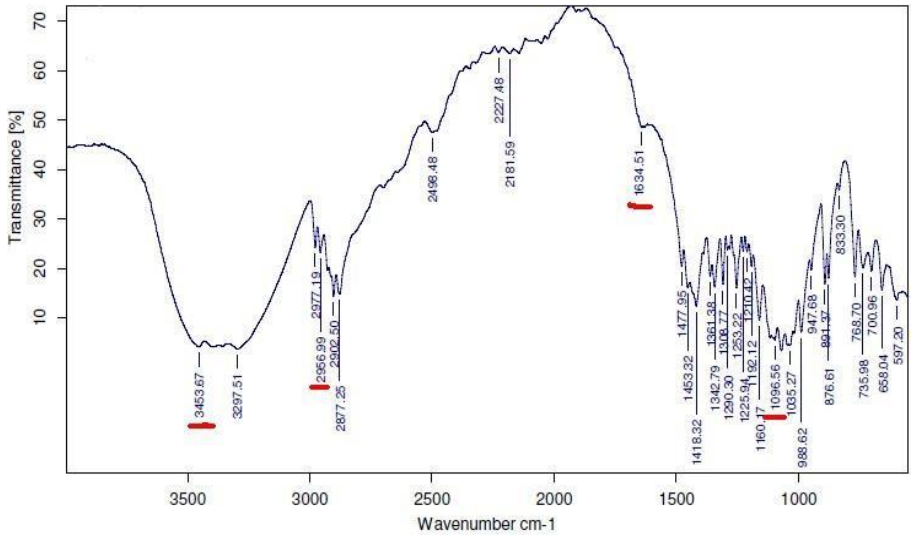
Preliminary studies

S. No	Drug	Angle ofRepose (degrees)	Bulk density (gm/ml)	Tappeddensity (gm/ml)	Carr's index(%)	Hausner ratio
1	Tolterodine	32.90	0.424	0.587	27.76	1.38

Drug excipient compatability studies



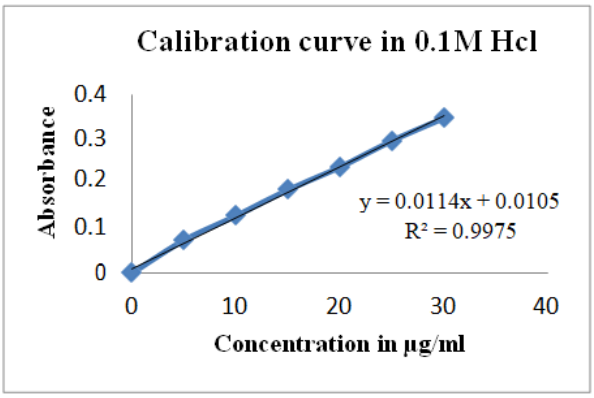
Characteristic peaks of pure Tolterodine



S. No.	Type ofbond	Type of vibration	Actual frequency	Observedfrequency	Conformation
1	N-H	Stretching	3500-3180	3465.29	Amide
2	C=O	Stretching	1680-1630	1668.52	Amide
3	C=O-O-C	Stretching	1270-1020	1097.87	Ether
4	C-H	Stretching	3100-2900	2957.73	Aromatic

The pure drug & optimized formulation were analyzed using FTIR, the peaks were observed at 3453.67,163451, 1096.56, 2966.99 frequencies which were indicating the presence of compatibility between the drug and excipient optimized formulation.

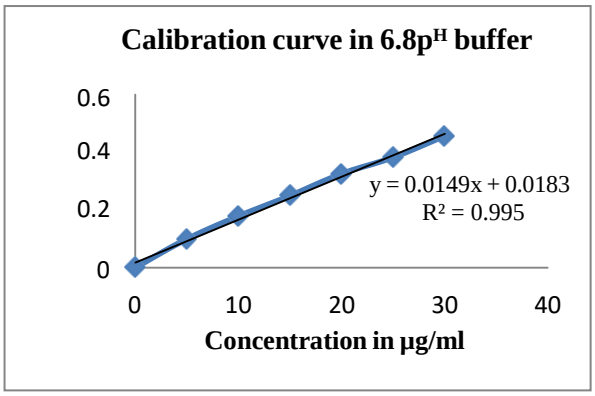
CALIBRATION CURVE



Calibration curve in 0.1N HCl

S. No	Concentration In µg/ml	Abs
1	0	0
2	5	0.074
3	10	0.129
4	15	0.187
5	20	0.238
6	25	0.297
7	30	0.348

Calibration values in 0.1N HCl



Calibration curve in 6.8p^{H} buffer

S.NO	Concentration In µg/ml	Abs
1	0	0
2	5	0.099
3	10	0.178
4	15	0.249
5	20	0.325
6	25	0.382
7	30	0.456

