Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: www.ijrpns.com

https://doi.org/10.36673/IJRPNS.2023.v12.i06.A21

COMPARATIVE STUDIES OF GENERIC AND BRANDED PRODUCT OF CIPROFLOXACIN HYDROCHLORIDE TABLETS

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ABSTRACT

The aim of this study was to evaluate the quality of ciprofloxacin hydrochloride tablets (500mg) of four brands which are available in Mangalore. Ciprofloxacin, a fluoroquinolone antimicrobial agent active against a broad spectrum of gramnegative and gram-positive organisms, including *Pseudomonas aeruginosa* and methicillin-resistant *staphylococcus aureus*. Quality test is a way to guarantee quality of drug products as many pharmaceutics can produce substandard drug products. In this project, ciprofloxacin hydrochloride of 500mg tablets were randomly selected from three manufactures of Bangladesh and has been assessed according to the United States Pharmacopoeia and British Pharmacopoeia. Those products were subjected to seven key tests such as-weight variation, hardness, dissolution test, drug content, disintegration test, friability and antimicrobial test. Assay of Ciprofloxacin Hydrochloride tablets showed that the samples of four brands had potency within limit. *In-vitro* release study showed that the amount of ciprofloxacin released in 30 minutes was not less than 80% of the labeled amount which is in accordance with the pharmacopeias requirements. Results of all tests are satisfactorily well, which shows a high-quality performance. This study will provide a basis for further *In-vivo* studies. The tested oral ciprofloxacin products distributed in our country were proven that those products had good quality.

KEYWORDS

Ciprofloxacin Hydrochloride, Generic drugs, Branded drugs and Friability.

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INTRODUCTION

Urinary tract infections (UTIs) are a severe public health problem and are caused by a range of pathogens, but most commonly by Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterococcus faecalis and Staphylococcus saprophyticus. Ciprofloxacin (CF) is an antibiotic which is available at a cheap cost and used to treat many bacterial infections[1].

It belongs to fluoroquinolones category and is a broad spectrum second generation antibacterial agent. It is mostly used to treat gram negative bacterial infections, urinary tract infections, skin, ophthalmic, respiratory, bone and joint, intraabdominal infections bacterial diarrheal infections and periodontal pathogens. But it is not effective against viral diseases. It is a nucleic acid synthesis inhibitor. It is one of the topmost selling antibiotics and numbers of researchers are working with this drug for different applications or improvements in its applications[2,3].

Branded drugs: It is the original product that has been developed by pharmaceutical company. It has sole right to manufacture and distribution for a period of time (patent). A brand name drug is a small medicine that's discovered developed and marketed, by pharmaceutical company. One'sa new drug is discovered, the company files for a patent to protect against other companies making copies and selling the drugs[4].

Generic drugs: It is used for identical (or biological) purposes on the original drugs, in doses, strengths, EFF accumulation and safely. According to FDA "a drug product that is comparable to branded product is dosage form strength route of administration, quality and performance, characteristics and intended use[5].

Ciprofloxacin Hydrochloride was shown to have activity against a wide range of bacteria and was particularly effective against the Enterobacteriaceae. Many of the strains tested by Wise *et al.*Were resistant to aminoglycosides or P-lactam antibiotics but sensitive to ciprofloxacin. The standard MIC method for determining antibacterial activity provides no information on initial killing kinetics[6].

Objectives of the study

Comparison of different branded and generic products of ciprofloxacin hydrochloride tablets (500mg).

Evaluation of Ciprofloxacin Hydrochloride tablets for

Weight variation

Hardness

Friability

Drug content

Disintegration time

Dissolution

To carry out antimicrobial study of branded and generic products of ciprofloxacin hydrochloride tablets

MATERIAL AND METHODS

Materials

Drugs: Generic- ciprofloxacin-500 (G1), Ciprofloxacin-500 (G2). Branded- Zoxan-500 (B1), Ciplox- 500 (B2).

