Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 13 [4] March 2024: 108-114

Online ISSN 2277-1808
Journal's URL: http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

A Comparison and Evaluation of B1- Selective Blocker Atenolol Generic Vs Brand Tablets

Yuvaraj .J[1], Karthikeyan B[2] And Balamurugan K[3*]
[1]Department of Pharmacy, FEAT, Annamalai University, Annamalai Nagar, Chidambaram – 608 002, Tamil Nadu, India.
[2]School of Pharmacy, Sri Balaji Vidyapeeth, SBV campus, Pillaiyarkuppam, Pondicherry - 607 402.
[3*]Department of Pharmacy, FEAT, Annamalai University, Annamalai Nagar, Chidambaram - 608002, Tamil Nadu, India
Corresponding Author: Email: placementbala@yahoo.co.in

ABSTRACT
Branded medicine is the original product that has been developed by a pharmaceutical company and generic medicine is a copy of the original branded product, marketed after the expiry date of the patent and hence supposed to be of low cost as compared to their branded versions. The main objective to undertake this study is to show a comparison between branded and generics products of Atenolol tablets. The study includes some of the specifications that should tested in the finished products in tablets such as appearance, thickness, diameter, weight variation, hardness, friability, disintegration time, dissolution, hardness and thickness as per pharmacopoeial & non pharmacopoeial tests were performed. The generic and brand Atenolol tablets quality control results showed within the range as per IP. Drug release of generic tablet was found to be satisfactory. Hence, it can be concluded that tablets were all found to be as per pharmacopoeial requirements.
Keywords: *Atenolol, generic, brand, quality control test*

Received 23.12.2023 Revised 22.01.2024 Accepted 04.03.2024

INTRODUCTION

Dosage form indicates a formulation that typically contains the API(s) and excipients in quantities and physical form designed to all the accurate and efficient administration of the API to the human or animal.[1] A variety of common dosage forms are available, such as pills, tablets, capsules, drinks, syrups, aerosols, inhalers, liquid injections, powder, solid crystals, and natural or herbal forms like plants or foods [2]. The dosage form of the chemical determines the route of administration for drug delivery. Heart arrhythmias, myocardial infarction, angina pectoris, and hypertension are all commonly treated with atenolol, a beta 1-selective blocker [3]. Several Pharmacopoeias emphasis atenolol biopharmaceutical property as being sparingly to little soluble in water [4]. Atenolol could be categorically placed in BCS Class III based on the biopharmaceutical data. The generic drugs are the copy of branded drugs whose patent has expired and the branded drugs is the original product that has been developed by innovator of a pharmaceutical company. Both products have same active ingredients, dosage form quality and performance and generic drug are manufactured by different pharmaceutical companies under different brand names and sold under different cost either lesser or cost subsidized. Still a significant proportion of lay people, doctors and pharmacists hold negative perceptions of generic medicines, perceiving generics as less effective, less safe, inferior in quality and more likely to cause side effects compared to their branded equivalents. The aim of present studies to throw away the blind belief of many people that branded drugs show better therapeutic activity than the generic drugs [6]. All the quality control tests for the pharmaceutical products are tested both in generic and brand drug as the pharmacopoeial specification are in-house specification as per pharmaceutical company [7]. To keep in mind the above false suspect, the current studies aim the comparison and evaluation of beta 1- selective blocker atenolol tablets generic and brand to throw away the blind belief of many people that branded medications have better therapeutic efficacy than the generic medications

MATERIAL AND METHODS

In the present study we are analyzing antihypertensive drug (atenolol) used for treating hypertension. There are many brands of Atenolol tablet (Aten (Zydus Cadila), Tenolol (Ipca Laboratories), Tenormin (Abbott) and etc.,] of different formulation bases and manufacture origin are present in the market, in our study one of the Atenolol which has same strength of generic and brand product was selected.

