

Design and Performance Evaluation of Tamsulosin Prolonged Release Matrix Tablets Using Different Polymers

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Abstract: The design and performance evaluation of a prolonged-release matrix tablet formulation of Tamsulosin Hydrochloride, an α -adrenoreceptor blocker frequently recommended for benign prostatic hyperplasia (BPH), are the main objectives of this study. The goal was to find an optimal formulation with improved release kinetics and tablet integrity while achieving prolong drug release using different polymers. The polymeric matrices included different amounts of sodium carboxymethyl cellulose (NaCMC), hydroxypropyl methylcellulose K100 (HPMC K100), ethyl cellulose (45 cps), and polyethylene oxide (PEO). Ethyl Cellulose, HPMC K100, and Na CMC were all present in equal concentrations in trials 1 through 3. PEO was added in Trial 4 at a concentration of 100 mg, and in Trial 5, its concentration was raised to 120 mg. Trial 5, which was made utilizing a fluidized bed processor and wet granulation, was determined to be the best formulation because of its excellent matrix integrity and regulated drug release profile. medication crystallinity was preserved by X-ray diffraction (XRD) studies, which showed no significant interaction between the medication and polymers. The modified matrix provided consistent extended release suitable for once-daily dosing, boosting patient compliance. According to this study, PEO is a significant polymer for developing strong, controlled-release oral drug delivery systems for α -adrenoreceptor blockers, such as tamsulosin.

Keywords: Tamsulosin, BPH (Benign Prostatic Hyperplasia), Prolong release matrix tablet.

INTRODUCTION

Prostate enlargement, another name for benign prostatic hyperplasia (BPH), is a benign expansion of the prostate gland. Loss of bladder control, poor urine flow, frequent urination, and trouble starting to urinate are common symptoms (Kim EH et al. 2016.,) (Prajapati A et al. 2013.,) BPH can result in persistent kidney problems, bladder stones, and urinary tract infections if it is not addressed. In (Ugare et.al 2014.,) One of the main causes of lower urinary tract symptoms (LUTS) in older men is benign prostatic hyperplasia (BPH). (Awedew et al 2019.,) (Carvalho-Dias E et al 2017.,) BPH becomes more common as people age. According to autopsy histological data, between 50 and 60 percent of men in their 60s and 80 to 90 percent of men in their 70s suffer with BPH. In (Sahu B et al 2011.,) The two primary types of α -receptors, α 1 and α 2, are present throughout the human body. (Roberts RO et al. 1995.,) α 2-receptors, which are often located pre-synaptically, (Bousquet P et al. 1983.,) work by reducing norepinephrine release through a negative feedback process that produces smooth muscle relaxation in response to stimulation. (Ratnaparkhi M. P et al., 2013) Alpha-1 receptors are post-synaptic receptors that control how the body reacts to signals from neurotransmitters. They are separated into three primary subtypes, α 1A, α 1B, and α 1D, each of which has distinct bodily sites and functions. (Jain et al. 2008.,) The main source of expression for the α 1A receptors are smooth muscle cells in the prostatic stroma. The smooth muscles of veins and arteries, as well as the microvasculature of the prostate gland, are the primary locations for α 1b receptors. (Chein Yie. W. (Ed.) et al. 2008.,) The spinal cord, where they aid in controlling parasympathetic activity through sympathetic pathways, and the bladder's dome and body are home to the majority of the α 1D receptors. (Dusane Abhijit Ratilal et al. 2011.,) Lower urinary tract symptoms' (LUTS) irritative aspects are mostly caused by these receptors. (Franco-Salinas et al. 2010.,) Alpha-adrenergic blockers, which include Tamsulosin, Prazosin, Terazosin, and Doxazosin, are frequently used to treat hypertension. (Chughtai et al. 2016.,) These

