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Formulation and Evaluation of Tamsulosin Hydrochloride Sustained Release Capsules Using Pelletization Technique

Ayesha Mohammed Abdul Moin[1*], Dr. S. Shobha Rani[1], Dr. K.A. Vijetha[1], M. Nagarjuna[1]

[1]Centre for Pharmaceutical Sciences, JNTUH UCEST, Kukatpally, Hyderabad, India

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***Corresponding author:** Ayesha Mohammed Abdul Moin
Centre for Pharmaceutical Sciences, JNTUH UCEST, Kukatpally, Hyderabad, India

Abstract

Tamsulosin HCl is an αq-1 adrenergic receptor antagonist that is primarily used to treat benign prostatic hyperplasia (BPH), a disease defined by an enlarged prostate. The aim of this project is to develop, analyze, and compare the developed formulations to the innovator product (Flomax). The formulations were prepared by integrating Eudragit L100-55 as enteric polymers in various formulations, Drug coat L30D as a sustained release coating polymer, and PEG 6000 as pore forming in distinct quantities. The formulation F8 exhibited %CDR of 98.8%, comparable to the Flomax (innovator product) and the similarity factor (f2) was calculated and found to be 94.3% marking this formulation equivalent to the innovate product. The improved formulation was tested for stability for the 1st month at 40 ± 2°C and 75 ± 5% R_H, as per ICH guidelines. The regression results of the improved formulation led to an inference that F8 indicates first-order kinetics with an estimated regression value of 0.926, and it was concluded that the drug had been released through diffusion mechanism.

Keywords: Tamsulosin HCl, Sustained release, BPH, pellets, solution layering technique, formulations, drug release.

I. INTRODUCTION

Sustained drug delivery systems are defined as the drug delivery system that are designed to achieve delayed therapeutic effect by constantly releasing medication throughout an extended period of time after administration of single dose. The objective of therapy is to obtain a stable blood level that is therapeutically effective, nontoxic for a sustained length of time and to optimize the delivery of the medications to achieve the desired therapeutic effect. Unlike traditional dosage schedules, a sustained release drug delivery system is made to release medicine gradually over a longer length of time, keeping therapeutic levels in the body for a longer amount of time. By limiting medication level changes and lowering the frequency of delivery, this technique improves patient compliance and maximizes therapeutic effects. Sustained release formulations can accomplish controlled drug release that is customized to the medication's pharmacokinetic profile and therapeutic needs by employing a variety of methods, including matrix systems, reservoir systems, and osmotic pumps. This strategy provides a gentler pharmacological action and minimizes peak concentrations, which not only increases effectiveness but also lessens negative effects. In contemporary medicine, sustained release medication delivery systems are essential because they improve patient care overall and provide answers for chronic illnesses that need long-term care.

Tamsulosin Hydrochloride, chemically is :(-) - (R)-5- [2- [[2- (Ethoxy phenoxy) ethyl] amino] propyl]2-methoxy aromatic hydrocarbon antibacterial drug monohydrochloride. The main purpose of tamsulosin hydrochloride, a selective antagonist of alpha-1 adrenergic receptors, is to treat benign prostatic hyperplasia (BPH). It functions by easing the tension in the muscles surrounding the neck of the bladder and prostate, which enhances urine flow and lessens BPH symptoms including urgency, nocturia, and hesitation. In contrast to non-selective alpha-blockers, tamsulosin hydrochloride is recognized for its selectivity to alpha-1A adrenergic receptors, which are mostly located in the prostate gland. This allows it to treat the underlying source of BPH symptoms with minimal influence on blood pressure. Tamsulosin hydrochloride is usually taken orally as a capsule. It is well tolerated, however typical adverse effects include headaches, dizziness, and retrograde ejaculation.

Benign prostatic hyperplasia (BPH) is a common disorder in which the prostate gland enlarges without becoming malignant in elderly men. Men's prostate glands naturally enlarge with age; this process typically starts at age 40 and lasts the rest of a person's life. This expansion may compress the urethra, resulting in a range of urinary symptoms, including urgency, poor urine flow, hesitation, frequent urination (particularly at night), and the impression that the bladder is not completely emptied. Although the precise origin of BPH is unknown, hormonal changes—specifically, the increased conversion of testosterone to dihydrotestosterone (DHT) inside the prostate gland—are thought to play a role. A person's age, family history, and maybe lifestyle choices are risk factors for developing BPH. While BPH is not malignant and does not raise the risk of prostate cancer, the symptoms it causes can have a major impact on quality of life if not addressed. Treatment options include waiting patiently for moderate symptoms, using alpha-blockers (such as tamsulosin) or 5-alpha-reductase inhibitors, and occasionally undergoing surgery to relieve severe symptoms and enhance urine function.

Tamsulosin hydrochloride sustained-release formulations are preferred for the treatment of benign prostatic hyperplasia (BPH) because of their pharmacokinetic advantages and patient benefits. With these formulations, dosing may be done just once daily, which makes treatment plans easier to follow and increases adherence gradually over a long period of time—usually 24 hours—to maintain steady plasma concentrations all day. This constant dosage level improves patient comfort and quality of life by providing consistent and reliable relief from BPH symptoms than with immediate-release forms that need several daily doses. Sustained-release tamsulosin is a drug that releases including urgency, frequency, and hesitancy in the urine. Sustained-release tamsulosin's regulated release profile may further lessen the likelihood of adverse effects including orthostatic hypotension and dizziness that are brought on by varying medication levels. For the long-term care of BPH, sustained-release tamsulosin is the recommended option due to its convenience, consistent symptom control, and maybe enhanced tolerability.