Drug Profile

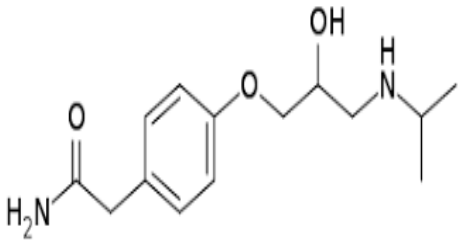

Fig 1: Structure of Atenolol

The IUPAC name - (RS)-2-{4-[2-Hydroxy-3-(propan-2-ylamino) propoxy] phenyl}acetamide ($C_{14}H_{22}N_2O_3$), molar mass 266.341 g·mol^{-1} [8]. Category is a antihypertensive, it is bioavailability 45% - 55% through oral. Administration routes includes oral and intravenous.

Mechanism of action

Cardio selective beta-1-adrenergic antagonists such as atenolol work by selectively binding to the beta-1 adrenergic receptors found in vascular smooth muscle and the heart, blocking the positive inotropic and chronotropic actions of endogenous catecholamines such as isoproterenol, norepinephrine, and epinephrine, Thereby reduces SNS stimulation of the heart [9], decrease heart rate [10], prolong sinoatrial (SA) node recovery [11], slow conduction rate through the AV node and decrease myocardial contractility, thus reducing myocardial oxygen demand [12].

Chemicals and reagents

The Atenolol tablets (both generic and brand) were purchased from one of the reputed pharmacy in Chidambaram, cuddalore district. Atenolol tablets manufactured by Zydus health care Ltd for brand and Pharmaceuticals and Medical Devices Bureau of India (PMBI) for generic tablets were selected in the research. Ingredients used were of analytical grade (AR grade) obtained from S.D Fine chemicals, Mumbai, India. Class A glassware's (Borosil Ltd., Mumbai, India) were used throughout the research work.

Methodology

Atenolol 25 mg uncoated tablet of both generic and brand was subjected for quality control test as per Indian pharmacopoeia 2018 [14].

EVALUATION TESTS FOR TABLETS

Tablets appearance

20 tablets were selected and visually inspected for their external characters such as color, shape, surface texture and shape, presence of grooves and surface defects [14].

Weight variation (%)

Twenty tablets from generic and brand were weighed individually using electronic balance (Shimadzu). Their individual weights (W_1) were measured and recorded. The average weight (W_A) of each sample was calculated and the deviation of each tablet weight from the average weight was determined.

$$\% \text{ weight variation} = (W_1 - W_A) \times 100 / W_A \text{ [14]}$$

Thickness (mm)

10 tablets from the representative sample were taken and individual tablet thickness was measured by using digital vernier calipers (Labpro). Average thickness and standard deviation values were calculated [14].

Hardness (kg/cm^2)

Tablet hardness was measured by using hardness tester (pfizer). From generic and brand, 10 tablets were observed and recorded for the hardness and average of ten values were noted along with standard deviation [14].

Friability (%)

6 tablets from generic and brand were accurately weighed and placed separately in the Roche friabilator (Erweka, Germany). Apparatus was operated at 25 rpm and tablets were observed while rotating. The tablets were taken after 100 rotations, de-dusted and reweighed. The friability was calculated as the percentage of weight loss.

$$\% \text{ Friability} = (W_1 - W_2) \times 100 / W_1$$

Where, W_1=Initial weight of tablets,
W_2=Final weight of tablets [14].

Disintegration time (min)

Disintegration time is considered to be one of the essential criteria in selecting the best formulation. The study was carried out using USP type II (Erweka,Germany) dissolution apparatus(paddle type) with water buffer as the disintegration medium. The medium was maintained at 37±0.5ºC at 28-32 cycles/min. The time point at which tablet completely disintegrates is noted as Disintegration time [14].