medications are frequently chosen to treat both hypertension and benign prostatic hyperplasia (BPH), as approximately 30% of men with BPH also have hypertension. The prostate's smooth muscle contains the majority of the $\alpha 1A$ receptors. The best course of treatment for BPH can be chosen by understanding the location and function of the various $\alpha 1$ -receptor subtypes. (Langan et al. 2019.,) Among the most popular α -adrenoreceptor blockers is tamsulosin. However, when compared to other comparable medications, the majority of trials have demonstrated that there are no appreciable differences in terms of efficacy or tolerability. In (Bousquet P et al. 1983.,) Whether the patients were hypertensive or had normal blood pressure, a large multicenter trial found no significant difference in the changes in systolic and diastolic blood pressure (Michel MC et al. 2010.,) between the Tamsulosin group and the placebo group. (Richards DA et al. 1976.,) Although it can be taken safely in conjunction with other blood pressure drugs, tamsulosin does not lower blood pressure in males with hypertension. The goal of this study is to create a straightforward, affordable, precise, and trustworthy process for creating and assessing tamsulosin hydrochloride as a matrix tablet with extended release. (Lerner LB et al. 2025.,)

Materials and Method

Table 1: Materials used in the formulation are mentioned below

S no.	Ingredients	Category
1.	Microcrystalline Cellulose	Diluent
2.	Polyethylene oxide (PEO)	Release modifying agent
3.	Hypromellose K100 (HPMC)	Release modifying agent
4.	Sodium carboxymethyl cellulose	Release modifying agent
5.	Ethyl cellulose 45 cps	Release modifying agent
6.	Butylated Hydroxy toluene (BHT)	Antioxidant
7.	Colloidal Silicon Dioxide	Glidant
8.	Magnesium stearate	Lubricant
9.	Isopropyl Alcohol	Solvent
10.	Purified Water	Solvent
11.	Opadry yellow	Film coating agent.

All the other reagents used in the experiment were of analytical grade, available in Mankind Pharmaceuticals Pvt. Ltd. (Research and Development), Manesar, Gurgaon.

Table 2: Equipment which are used during process.

S. No.	Equipment/Processing aids
1.	Mechanical vibratory sifter (SS sieves: ASTM #24, #30, #60)
2.	S.S vessel for drug dispersion preparation
3.	Stirrer (Mechanical / Pneumatic)
4.	Fluidized bed processor (FBP) {With finger bag (5 μ m) and Dutch mesh sieve (100 μ m)}
5.	Qudro co-mill {Screen: 0.8 mm}
6.	Weighing Balances
7.	Moisture Analyzer
8.	Bin blender
9.	Compression machine with change parts and tooling
10.	Coating machine
11.	Filtration pot (#80 sieve for filtration)
12.	Hardness Tester

METHODS

Process selection

The early stages of method development involved the evaluation of a number of traditional processing approaches. The impurity levels were significantly raised by these methods, though, most likely as a result of uneven mixing and insufficient heat/mass transmission. In order to get over these obstacles, a fluidized bed processor was chosen for the procedure. By improving consistency and providing more control over processing parameters, this equipment significantly lowers contaminants. The fluidized bed environment facilitates effective mixing, uniform temperature distribution, and enhanced drying or coating performance—all of which are essential for preserving the final product's intended quality.

Wet Granulation by Fluidized Bed Processor

A product's granulation, coating, and drying can be achieved with the use of fluid bed processing, resulting in uniform coating and drying. (Soeishi et al. 1996.,) Such techniques may use the tangential spray process, top spray, or bottom spray as their underlying concept. (Dunn et al. 2002.,) The spray gun's placement within the apparatus determines these principles. The top spray method aids in achieving consistent granulation or palletization which is used for the formulation. (Pusapati RT et al. 2014.,)

Table 3: Different Trials for Composition of Tamsulosin prolong Release tablets.