Methods

Pre-formulation studies

Comparison of strips and blister packs of Ciprofloxacin Hydrochloride for labelling contents to check whether the package is blister or strip. Label claim: Warning schedule H, Batch no., Expiry date, manufactured date, Company Address.

UV-VISIBLE SPECTROSCOPY

Preparation of Stock Solution[7]

Preparation of standard stock solution A: (10µg/ml)

0.1g of drug was accurately weighed and transferred into 100ml volumetric flask. Then make up to 100ml water.

Preparation of standard stock solution B: (10µg/ml)

10ml of above solution will be pipetted into 100ml volumetric flask. Then make up to 100ml with water.

Determination of Absorption Maxima (λ-max) of Ciprofloxacin Hydrochloride

The solution containing 10µg/ml concentration of Ciprofloxacin Hydrochloride was prepared using water and was scanned between the range of 200-400nm against blank reagent using UV visible spectrophotometer.

Standard curve

10mg of Ciprofloxacin Hydrochloride was weighed and transferred to 100ml volumetric flask. Aliquots of the stock standard solution were diluted to obtain standard solutions of 2-10µg/ml concentrations.

Standard solutions of 2-10µg/ml were scanned at 276nm to obtain the standard curve[8].

Drug content

20 tablets from each generic and brand were weighed and powdered using mortar and pestle. Quantity of powder equivalent to 0.1gm of Ciprofloxacin Hydrochloride was taken carefully and transferred to 100ml volumetric flask. The volume was made up to 100ml with distilled water and contents were thoroughly shaken and filtered in order to get a clear solution. 5ml of this clear solution was taken and further diluted to 50ml with water acid and optical density was measured at 276nm.

% Drug content=Concentration/1000 ×*DF*×100

Weight variation

20 tablets of each generic and branded were collected randomly and weight of individual tablet was determined. The average weight of the 20 tablets was calculated. Percentage deviation in weight of each tablet from the average weight was determined from the following formula[9].

Positive % Deviation= (Maximum Weight−Average weight)/ (Average weight) ×100 Negative % Deviation= (Minimum Weight−Average weight)/ (Average weight) ×10"0"

Hardness test

The crushing strength of tablets was determined using Monsanto hardness tester (10) sample tablets from each generic and brand were taken. A tablet was placed between the spindle of hardness tester machine until the tablet breaks. Pressure required to break the tablet was determined and expressed in kg/cm2[10].

Friability test

Six tablets of each generic and brand were weighed and subjected to abrasion using Rocher friabilator at 100 revolutions at 25rpm. After 100 revolutions the tablets were dedusted and weighed again Percentage friability was calculated using following formula. % Friability= (Initial weight- Final weight) × 100/ Initial weight[11].

Disintegration test

The disintegration time of the tablet was determined according to IP procedure for Tablets Disintegrating Test machine. One Tablet was placed in each of six tubes of the basket disc was added to each tube and apparatus was operated using water as medium maintained at 37 ±2ºC. The time was noted for all the six tablets to disintegrate[12].

Dissolution test

The tablets were evaluated for *in vitro* drug release using USP dissolution apparatus II. The dissolution was carried out in 900ml of water with rotating peddle at 100rpm and at 37 ± 0.5°C. Aliquot of 1ml was removed from each flask, filtered by Whatman filter paper and diluted up to 10ml with water. The sample was analyzed for the quantity of drug released at 276nm using UV visible double beam spectrophotometer. The dissolution medium was replenished with an equal volume of the fresh medium after each removal.

Antimicrobial Study

The antimicrobial activity of Branded and Generic marketed tablet of CiprofloxacinHydrochloride was evaluated against Staphylococcus aureus. 20 tablets of each Branded and Generic marketed tablet of Ciprofloxacin hydrochloride were weighed accurately to obtain the average tablet weight, The tablets were crushed and triturated in a mortar and amount of the powder equivalent to 10mg was weighed accurately and taken into a 10ml volumetric flask. The powder was dissolved in 10ml of the water. Dilution from this solution was made and the clear solutions was made to obtain a concentration which contains 1000µg/ml of the standard solution from this stock solution 1ml was pipette out and diluted up to 10ml with water. This solution was made to obtain a concentration which contains 100µg/ml from this solution take 0.5µg/ml and it was injected to agar medium plate containing *Staphylococcus aureus* in the proportion of 5.0% and incubated at 37°C for 48 hr[13].

