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Development of alfuzosin gastro resistant prolonged release tablet and evaluate using HPLC

Singh Jaidev*[1], Agrawal Ankit[2], Singh Gurdeep[1], Gupta M K[1]

[1]Oriental College of Pharmacy & Research, Oriental University, Indore, Madhya Pradesh, India

[2]Chameli Devi Institute of Pharmacy, Indore, Madhya Pradesh, India

ABSTRACT

Alfuzosin belongs to a class of drugs known as alpha blockers. As an antagonist of the alpha 1 adrenergic receptor, it works by relaxing the muscles in the prostate and bladder neck, making it easier to urinate. Alfuzosin gastro resistant prolonged release tablet was prepared as the prepared tablet will improve the bioavailability as well dosing frequency. The prepared gastro resistant prolonged release tablet was evaluated using HPLC. The release profile of each film coated prolonged release tablet contains Alfuzosin HCl IP. 10 mg was found to be range from 23.27 % to 93.58 % from 1st hour to 20th Hour of the release time. From the above study it was concluded that the prolonged release tablet of alfuzosin was found to be effective for long term therapy.

Keywords: Alfuzosin, Gastro Resistant, Prolonged Release, HPLC

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***Address for Correspondence:**

Mr. Jaidev Singh, Research Scholar, Oriental College of Pharmacy & Research

INTRODUCTION

Pharmaceutical invention and research are increasingly focusing on delivery systems which enhance desirable therapeutic objectives while minimizing side effects. Oral drug delivery system represents one of the frontier areas of controlled drug delivery system. Such a dosage forms having a major advantage of patient compliance. Sustained or prolonged release dosage forms are designed to release a drug at a predetermined rate in order to maintain a constant drug concentration for a specific period of time with minimum side effects. Now days as very few drugs are coming out of research and development and already existing drugs are suffering the problem of resistance due to their irrational use specifically in case of drugs like antibiotics.[1,2] Alfuzosin is freely soluble in water[3], and thus readily absorbed after administration. The absorption is significantly aided by the presence of food. The dose of immediate release alfuzosin tablet is 2.5mg thrice daily, elimination half life is 3-5 hr and pka is 8.1.[4] Recently 10 mg once daily extended release formulation has become available in the market[5] which is more convenient for older patients. Marketed alfuzosin formulation is a three layered Geo matrix tablet that requires special facilities, high cost, time consuming and complex operation than conventional formulations. [6] The objective of development activities was to develop pharmaceutically equivalent, stable, cost effective, quality improved and robust formulation of Alfuzosin tablets 10mg.Hence, change in the operation is a suitable and optimized way to make the some drug more effective by slight alteration in the drug delivery. Sustained or prolonged Release is also providing promising way to decrease the side effect of drug by preventing the fluctuation of the therapeutic concentration of the drug in the body. [7]

MATERIALS & METHODS

Table 1: Formulation for uncoated tablets

Sr. No.	Ingredients (Grade)	Standard Quantity per tablet in mg					
Formulation		**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Intragranular							
1	Alfuzosin Hydrochloride* (IP)	10.00	10.00	10.00	10.00	10.00	10.00
2	Microcrystalline cellulose Powder** (USP/BP)	153.10	135.10	65.10	81.10	56.10	54.10
3	Hydroxypropylmethylcellulose K-100M (USP/BP)	20.00	34.00	34.00	22.00	45.00	35.00
Binder							
4	PVP K 30 (USP/BP)	6.000	6.000	6.000	6.000	6.000	6.000
5	Iso Propyl Alcohol (IPA)# USP/BP	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.
Lubrication							
6	Hydroxypropylmethylcellulose K-100 M (USP/BP)	6.00	6.00	10.00	6.00	8.00	20.00
7	Aerosil (Colloidal silicon dioxide) (USP/BP)	0.400	0.400	0.400	0.400	0.400	0.400
8	Purified Talcum (USP/BP)	1.500	1.500	1.500	1.500	1.500	1.500
9	Magnesium Stearate (USP/BP)	3.000	3.000	3.000	3.000	3.000	3.000
Average Total weight		200.0	200.0	135.0	130.0	133.0	130.0

Table 2: Formulation for uncoated tablets

Sr. No.	Ingredients (Grade)	Standard Quantity per tablet in mg		
Intragranular				
1	Alfuzosin Hydrochloride* (IP)	10.00	10.00	10.00
2	Microcrystalline cellulose Powder** (USP/BP)	54.10	48.10	58.10
3	Hydroxypropylmethylcellulose K-100M (USP/BP)	35.00	35.00	30.00
Binder				
4	PVP K 30 (USP/BP)	6.000	12.000	12.000
5	Iso Propyl Alcohol (IPA)# (USP/BP)	q. s.	q. s.	q. s.
Lubrication				
6	Hydroxypropylmethylcellulose K-100 M (USP/BP)	20.00	20.00	15.00
7	Aerosil (Colloidal silicon dioxide) (USP/BP)	0.400	0.400	0.400
8	Purified Talcum (USP/BP)	1.500	1.500	1.500
9	Magnesium Stearate (USP/BP)	3.000	3.000	3.000
Average Total weight		130.0	130.0	130.0
Film Coating				
10	Hydroxy propyl methyl cellulose (HPMC E-15) (USP/BP)	1.900	1.900	1.900
11	PEG 6000 (USP/BP)	0.400	0.400	0.400
12	Colour Titanium Dioxide (IP)	0.500	0.500	0.500
13	Purified Talcum (USP/BP)	0.200	0.200	0.200
14	Isopropyl alcohol (IPA)# (USP/BP)	q.s.	q.s.	q.s.
15	Dichloro methane (MDC)# (USP/BP)	q.s.	q.s.	q.s.
Average Total weight of coated tablet		133.00	133.00	133.00