In-vitro dissolution studies

Drug dissolution testing is routinely used to provide critical in vitro drug release information for both quality control purposes [13]. The Atenolol tablets are added to 900ml of dissolution media (phosphate buffer PH 7.4: Dissolve 6.8 g of potassium dihydrogen orthophosphate and 1.56 g of sodium hydroxide in 900 ml of water adjust the pH 7.5 with sodium hydroxide solution and dilute with water to produce 1000 ml)[14]. Contained in USP dissolution apparatus II and stirred at a speed of 60rpm at 37 ± 0.5 °C. 10ml aliquots were withdrawn at interval of 10, 20, 30, 40, 50, 60 min and replaced by 10ml of fresh dissolution media (37 °C). The samples were collected and analyzed after suitable dilution at 241nm using Shimadzu 1700 UV-Visible spectrophotometer [13].

Assay of Atenolol tablet

Weighed and powdered 20 tablets and equivalent quantity of the powder containing 0.2 g of Atenolol, transferred to a 500 ml of volumetric flask using 300 ml of methanol, heated the resulting suspension to 60^0C and shacked for 15 min. Cooled, diluted to 500 ml with methanol, filtered through a fine glass micro-fibre filter paper (Whatman GF/C) and diluted a suitable volume of filtrate with sufficient methanol to produce a solution containing 0.01 per cent w/v of Atenolol. Measured the absorbance of the resulting solution at the UV-spectroscopy at about 241 mm. calculated the content of $C_{14}H_{22}N_2O_3$ taking 97 as the specific absorbance at 241 nm [14].

UV Method

Preparation of standard stock solution

To prepared standard stock solution of Atenolol, weigh the drug sample and dissolve it in a 100ml volumetric flask. Add methanol as a solvent to bring the volume up to 100ml, which will yield a concentration of 100µg/ml.

Preparation of calibration curve and λmax of Atenolol determination

Fresh aliquots were pipette out of the above-prepared standard stock solution and properly diluted with methanol to obtain a final concentration in the range of 5–30µg/ml. After scanning the generated dilutions between 200 and 400 nm in wavelength, a strong peak was detected at 241 nm. Calibration curve was plotted by taking concentration of solution on the x-axis and its absorbance on the y-axis [15].

Procedure

Weigh about 20 tablets of Atenolol, powdered and weighed equivalent amount of drug about 10mg and transferred into a 100ml volumetric flask. Then, pour the mixture into a 100 ml volumetric flask. Methanol was used to make up the difference in the final volumes. Followed filtration in using Whatman filter paper, the absorbance of the solution was determined by contrasting it with a blank.

RESULT AND DISCUSSION

Table 1: Label contents

Item	Cost of tablets - For 14 tablets Rs.	Batch No.	Manufacture Date	Expiry Date	Manufacturer
Generic	6	ATCT1006	11/2022	10/2024	Pharmaceuticals and Medical Devices Bureau of India (PMBI)
Brand	27.90	1301582	04/2023	03/2025	Zydus Health Care Limited

Table 2: Result of appearance features of the different brands of Atenolol 25 mg tablets

Parameter	Generic	Brand
Shape & Color	Round & white	Round & white
Surface texture & Convexity	Smooth & flat with beveled edges	Smooth & flat with beveled Edges
Presence of cracks & chips	None	None

Table 3: Evaluation test for Tablets

Evaluation Test for Tablets								
Drug	**Average weight (mg)**	**% weight variation**	**Hardness test**	**Thickness test**	**Friability**	**disintegration test**	**Dissolution rate**	**Assay**
	Standard as per IP	7.5%	3-10 kg/cm^2	± 5 %	<1%	30min	Not less than 70%	90-110%
Generic	185	3.120	6.7	0.426	0.904	1min 7sec	98.72	98.18
Brand	188	2.955	6.9	0.413	0.713	1min22 sec	99.09	106.03

Table 4: Results of Calibration curves data of Atenolol using pH 7.4 phosphate buffer

S.no	Concentration (µg / ml)	Absorbance
1	5	0.015
2	10	0.034
3	15	0.058
4	20	0.071
5	25	0.095