RESULTS AND DISCUSSION

Pre-formulation studies of ciprofloxacin hydrochloride

Comparisons of strips and blister packs of ciprofloxacin hydrochloride for labelling contents was found accurate.

UV-Visible spectroscopy

The λ-max of Ciprofloxacin Hydrochloride was determined by water which was scanned between 200-400nm in the UV spectrophotometer. The absorption maxima (λmax) of 276nm was selected for the present study.

Standard curve

The standard curve was constructed by using water. The slope of the graph was found to be 0.0908 and with regression coefficient R2 = 0.9981.

Drug content

Drug content of the generic and branded tablets was found to be in the range between 92.6%- 100.6%. According to I.P specification tablet should not contain less than 90% and not more than 110%. All the tablets found to have satisfactory drug content.

Weight variation

According to I.P. specification, tablet weighed above 300mg can have the maximum of ±5% deviation. From the obtained results, it was observed that, no single tablet of generic and branded product crosses the percentage deviation.

Hardness test

The hardness was found in the range of 1.5-3Kg/cm2. According to IP specification, tablet hardness of ciprofloxacin hydrochloride should range between 1- 4Kg/cm2. Depending on this specification, it can be observed that hardness values were greater for branded tablets when compared to generic tablets but both were within the limits.

Friability test

Friability is a non-official test. % friability was ranged from 0.262-0.872%. Tablets having % loss less than 1% is usually considered acceptable.

Disintegration test

Disintegration test measures the time required for the tablet to disintegrate into particles. Results of disintegration were ranged from 7.32-8.50min. Both generic and branded marketed products of ciprofloxacin hydrochloride have shown good disintegration rate.

Dissolution test

All the generic and branded drugs in the dissolution study found to have good %CDR that is in the range of 85.3% to 89.9 % within 30min. Generic tablets G1 and G2 showed 88.9% and 89.9% respectively in comparison with branded tablets B1 and B2 which showed 85.3.% and 86.4.% respectively at 30min. The I.P. stipulates that at 30 minutes all tablets should have released into dissolution medium an amount not less than 80% of labeled amount of drug.

Antimicrobial Study

Both generic and branded marketed products of ciprofloxacin hydrochloride were compared to standard drug ciprofloxacin hydrochloride in antimicrobial assay. The zone of inhibition was ranged from 17-25mm. Both generic and branded marketed products of ciprofloxacin hydrochloride have shown good antibacterial activity.

Table No 1: Calibration curve for Ciprofloxacin hydrochloride

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.179±0.004
3	4	0.3625±0.003
4	6	0.517±0.006
5	8	0.745±0.003
6	10	0.909±0.005

Table No.2: Drug content

S.No	Product Name	% Drug Content	Comments
1	Zoxan – 500 (B1)	99.5±0.95%	Complies
2	Ciplox – 500 (B2)	92.6±0.53%	
3	Ciprofloxacin – 500 (G1)	95.3±0.15%	
4	Ciprofloxacin – 500 (G2)	100.6±0.45%	

Table No.3: Weight variation

S.No	Product Code	Average Weight (mg)	Maximum Weight (mg)	Minimum Weight (mg)	Positive % deviation (%)	Negative % deviation (%)	Permitted Value	Comments
1	Zoxan – 500 (B1)	753	760	730	0.929	-3.054	±5%	Complies
2	Ciplox - 500 (B2)	699	770	680	1.573	-2.718		
3	Ciprofloxacin – 500 (G1)	754	770	740	2.122	-1.856		
4	Ciprofloxacin – 500 (G2)	677	690	650	1.920	-3.988		