Calibration values in 6.8p^{H} buffer

Calibration curve of Tolterodine was plotted by preparing different concentrations of solutions in Tolterodine 0.1MHcl, 6.8 p^{H} phosphate buffer and observed at 286nm in U. V. visible spectrophotometer.

EVALUATION STUDIES

Pre Compression Parameters

Data for pre compression studies of the blends

Formulation Code	Angle of Repose (in degrees)	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility Index	Hausner's ratio
F1	29.37±0.98	0.418±0.006	0.530±0.003	21.08±0.71	1.26±0.01
F2	25.57±0.49	0.434±0.005	0.530±0.002	18.63±0.66	1.23±0.01
F3	23.26±1.33	O.486±0.006	0.590±0.001	17.56±0.94	1.26±0.11
F4	28.75±1.24	0.404±0.006	0.504±0.006	19.86±2.33	1.25±0.04
F5	24.92±0.85	0.427±0.004	0.530±0.004	19.47±0.23	1.25±0.01
F6	26.67±0.46	0.436±0.006	0.546±0.006	20.13±1.76	1.25±0.02
F7	25.64±0.89	0.508±0.01	0.636±0.005	19.98±1.17	1.25±0.02
F8	23.79±0.55	0.547±0.009	0.670±0.008	18.40±0.31	1.23±0.01
F9	24.97±1.14	0.476±0.005	0.574±0.005	16.91±0.30	1.20±0.01
F10	24.07±0.76	0.499±0.004	0.596±0.004	16.20±0.94	1.19±0.01
F11	25.13±0.72	0.457±0.004	0.547±0.005	17.50±2.21	1.19±0.01
F12	24.89±0.67	0.492±0.005	0.588±0.003	16.32±0.52	1.67±0.41
F13	24.48±0.77	0.525±0.003	0.644±0.001	18.48±0.35	1.23±0.01

The prepared blends were evaluated for precompression parameters-angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio. All the parameters were in the accepted limits showing that the blend has good flow in which the blend can subject for direct compression.

POST COMPRESSION PARAMETERS

Data for post compression studies of the prepared tablets

Formulation Code	Average Wt (mg)	Average Hardness (Kg/cm^2)	Average Thickness (mm)	Friability (%)
F1	200.15±1.78	8.50±0.33	3.60±0.09	0.20
F2	199.60±1.44	8.70±0.53	3.55±0.19	0.15
F3	199.56±1.94	8.30±0.58	3.69±0.02	0.18
F4	201.20±1.60	10.36±0.78	3.55±0.08	0.22
F5	202.35±1.53	10.55±0.50	3.56±0.11	0.24
F6	200.33±1.96	8.40±0.57	3.55±0.08	0.21
F7	200.15±1.48	8.35±0.03	3.68±0.05	0.16
F8	200.32±1.77	8.55±0.68	3.70±0.03	0.21
F9	199.62±2.09	8.60±0.77	3.73±0.02	0.21
F10	199.75±2.54	8.55±0.55	3.58±0.06	0.19
F11	198.45±2.13	8.40±0.56	3.61±0.06	0.20
F12	201.40±2.23	8.75±0.42	3.67±0.05	0.14
F13	199.75±2.97	8.45±0.64	3.62±0.04	0.12

The post compression parameters were given in the table. The prepared tablets were evaluated for post compression parameters - weight variation, hardness, thickness and friability. All the parameters were in the acceptable limits showing that the tablets prepared were good. But the formulations F4 and F5 formulated with ethyl cellulose had higher hardness values (10.36, 10.55 kg/cm^2respectively) comparatively than the accepted limit-≤10 kg/cm^2. Though theformulations were hard they were further studied for *in vitro* drug release studies.