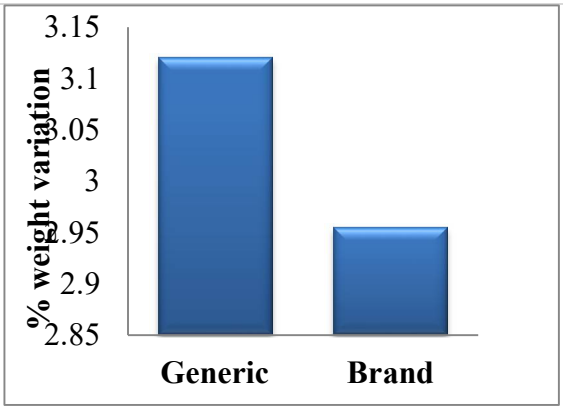

Fig 2 : % of weight variation of Atenolol tablets

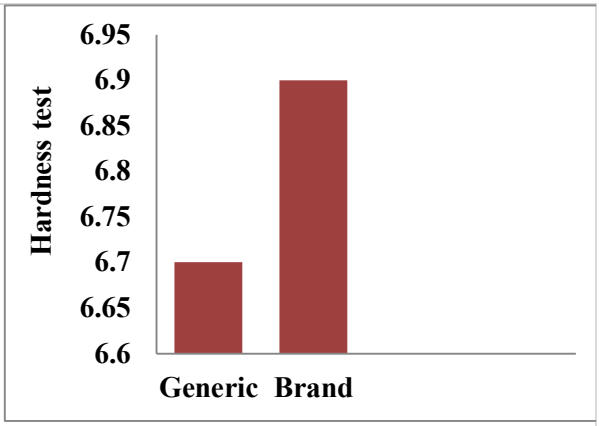

Fig 3 : Hardness of Atenolol tablets

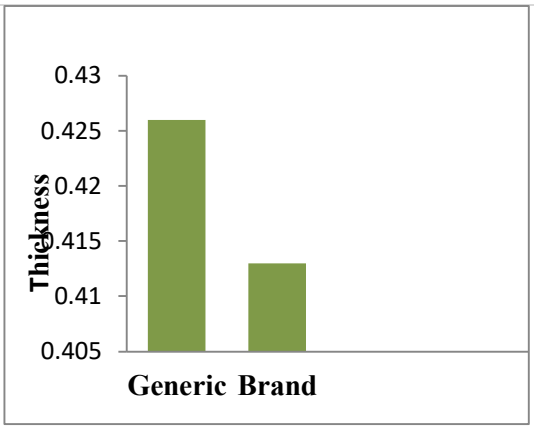

Fig 4 : Thickness of Atenolol tablets

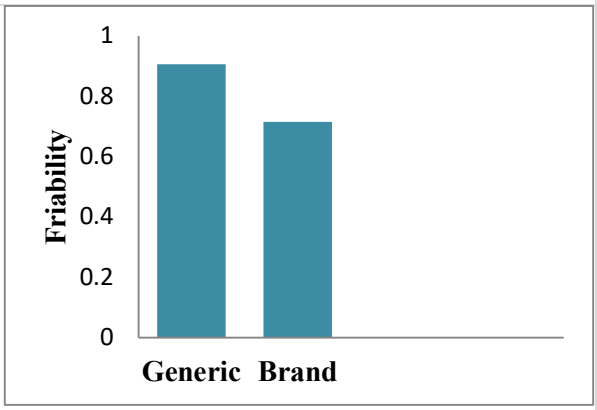

Fig 5 : Friability of Atenolol tablets

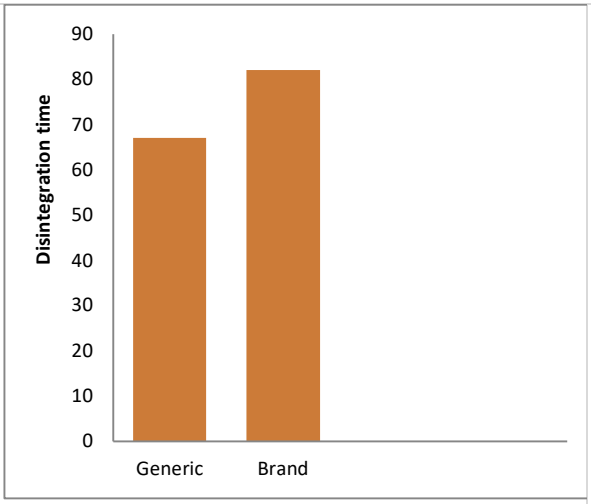

Fig 6 : Disintegration time of Atenolol tablets

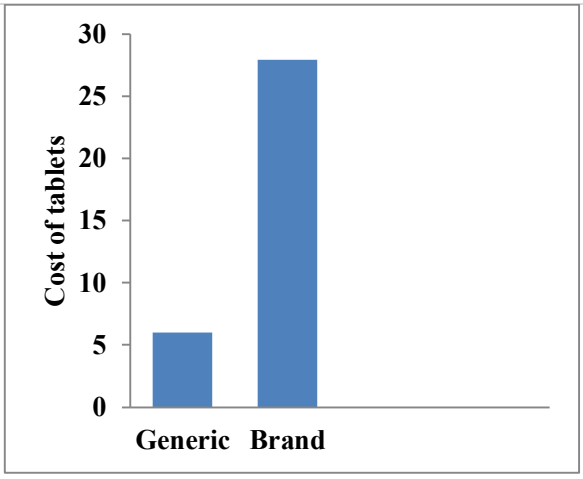

Fig 7 : Cost of Atenolol tablets

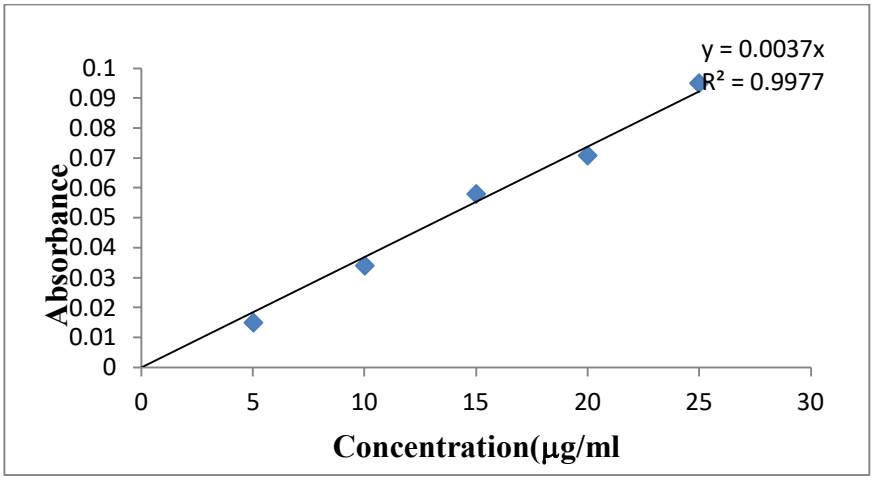

Fig 7: Calibration curve of atenolol drug

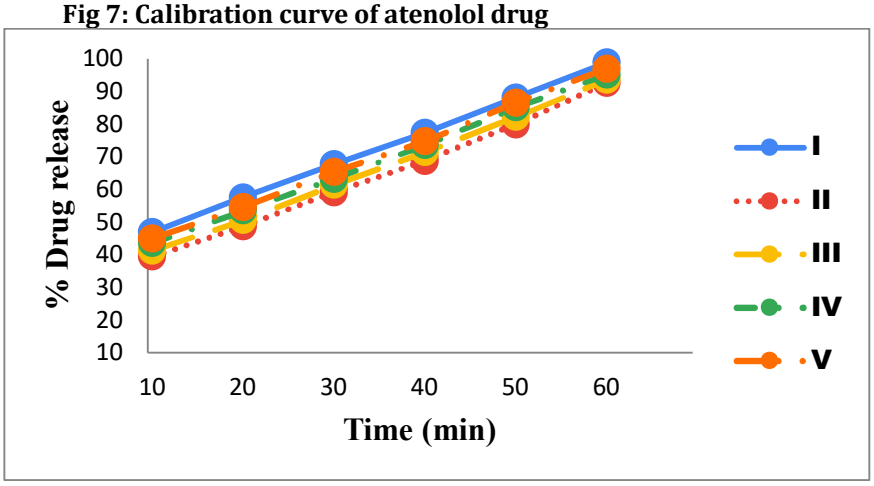

Fig 8: Dissolution profile of generic drug

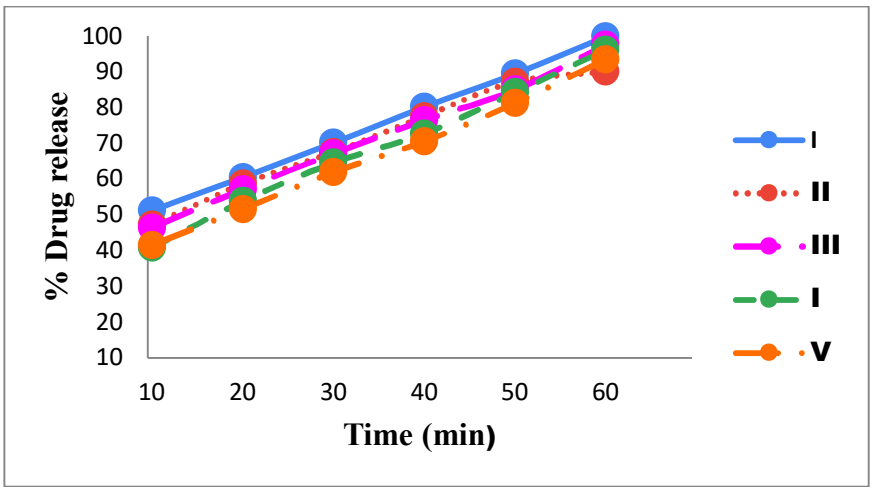

Fig 9: Dissolution profile of brand drug

The results of our research work conducted on generic and brands of antihypertensive atenolol tablets, met the IP requirements of quality control tests within specified limits. The various physical parameters of tablets like Shape (brand -round, generic-round) & Color (brand --white, generic-white, Surface texture (brand -smooth, generic- smooth) & Convexity (brand –flat with beveled edges, generic - flat with beveled