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FORMULATION AND *IN VITRO* EVALUATION OF TAMSULOSIN HCL SUSTAINED RELEASE PELLETS IN CAPSULES

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ABSTRACT
Tamsulosin HCl is used for the treatment of benign prostatic hyperplasia (BPH). As it acts as an antagonist of alpha 1A adrenoceptor in the prostate. Its plasma half life is 2-4 hours. The present work was aimed to develop the sustained release Tamsulosin Hcl pellets loaded capsules using Ethylcellulose N45 as a sustained release polymer and Eudragit L100-55 as an enteric coating polymer in different formulations and polyvinyl pyrrolidone used as a pore former, Tri ethyl citrate as a plasticizer, Iso propyl alcohol and purified water used as solvents in solution layering technique by coating technology, should release the drug equivalent to the innovator product. The prepared Tamsulosin Hcl pellets were characterized by various evaluation studies and compare with the marketed innovator product drug release profile and further performed the stability test for selected or optimized formulation. It was finally brought down that the optimized formulation TC8 follows zero order release whose regression value was found to be 0.890. It was also found that the drug was released by diffusion as the regression in Higuchi's plot was 0.858. All formulations are determined for similarity factor, formulation TC8 drug release profile was very close to the innovator drug dissolution profiles and whose f2 values was found to be 88.3. It was concluded that stability studies of the optimized TC8 was carried out to the sample at temperatures 40^0C / 75% RH for a period one month. The capsules are checked and there is no indicative change in the release pattern.

KEYWORDS: Tamsulosin HCl, Benign prostatic hyperplasia, Sustained release capsule, Innovator product.

INTRODUCTION
Benign prostatic hyperplasia (BPH) is a non-malignant enlargement of the prostate, a wedge-shaped gland which surrounds the male urethra as it emerges from the bladder. This enlargement is a normal consequence of aging but it may be associated with symptoms which although rarely life-threatening, can be distressing. BPH firstly affects the inner parts of prostate. Enlargement of prostate gland causes a gradual squeezing of urethra, sometimes it causes difficulty in micturition and may create other urinary problems. However, it is possible for a man to have both BPH and prostate cancer. The current work entitled Tamsulosin Hcl pellets loaded into capsules is needed for the following reasons. To prolong the drug release in a sustained manner and treat BPH(Benign prostatic hyperplasia). To reduce the side effects reducing the dosing frequency and improve the patient compliance. Finally developing a formulation similar to that of the Innovator product.

MATERIALS AND METHODS
Tamsulosin Hcl was obtained as gift sample from RA chem pharma Pvt. Ltd., Sugar pellets (20#25) was obtained from Arun pharm Pvt. Ltd., Ethylcellulose N 45 was obtained from Shinetsu company, Eudragit L30D55 was obtained from Evonik company, Eudragit L100-55 was obtained from Evonik company**,** PVPK-30 was obtained from laxmi chem Pvt. Ltd.**,** Triethyl citrate was obtained from Qualigens fine chemicals Pvt. Ltd., Isopropyl alcohol was obtained from SD fine chemicals Pvt. Ltd.

A. METHOD OF PREPARATION OF SR PELLETS
1. Preformulation studies
For any drug substance to formulate into a dosage form, it is necessary to study the physico chemical properties of a drug like physical appearance, solubility, compatibility. The physical appearance of the Tamsulosin Hcl was done by visual observation. The important physicochemical properties of any drug is its solubility which ultimately effects on bioavailability. An excess amount of drug was taken and dissolved in a measured volume of ethanol, methanol, water in a separate glass vials to get a saturated solution. The solutions was sonicated and kept at room temperature for the attainment of equilibrium.

2. Construction of calibration curve

The calibration curve was established by preparing a stock solution (1mg/mL). 100mg of Tamsulosin Hcl was dissolved in 10mL of buffer in a 100mL standard flask and this solution was made up to 100mL with buffer. From the stock solution 10mL solution was transferred to a 100mL standard flask and volume was made up to 100mL with buffer. From the working standard solution different concentrations ranging between 20,40,60,80, 100µg/mL were prepared and it was determined by using HPLC method. From this data, the calibration curve of Tamsulosin Hcl was obtained by taking concentration on X-axis and peak area on Y-axis. The results were tabulated in Table. No.3 and calibration plot was represented graphically in Figure.no.1.

3. Drug –Excipient compatability studies

The infrared (IR) spectra were recorded using an FTIR by the KBr pellet method and spectra were recorded in the wavelength region between 4000 and 400 cm–1. The spectra obtained for Tamsulosin Hcl pure drug, polymers and physical mixtures of Tamsulosin Hcl were compared. Disappearance of Tamsulosin Hcl peaks or shifting of peak in any of the spectra was studied. The results were mentioned in figure no.2.