Assay data of the prepared tablets

Formulation code	Test Absorbance	Average Wt (mg)	Drug Content (Assay) mg/tab	Assay(%)
F1	0.023	200.15±1.78	2.44	102.98
F2	0.022	199.60±1.44	2.73	98.23
F3	0.022	199.56±1.94	2.87	99.12
F4	0.021	201.20±1.60	2.17	94.52
F5	0.022	202.35±1.53	2.93	99.58
F6	0.022	200.33±1.96	2.78	98.59
F7	0.022	200.15±1.48	2.77	98.5
F8	0.023	200.32±1.77	2.32	102.17
F9	0.022	199.62±2.09	2.73	98.24
F10	0.023	199.75±2.54	2.28	101.88
F11	0.0224	198.45±2.13	2.91	99.44
F12	0.0224	201.40±2.23	2.13	100.92
F13	0.0222	199.75±2.97	2.95	99.65

The drug content uniformity was performed for all the formulations. The uniformity of drug distribution with in the batch tablets was confirmed by the assay values of 2.17 to 2.44, 1mg/tablet and 94.52 to 102.98 %for all the formulations. All the formulations were within the accepted limits- 90% to 110%. Except the F4 formulation with 94.52% all other formulations werenear to 100% representing uniform drug content.

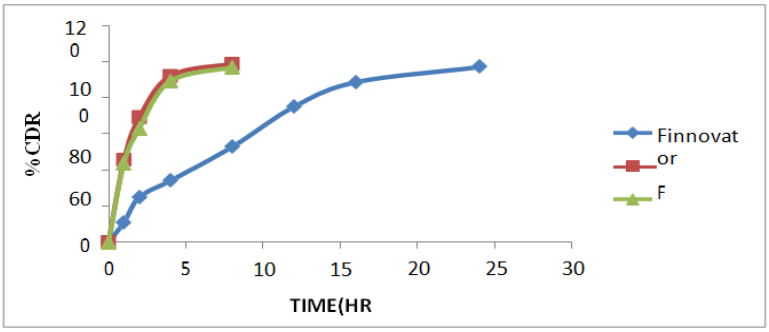
IN-VITRO DRUG DISSOLUTION STUDIES OF THE PREPARED FORMULATIONS

***In-vitro* drug release data**

Time Hrs	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)
0	0	0	0	0	0	0	0
1.	45.5±0.8	43.6±0.82	25.23 ±0.98	29.15±0.76	26.13±0.52	29.16±1.1	26.13±1.16
2	69±0.89	63±0.98	41.84±1.2	35.89±0.9	33.72±0.9	45.14±0.6	33.72±1.2
4	92±0.5	89±1.03	59.04±1.4	57.13±0.8	47±1.04	62.19±0.89	50.67±0.55
8	98.5±0.7	96.5±0.89	85.9±0.57	79.1±1.3	68.37±0.57	87.11±1.1	78.74±1.10
12	_	_	_	91±1.6	89.93±0.98	_	91.39±0.5

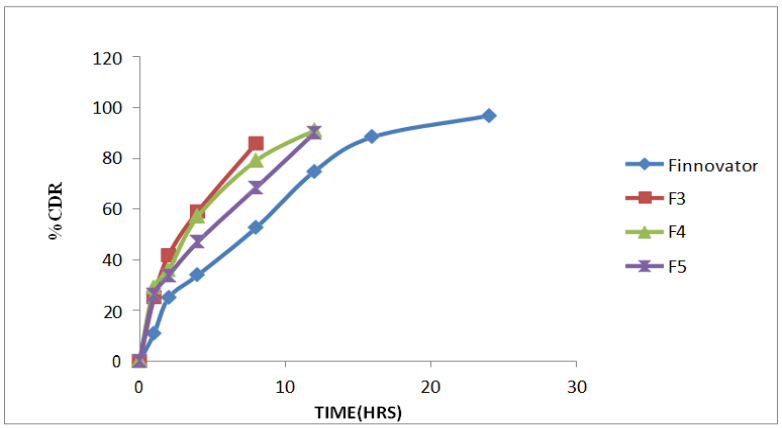
Time Hrs	F8 (%)	F9 (%)	F10(%)	F11(%)	F12(%)	F13(%)	Innovator (%)
0	0	0	0	0	0	0	0
1	22.3±0.53	19±2.62	15.7±3.76	11±0.73	8.7±0.5	7.9±2.1	10.9±2.72
2	29.56±0.59	29±2.24	24.8±2.33	21±0.9	19±1.04	15±6.2	25±3.00
4	45.31±1.43	46.9±2.36	39.9±2.14	32.9±0.8	31.9±0.8	29±1.61	33.89±3.52
8	63.46±0.82	71.8±2.28	64.5±3.17	51.1±0.49	50±0.6	48.8±2.77	52.6±2.89
12	71.42±1.14	83.5±3.52	79.1±2.75	73.8±1.43	73±0.94	72.5±1.09	74.8±2.72
16	87.3±0.42	94.8±2.73	85.4±3.04	88.4±0.7	86.5±0.23	85.5±0.3	88.4±1.61
24	_	_	92.8±4.2	95.5±0.6	90±0.7	89±1.4	96.8±1.61