Table 3: Different Trials for Composition of Tamsulosin prolong Release tablets.							
S. No.	Ingredients	Category	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
			Qty. (mg/unit)	Qty. (mg/unit)	Qty. (mg/unit)	Qty. (mg/unit)	Qty. (mg/unit)
Intra-granular material							
1.	Microcrystalline Cellulose (Avicel PH 102)	Diluent	146.300	146.300	146.300	146.300	126.300
2.	Sodium carboxymethyl cellulose	Release modifying agent	100.000	~	~	~	~
3.	Hydroxypropyl Methyl Cellulose K100	Release modifying agent	~	100.000	~	~	~
4.	Ethyl cellulose 45cps	Release modifying agent	~	~	100.000	~	~
5.	Polyethylene oxide (PEO)	Release modifying agent	~	~	~	100.000	120.000
Drug dispersion							
6.	Tamsulosin	Active	0.400	0.400	0.400	0.400	0.400
7.	Butylated Hydroxy toluene (BHT)	Anti-oxidant	1.500	1.500	1.500	1.500	1.500
8.	Isopropyl alcohol (IPA)	Solvent	Q. s	Q. s	Q. s	Q. s	Q. s
Pre-lubrication							
9.	Colloidal Silicon Dioxide (Aerosil 200)	Glidant	0.800	0.800	0.800	0.800	0.800
Lubrication							

10.	Magnesium stearate	Lubricant	1.000	1.000	1.000	1.000	1.000
Core tablet weight (mg)			250.000	250.000	250.000	250.000	250.000
Film Coating							
11.	Opadry Yellow	Coating Agent	5.000	5.000	5.000	5.000	5.000
12.	Isopropyl alcohol (IPA)	Solvent	Q. s	Q. s	Q. s	Q. s	Q. s
13.	Purified Water	Solvent	Q. s	Q. s	Q. s	Q. s	Q. s
Coated tablet weight (mg)			255.000	255.000	255.000	255.000	255.000

Granulation – Wet Granulation by Fluidized Bed Processor (Top-Spray Method)

Step 1: Drug Dispersion Preparation

Tamsulosin hydrochloride was dispersed in purified water containing Butylated Hydroxy Toluene (BHT). Isopropyl alcohol (IPA) was used as a co-solvent to ensure uniform dispersion.

Step 2: Granulation

The intra-granular ingredients (API + polymers + diluents) were dry-sifted and loaded into the FBP chamber. The drug dispersion was sprayed over the fluidized mass using a top-spray nozzle under the following optimized conditions mentioned in table 4:

Table 4: Optimized Process Parameters for Fluidized Bed Granulation

Parameters	Recommendations
Stage: Pre-warming	
Inlet temperature of air (°C)	35-60
Temperature of product (°C)	35-45°C
Exhaust air temperature (°C)	35-45°C
Inlet air flow (CFM) ^{\$}	2000-2500
Stage: Granulation	
Inlet air temperature (°C)	35-60
Product temperature (°C)	35-45°C
Exhaust air temperature (°C)	35-45°C
Inlet air flow (CFM) ^{\$}	2000-2500
Atomization air pressure (Bar)	1-2
Spray pump speed (RPM)	2-20
Mode of synchronization	Synchronized
Nozzle Size	1mm
^{\$} Set value to obtain required air flow (CFM) Note: If gun choking observed, clean the gun and continue the process.	
Stage: Drying	
Inlet air temperature (°C)	35-60
Product temperature (°C)	35-45°C
Exhaust air temperature (°C)	35-45°C
Inlet air flow (CFM) ^{\$}	2000-2500
LOD (% w/w) at 60°C	1-3

Step 3: Drying After spraying, the granules were dried until a desired LOD (Loss on Drying) below 2% was achieved.

Step 4: Milling of dried granules

Dried granules were milled using a Quadro co-mill (0.8 mm screen) and parameters are mentioned in table 5.