4. Method of preparation of Tamsulosin Hcl pellets by using solution layering method

The dispensing of Active Pharmaceutical Ingredient and Excipients is carried out as per the manufacturing formula (table no.2) Disperse Tamsulosin Hcl in iso propyl alcohol with continuous stirring till a uniform suspension is obtained. The sustained release coating solution preparation was done by dispersing ethyl cellulose N 45 in iso propyl alcohol and pvp k 30as pore former (for last two trails in f7 and f8) was added and it is dissolved in water and after that tri ethyl citrate was added and stirred until a clear solution is obtained. Drug solution was transferred into the coating solution and were continuously stirred until a uniform suspension was obtained. The sugar pellets(or)spheres (20#-25#) were loaded into coating pan. The sugar pellets(or)spheres were coated by top spray coating technology by maintaining 40-50˚c bed temperature at peristaltic pump whose rpm at 15-20 and atomizing air pressure of 2.0-5.0 Kg/cm^2 till the coating solution was completed. The coating solution was sprayed completely and after the completion of drug solution, drying was done for 10-15 minutes. The sustained drug layered pellets were unloaded from coating pan and it is ready for enteric coating.

5. Method of preparation of Tamsulosin Hcl pellets by using enteric coating method

After completion of solution layering method the pellets were unloaded from the pan and sent for enteric coating. In enteric coating solution preparation two polymers were used. Firstly, Eudragit L30D55 (or) Eudragit L100-55 were dissolved in respective solvents like IPA(or) water along with the tri ethyl citrate kept under stirring until uniform suspension was obtained. The dried sustained coated pellets were loaded into another coating bowl. The enteric coating on pellets were done by top spray at peristaltic pump rpm of 15-20 by maintaining 40-50˚c bed temperature and atomizing air pressure of 2.0-5.0 Kg/cm^2 till the coating solution was completed. The coating solution was sprayed completely and after the completion of coating solution drying was done for 10-15 minutes. The drug layered pellets were unloaded from coating pan and were sifted prior to be filled into capsules. Sift the coated dried pellets through the #20 and collect retains and downs separately. To prepare Tamsulosin Hcl capsules 0.4mg by taking Tamsulosin Hcl pellets 200 mg from the formulation is taken and filled. Before filling pellets into capsules the parameters like physical appearance, %moisture content, %drug content is evaluated. The pellets were loaded in hard gelatin capsule size-3 which has peach color body and grey color cap with capsule filling machine and spread equally.

B. *IN VITRO* EVALUATION TESTS FOR TAMSULOSIN HCL PELLETS

1. Evaluation for prepared Tamsulosin Hcl pellets

a. Physical appearance

0.5g of pellets were transferred into a dry petri dish or dispensed on a white card. The content was visually observed. The results were represented in Fig.No.3.

b. % Moisture content

Methanol was taken in dried Karl Fischer titration flask and titrated with KF reagent til the end point to neutralize the free water. Tamsulosin Hcl pellets were powdered finely. Accurately weighed quantity of sample was transferred to the titration flask and dissolved by stirring and titrated with KF reagent to the end point whose percentage water content was calculated by following formula. The results were tabulated in Table.No.4.

% Water Content = V×F×100/W×100

Where,
V = KF reagent volume consumed
F = KF reagent factor
W= Sample weight (grams)

c. Assay for tamsulosin Hcl pellets

Standard solution was prepared by weighing accurately about 50mg of Tamsulosin Hcl drug into a 100 ml of volumetric flask with 20mL of buffer, occasionally sonicate and shake to dissolve the content and make up to mark with buffer. Transfer 2mL of above solution into a 40mL volumetric with 7.2 phosphate buffer and finally filter the solution.

Sample solution was prepared by crushing 20 capsules of pellets and take 0.4mg Tamsulosin Hydrochloride equivalent weight of crushed sample powder into a 100ml of volumetric flask and add 20ml of buffer, occasionally sonicate and shake to dissolve the content

and make up to mark with 7.2 phosphate buffer and finally filter the solution.

100µl, of standard solution of replicate injects and sample injections were injected. The peak response was measured and recorded as chromatograms. The % drug content was calculated by using following formula.

Assay was calculated by using formula

$$\frac{A_{T1}}{A_{S1}} \times \frac{W_{S1}}{100} \times \frac{2}{40} \times \frac{40}{W_T} \times \frac{P}{100} \times AW \times 100$$

Where,
$\mathbf{A_T}$ = Test sample solution peak area.
$\mathbf{A_S}$ = The standard solution peak area.
$\mathbf{W_S}$ = Amount of the sample in standard working solution (mg)
$\mathbf{W_T}$ = Amount of sample (mg)
P = Potency of the sample working standard used.
AW = Average fill weight of the capsules.