IN-VITRO DRUG DISSOLUTION GRAPHS OF THE PREPARED FORMULATIONS



***In-vitro* drug release profile of Formulations F 1, F2 & Innovator**

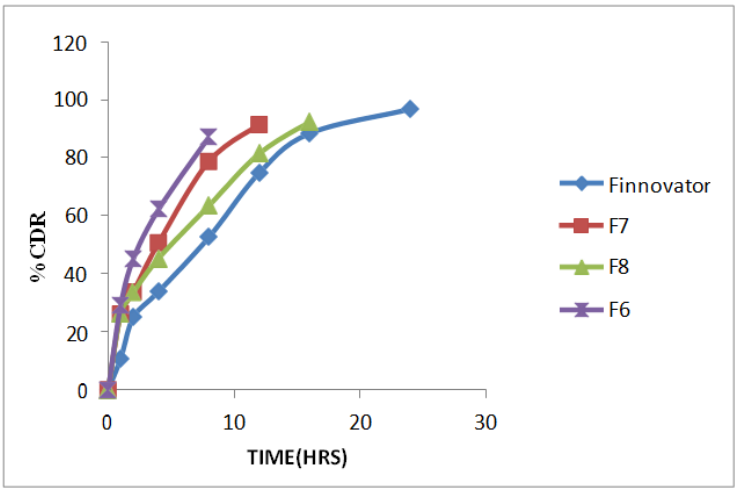
In-vitro drug release for the two formulations was performed as discussed in the experimental procedure. The two formulations F1 and F2 prepared by using Xanthan gum in concentration ranges from 15 to 20% were not extended their drug release up to 24 hrs. As the polymer concentration increases the drug release would be slower. The formulation F1 with 15% concentration the drug release was 98.5% within 8 hrs, F2 with 20% release was 96.5% within 8hrs.



***In-vitro* drug release profile of Formulations F 3, F4, F5 & Innovator**

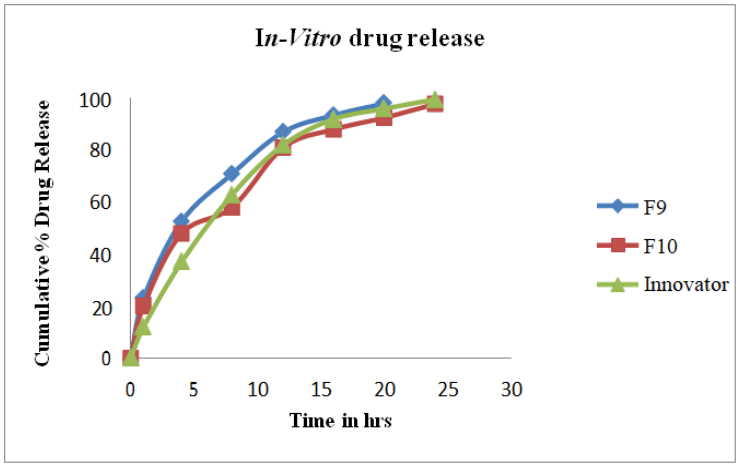
In-vitro drug release for the three formulations (F3-F5) was performed as discussed in the experimental procedure. The formulation F3 with 30% concentration of xanthun gum the drug release was 85.9% with in 8 hrs. The two formulations F4, F5 prepared by using Ethyl cellulose inconcentration ranges from 15 & 30% were not extended their drug release up to 24 hrs. As the polymer concentration increases the drug release would be slower. The formulation F4 with 15% concentration releases drug with in 12 hrs, F5 with 20% releases with in 12hrs.

