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FORMULATION DEVELOPMENT AND EVALUATION OF TAMSULOSIN HCL SUSTAINED RELEASE TABLETS BY WET GRANULATION TECHNIQUE

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ABSTRACT

This research work was aimed towards developing an oral dosage form having Tamsulosin HCL sustained release (SR). Compressed tablets were tested for in-vitro drug release as per the official dissolution profile. There are various polymers used in trial and error method, among these Eudragit$_{RSPO}$ and HPMCK$_{100M}$ were taken in the ratio 1:3, had successfully retarded the release of Tamsulosin hydrochloride for 24 hrs in a rate controlled manner. Hence the present work suggests HPMCK$_{100M}$ as suitable rate retarding polymer for control release formulation of Tamsulosin hydrochloride and the study recommends *in vivo* evaluation of the best optimized formula. As per the proto type evaluation results it was concluded that wet granulation is the best possible method of granulation for the present work. Pre-formulation studies were conducted to evaluate the drug and excipients compatibility study. The granules were evaluated for tests like bulk density, tap density, compressibility index before compression.

KEYWORDS

Tamsulosin HCL, Sustained release, Eudragit$_{RSPO}$, HPMCK$_{100M}$ and Pre-formulation studies.

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INTRODUCTION

Oral drug delivery systems are the largest and oldest technology among all drug delivery systems. This is the fastest growing and most preferred mode of drug delivery. Oral drug delivery systems have been known for decades as the most common route of administration among all routes studied for systemic delivery of drugs via various pharmaceuticals in various dosage forms[1-3].

The term modified release drug is used to describe products that alter the timing and/or rate of drug release. A modified-release dosage form is defined as "a selected release of drug over time and/or place to achieve a therapeutic or functional purpose not achieved by conventional dosage forms such as solutions, ointments, or fast-dissolving dosage forms. Defined as "characteristics". Advantages include achieving sustained or sustained release, avoiding gastric release (enteric coating), targeting different parts of the gastrointestinal tract (intestinal delivery) and gastric release[4-9], Drug selection criteria: Selection of compounds with half-life 2-8 hours, no extensive first-pass metabolism, stability in GIT, high partition coefficient Included in GIT[10-16].

Techniques for preparing sustained release formulations

Based on drug modification

Complex Formation

The dissolution rate of solid complexes in biological fluids and the dissociation rate of complexes in solution are taken into consideration and rely on the pH and composition of the gastric and intestinal fluids.

Drug Adsorbent formulation

Insoluble in this product. Drug availability is determined by absorption rate.

Synthesis of prodrugs

These are inactive and require enzymatic hydrolysis for refolding. The prodrug's solubility and absorption should be lower than that of the parent drug.

Ion Exchange Resins

These are water-insoluble cross-linked polymers with salt-forming groups. Drugs are bound to resins using chromatographic columns or by prolonged contact. Drug release from this complex and depends on pH and resin properties[17-20].

The primary objective of this study is to design and develop a solid oral dosage form of tamsulosin hydrochloride at a concentration of 0.8mg. The primary objective of this study was to develop and evaluate a tamsulosin HCL extended-release tablet formulation by wet granulation. Tamsulosin HCL tablets have improved plasma drug control, improved efficacy and safety, maintained drug concentrations within the therapeutic window, and improved patient compliance compared to the novel tablets[21-26].

MATERIAL AND METHODS UTILIZED

Materials used

Tamsulosin hydrochloride (Rachem ltd), Dibasic calcium phosphate dehydrate (Innophos), HPMC K100M (Shin etsu), Eudragit RS PO (Evonik Degussa), Eudragit RL PO (Evonik Degussa), Povidone (ISP, U.S.A), PEG 20,000 (Clarient), Lubritab (JRS pharma), Lactose monohydrate (Rachem ltd), Cross povidone xl 10 (Rachem ltd), Magnesium stearate (Rachem ltd), Iso propyl alcohol (Rachem ltd), Opadry code (Colorcon) were purchased.

Instruments used

Electrical balance (V-Tech), Multiple rotary punching machine (Rimek Phase-I), Vernier caliper (Mitutoya), Hardness tester (Monosanto), Friabilator (Nunes), Hydrolic press hardness tester (Dharma scientific products), Dissolution apparatus (Lab India), Sonicator (bath) (Remi equipment Pvt Ltd), Dryer (Techno- Tray dryer), Micro centrifugator (Remi Rsearch Centrifugur), Micro syringe, Hot air ovan (NSW India), Bulk density test apparatus (Konark Instruments), Cyclo mixer (Rapid).