Table No.4: Hardness

S.No	Product Code	Average hardness (Kg/cm^2)	Specifications	Comments
1	Zoxan – 500 (B1)	3	1-4(Kg/cm^2)	Complies
2	Ciplox - 500 (B2)	2.5		
3	Ciprofloxacin – 500 (G1)	1.5		
4	Ciprofloxacin – 500 (G2)	2.7		

Table No.5: Friability

S.No	Product Code	% Friability	Specifications	Comments
1	Zoxan – 500 (B1)	0.654±0.253	NMT 1%	Complies
2	Ciplox - 500 (B2)	0.282±0.015		
3	Ciprofloxacin – 500 (G1)	0.262±0.145		
4	Ciprofloxacin – 500 (G2)	0.872±0.055		

Table No.6: Disintegration

S.No	Product Code	Disintegration Time (min)
1	Zoxan – 500 (B1)	**8.50**±0.02
2	Ciplox - 500 (B2)	**8.15**±0.13
3	Ciprofloxacin – 500 (G1)	**7.49**±0.05
4	Ciprofloxacin – 500 (G2)	**7.32**±0.09

Table No.7: Percentage cumulative drug release (% CDR)

S.No	% Cumulative drug release				
	Time (min)	**Zoxan – 500 (B1)**	**Ciplox - 500 (B2)**	**Ciprofloxacin – 500 (G1)**	**Ciprofloxacin – 500 (G2)**
1	0	0.0	0.0	0.0	0.0
2	5	51.0±0.12	53.2±0.43	52.6±0.90	58.5±0.28
3	15	62.1±0.59	64.4±0.80	66.2±0.26	68.2±0.68
4	30	85.3±0.27	86.4±0.28	88.9±0.53	89.9±0.53
5	45	87.6±0.18	88.4±0.19	92.5±0.97	94.2±0.98
6	60	95.2±0.69	96.2±0.64	96.2±0.36	97.2±0.84

Table No.8: Antimicrobial study

S.No	Product Code	Zone of inhibition (mm)
1	Standard (Ciprofloxacin hydrochloride)	24±2
2	Zoxan-500 (B 1)	17±1
3	Ciplox - 500 (B2)	20±3
4	Ciprofloxacin – 500 (G1)	25±2
5	Ciprofloxacin – 500 (G2)	23±1

CONCLUSION

The current study is the successful attempt to compare and evaluate the characteristics of the Ciprofloxacin Hydrochloride tablets. From the reproducible results of conducted experiment, it can be concluded that; the study covered only some selected branded and generic products of Ciprofloxacin Hydrochloride tablet. The tablets can be evaluated for various parameters like weight variation, hardness test, friability test, disintegration, dissolution, antimicrobial study. Standard curve- Standard curves are graphs of light absorbance versus solution concentration which can be used to figure out the solute concentration in unknown samples. Drug content- The examination of the contents of active ingredient in a product. Pre-formulation studies- showed good results in terms of appearance, shape, colour. Weight variation- weight variation was ranged from -3.988% to 2.122%. More negative deviation was shown by generic product (G2). Highest positive deviation was shown by generic product (G1). Friability – Results of friability test were ranged from 0.262%-0.872%. Both lowest and highest %friability was shown by generic products G1 and G2 compared to branded products B1 and B2. Disintegration-Results of disintegration were ranged from 7.32-8.50min. Lowest time taken to disintegrate was by generic product (G2), Highest time taken to disintegrate was by branded product zoxan-500 (B1). Dissolution-Results of dissolution were ranged from 97.2-95.2% at 60min. Highest %CDR was shown by generic product (G2) and lowest %CDR was shown by brandedproduct zoxan-500 (B1).

ACKNOWLEDGEMENT

I express my sincere thanks to management of Srinivas College of Pharmacy and Vision Group of Science and Technology for providing necessary facilities to carry out the project work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Deekshitha K *et al*. Comparative studies of generic and branded product of ciprofloxacin hydrochloride tablets, *International Journal of Research in Pharmaceutical and Nano Sciences,* 12(6), 2023, 189-195.