edges) presence of cracks & chips (brand -none, generic--none). The various physical parameters of tablets like weight variation (brand –1.716%, generic-1.519%), hardness (brand –6.9 kg/cm^2, generic-6.7 kg/cm^2), thickness (brand –0.426%, generic - 0.413%), friability (brand - 0.904%, generic-0.713%), dissolution(brand –99.09%, generic - 98.72%), assay (brand -106.03%, generic - 98.18%) and disintegration time (brand –1min 22sec, generic-1 min 7sec) for both generic and brand tablets were found to be similar in appearance. There were no cracks and chips in any of the tablets. Cost of the generic tablet was Rs 6 per 14 tablets, whereas cost of the brand tablet was found to be Rs 27.90 per 14 tablets. The generic tablet was cheaper than branded tablets. Drug release of generic tablet was found to be 95.3 % in 60 min which is comparatively lesser than the branded tablets which showed drug release 98.8% in 60 min. Hence, it can be concluded that tablets were all found to be as per pharmaceutical specifications.

CONCLUSION

Finally, research concludes that generic and branded medications shown equal outcomes. Thus, it would be wise to prescribe the drug's generic version more frequently in order to lower prescription costs and make therapy more affordable. The generic tablet was less cost than branded tablets. Always for better therapy as per USFDA *in vitro – in vivo* correlation (IVIVC) can be predicted mathematical model describing the relationship between the *in vitro* property of an oral dosage form and relevant *in vivo* response. However, the *in vitro – in vivo* correlation (IVIVC) allows prediction of the *in vivo* performance of a pharmaceutical product based on its *in vitro* drug release profiles and can be used to optimize formulations, set dissolution limits, reduce the number of bioequivalence studies during product development, and facilitate certain condition. In our research manual laboratory equipment's were used for the studies and should be correlated with digital and modern equipment's. Generic medicine contains the same active ingredient that had undergone all clinical trials and quality testing during its patent when it was manufactured by a brand as the non-generic medicine. Therefore, these are considered to be safe further the Pharmacovigilance centers monitor the safety and side effects of medications.