Methodology

Pre-formulation testing is a study of the physical and chemical properties of the drug alone and in combination with excipients. This is the first rational development of dosage forms. Tamsulosin HCL extended-release tablets have been experimentally tested in wet granulation is suitability. A general evaluation was performed to validate the granulation technique, which can be modified during product manufacturing to provide consistent results for the final product across test batches. The bioequivalence study was performed on innovator samples and was consistent with drug delivery studies.

Procedure for Tamsulosin tablet manufacturing by wet granulation method

Accurately weighed amounts of drug and excipients are taken according to a standard protocol. All excipients were sieved with mesh No.30 and then poured into the dry mixture. These approved materials are mixed in the RMG for 2 minutes. The binding solution is prepared by dissolving povidone, tamsulosin HCl in isopropyl alcohol. The binding solution is slowly poured into the dry mixture to prepare a wet mass. Later, the wet mass is kept in a tray dryer at a temperature of 450°C for 1 hour. Then the mass is passed in half through sieve No.20 (bulk sieve). Then, after drying, these granules are passed through sieve No.20. These granules are lubricated with lubricants and if there are additional granular materials. These granules are compressed into tablets using a compression machine. These tablets are coated with a coating solution.

RESULTS AND DISCUSSION

Pre-formulation Charecterstics of blend of all formulations

Pre-formulation study of the Blend - Bulk density, Compressibility index, Tapped density and Hausner's ratio are given in Table No.1.

Evaluation of tablets

The following parameters of size and shape, thickness, hardness, Friability, Dissolution Study of tablets were performed.

Size and Shape

The size and shape of tablets can be dimensionally described, monitored, and control. The compressed tablet's shape and dimensions are determined by the tooling during compression process.

Thickness

The thickness of a tablet was the only dimensional variable related to the process. 10 tablets were measured for their thickness and diameter with vernier calipers. Average thickness and diameter were calculated.

Hardness

Tablet hardness has been defined as the force required breaking a tablet in a diametric compression test. To perform this test, there is a Tablet Hardness apparatus. The tablet is placed between two anvils, force is applied to the anvils and the crushing strength that just causes the tablet to break is recorded. Hardness is thus sometimes termed as the tablet crushing strength.

Friability

20 tablets were taken and weighed. After weighing the tablets were placed in the friabilator and subjected to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25rpm for 4 minutes dropping the tablets from a distance of six inches with each revolution. After operation the tablets were deducted and reweighed. Physical parameter of tablet compression given in Table No.2.

Dissolution Study

Dissolution Parameters

Medium : 500ml of Acid stage medium and followed by Polysorbate 80 solution

Apparatus : USP Type-II (Paddle)

RPM : 100

Temperature : 37 ± 0.5°C

Time intervals : every 1 Hr once

Preparation of acid stage medium

Dissolve 15.0g of sodium chloride in 43.5mL of hydrochloric acid, and add water to make up to 10000ml.

Preparation of Polysorbate 80 solution

Take 5.0ml of Polysorbate 80 into a 1000ml of water and sonicate to dissolve and makeup 10000ml with volume.

Preparation of diluents

Prepare a mixture of water and acetonitrile in the ratio 70:30.

Preparation of Standard Solution: (Acid stage standard)

Weight accurately about 50mg of Tamsulosin Hydrochloride working reference standard transfer 100mL volumetric flask add 70ml of diluent, sonicate to dissolve the content and make up to the mark with diluent. Transfer 2ml of above solution into a 50ml volumetric flask and make upto the mark with acid stage medium. Transfer 2ml of above solution into a 50ml volumetric flask and make upto the mark with acid stage medium. Filter the solution through 0.45µ membrane filter.

Calibration curve of Tamsulosin Hydrochloride were given in Table No.3 and Figure No.1.

Preparation of Sample Solution

Set the parameters of dissolution apparatus as mentioned above, Transfer the tablets in to an each of the six dissolution vessel, run the apparatus and immediately. Then withdraw the sample as per the time interval from each dissolution vessel and replace the same volume. Filter the solution through 0.45µ membrane filter.

Procedure

Separately inject 100µL of dissolution media, five replicate injections of standard solution and single injection of Sample solutions into the chromatograph, record the chromatograms and measure the peak responses.