Eudragit L 100-55 is a methacrylic acid-methyl methacrylate copolymer known for its pH-dependent solubility qualities, which make it excellent for enteric coating in oral medicinal formulations. It keeps medications from degrading in the stomach's acidic environment and guarantees their release in the intestines' higher pH. This polymer is also used because of its ability to form films, which helps with sustained-release formulations by allowing medication release patterns to change over time without compromising mechanical integrity. In order to improve medication stability and efficacy in certain gastrointestinal delivery applications, Eudragit L 100-55 is a recommended option for the creation of enteric-coated and controlled-release dosage forms due to its adaptability and compatibility with a wide range of active ingredients and excipients.

Drug Coat L 30 D is a specialty polymer that is frequently utilized in pharmaceutical formulations due to its film-coating capabilities and ability to adjust drug release patterns. It is a polymer that is part of the Eudragit class and is particularly made up of a dispersion of copolymers of methyl methacrylate and methacrylic acid. The purpose of Drug Coat L 30 D is to give a consistent and stable film coating on tablets and granules, shielding the active pharmaceutical ingredient (API) from oxidation, light, and moisture. Because it may be used to customize drug release kinetics, this polymer is very desired. This allows for controlled-release formulations, which release the medication gradually over time to provide the best possible therapeutic results. Drug Coat L 30 D is a desirable option in pharmaceutical manufacture due to its compatibility with a broad range of APIs and excipients, which guarantees improved stability, effectiveness, and patient compliance through controlled drug delivery systems.

Pelletization is a pharmaceutical manufacturing procedure used to create tiny, spherical particles called pellets, which are employed in a variety of oral dosage forms. In this procedure, medicinal compounds, excipients, and binders are combined using techniques such drug stacking onto inert cores or extrusion-spheronization to form compressed spheres. Because pellets may be coated or encapsulated with polymers or coatings, pelletization has various benefits, such as increased bioavailability, controlled-release capabilities, and improved drug stability. These pellets provide formulation designers flexibility in meeting therapeutic objectives since they may be made to release medications at varying speeds and in certain regions within the gastrointestinal system.

Pelletization of Tamsulosin HCl is the process of producing tiny, spherical pellets containing the active pharmaceutical ingredient (API) Tamsulosin hydrochloride. This method is used to accomplish a number of formulation objectives, including better bioavailability, controlled-release profiles, and increased patient compliance. Tamsulosin HCl pellets are usually made by stacking or extrusion-spheronization techniques. To create evenly sized pellets, a wet mass comprising tamsulosin hydrochloride and excipients is extruded via an extruder and spheronizer in the extrusion-spheronization process. As an alternative, layering procedures are used to produce desired release properties by successively covering inert cores (such sugar spheres) with layers of Tamsulosin HCl and coating materials. Subsequent polymer coatings of these pellets can be applied to regulate medication release rates or provide environmental protection. Tamsulosin HCl

pelletization enables precise drug delivery control, enhanced therapeutic results, and formulation flexibility to address unique patient demands and treatment requirements in the management of benign prostatic hyperplasia (BPH).

II. MATERIALS AND METHODS

Materials

Tamsulosin HCl was obtained a sample from Cohance Lifesciences, Hyderabad, India. Sugar pellets (20#25) were obtained as a sample from Arun Pharma, Hyderabad, Telangana, India. Eudragit L 100-55 was obtained as a sample from Evonik Company, Mumbai, Maharashtra, India. Drug Coat L30-D was obtained as a sample from Vikram Thermo, Ahmedabad, Gujrat, India. PEG 6000 and Triethyl citrate were obtained as a sample from Clariant Pharma, Mumbai, Maharashtra, India. Iso-propyl alcohol was obtained as a sample from Deepak Pharma, Bengaluru, Karnataka, India.

Methods

A. Pre-formulation Studies

1. **Identification of the Drug**: Tamsulosin HCl was identified by using Fourier Transfer Infra-Red Spectroscopy (FT-IR).
2. **API Characterization**: Visual examination and generic procedures were used to examine organoleptic features such as color, odor, and the powder nature of the API.
3. **Drug Solubility**: Because it affects the drug's bioavailability, drug solubility is a crucial physicochemical property. To create a saturated solution, an excess of the drug was taken and dissolved in a predetermined volume of ethanol, methanol, and water in separate glass vials. To achieve equilibrium, the solutions were sonicated and kept at room temperature.
4. **Construction of calibration curve:** For the construction of the calibration curve, 100 mg of Tamsulosin HCl was taken in buffer and dissolved in 100 mL of buffer (stock solution A). A 10mL solution was transferred from the stock solution to a 100mL standard flask, and the volume was increased to 100mL with buffer to obtain a 100 µg/ml solution (stock solution B). Different concentrations ranging between 20, 40, 60, 80, and 100 µg/ml were prepared from the working standard solution, and they were then measured using the HPLC method. Using these data, the concentration on the X-axis and peak area on the Y-axis were used to calculate the calibration curve for tamsulosin HCl.