The maximum concentration of ethyl cellulose was used in F5 formulation but the drug releasewas not up to 24 hrs. Also the F4 &F5 formulations had shown higher hardness than the prescribed limits. Hence ethyl cellulose was not further used in formulations in combination with other polymers.



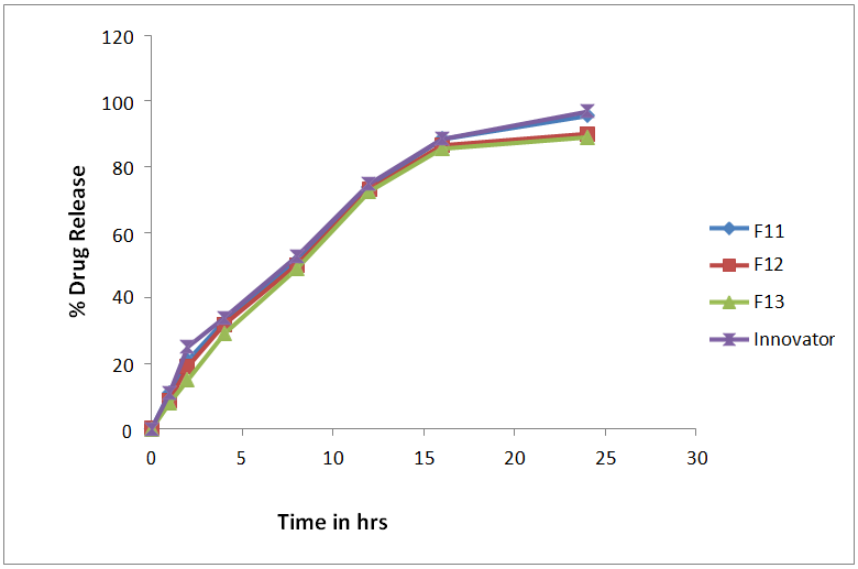
***In-vitro* drug release profile of Formulations F 6, F7, F8 & Innovator**

In-vitro drug release for the three formulations (F6-F8) was performed as discussed in the experimental procedure. The three formulations F6-F8 prepared by using HPMC K4M in concentration ranges from 10 - 30% were not extended their drug release up to 24 hrs. As the polymer concentration increases the drug release would be slower. The formulation F6 with 10% concentration the drug release was 87.11% with in 8 hrs, F7 with 20%the drug release was 91.39%with in 12hrs and F8 with 30%the drug release was 87.3% with in 16hrs.



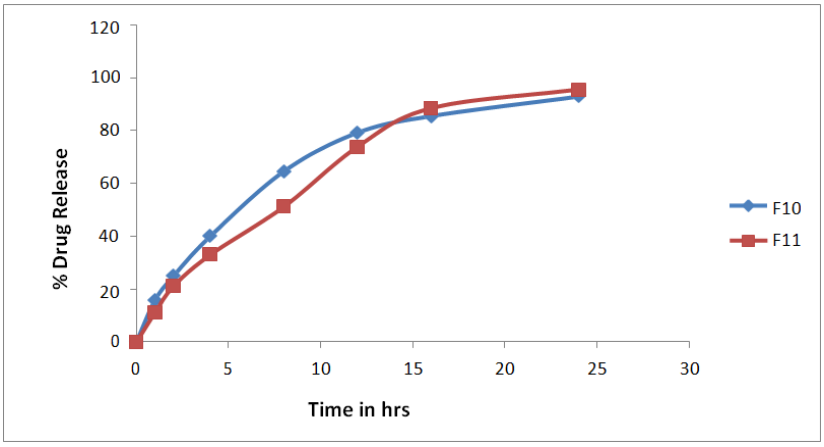
***In-vitro* drug release profile of Formulations F 9, F10 & Innovator**

In-vitro drug release for the two formulations (F9-F10) was performed as discussed in the experimental procedure. The two formulations F9 &F10 prepared by using HPMCK4M and Xanthan gum combination. The formulation F9 with 30% Xanthan gum and 20% HPMCK4M thedrug release was 94.8% with in 16 hrs, F10 with 25% Xanthan gum and 25% HPMCK4M the drug release was 92.8 % with in 24 hrs. F10 formulation was showing drug release up to 24 hrs. Hence it was further performed the similarity factor with innovators tablets.