The results were tabulated in Table.No.4.

Dissolve 8.7 ml of perchloric acid and 3.0 g of sodium hydroxide in 1900ml of water. Adjust with 1N sodium hydroxide solution to a PH of 2.0 and filter. Prepare filtered mixture of PH 2.0 solution and Acetonitrile in the ratio 1400:600 as mobile phase.

Chromatographic conditions

Table No. 1: Table showing chromatographic conditions for assay.

Column	OD-3V,C18 150x4.6mm,5 µm
Flow rate	1.3ml/min
Detector	UV,225nm
Injection volume	10 µL
Column temperature	40C
Run time	20minutes

2. Evaluation tests for capsules containing Tamsulosin Hcl pellets

a. Weight variation test

20 intact capsules were selected randomly, individual weights were caluculated and average weight was calculated. Weight of individual capsule should not be less than 90% and greater than 110% of average weight.

The results were tabulated in Table.No.5
Weight variation is calculated by following formula,

$$\text{Weight variation} = \frac{\text{(Weight of capsule-Average weight)}}{\text{Average weight of capsules}} \times 100$$

b. Disintegration Time

The capsules are placed in disintegration test appartus, which were observed over the time described in the individual monograph. Two capsules must disintegrate completely into a soft mass having no palpably firm core, and only some fragments of the gelatin shell. The results were tabulated in Table.No.5.

c. *In-vitro* drug dissolution studies

Place 900ml of dissolution medium in each vessel with temperature of 37 ± 0.5ºC provided with basket type of stirrer at 100 rpm stirrer speed using pH 1.2 buffer solution for 2 hrs and pH 7.2 Phosphate buffer solution for 8 hrs. collect 10mL of the sample solution from each vessel by maintaining sink conditions and filter the solution through 0.45microns membrane filter and samples were analyzed using uv-visible spectrophotometer for its absorbance finally %CDR is calculated whose values are tabulated in table no.10.

In order to demonstrate the mechanism and mode of drug release, the *in vitro* drug release data was transformed and elucidated at graphical level using various kinetic models. The *in vitro* dissolution release profile from various formulation in 1.2 pH phosphate buffer solution was applied to different kinetic models. The release mechanism and kinetic data were estimated by various plots like Zero order, First order, Higuchi model and Kores Meyer Peppa's model. when R^2 value of zero order and first order were compared it was found that the drug release from capsules follow zero order release, further the release data is incorporated in higuchi and koresmeyer peppas model and finally found TC8 as optimized formulation, which follow zero order whose regression value was found to be 0.890 which was already tabulated in table no. 10.

d. Dissolution profile comparision using Similarity and Dissimilarity Factors.

f1=Dissimilar factor
f2=Similar factor

A dissolution profile helps to assure similarity in product performance and bioequivalence. The component f1 is proportional to the average in distinctness between two profiles, where as component f2 inversely proportional to the average squared in distinctness between two profiles. The component f2 measures the intimacy between two profiles. FDA has set a public standard of f2 value between 50-100 to indicate likeness between two profiles. Results were tabulated in Table.No.9.

$$f1 = \Sigma D\ (1/\Sigma t)\ 100$$

$$f2 = 50 \times \ln\{1/1+\Sigma\ (Rt-Tt)^2\}$$

E. Stability studies

This will include storage of formulations at both normal and exaggerated temperature conditions. The design of the stability studies for the drug product should be done at $40\pm2^0C/75\pm5\%$ RH initially for 1 month based on the behaviour and properties of the drug substance and results were tabulated in table no.12.

RESULTS AND DISCUSSION

A. Formulation design of Tamsulosin Hcl pellets

Table No.2: Formulation table showing the design of Tamsulosin Hcl pellets.

S.No	Drug loading (S.R.coating)	Category	T1 %w/w	T2 %w/w	T3 %w/w	T4 %w/w	T5 %w/w	T6 %w/w	T7 %w/w	T8 %w/w
1	Tamsulosin Hcl	API	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
2	Sugar spheres	Core	96.3	94.3	93.3	94.3	93.3	92.3	88.3	87.3
3	Ethyl cellulose N45	S.R.polymer	2	3	4	4	5	5	6	6
4	Pvpk-30	Pore former	-	-	-	-	-	-	3	4
5	Tri ethyl citrate	Plasticizer	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
6	Iso propyl alcohol	Solvent	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
7	Purified water	Solvent	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
	Enteric coating									
8	Eudragit L30-D55	E.C. polymer	1	2	2	-	-	-	-	-
9	Eudragit L100-55	E.C. polymer	-	-	-	1	1	2	2	2
10	Tri ethyl citrate	Plasticizer	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
11	Iso propyl alcohol	Solvent	-	-	-	Q.S	Q.S	Q.S	Q.S	Q.S
12	Water	Solvent	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
13	Total %		100%	100%	100%	100%	100%	100%	100%	100%

1. Preformulation studies

An excess amount of pure drug was taken and dissolved in excess volume of ethanol, methanol and water. It is evident that the drug is freely soluble in water.