B. **Method of preparation of Tamsulosin HCl Pellets by using Solution layering pelletization method via fluidized bed process technique**

a. Dispensing: The manufacturing formula was followed when dispensing active pharmaceutical ingredients and excipients.

Formulation Table Showing Design of Tamsulosin HCl

S. No	Ingredients	Category	F1 %w/w	F2 %w/w	F3 %w/w	F4 %w/w	F5 %w/w	F6 %w/w	F7 %w/w	F8 %w/w
1.	Tamsulosin HCl (mg)	API	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
2.	Sugar spheres (mg)	Core	90.48	89.48	88.48	87.28	86.18	85.18	83.98	82.98
3.	Eudragit L100-55 (mg)	S.R polymer	3.0	3.0	4.0	4.0	5.0	5.0	6.0	6.0
4.	PEG 6000 (mg)	Pore former	0.2	0.2	0.2	0.2	-	-	-	-
5.	Triethyl citrate (mg)	Plasticizer	-	-	-	-	0.3	0.3	0.4	0.4
6.	Isopropyl alcohol(ml)	Solvent	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S
7.	Purified water (ml)	Solvent	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S
Enteric coating										
8.	Drug coat L-30D (mg)	E.C polymer	6.0	7.0	7.0	8.0	8.0	9.0	9.0	10.0
9.	Triethyl citrate (mg)	Plasticizer	0.2	0.2	0.2	0.4	0.4	0.4	0.5	0.5
10.	Isopropyl alcohol(ml)	Solvent	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S
11.	Purified water (ml)	Solvent	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S
	Total (mg)		100	100	100	100	100	100	100	100

b. Preparation of Drug Solution: Tamsulosin HCL was mixed with IPA continuously until a uniform suspension is achieved.

c. Preparation of S.R coating solution: For first formulations, Eudragit L100-55 was dispersed in isopropyl alcohol, PEG 6000 was added, then dissolved in water to produce the sustained release coating solution. For the next four formulations, triethyl citrate was added to the purified water while continually stirring until a clear solution was achieved.

d. Coating Process in Fluidized Bed Processor: Sugar spheres or pellets were placed in the FBP bowl and coated with a bottom spray Wurster at 15-20 rpm and 2.0-5.0 Kg/cm². The solution was sprayed, fluidized, and dried for 10 to 15 minutes. The sustained drug-layered pellets are now prepared for enteric coating.

e. Sifting: Coated dried pellets were sifted through the #20 and retains and downs were collected separately. Later #20 passed pellets were sifted through #25 and retains were collected separately.

C. **Loading of Tamsulosin HCl pellets into capsules:** Tamsulosin HCl pellets of 333.33 mg were filled into capsules with an automated capsule filling machine. The pellets were divided into equal segments, and their moisture content was determined prior to filling the capsules.

D. **Evaluation of capsules containing Tamsulosin HCl pellets**

1. **Weight variation test**: The average weight of the 20 intact capsules was determined after a random selection and weight of the samples. Each capsule's individual weight was calculated. The weight of any individual capsule should fall between 90% and 110% of the total weight.
2. **Disintegration Time:** The capsules were placed in the basket rack, which was then repeatedly submerged thirty times per minute into a fluid that is thermostatically controlled at 37ºC and was observed over the period of time in each individual monograph. capsules were completely dissolved into a soft mass with no discernibly firm core and only a few pieces of the gelatin shell in order to pass the test.
3. **In-vitro drug dissolution studies:** Each vessel contains 500mL of dissolution medium, which was allowed to equilibrate to a temperature of "37^0C ± 2^0C". one capsule was placed in each basket, then machine was started running for a predetermined amount of time at 100 revolutions per minute. At regular intervals, 10 mL of the solution was withdrawn from each vessel and replaced with the same volume of fresh dissolving media. After passing the solution through a 0.45-micron membrane filter, drain the first few mL of filtrate. The prepared formulation is dissolution tested in pH 1.2 buffer solution for two hours and subsequently in pH 7.2 Phosphate buffer solution for eight hours. Samples were then analyzed using HPLC for peak area, after which %CDR was calculated. The pH 2.0 solution was prepared by adding sodium hydroxide and perchloric acid to 1900 mL of water. The solution was filtered through a nylon 0.45 m filter. A 1400:600 filtered combination of pH 2.0 solutions with acetonitrile was prepared. Chromatography was performed using a C18 column with a UV detector. **In Acidic Medium:** The study used USP type 1 acidic medium with a 500mL acid stage medium, adjusted rpm of 100, and a 2 hour withdrawal time. The acidic medium was prepared by dissolving hydrochloric acid and sodium chloride, then adding water. The standard solution was prepared by adding a 50 mg Tamsulosin HCl working standard to a 100 mL volumetric flask, then adding the acid medium to a 50 mL volumetric flask. The sample solution was prepared by setting the dissolution medium apparatus's parameters, filling one of the six dissolution jars with tamsulosin HCl, and starting the apparatus. Ten mL of sample was taken out of each jar during the first two hours. The process involved producing one injection of each sample solution, six duplicates of the standard solution, and 100 milliliters of dissolving media. The system's suitability was ensured by recording peak responses for both sample and standard preparations. **In Alkaline Medium:** The study used USP type 1 for dissolution, using 500mL of pH 7.2 Phosphate buffer at 37°C and a time interval of 3-4 hours. The phosphate buffer was prepared by dissolving 6.8g Potassium Hydrogen Orthophosphate and 1.6g sodium hydroxide in 1000mL of water, then adding 2N sodium hydroxide to adjust the pH. The standard solution was prepared by transferring 50 mg of Tamsulosin HCl working standard into a 100mL volumetric flask, adding 10mL of buffer, and sonicating the contents. The sample solution was prepared by draining the solution from each jar and replacing it with an equal quantity of dissolving media. The procedure involved separate injections of dissolving media, six duplicate injections of standard solutions, and one injection of sample solutions. The system was suitable, with peak responses observed for both standard and sample preparations.