Table No.1: Results of pre-formulation study of the blend

Trial	Bulk Density g/cm³	Tapped Density g/cm³	Hausner Ratio	Compressibility Index (%) I=1-V0/V	Angle of Repose (º)
F1	0.56	0.65	1.16	13.84	27.5
F2	0.54	0.63	1.16	14.28	26.8
F3	0.53	0.62	1.15	14.51	26.5
F4	0.52	0.60	1.15	13.5	27.8
F5	0.53	0.61	1.15	13.1	27.6
F6	0.58	0.63	1.14	14.6	26.9

Table No.2: Results of the tablet compression parameters

Trail	Thickness (mm)		Hardness (N)		Friability (% w/w)	
	Min	Max	Min	Max	Min	Max
1	3.89	4.11	67.8	80.1	0.52	0.98
2	3.99	4.33	70.4	75.3	0.43	0.86
3	3.87	4.12	61.3	78.6	0.48	0.92
4	3.95	4.23	64.5	79.3	0.55	0.91
5	3.95	2.14	69.9	77.6	0.41	0.89
6	3.96	4.21	68.8	76.9	0.53	0.85
7	3.88	4.28	72.4	79.9	0.42	0.88
8	3.84	4.17	74.8	78.3	0.49	0.94
9	3.87	4.10	71.2	76.4	0.44	0.91
10	3.91	4.29	63.4	75,2	0.59	0.92
11	3.93	4.20	69.5	76.5	0.57	0.90
12	3.81	4.22	63.4	77.1	0.51	0.81

Table No.3: Standard calibration curve of tamsulosin HCL

S.No	Concentration (µg/ml)	Peak area
1	0	0
2	20	36782
3	40	73160
4	80	141534
5	120	220216
6	160	293103
7	200	376210
8	240	440213

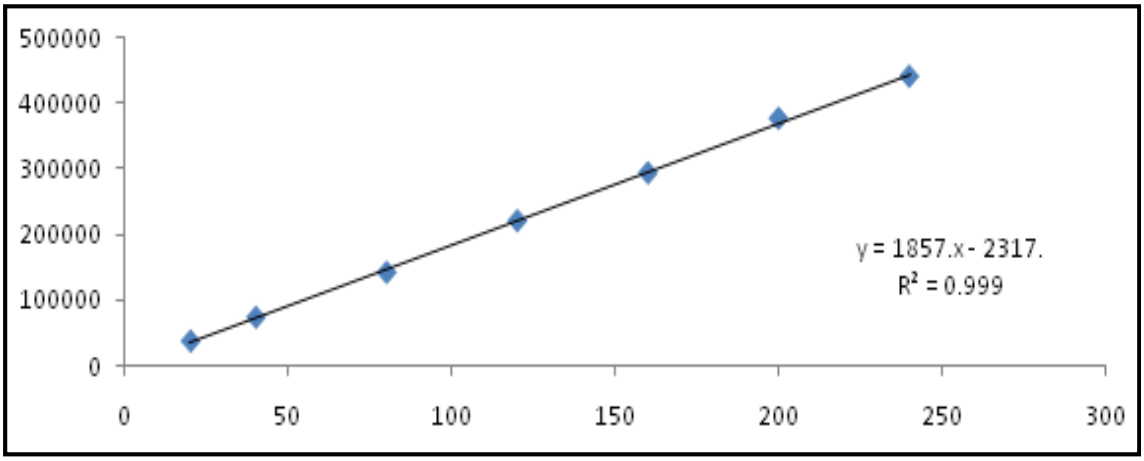

Figure No.1: Standard calibration graph of tamsulosin hydrochloride

SUMMARY AND CONCLUSION

The focus of this research was the development of an oral sustained release dosage form of tamsulosin hydrochloride tablets. Based on the prototype evaluation results, it was concluded that wet granulation is the best granulation method for the current work. A pre-formulation study was performed to verify the compatibility of the drug polymer and excipients, resulting in the confirmation of compatibility between them.

Granules were evaluated in tests such as pre-compression bulk density, tapped density and compressibility. Compressed tablets are tested for in vitro drug release according to official dissolution procedures. Among all dissolution profiles, it was concluded that study 6 using Eudragit$_{Rspo}$ and HPMCK100M in a 1:3 ratio successfully delayed the release of tamsulosin HCl for 30 hours in a rate-controlled manner. Therefore, in this study, we propose that HPMCK100M is a suitable rate-retarding polymer for controlled-release formulations of tamsulosin hydrochloride and this study recommends *in vivo* evaluation of the most optimized formulations.

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CONFLICT OF INTEREST

The entire author's declared as no conflict of interests.

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