2. Construction of calibration curve

The standard plot was drawn for Tamsulosin Hcl by taking concentration on x-axis and peakarea on y-axis by using HPLC, its R^2 value found to be 0.999.

Table No.3: Standard graph for Tamsulosin Hcl drug.

S.No	Concentration (mcg/mL)	Peak Area (mV.s)
1	0	00000
2	20	2067094
3	40	4134188
4	60	6201282
5	80	8268376
6	100	10035470

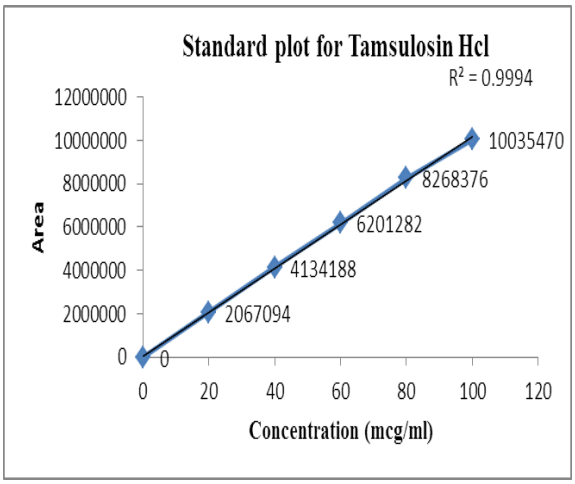
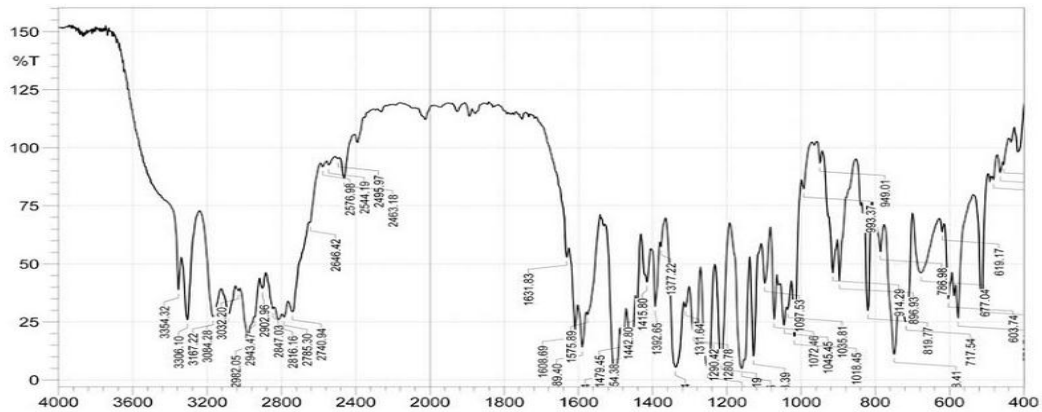


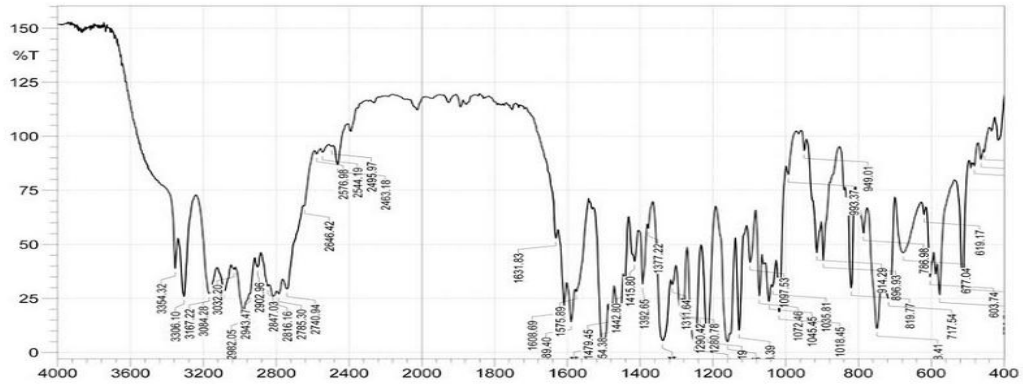
Fig. No. 1: Graphical representation showing standard plot for Tamsulosin Hcl.

3. Drug-Excipient compatability studies

The physical and chemical compatibility of drug and excipients was attained by FT-IR profiles and the results were tabulated.



Graph showing FTIR spectra of pure drug of Tamsulosin Hcl.