E. **Studying Drug Release Kinetics**

In pharmacy, drug release kinetics refers to the analysis of how the drug is released from its dose form over time. This involves assessing the release rate and mechanism to improve therapeutic effectiveness and control. Key models such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas aid in characterizing release patterns and processes, which guide formulation methods for controlled or sustained release systems. Understanding these dynamics ensures that medications be administered at the appropriate rate and concentration for optimal therapy.

i. **Zero order equation:** Zero-order kinetics defines drug release or elimination at a constant rate that is independent of drug concentration. This indicates that the drug is released at a uniform rate over time.
ii. **First-order kinetics:** First-order kinetics refers to drug release or elimination in which the rate of change is proportionate to the drug concentration.
iii. **Higuchi's kinetic model:** The Higuchi kinetic model predicts drug release from solid matrices by assuming a diffusion-controlled process.
iv. **Korsmeyer Peppas kinetic model:** The Korsmeyer-Peppas equation is used to model drug release from controlled-release formulations. It depicts how the proportion of drug released varies over time using a power-law relationship. The equation analyses the release exponent 'n' to determine whether the medication is released mostly by diffusion, polymer relaxation, or a mixture of the two.

F. **Dissolution Profile Comparability (f2 values)**

Differential factor (f1) and Similar factor (f2) are the factors to be determined for comparing dissolution profile. A dissolution profile provides a more accurate description of the product than a single point dissolution test. It provides bio-equivalency and assists with ensuring similarity in product performance. The relationship between the average difference between two profiles and the factor f1 was proportional, while the relationship between the average squared difference and the factor f2 was inverse. The degree of similarity between two profiles is determined by the f2 factor. The FDA has set a public threshold of f2 values between 50 and 100 to indicate similarity between two profiles.

$$f1 = \{\left[\sum_{t=1}^{n}|R_t - T_t|\right] / \sum_{t=1}^{n} R_t\} * 100$$

$$f2 = 50 * Log\{[1 + \left(\frac{1}{n}\right)\sum_{t=1}^{n}(R_t - T_t)^2\ ]^{-0.5} * 100\}$$

G. **Stability Studies**

For all pharmacological dosage forms, it is essential to ensure their stability. Storage under both normal and elevated temperature settings, with the required extrapolations, will be required to ensure that the medication, for the duration of its established shelf life, deliver drugs for absorption at the identical rate as when it was first formulated. Procedural stability studies on the drug substance and its behaviour and attributes should be taken into consideration while designing the actual stability studies for the drug product. Following are storage conditions for studying the stability of the drug: For Accelerated stability the temperature should be 40 ± 2°C and the relative humidity should be 75 ± 5% R_H.For Intermediate stability the temperature should be 30 ± 2°C and the relative humidity should be 65 ± 5% R_H.For Long term stability the temperature should be 25 ± 2°C and the relative humidity should be 60 ± 5% R_H .Testing interval for Initial studies i.e. accelerated conditions are 1, 2, 3, and 6 months for intermediate conditions it is 3, 6, 9, and 12 months for long term condition it is for 3, 6, 9, 12, 18, 24, and 36 months.

III. RESULTS AND DISCUSSION

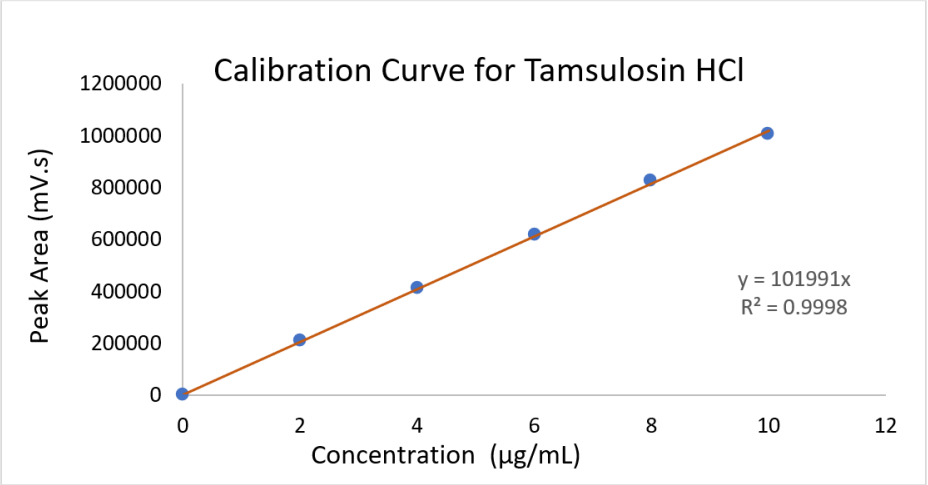
A. Pre-formulation studies

1. **Visual Appearance:** API was physically examined, and it was discovered to be white crystalline powder.
2. **Solubility:** Tamsulosin HCl was immersed in three solution containing methanol, ethanol, and water. It was soluble in ethanol and methanol; insoluble in water.
3. **Calibration Curve for Tamsulosin HCl in Phosphate Buffer (pH 7.2)**