Remarks:

*API quantity calculated as per Minimum Assay & Maximum Water

**Actual quantity of API after assay & LOD calculation to be compensated using microcrystalline cellulose Powder as filler.

does not appear in the final product.

Manufacturing of Tablet: [8,9]

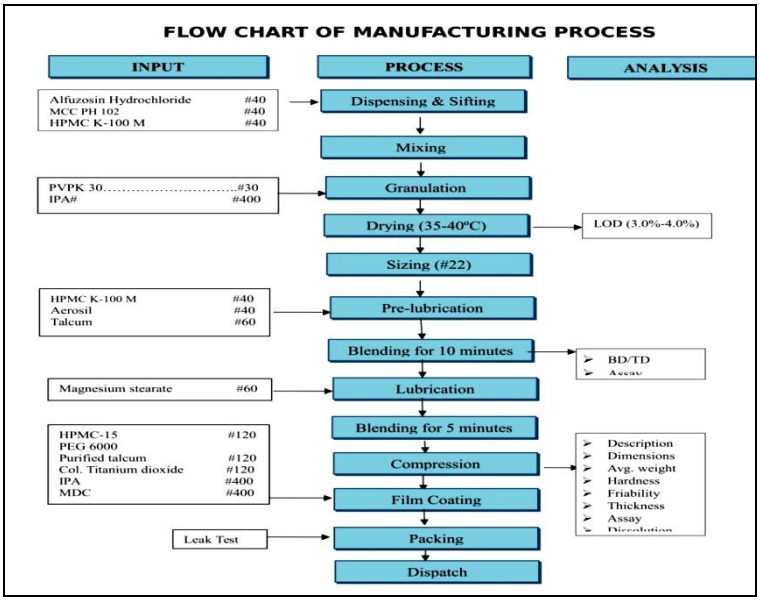


Figure 1: Flow Chart of manufacturing process of Alfuzosin tablets

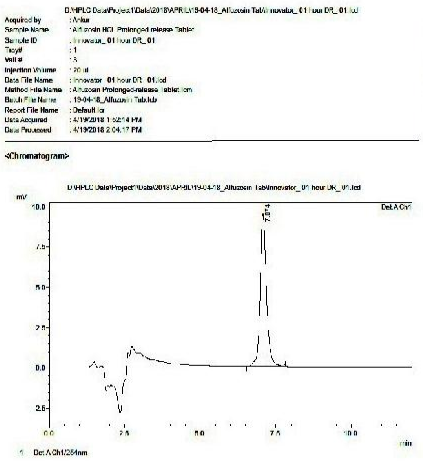
RESULT & DISCUSSION

S. No.	Parameters	Specifications	Results
	Description	White colored round shaped biconvex film coated tablet plain on both sides.	White colored round shaped biconvex film coated tablet plain on both sides.
	Identification of Alfuzosin **(By HPLC)**	In the assay, the retention time of principle peak of Alfuzosin obtained in chromatogram of test solution corresponds to the chromatogram obtained with the Standard Solution.	In the assay, the retention time of principle peak of Alfuzosin obtained in chromatogram of test solution corresponds to the chromatogram obtained with the Standard Solution.
	Average Weight	133 mg ± 5%	126.8 mg
	Uniformity of Weight	Average weight ± 5.0%	Complies
	Dissolution (By HPLC) Each film coated prolonged release tablet contains: Alfuzosin HCl IP.....10 mg eq. to Alfuzosin 1st Hour 6th Hour 20t Hour	 NMT 35 % Between 30 % to 75 % NLT 80 %	 Min : 20.98 % Max : 25.57 % Avg : 23.27 % Min :59.76 % Max : 69.68 % Avg : 64.72 % Min :93.34 % Max : 94.64 % Avg : 93.58 %
	Assay (By HPLC) Each film coated prolonged release tablet contains: Alfuzosin HCl IP.....10 mg eq. to Alfuzosin	95 % to 105 %	% (mg/ Tab)
	Additional Tests Diameter Thickness	7.00 mm ± 0.2 mm 3.40 mm ± 0.2 mm	7.12 mm 3. 48 mm