Table 5: - Parameters for milling of granules

Parameters	Recommendations
Quadro-mill screen	0.8 mm
Speed of Quadro mill (rpm)	2000-3500

Step 5: Blending

Table 6: Parameters for Blending

Load the sized granules in a blender & mix as per below mentioned parameter.	
Stage: Blending	
Parameters	Recommendations
Blender speed (rpm)	16
Blending time (minutes)	10

Step 6: Pre-lubrication:

Table 7: Pre lubrication stage parameters

Load the pre-sifted material of step II to the blended material of step VII in the blender & mix as per below mentioned parameter.	
Stage: Pre lubrication	
Parameters	Recommendations
Blender speed (rpm)	16
Blending time (minutes)	10

Step 7: Lubrication:

Table 8: - Lubrication parameters

Add pre-sifted material of step II to the blender with material of step VIII and lubricate the granules as per following parameters.	
Stage: Lubrication	
Parameters	Recommendations
Blender speed (rpm)	16
Blending time (minutes)	5
Lubricated blend description	White to off-white granules

Step 8: Compression:

Table 9: Compression machine parameters.

Assemble the compression machine with tooling.	
0.4 mg	9.0 mm, round, and concave, beveled edge plain on both sides punches.
After assembling, load the lubricated granules in hopper and compress the tablet as per mentioned below parameters:	
Parameters	Specifications
Description	White to off white, round, uncoated tablet, plain on both sides.
Average weight (mg)	250.000 \pm 5 %
Uniformity of weight (mg)	250.000 \pm 7.5 %
Thickness (mm)	4.20 \pm 0.40
Hardness (N)	80 - 100 N
Friability (% w/w)	NMT 1.0

Step 8: Coating

Core tablets were coated using Opadry Yellow dispersion (in IPA and purified water) in coating machine to achieve a uniform film. Final coated tablet weight: 255 mg.

Table 10: Coating machine parameters.

Film coating dispersion 7 % w/w (IPA: Purified water = 8:2) w/w preparation: Take Isopropyl alcohol in a suitable SS Container; add Opadry yellow under continuous stirring. Add Purified water into it slowly under continuous stirring till homogeneous coating dispersion is obtained. Record the time of mixing (Not less than 45 minutes). Filter the dispersion through #80 sieve ASTM. Load the tablets into coating machine and complete the film coating as per following parameters:		
S. No.	Film Coating Parameters	Recommendations
Pre-warming stage		
	Product temperature (°C)	35 ± 10
	Drum speed (rpm)	8
	Pre-warming time (minutes)	10
Film coating Stage		
	Inlet air temperature (°C)	20 - 70
	Product temperature (°C)	35 ± 10
	Drum speed (rpm)	8
	Spray pump speed (rpm)	5
	Final coat weight builds up (w/w %)	3.0 ± 1.0
Drying stage		
	Inlet air temperature (°C)	20 - 70
	Product temperature (°C)	35 ± 10
	Drum speed (rpm)	2
	Drying time (minutes)	NLT 10
Film Coated Tablet Parameters:		
Film coated tablet parameters		Specifications
Description		Yellow to dark yellow, round, film coated tablet plain on both sides.
Average weight (mg)		250.000 ± 5 %
Thickness (mm)		4.50 ± 0.40

ANALYTICAL METHODS FOR TABLET EVALUATION

Description: Examine 10 tablets in petridish or on a white paper and observe for color, shape, scoring, engraving etc. of the tablets

Identification: By UV: After preparation of Reference and Sample solution. Inject standard solution and sample solution into HPLC system using photo diode array detect in the range of 210 nm to 400 nm of the solution prepared in the Assay. Acceptance Criteria: Absorbance of Solution as prepared in Assay exhibit a single maximum at 225nm.

By HPLC: According to the assay method, the principal peak in the chromatogram of the Reference standard solution and the retention time of the principal peak in the chromatogram of the sample solution match.