***In-vitro* drug release profile of Formulations F 11, F12, F13 & Innovator**

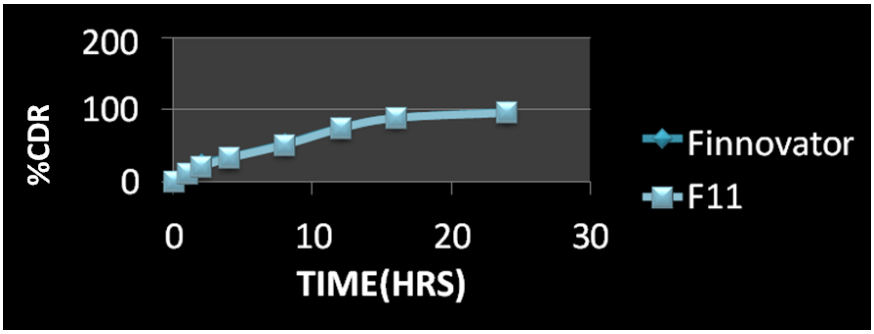
In-vitro drug release for the three formulations (F11-F13) was performed as discussed in the experimental procedure. The three formulations F11- F13 prepared by using HPMCK4M and HPMC K100M combination. The formulation F11 with 35% HPMCK4Mand 5% HPMCK100M the drug release was 95.5% with in 24 hrs, F12 with 40% HPMCK4M and 5% HPMCK100M thedrug release was 90% with in 24 hrs and F13 formulation with 45% HPMCK4M and 5% HPMCK100M the drug release was 89% with in 24 hrs.



***In-vitro* drug release profile of Formulations F 10 & F 11**

In-vitro drug release for the two formulations (F10-F11) was performed as discussed in theexperimental procedure. The two formulations F10 & F11 prepared by using HPMCK4M and Xanthan gum and HPMCK4M and HPMCK100M respectively. The formulation F10 was showingsimilar drug release with innovators tablets but initially the drug was

released faster up to 8hrs then followed slow drug release. The formulation F11 was showing similar drug release with innovators tablets. Hence F11 was selected as optimized formula and the both formulations were performed the similarity factor.



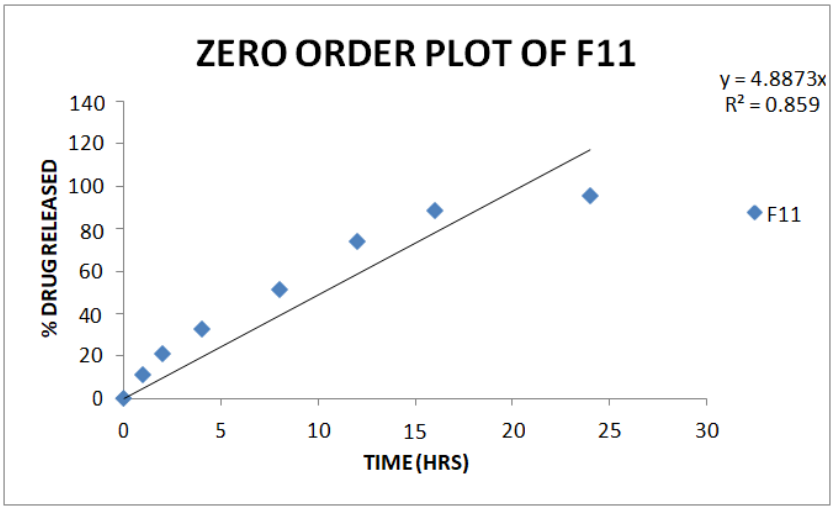
In-vitro **drug release profile of Formulations F 11 & Innovator**