Graph showing FTIR spectra of pure drug with Eudragit L100-55
Figure No.2: FTIR spectra data for pure Tamsulosin Hcl.

FTIR spectral analysis of tamsulosin HCl pure drug shows the peaks at wave number of 1215 (C-N) 2847 (C-H Alkane) 1630 (N-H Bending) 1159 (OCH_3- stretching) 3306(C=C) which confirms the purity of drug with standard. In physical mixture of Tamsulosin Hcl with EthylcelluloseN45 major peaks of Tamsulosin HCL were 1219(C-N) 2850(C-H Alkane) 1639(N-H Bending)1212(OCH_3- stretching) 3312(C=C) wave numbers. In physical mixture of Tamsulosin Hcl with Eudragit L100-55 major peaks of Tamsulosin HCL were 1217(C-N) 2850(C-H Alkane) 1646(N-H Bending) 1219(OCH_3- stretching) 3318(C=C) wave numbers. However some additional peaks are observed which evident the presence of excipient and can be concluded that there was no chemical interaction between the drug and excipient from the spectrum.

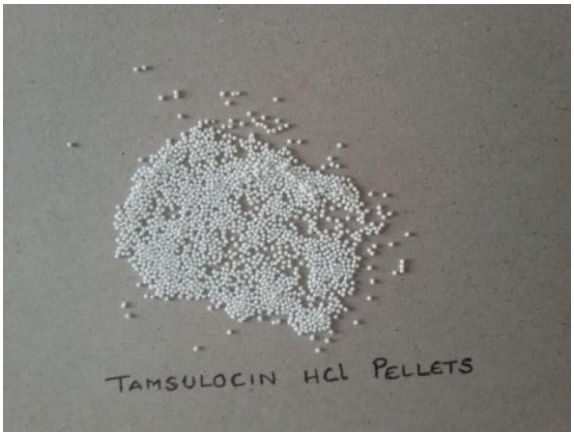


Fig. No.3: Showing picture of Tamsulosin Hcl pellets.

B. *INVITRO* EVALUATION TESTS

1. Evaluation of Prepared Tamsulosin Hcl pellets

a. Physical appearance: Tamsulosin Hcl pellets were found to be white crystalline solid.

b. Estimation of %Moisture content and %Drug content.

Table No.4: Results showing % Moisture content & % Drug content for TP1 to TP8.

S. No	Formulation code	% Moisture Content (± SD) n=3	%Drug content (± SD) n=3
1	TP1	2.75±0.174	97.5 ± 0.577
2	TP2	2.03±0.425	98.2 ± 0.556
3	TP3	2.38±0.189	98.1 ± 0.556
4	TP4	2.46±0.156	98.2 ± 0.608
5	TP5	2.30±0.266	98.2 ± 0.551
6	TP6	2.47±0.340	98.6 ± 0.351
7	TP7	1.82±0.068	98.8 ± 0.305
8	TP8	1.77±0.104	99.2 ± 0.202

% moisture content achieved for formulation from TP1-TP8 were noticed to be within the bound of limits 2±1%. % Drug content performed for formulations from TP1-TP8 were between the boundaries of limits 98 ± 1%.

2. Evaluation tests for capsules containing Tamsulosin Hcl Pellets

a. Estimation of Weight variation, Disintegration time

Table No.5: Results showing weight variation test for formulations TC1 to TC8.

S. No	Formulation code	Weight variation (mg) (± SD) n=3	Disintegration time (mns) (± SD) n=3
1	TC1	200.08±0.160	5.13 ± 0.208
2	TC2	200.67±0.204	5.66 ± 0.210
3	TC3	200.17±0.365	5.15 ± 0.596
4	TC4	200.69±0.279	5.43 ± 0.416
5	TC5	200.13±0.568	5.30 ± 0.152
6	TC6	200.58±0.275	5.12 ± 0.264
7	TC7	200.41±0.229	5.07 ± 0.350
8	TC8	200.12±0.208	5.06 ± 0.115

Weight variation test was conducted for all formulations mentioned below were within the boundary of limits 200±1 and their disintegration time were found within the boundary of limit 5±1 min.

C. *In- vitro* drug release studies for Innovator product (FLOMAX)

As a innovator product FLOMAX capsules manufactured by boehringer ingelheim limited, USA with 0.4 mg dose in oral route with 10 hrs duration of action are selected, dissolution profile was given below in a table and with a graph.

Table No.6: Results showing Innovator(FLOMAX)dissolution profile.