Average weight: Weigh twenty tablets precisely. The average weight determined by dividing the total weight by 20. Average weight = $\frac{\text{Total weight of 20 tablets}}{20}$

Weight uniformity: Take 20 tablets taken for average weight. Weigh each tablet individually, select minimum and maximum weight and calculate variation by formula as given below:

For (-) variation (%) = $\frac{(\text{Minimum Weight}-\text{Average weight})}{\text{Average weight}} \times 100$

Average weight

For (+) variation (%) = $\frac{\text{Maximum Weight}-\text{Average weight}}{\text{Average weight}} \times 100$

Average weight

Dissolution: (By HPLC)

Apparatus: Paddle (USP Apparatus-2) with Sinkers (Spring style capsule sinker, 19.3 x 7 mm)

Medium: 0.1 N Hydrochloric acid

Volume: 900 mL Speed: 100 rpm

Temperature: $37.0 \pm 0.5^\circ\text{C}$

Time: a. Routine Time: 2, 6, and 20 hours

b. Profiling Time: 1, 2, 3, 4, 6, 8, 10, 12, 16, 20 and 24 hours.

Stability Studies:

A drug's stability in a dosage form under various environmental circumstances is crucial since it establishes the formulation's expiration date. The drug's instability is indicated by changes in the formulation's texture, taste, color, odor, or physical appearance. On the Basis of physiochemical evaluation of the in-vitro release characteristics, Design Batch trial-5 was chosen for stability tests among the formulations of sustained-release tablets. The stability tests were conducted using $75 \pm 5\%$ at $40^\circ\text{C} \pm 2^\circ\text{C}$.

Powder X-Ray Diffraction study [PXRD]:

Twenty Tablets were taken randomly (sufficient) quantity to get 500mg powder) into a mortar. These Tablets were then triturated gently with the help of a pestle and coating lumps were removed. Then, the fine powder sample was filled uniformly in the groove of the sample holder and the sample was pressed using the back loading sample preparation holder.

Placebo was prepared and run separately. The sample was loaded into the sample magazine placed inside the PXRD instrument and the shutter was closed. The scan was started using the given parameters which are mentioned in the Table 11.

Table 11: PXRD Instruments Parameters

Instrument	X'Pert3Powder
Make	PANalytical
Detector	X'Celerator#
Scan Axis	Gonio
Start position[2 θ]	14.5084
End position [2 θ]	16.4804
Step size [2 θ]	0.0170
Scan step time [s]	2000.2500
Scan Type	Continuous
PSD Mode	Scanning

RESULTS AND DISCUSSION

Tablets parameters after compression:

Wet granulation and dry mixing were used to create tamsulosin tablets. Important quality characteristics like weight variation, hardness, thickness, content consistency, and friability were examined. These tests' results are shown in Table 11.

Table 11: Tamsulosin Tablets Post - compression parameters.

Formulations	Avg. wt.(mg) Mean \pm PXRD	Hardness (N)	Friability (% wt. loss)	Thickness (mm)
1	1534	180.26	0.25	8.15
2	1530	185.11	0.11	8.26
3	1536	189.24	0.65	8.25

4	1534	190.28	0.45	8.22
5	1529	196.18	0.28	8.27

Formulation (Development trials)

In-vitro dissolution data of formulations:

In vitro drug release tests were conducted utilizing the USP Apparatus II (Paddle) with a sinker for the α -adrenoreceptor blocker formulation of Tamsulosin. The test was carried out over a 12-hour period at $37.0 \pm 0.5^\circ\text{C}$ in 900 mL of 0.1N HCl. 5 mL samples were taken out at certain intervals—1, 2, 3, 6, 8, 10, and 12 hours—and an equivalent volume of new dissolving medium was added to keep the conditions constant. Table 50 lists the percentage of drug released at each interval, and Figure 13 displays the drug release curve. Table 12: - Percent drug release data of reference drug and Trials.