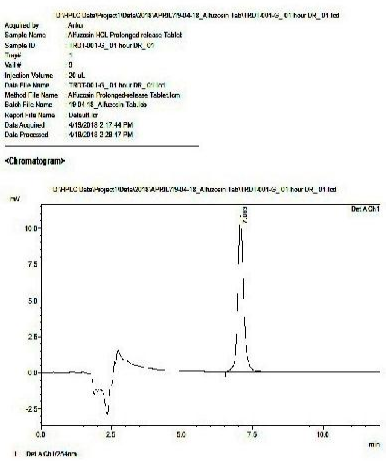
Dissolution Release Profile

Result 1 hour

Reference

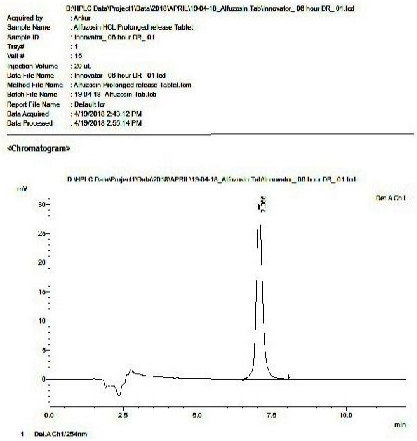


Trial



Result 6 hours

Reference



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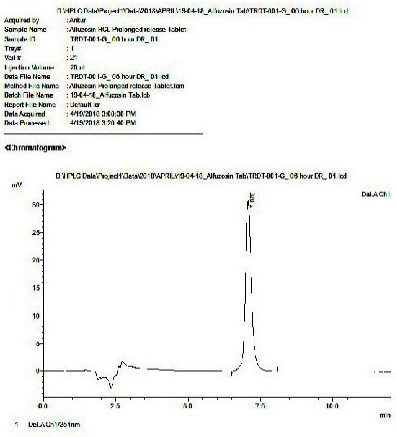

Result 20 hours

Reference

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Acquired by	: Ankur
Sample Name	: Alfuzosin HCL Prolonged release Tablet
Sample ID	: Innovator_ 20 hour DR_ 01
Tray#	: 1
Vail #	: 27
Injection Volume	: 20 uL
Data File Name	: Innovator_ 20 hour DR_ 01.lcd
Method File Name	: Alfuzosin Prolonged-release Tablet.lcm
Batch File Name	: 19-04-18_Alfuzosin Tab.lcb
Report File Name	: Default.lcr
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Data Processed	: 4/19/2018 3:45:10 PM

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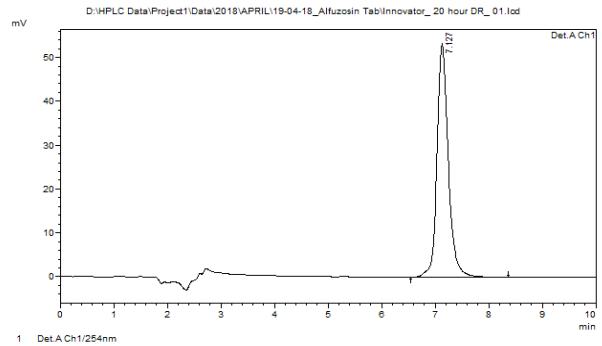

Trial

D:\HPLC Data\Project1\Data\2018\APRIL\19-04-18_Alfuzosin Tab\TRDT-001-G_ 20 hour DR_ 01.lcd

Acquired by	: Ankur
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Sample ID	: TRDT-001-G_ 20 hour DR_ 01
Tray#	: 1
Vail #	: 33
Injection Volume	: 20 uL
Data File Name	: TRDT-001-G_ 20 hour DR_ 01.lcd
Method File Name	: Alfuzosin Prolonged-release Tablet.lcm
Batch File Name	: 19-04-18_Alfuzosin Tab.lcb
Report File Name	: Default.lcr
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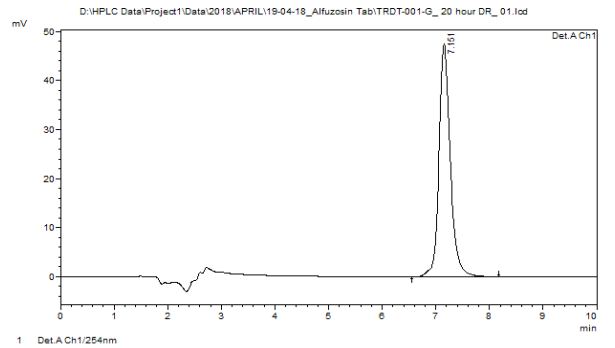

CONCLUSION

There are number of drugs are formulated now in a variety of different per oral extended-release dosage forms. However, only those that will result in a significant reduction in dose frequency and/or a reduction in toxicity resulting from high concentration in the blood or gastrointestinal tract are likely to improve therapeutic outcomes. To formulate a successful extended-release product, the drug must be released from the dosage form at a predetermined rate, dissolve in the gastrointestinal fluids, maintain sufficient gastrointestinal residence time, and may be absorbed at a rate and will replace the amount of drug being metabolized and excreted. The oral extended or prolonged release formulations must have the following properties. They exhibit neither very slow nor very fast rates of absorption and excretion. They are uniformly absorbed from the gastrointestinal tract. They are administered in relatively small doses. They possess a good margin of study and they are used in the treatment of chronic rather than acute conditions.

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