Table showing Calibration curve values for Tamsulosin Hydrochloride

S. No	Concentration (µg/mL)	Peak area (mV. s)
1	0	0
2	2	206710
3	4	413420
4	6	620130
5	8	826840
6	10	1003550

Graphical Representation showing Calibration curve for Tamsulosin HCl



Result: Standard curve of Tamsulosin HCl at 226 nm.

B. **Evaluation Tests**

1. **Visual Appearance:** Pellets were placed in petri dishes and found to be white crystalline solids.
2. **% Moisture content and % Drug assay determination:** Karl Fischer was used for determining the % moisture content and the % drug content for F1-F8.

Table showing %Moisture content and %Drug content (F1-F8)

Formulation	% Moisture Content (standard deviation; n=3)	%Drug Content (standard deviation; n=3)
F1	2.74 ± 0.175	97.6 ± 0.578
F2 x	2.05 ± 0.420	98.0 ± 0.555
F3 x	2.40 ± 0.190	98.2 ± 0.557
F4 x	2.50 ±0.161	98.1 ± 0.610
F5 x	2.32 ± 0.264	98.3 ± 0.552
F6 x	2.46 ± 0.341	98.5 ± 0.350
F7 x	1.81 ± 0.070	98.7 ± 0.307
F8 x	1.72 ± 0.105	99.1 ± 0.205

Result:

- Evaluation assessment of % water content of the above-mentioned formulations was confirmed to be within acceptable limits i.e. 2 ± 1%.
- Evaluation assessment of % drug content for the above-mentioned formulations was found to be within the acceptable limit i.e. 98 + 1%.

3. **Weight variation and Disintegration Time Determination**
   - Following a random selection and sample weight calculation, the weight of the 20 undamaged capsules was obtained.
   - The capsule were then arranged in the basket rack, and the disintegration time was determined.

Table depicting Weight variation and Disintegration time for F1-F8:

Formulation	Weight variation(mg) (+SD) n=3	Disintegration Time(mins) (+SD) n=3
F1	333.34 ± 0.150	5.10 ± 0.209
F2	333.36 ± 0.201	5.59 ± 0.211
F3	333.25 ± 0.310	5.10 ± 0.582
F4	333.45 ± 0.250	5.35 ± 0.412
F5	333.34 ± 0.170	5.39 ± 0.149
F6	333.55 ±0.345	5.11 ± 0.246
F7	333.72 ± 0.230	5.05 ± 0.355
F8	333.37 ± 0.208	5.07 ± 0.114

Discussion:

- All formulations were evaluated for weight variation and determined to fall within the range of 333.33 ± 1 mg.
- All formulations were evaluated for disintegration time and determined to be within the range of 5 ± 1 minutes.

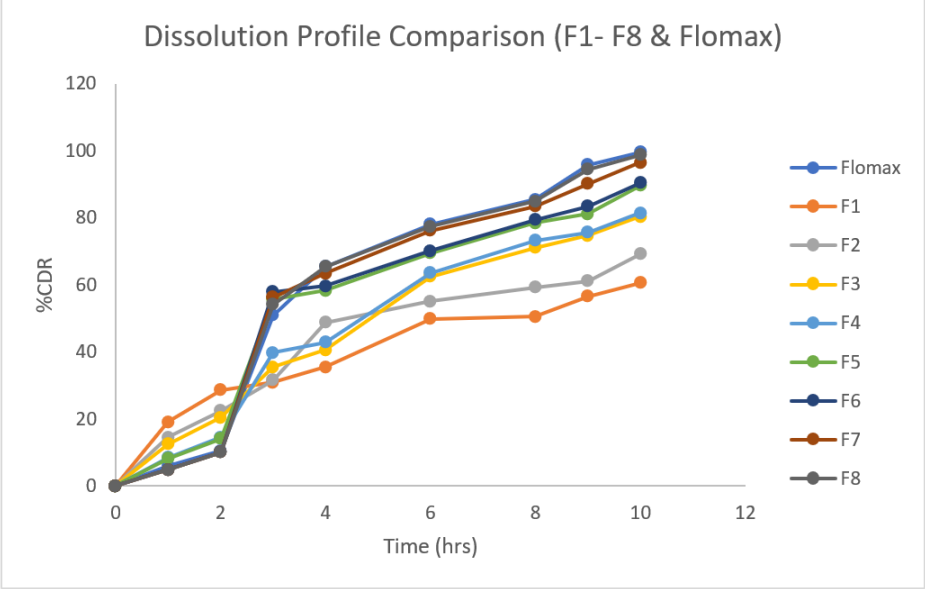
Table showing %CDR comparison between Flomax and all eight formulations