Batch no.	Reference drug	Trials containing Tamsulosin				
		Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Time points (Hr.)	%DR	%DR	%DR	%DR	%DR	%DR
1	5	38	24	41	15	8
2	12	46	30	56	28	16
3	28	53	47	69	34	35
6	46	78	65	77	59	51
8	69	86	74	83	71	74
10	87	95	89	96	88	92
12	98	99	100	97	98	101

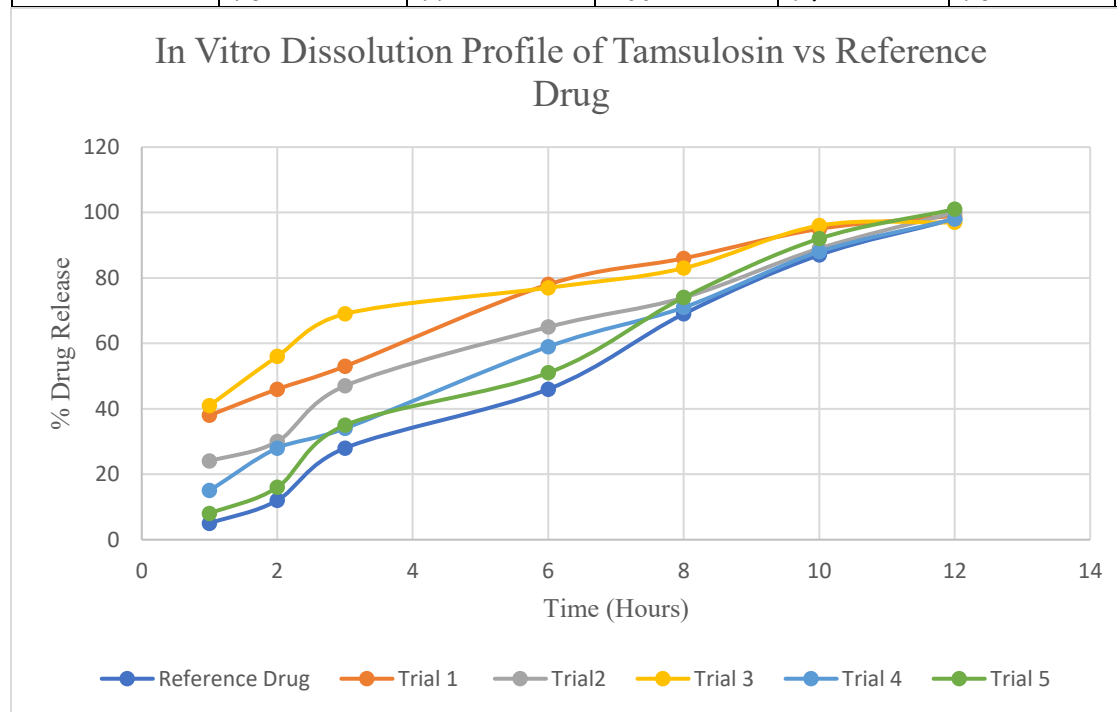


Figure 1: - Comparative dissolution profiles of reference drug and Trial 1, 2, 3, 4 and 5 containing Tamsulosin in 0.1N HCl