REFERENCES

1. Loyd V. Allen, Jr, (2018). Ansel's pharmaceutical dosage forms and drug delivery systems. Lippincott Williams Wilkins; 2018 Dec 23.
2. Solate JT. (2020). Dictionary of Pharmaceutical Dosage Forms. CRC Press; Nov 11.
3. Beţiu AM, Noveanu L, Hâncu IM, Lascu A, Petrescu L, Maack C, Elmér E, Muntean DM. (2022). Mitochondrial effects of common cardiovascular medications: The good, the bad and the mixed. International Journal of Molecular Sciences. 7;23(21):13653.
4. Husain T, Shoaib MH, Ahmed FR, Yousuf RI, Farooqi S, Siddiqui F, Imtiaz MS, Maboos M, Jabeen S. (2021). Investigating halloysite nanotubes as a potential platform for oral modified delivery of different BCS class drugs: characterization, optimization, and evaluation of drug release kinetics. International Journal of Nanomedicine. 1:1725-41.

5. Usman, Shahnaz. (2014). Biowaiver Studies of Atenolol Tablets (100mg) - An Alternative to In Vivo Bioequivalence Studies. Natural Products Chemistry & Research. 2. 10.4172/2329-6836.1000125.
6. Jain A, Chaudhary J, Saini A, Mehan N. (2019). Quality assessment and comparative study of different marketed brands of metformin. Research Journal of Pharmacy and Technology.12(3):1357-60.
7. Warthin IK, Berik J, Podolsky D, Raghavendran V, Reddy R, Chang J, Porter N, Garito N. (2020). Commentary on the benefits of US pharmacopeial standards: a generic pharmaceutical industry survey. Journal of pharmaceutical sciences. 1;109(2):944-9.
8. Singh M. (2019). Enantiomeric separation of (RS)-Atenolol Using (S)-Ibuprofen as Chiral Derivatizing reagent. Think India Journal. 22(37):1371-6.
9. Sree Ranjani P. (2010). Design and Development of Proliposomal Dry Powder Inhalation for Pulmonary Delivery of Antihypertensive Drug (Doctoral dissertation, CL Baid Metha College of Pharmacy, Chennai).
10. Ostrom KF, LaVigne JE, Brust TF, Seifert R, Dessauer CW, Watts VJ, Ostrom RS. (2022). Physiological roles of mammalian transmembrane adenylyl cyclase isoforms. Physiological reviews. 1;102(2):815-57.
11. Dashwood A, Cheesman E, Beard N, Haqqani H, Wong YW, Molenaar P.(2020). Understanding how phosphorylation and redox modifications regulate cardiac ryanodine receptor type 2 activity to produce an arrhythmogenic phenotype in advanced heart failure. ACS Pharmacology & Translational Science.1;3(4):563-82.
12. Federico M, Valverde CA, Mattiazzi A, Palomeque J. (2020). Unbalance between sarcoplasmic reticulum Ca2+ uptake and release: a first step toward Ca2+ triggered arrhythmias and cardiac damage. Frontiers in physiology. 23;10:1630.
13. Iman IS, Nadia AS, Ebtsam MA. (2010). Formulation and stability study of chlorpheniramine maleate transdermal patch. Asian Journal of Pharmaceutics (AJP). 4(1).19-23
14. Indian Pharmacopoeia,2018, 8th edition, volume 1.
15. Lokhande SK. (2009). Design and Evaluation of Sustained Release Matrix Tablets of Atenolol (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India).

CITATION OF THIS ARTICLE

Yuvaraj .J, Karthikeyan B And Balamurugan K. A Comparison and Evaluation Of B 1- Selective Blocker Atenolol Generic Vs Brand Tablets. Bull. Env.Pharmacol. Life Sci., Vol 13 [4] March 2024: 108-114