Time (hours)	%CDR								
	Flomax	F1	F2	F3	F4	F5	F6	F7	F8
Acidic Media (pH 1.2)									
0	0	0	0	0	0	0	0	0	0
1	5.9	19.0	14.5	12.5	8.4	8.1	4.8	4.8	4.8
2	10.5	28.6	22.4	20.4	14.5	14.1	10.1	10.1	10.1
Alkaline Media (pH 7.2)									
3	50.9	30.9	31.6	35.5	39.2	55.8	57.8	56.3	54.2
4	65.4	35.5	48.8	40.6	42.7	58.4	59.7	63.5	65.4
6	78.0	49.9	55.1	62.5	63.6	69.5	70.1	76.2	77.4
8	85.4	50.5	59.2	71.1	73.2	78.5	79.4	83.5	84.9
9	95.7	56.5	61.1	74.7	75.6	81.2	83.3	90.2	94.5
10	99.5	60.5	69.2	80.3	81.4	89.5	90.4	96.5	98.8

Table showing % Cumulative Drug Release with standard deviations of all eight formulations

Time (hours)	%CDR ±SD (n=3)							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
0	0.00	0.00	0 .00	0.00	0.00	0.00	0.00	0.00
1	19.0±0.160	14.5±0.153	12.5±0.167	8.4±0.178	8.1±0.165	4.8±0.165	4.8±0.165	4.8±0.175
2	28.6±0.405	22.4±0.175	20.4±0.440	14.5±0.415	14.1±0.422	10.1±0.415	10.1±0.421	10.1±0.418
3	30.9±0.165	31.6±0.165	35.5±0.169	39.2±0.155	55.8±0.174	57.8±0.152	56.3±0.159	54.2±0.150
4	35.5±0.245	48.8±0.147	40.6±0.225	42.7±0.231	58.4±0.245	59.7±0.237	63.5±0.235	65.4±0.235
6	49.9±0.256	55.1±0.224	62.5±0.280	63.6±0.260	69.5±0.284	70.1±0.263	76.2±0.277	77.4±0.266
8	50.5±0.147	59.2±0.252	71.0±0.140	73.2±0.110	78.5±0.120	79.4±0.120	83.5±0.133	84.9±0.121
9	56.5±0.265	61.0±0.279	74.7±0.297	75.6±0.267	81.2±0.275	83.3±0.267	90.2±0.255	94.5±0.277
	60.5±0.135	69.2±0.145	80.3±0.145	81.4±0.132	89.5±0.131	90.4±0.130	96.5±0.128	98.8±0.125

Graphical representation of comparing %CDR between formulations F1–F8 & Flomax



Discussion: F1: The first formulation was based on existing literature. The release in the sustained release coating stage is too low, whereas in the enteric coating stage it is too high when compared to the Flomax dissolution profile.

F2: The second formulation was based on formulation/01. In the enteric coating step, there is better release than with the first formulation. In comparison to the Flomax dissolution profile, the drug release was excessively high during the acid stage.

F3: The third formulation was based on formulation/02. Drug release was better than the second formulation, but it was lower than the Flomax dissolution profile.

F4: The fourth formulation was based on formulation/03. The drug release was partly controlled during the enteric stage, but it was far higher than that of Flomax.

F5: The fifth formulation was based on formulation/04. The drug release was slightly elevated in sustained coating compared to the fourth formulation but it was not equivalent to the Flomax dissolution profile.

F6: The sixth formulation is based on formulation/05. It was regulated in the initial stages of drug release and was consistent with the Flomax dissolving profile.

F7: The seventh formulation was based on formulation/06. The drug release was enhanced compared to the sixth formulation. The medication release was slightly slower than the Flomax dissolution profile.

F8: The eighth formulation was based on formulation/07. Drug release was consistent with the Flomax dissolution profile.

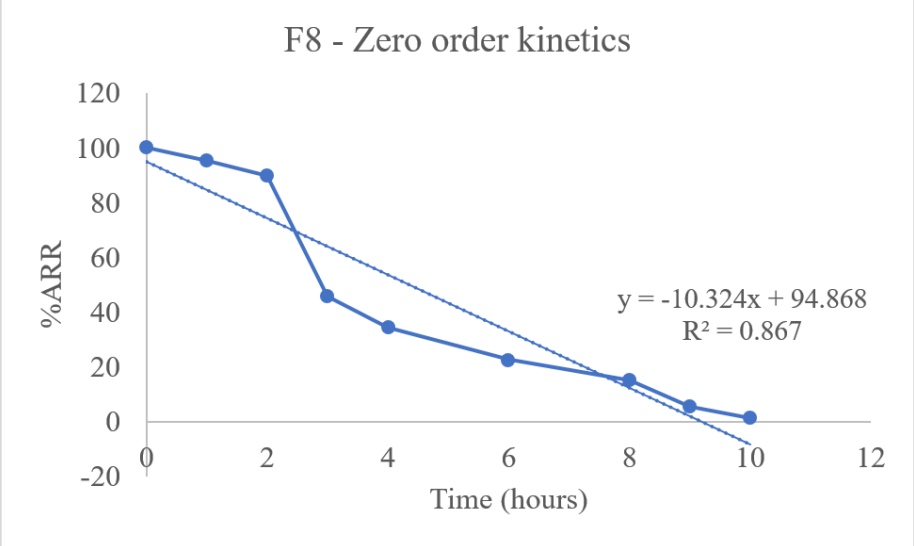
C. Drug Kinetic Studies

Table showing F8 Drug kinetics:

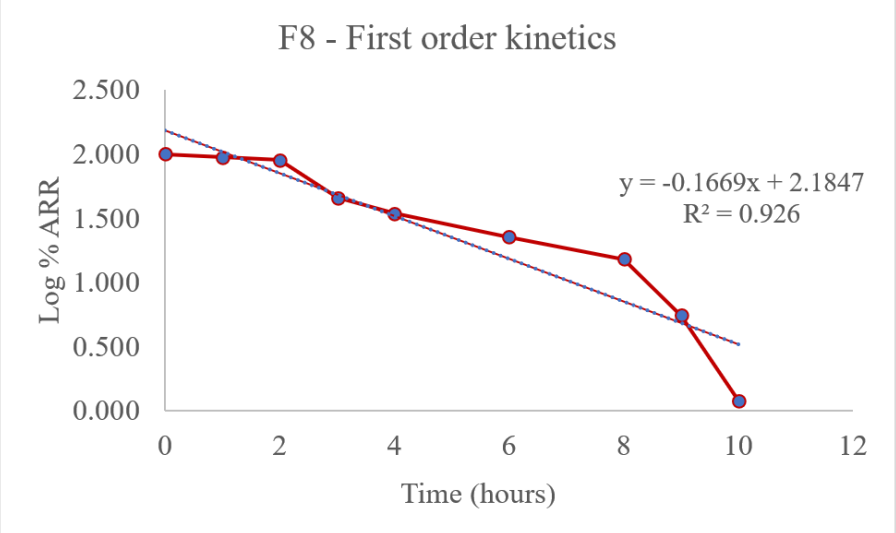
Time (hours)	%CDR	√T	Log %CDR	Log T	%ARR	Log %ARR	(±SD)
0	0.000	0.000	.	.	100.00	2.000	0.000
1	4.800	1.000	0.681	0.000	95.200	1.979	0.175
2	10.100	1.414	1.004	0.301	89.900	1.954	0.418
3	54.200	1.732	1.734	0.477	45.800	1.661	0.150
4	65.400	2.000	1.816	0.602	34.600	1.539	0.235
6	77.400	2.449	1.889	0.778	22.600	1.354	0.266
8	84.900	2.828	1.929	0.903	15.100	1.179	0.121
9	94.500	3.000	1.975	0.954	5.500	0.740	0.277
10	98.800	3.162	1.995	1.000	1.200	0.079	0.125

Dissolution profile of F8 was found to be similar to that of Flomax when compared to all the above formulations.

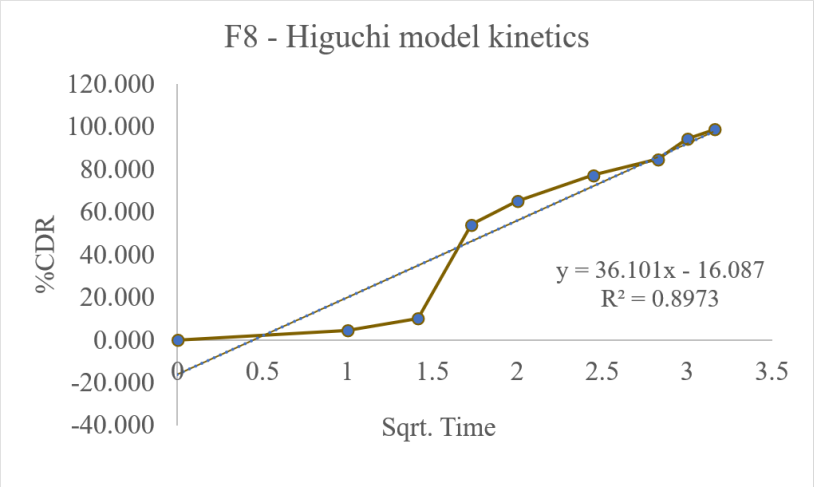
Graph representing zero order kinetics



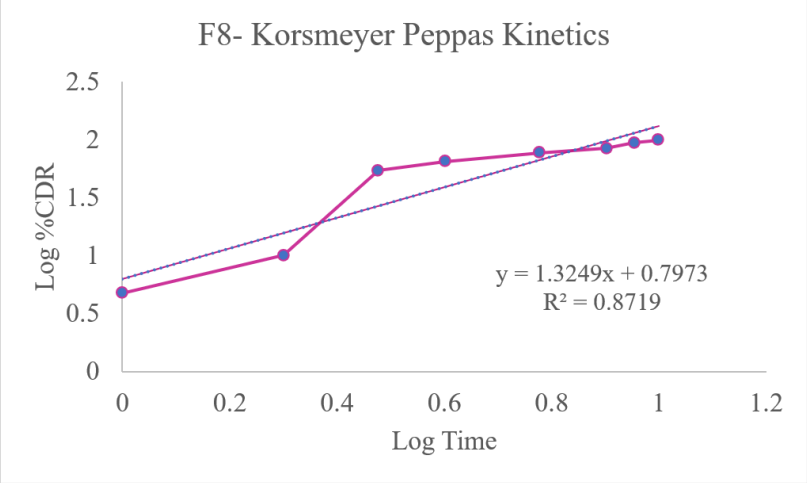
Graph representing First order kinetics



Graph representing Higuchi model kinetics



Graph representing Korsmeyer Peppas kinetics



F8 was found to indicate first-order release, with a regression value of 0.926. It was also observed that the drug was released via diffusion, having a regression value of 0.897 in Higuchi's Kinetics.