RELEASE PROFILE OF TRIAL 5

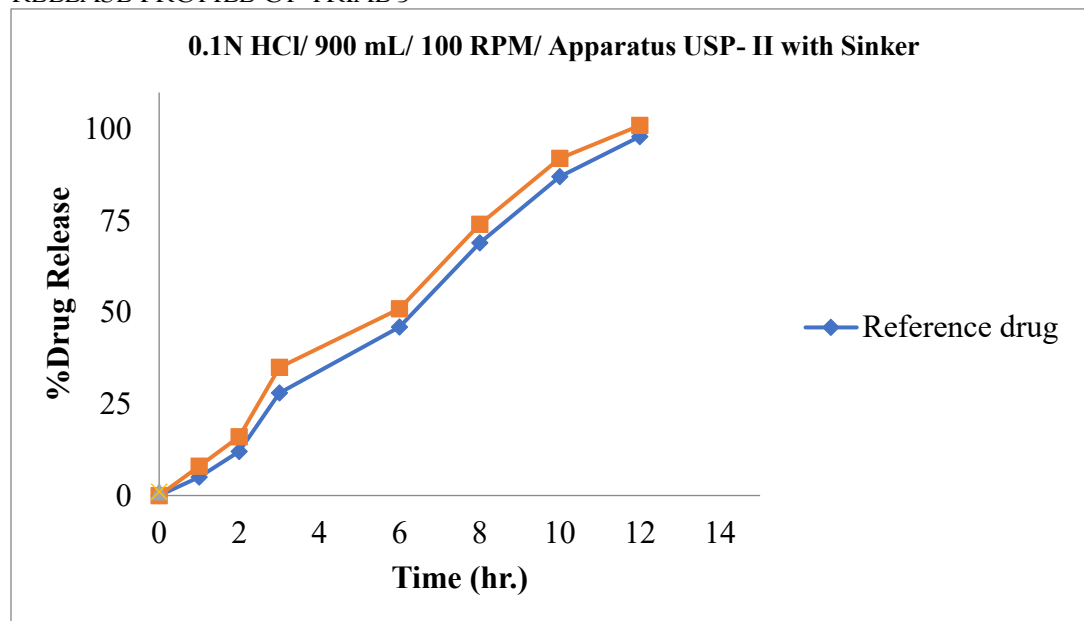


Figure 2: - Comparative dissolution profiles of reference drug and Trial 5 of Tamsulosin in 0.1N HCl
Inference:

In vitro dissolution study revealed that all Tamsulosin matrix tablet formulations (Trial 1-5) demonstrated significantly higher and faster drug release profiles compared to the reference drug. Among them, Trial 5 (Optimized) showed the most desirable release pattern, achieving nearly 100% drug release by the 12th hour, closely resembling a sustained-release profile. This indicates that the optimized formulation has the potential to provide prolonged therapeutic action, improved bioavailability, and better patient compliance when compared to the reference. These findings support the suitability of the developed Tamsulosin formulation for further in vivo evaluation.

Study of Powder X-Ray Diffraction [PXRD]:

The PXRD spectra of formulations containing Tamsulosin showed same characteristic peaks after 3 months accelerated (40°C/75%RH) stability condition.

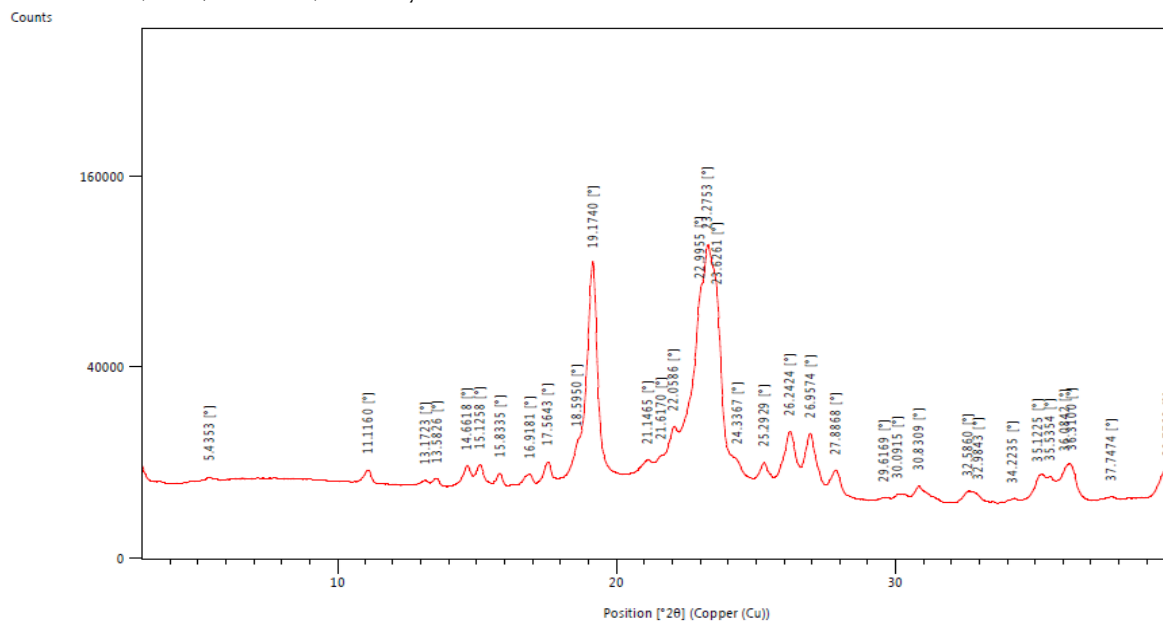


Figure 3: - PXRD Diffractogram of Formulation [Accelerated 3M (40°C/ 75%RH)]

Inference: After 3 months (40°C/75%RH) accelerated stability showed no polymeric conversions when compared with API and drug product samples along containing Drug. The characteristic 2Φ values were found to be intact in drug product formulations up-to 3M stability studies.