IN-VITRO DRUG RELEASE KINETICS

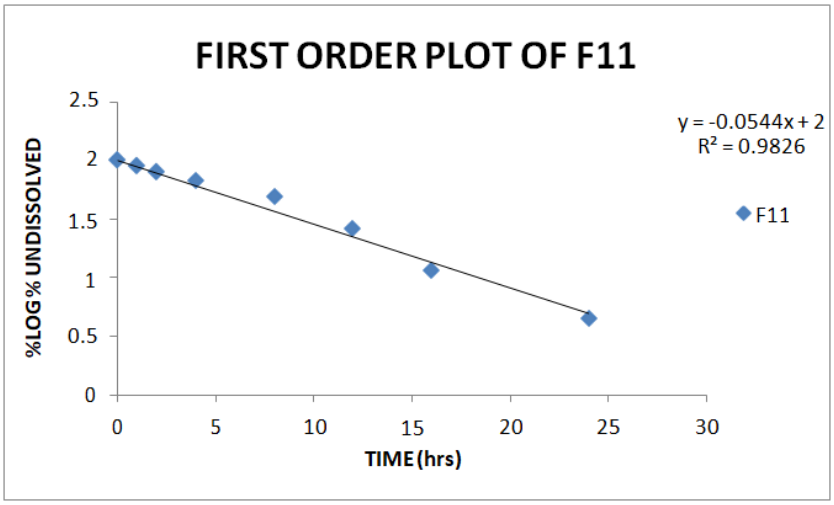
The drug release kinetics of the prepared formulations

Formulationcode	Zero order		First order		Higuchi		Korsmeyer-peppas	
	r^2	Slope	r^2	Slope	r^2	Slope	r^2	Diffusion exponent (n)
F-1	0.734	11.60	0.989	-0.236	0.934	36.71	0.681	0.43
F-2	0.734	10.53	0.954	-0.169	0.949	35.83	0.691	0.37
F-3	0.921	9.9	0.994	-0.104	0.995	30.93	0.749	0.36
F-4	0.891	6.874	0.994	-0.087	0.995	27.27	0.783	0.52
F-5	0.936	6.64	0.968	-0.073	0.993	25.69	0.809	0.52
F-6	0.894	9.85	0.956	-0.077	0.998	31.28	0.795	0.29
F-7	0.924	7.06	0.991	-0.088	0.994	27.51	0.810	0.23
F-8	0.922	7.06	0.961	-0.067	0.997	22.97	0.859	0.35
F-9	O.835	3.985	0.996	-0.071	0.973	22.47	0.631	0.29
F10	0.883	03.985	0.951	-0.064	0.984	21.97	0.680	0.29
F11	0.859	4.11	0.982	-0.056	0.966	22.11	0.988	0.694
F-12	0.902	3.974	0.967	-0.045	O.969	21.49	0.781	0.67
F-13	0.906	4.013	0.961	-0.04	0.988	21.57	0.812	0.79
F(I)	0.910	4.11	0.984	-0.062	0.981	22.13	0.733	0.6