S.No	Time (hrs)	%CDR
Acidic media (pH 1.2)		
1	**0**	**0**
2	**1**	**5.8**
3	**2**	**10.6**
Alkaline media (pH 7.2)		
4	**3**	**50.8**
5	**4**	**65.5**
6	**6**	**78.1**
7	**8**	**85.5**
8	**9**	**95.6**
9	**10**	**99.4**

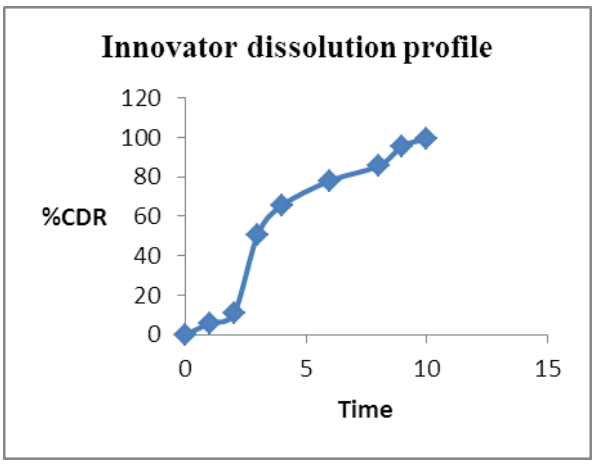


Fig. No.4: Graphical representation of *In-vitro* dissolution profile of Innovator.

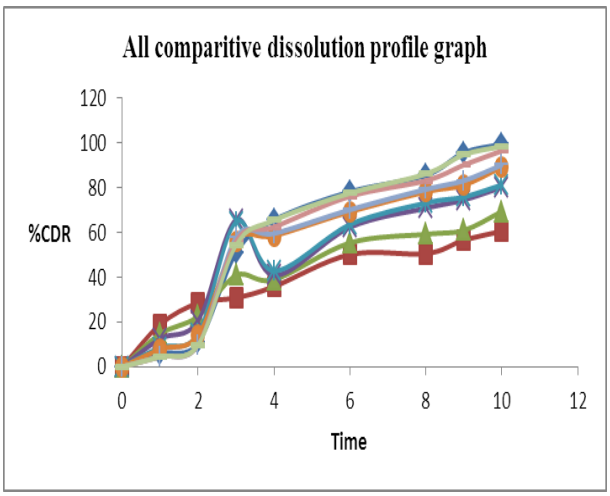


Fig. No.5: Graphical representation showing comparative *In-vitro* drug release studies for all formulations TC1-TC8 and Innovator.

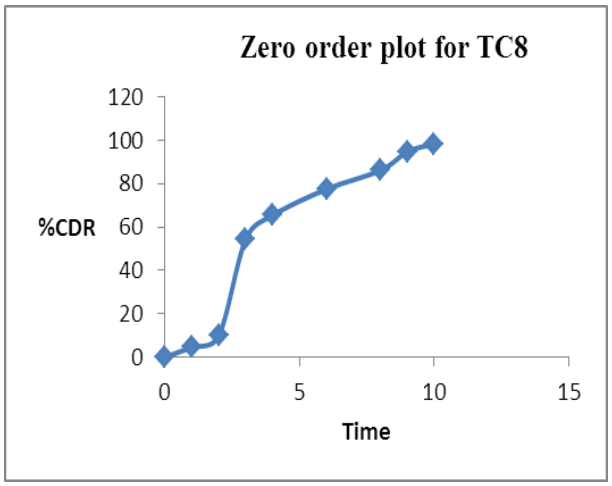
In first formulation, sustained release coating stage the release is too low and in enteric coating stage the release was too high, when compared with innovator product. In second formulation, release was better compared to 1st formulation in enteric coating stage the drug release was too high in acid stage when compared with innovator product. In **t**hird formulation, drug release was better compared to 2nd formulation but drug release was low when compared with the innovator profile. In fourth formulation, drug release was somewhat controlled in enteric stage but in compared with the innovator it is high. In fifth formulation drug relese was increased in sustained coating compared to 4th formulation but it is not matching with the innovator product. In sixth formulation, drug release was controlled the intial points of drug release is matching with the innovator product drug release. In Seventh formulation, drug release was increased compared to 6th formulation and was slow compared to Innovator drug release profile. In Eight formulation drug release was matching with the Innovator product.