Stability studies:

The stability studies carried out at 40°C ± 2°C with 75± 5% for 1.5 and 3 months which are shown in Table 13.

Table 13: - Stability Study Data

S.No.	Tests	Initial	1.5 month	3 months	Specifications (As per USP)
1.	Description	Complies	Complies	Complies	Yellow tablets that are round, biconvex, and have film covering on both sides.
2.	Identification	Complies	Complies	Complies	The assay method determines that the main peak in the chromatogram of the working or USP reference standard solution has the same retention period as the main peak in the chromatogram of the sample solution.
3.	Average weight (mg)	250	250	250	For information
4.	Water content (%w/w by KF)	1.8	1.4	1.7	Not more than 10.0
5.	Related substances	ND 0.1 ND 0.3 0.4	ND 0.2 ND 0.2 0.4	ND 0.1 ND 0.2 0.3	Impurity A: 0.5% Impurity B: 0.5% Impurity C: 0.5% Any individual impurity: 0.7% Sum of all individual impurities: 1.5%
5.	Dissolution: 0.1N HCl, 900 mL, 100 rpm, Apparatus USP- II (Paddle)				
	Tamsulosin	2 hr- 16% 8 hr- 74%	2 hr- 18% 8 hr- 72%	2 hr- 15% 8 hr- 78%	2 hr.- 10-30% 8 hr.- 70-80%
6.	Assay				
	Tamsulosin (0.4 mg)	0.396 mg (99.9%)	0.390 mg (97.5%)	0.392 mg (98.0%)	Not less than 90.0 % and Not more than 110.0 %

Inference: In terms of its average tablet weight, appearance, hardness, drug content, and drug release, the produced formulation did not exhibit any significant modifications. Even after three months of storage, the original medication content didn't change. Additionally, there was no discernible fluctuation in the drug release profile, suggesting the stability of the formulation. Consequently, it can be said that within a three-month period, the formulation stayed stable and retained its medicinal properties. The developed formulation will be subjected to more research.

CONCLUSION

In the current work, different polymers were used to enhance the physicochemical properties of a BCS Class I drug. Polyethylene oxide (PEO) was the polymer that showed the highest dissolution enhancement for the drug under investigation when compared to other polymers that were investigated. The levels of drug: polymer

that were studied showed that the best outcomes were obtained at the 1:0.5 ratio since it had the highest similar drug release out of all the polymers of Screening Batches. The present study successfully achieved its goal to make a prolong release tablet with similar dissolution of the BCS III drug.

In this study, the content uniformity and impurity were a challenge of Tamsulosin. Out of all the polymers Polyethylene oxide (PEO) was chosen as a final polymer on the root of drug release profile and in-vitro results. Among these, Trial 5 with a drug to ratio of polymer of 1:0.5, exhibited the highest drug release in dissolution studies, confirming its efficacy in similar drug release as reference drug. By using final optimized ratio of polymers, it can be converted into Prolong release tablet.

Five different Formulations were being Formulated by using different excipients out of which F5 Formulation is giving the best Results. XRD analysis confirmed that the formulated F5 maintained the characteristic peaks of Drug, indicating no chemical interaction with excipients. Furthermore, dissolution profiles in media showed that F5 closely matched the innovator formulation, meeting bioequivalence criteria. Thus, Trial 5 (1:0.5) was identified as the optimal formulation, offering similar drug release and bioequivalence to the standard product.

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