IN-VITRO **DRUG KINETICS OF OPTIMIZED FORMULA**

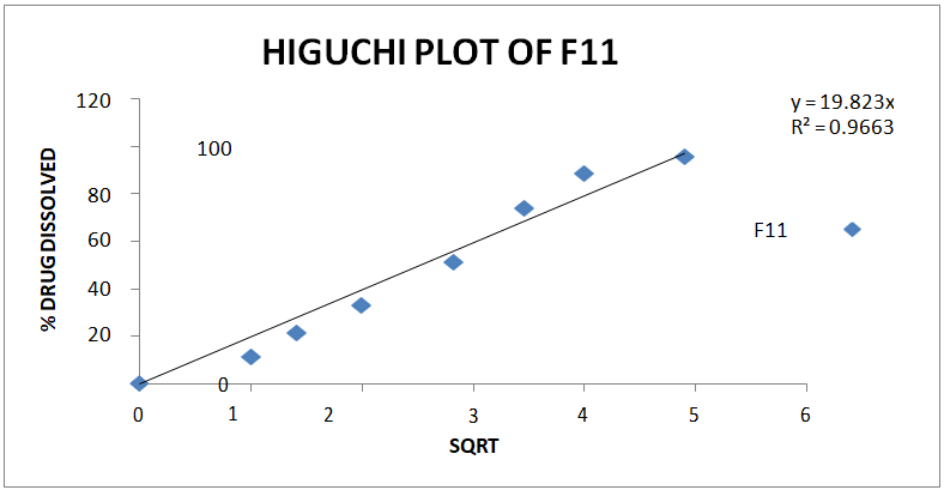


The Zero order release kinetics of optimized formula F-11



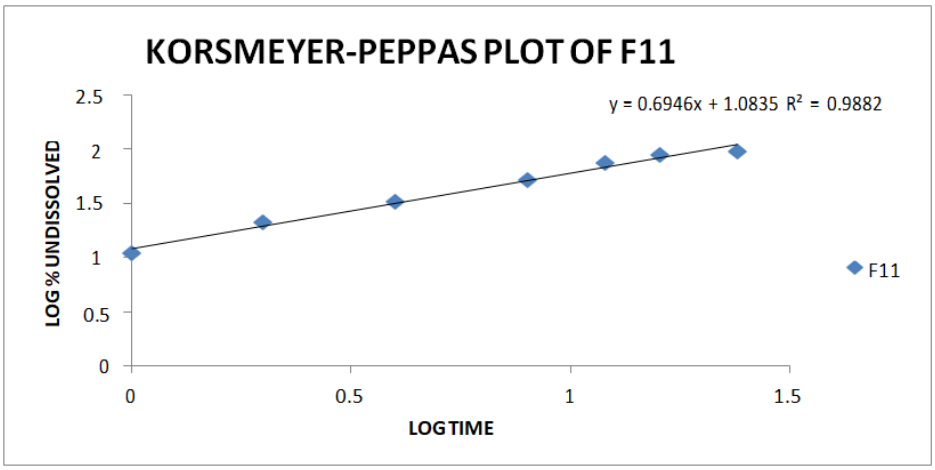
The first order release kinetics of optimized formula F-11

HIGUCHI MODEL



The Higuchi release kinetics of optimized formula F-11

KORSMEYER PEPPAS MODEL



The korsmeyer-peppas model release kinetics of optimized Formula F-11

The *in vitro* drug release kinetic models- zero order, First order, Higuchi. The figuresfrom the graphical representation of release kinetics of the optimized formula F11. Korsmeyer-Peppas model were performed for all the formulations and was based on the 'diffusion exponent n' of korsmeyer-peppas model where specifications were mentioned in the table. Based on the regression values mentioned in table the drug product follows the Firstorder kinetic model.

STABILITY STUDY REPORT

The stability study was performed for 200 tablets of final formulation F-11 at accelerated conditions(40°C/75% RH) for two months and at stress conditions (50°C/90% RH) for one month stability chambers. The parameters like Description, Dissolution, Identification, Average weight, moisture content, Assay and related impurities were performed initiallyto report that the tablets results were in limits. All these parameters were performed again after one month and two months time period and observed no physical reactions and incompatibilities. All the results were found to be in mentioned limits. Hence the formulated optimized batch F-11 was found stable and successful.

Stability Summary data of formulation-11

Test Name	Limits	Initial	40°C/75% RH		50°C/90 % RH
			1 month	2 months	1 month
Description	Orange colored, round biconvex filmcoated tablets with plain surface on both sides	Complies	Complies	Complies	Complies
Dissolution by UV Method (%w/w) InAcid Stage	NLT 25% in 1hr	12%	12.4%	13%	11.8%
Dissolution by UVMethod (%w/w) inpH 6.8 Buffer stage	NLT 85% at 24th hr	99.2%	99.4%	99.2%	98.8%
Identification byHPLC	To match withStandard	Complies	Complies	Complies	Complies
Average wt	206mg±2%	206.1	206.3	206.2	206.4
Water by KF (% W/W)	NMT 3.5%	2.2	2.7	2.4	2.7
Assay	NLT 90.0 and NMT 110.0	100.1	99.0	99.6	98.8

CONCLUSION

The study aimed to develop and evaluate Tolterodine Extended Release matrix tablets usingvarious grades and ratios of hydroxy propyl methyl cellulose (HPMC), Xanthan gum, and Ethyl cellulose as rate controlling hydrophilic polymers. The drug was compatible with the formulation components, and the formulation followed the first order release model. The dissolution profile of the optimized formulation F11 was above 50, indicating a match with the innovator's tablet. Stability studies were performed at accelerated and stress conditions, indicating the formulation was stable. The combination of high and low viscous hydroxy propyl methyl cellulose polymers was used to create a formula similar to the innovator's product Detrol.

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