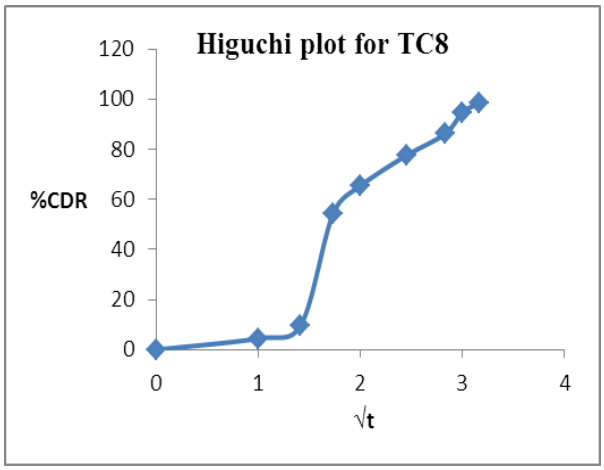
d. Drug Kinetic studies

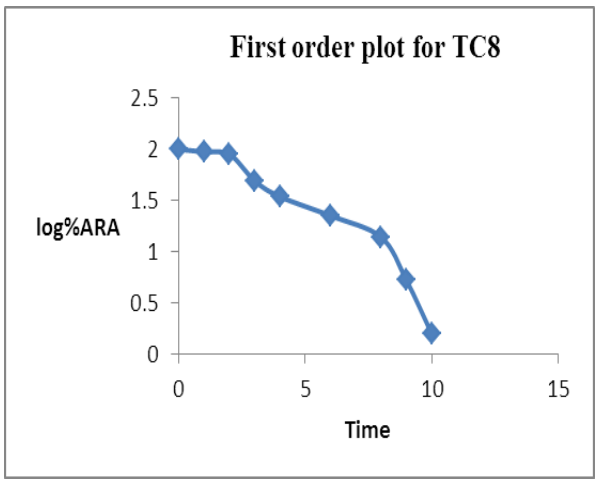
From all the formulations, TC8 formulation drug profile was equivalent with the Innovator product. Drug release Kinetic data for TC8 were tabulated below.

Table No.7: Showing results Kinetic data for TC8.

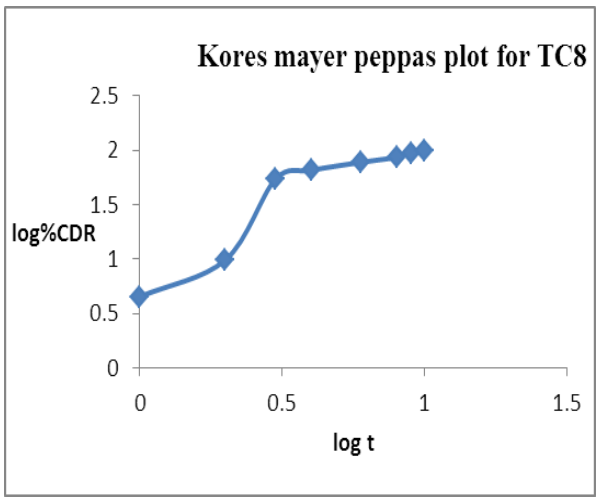
Time	%CDR	√ T	Log %CDR	Log T	%ARA	Log %ARA	(+ SD) n=3
0	0	0	1	1	100	2	0
1	4.5	1	0.653213	0	95.5	1.980003	0.173
2	9.8	1.414214	0.991226	0.30103	90.2	1.955207	0.4163
3	54.3	1.732051	1.73348	0.477121	45.7	1.659916	0.1527
4	65.4	2	1.815578	0.60206	34.6	1.539076	0.236
6	77.5	2.44949	1.889302	0.778151	22.5	1.352183	0.264
8	86.1	2.828427	1.935003	0.90309	13.9	1.143015	0.123
9	94.7	3	1.97635	0.954243	5.3	0.724276	0.278
10	98.4	3.162278	1.992995	1	1.6	0.20412	0.124







Graph No.6: The above graph shows zero order & First order plot plot of TC8.



Graph No.7: Graphical representation showing Higuchi & kores mayer peppas for TC8.

Table No. 8: Drug kinetic results for optimized formulation (TC8).

S.no	Order of kinetics	Regression value(R^2 /n)
TC8	Zero order	0.890
TC8	First order	-3.88
TC8	Higuchi	0.858
TC8	Koresmeyer peppas (n)	0.364

It was ascertained that the optimized formulation TC8, follows zero order release whose regression value was found to be 0.890. It was concluded that the drug was released by diffusion as the regression in Higuchi's plot was 0.858.

e. Similarity factor determination for various formulations

The FDA prescribed the range of 50-100 for similarity between two dissolution profile. Accordingly TC5, TC6, TC7, TC8 formulations had similarity to innovator product. However, other formulations were not similar. But TC8 drug release profile was very close to the innovator drug dissolution profiles and whose f2 values was found to be 88.3 and the results were tabulated below.

Table No.9: Results showing similarity values of all formulations TC1-TC8.

S.No	Formulations	*f2* value	Similar/dissimilar factor
1	TC1	21.2	Dissimilar
2	TC2	30.5	Dissimilar
3	TC3	38.6	Dissimilar
4	TC4	41.9	Dissmilar
5	TC5	53.6	Similar
6	TC6	55.9	Similar
7	TC7	73.9	Similar
8	TC8	88.3	Similar

f. *In-vitro* drug release data for all formulations TC1-TC8

Table No.10: Results showing *In-vitro* drug release studies comparison between TC1-TC8 to Innovator.