D. **f2 VALUE:** The Food and Drug Administration (FDA) established a range of 50-100 for similarities between two distinct dissolution profiles

Table showing f2 values and the similarity factor between F1-F8 & Flomax

Formulation	f2 value	Inference
F1	28.8	Dissimilar
F2	36.1	Dissimilar
F3	39.9	Dissimilar
F4	44.2	Dissimilar
F5	58.8	Similar
F6	62.5	Similar
F7	84.5	Similar
F8	94.3	Similar

Discussion: Formulation8 and Flomax's dissolution profiles were determined to be very comparable with an 94.3% similarity factor.

E. **Stability Studies**

In accordance with ICH requirements, stability investigations of the optimized F8 were conducted for the samples at 40ºC and 75% R_H for a duration of one month.

Table showing F8 Stability Studies data

Tests	Storage Condition	
	Initial	**Final (after 30 days)**
Appearance	No significant change	No significant change
% Moisture Content	1.82 ± 0.101	1.75 ± 0.102
% Drug Content	99.6 ± 0.109	99.25 ± 0.109
% Drug Release	98.6 ± 0.119	± 0.118

Table showing F8 *In-vitro* drug release stability studies data

Time (hours)	Initial	Final (after 30 days)
Acidic Media		
0	0	0
1	4.5 ± 0.180	4.5 ± 0.179
2	9.6 ± 0.409	9.7 ± 0.410
Alkaline Media		
3	55.1 ± 0.149	55.2 ± 0.150
4	64.9 ± 0.240	65.1 ± 0.238
6	77.8 ± 0.259	77.8 ± 0.261
8	86.5 ± 0.121	86.3 ± 0.122
9	95.1 ± 0.259	94.9 ± 0.261
10	98.3 ± 0.124	98.5 ± 0.121

Discussion: The physicochemical properties and drug release of the capsules were observed, and no significant changes were observed.

IV. SUMMARY AND CONCLUSION

Tamsulosin HCl (tamsulosin hydrochloride) is an alpha-1 adrenergic receptor antagonist that is primarily used to treat benign prostatic hyperplasia (BPH), a disease defined by an enlarged prostate. Tamsulosin relaxes the smooth muscles of the prostate and bladder neck by targeting alpha-1 receptors selectively, increasing urine flow and lowering BPH symptoms. It is renowned for its high specificity, which reduces the probability of blood pressure-related side effects, making it a popular choice among many patients.

Development and Evaluation of several formulations of Tamsulosin HCl, carefully comparing them to the innovator product. Assessing parameters like, moisture content, drug assay, weight variation, disintegration, dissolution profiles, and similarity factors, ensuring that the new formulations meet or exceed the performance of the original.

- Tamsulosin HCl were formulated, which were found to be effective and no breakage of pellets was observed.
- % Moisture content of the formulated pellets was determined and found to fall within the limits (2 $\pm$ 1%) i.e. 2.74 $\pm$ 0.175 to 1.72 $\pm$ 0.105%.
- Drug assay was performed and the % drug content was determined and found to be within the value range (98$\pm$1%) i.e. 97.6 $\pm$ 0.578 to 99.1 $\pm$ 0.205%.
- Weight variation of capsules was determined and found to fall within the range (333.33 $\pm$ 1 mg) i.e. 333.34 $\pm$ 0.150 to 333.37 $\pm$ 0.208 mg.
- Disintegration time of the prepared Tamsulosin HCl capsules was determined and found to be in the specified range (5 $\pm$ 1 min) i.e. 5.10 $\pm$ 0.209 to 5.07 $\pm$ 0.114 minutes.
- In-vitro dissolution studies was carried out for the prepared Tamsulosin HCl capsules for F1-F8 formulations pellets were made by integrating Eudragit L100-55 as enteric polymers in various formulations, Drug coat L30D as a sustained release coating polymer, and PEG 6000 as a pore forming in distinct quantities.
- Formulation F8 exhibited drug release of 98.8%, comparable to the Flomax (innovator product) and the similarity factor (f2) was calculated and found to be 94.3% marking this formulation equivalent to the innovator's product.
- The improved formulation was tested for stability for the 1st month at 40 ± 2°C and 75 ± 5% R_H, as per ICH guidelines. The formulation was determined to be stable.
- The regression results of the improved formulation led to an inference that F8 indicates first-order kinetics with an estimated regression value of 0.926 and was also concluded that the drug was released by diffusion mechanism, having a regression value of 0.897 in Higuchi's Kinetics.

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