S.No	Time	Innovator %CDR	TC1 %CDR	TC2 %CDR	TC3 %CDR	TC4 %CDR	TC5 %CDR	TC6 %CDR	TC7 %CDR	TC8 %CDR
Acidic media (pH 1.2)										
1	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
2	**1**	**5.8**	**18.9**	**14.7**	**12.5**	**8.6**	**7.9**	**4.5**	**4.5**	**4.5**
3	**2**	**10.6**	**28.4**	**22.5**	**20.6**	**14.8**	**14.2**	**9.8**	**9.8**	**9.8**
Alkaline media (pH 7.2)										
4	**3**	**50.8**	**30.8**	**40.8**	**65.7**	**64.7**	**55.9**	**57.9**	**56.2**	**54.3**
5	**4**	**65.5**	**35.8**	**38.9**	**40.8**	**42.8**	**58.5**	**59.5**	**62.4**	**65.4**
6	**6**	**78.1**	**50.1**	**55.3**	**62.3**	**63.5**	**69.2**	**70.1**	**76.1**	**77.5**
7	**8**	**85.5**	**50.5**	**59.15**	**70.8**	**73.1**	**78.1**	**79.2**	**83.1**	**86.1**
8	**9**	**95.6**	**56.8**	**60.9**	**74.5**	**75.8**	**81.1**	**83.1**	**90.1**	**94.1**
9	**10**	**99.4**	**60.5**	**69.3**	**80.2**	**81.2**	**89.2**	**90.1**	**96.4**	**98.4**

g. Stability Results for optimized formulation(TC8).

Table No. 11: Stability data results of optimized formulation TC8.

S.No	Test	Storage Condition 40^0C /75%RH	
		Initial	30 days
1	Physical Appearance	No change	No change
2	% Moisture Content	1.77± 0.104	1.76± 0.104
3	%Drug Content	99.2 ± 0.202	99.19 ± 0.201
4	%Drug Release	98.4 ± 0.124	98.3 ± 0.123

Table No. 12: Stability data of *In-vitro* drug release studies of TC8.

S.No	Time (hrs)	Intial	30days %CDR at 40^0C/75%RH
Acidic media			
1	0	0	0
2	1	4.5 ± 0.173	4.49 ± 0.174
3	2	9.8 ± 0.416	9.8 ± 0.417
Alkaline media			
4	3	54.3 ± 0.152	54.29 ± 0.153
5	4	65.4 ± 0.236	65.38 ± 0.236
6	6	77.5 ± 0.264	77.5 ± 0.265
7	8	86.1 ± 0.123	86.12 ± 0.126
8	9	94.1 ± 0.278	94.1 ± 0.276
9	10	98.4 ± 0.124	98.3 ± 0.123

It was concluded that stability studies of the optimized TC8 was carried out to the sample at temperatures 40^0C / 75% RH for a period one month. The capsules are observed and there is no indicative change in physicochemical property and drug release pattern from capsules.

SUMMARY AND CONCLUSION

In the present work, sustained release Tamsulosin Hcl pellets were prepared by solution layering method using coating technology. All the formulations were subjected to weight variation, drug content, moisture content, disintegration time and dissolution test. Based on the above study following summary can be drawn.

Tamsulosin Hcl Pellets prepared by two coatings technology by using solution layering method without any breaking of pellets. The % moisture content, %drug content, weight variation and disintegration time of capsules are found to be within the boundaries of limits 2±1%, 98±1%, 200±1mg, 5±1min respectively. *In-vitro* dissolution studies for the formulation TC8 showing drug release of 98.4% matching the innovator product and its similarity factor(f_2) value was found to be 88.3. TC1 to TC8 formulations were done by using Ethyl cellulose N45 as sustained release polymer, Eudragit L100-55 and Eudragit L30-D55 used as Enteric polymers in different formulations. All the formulations are carried out for various evaluation tests, the results are found to be within the range of limits. Finally, in this study Tamsulosin Hcl SR pellets loaded capsules were developed. Both innovator's product and the formulation TC8 showed almost identical cumulative drug release profiles. Hence, both of them were considered as pharmaceutically equivalent. Stability study is carried out for finalised formulation for month at 40^0C±2^0C/ 75%±5% RH, the formulation was found to be stable. Based on the regression values it was concluded that the optimized formulation, TC8 follows zero order release where the regression value was found to be 0.890. It was also found that the drug was released by diffusion as the regression in Higuchi's plot was 0.858. All formulations are determined for similarity factor, formulation TC8 drug release profile was very close to the innovator drug dissolution profiles and whose f2 values was found to be 88.3. It was concluded that stability studies of the optimized TC8 was carried out to the sample at temperatures 40^0C / 75% RH for a period one month which shows uniform release patterns.

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