Original Article

A Study on Antimicrobial Evaluation of Different Generic and Branded Tablet of Ciprofloxacin HCl Marketed in Wardha District

Sachin J. Dighade[1], Shramika A Chore[2,*], Sunit D Gaurkar[3]

[1]Department of Pharmaceutical Chemistry, Institute of Pharmacy and Research, Badnera, Amravati, Maharashtra, INDIA.
[2]Department of Pharmaceutics, Institute of Pharmacy and Research, Badnera, Amravati, Maharashtra, INDIA.
[3]Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha, Maharashtra, INDIA.

ABSTRACT

Bacterial infection is responsible for various activity including respiratory, urinary tract, gastrointestinal and abdominal infections. Ciprofloxacin HCl, a second-generation fluroquinolone antibiotic that can treat a number of bacterial infections. The aim of this work was to evaluate antimicrobial activity of different generic and branded drug formulation marketed in Wardha district. i.e. Cifran and Zoxan. All the formulations obtained from the market were in compliance with the control samples in respect of Preformulation study, Disintegration, *in vitro* drug release, and antimicrobial potential. Thus, the antimicrobial activity of marketed and control sample was also same shows satisfactory results against *Staphylococcus aureus* as compare to *Escherichia coli*, but *Staphylococcus aureus* was shows better microbiological assay response as compare to *E. coli*.

Keywords: Ciprofloxacin HCl, Preliminary, Branded and Generic drug, Cifran, Zoxan, Antimicrobial potential etc.

INTRODUCTION

Antibiotics are the most common medications in modern age, and is used for control of microbial infections. Ciprofloxacin is the most potent fluoroquinolone derivative having a broader spectrum of antibacterial activity against Gram-negative and Gram-positive aerobic and anaerobic organisms. It's inhibited the bacterial cell wall. The aim of this study to ensure the level of quality of tablet in pharmaceutical industry should contain the appropriate amount of active pharmaceutical ingredient and checking the purity of drug. So that the people were about the safety and efficacy of marketed drug.

MATERIALS AND METHODS

Materials

Ciprofloxacin HCl was provided as gift sample by Cipla Ltd. Pune. Methanol, Potassium Hydrogen Phospahte (AR), Sodium Hydrogen Phosphate (AR) were purchased from Loba Chemical (Mumbai). All other chemicals were of analytical grade.

Methods

All the tablet (brand and generic) of Ciprofloxacin HCl were labeled to contain 500 mg of Cifran per tablet and coded as A, A1, A2, A3, A4 and A5 (Brand A) and B, B1, B2, B3, B4 and B5 (Brand B). The study was done by performing various UV absorbance, IR Spectroscopy, Preliminary studies, Uniformity of weight, Hardness, Thickness, Diameter, Friability,

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Address for correspondence:
Ms. Shramika A. Chore,
Lecturer, Department of Pharmaceutics, Institute of Pharmacy and Research, Badnera, Amravati -444701, Maharashtra, INDIA.
Email id: shramikachore16@gmail.com

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Table 1: Details of generic Ciprofloxacin HCl tablets used in study (Brand A).

Code	Brand Name	Sample	Label Strength	Manufactured by
A	Cifran	Control	500 mg	Sun Pharma, Mumbai
A^1	Cifran	Marketed	500 mg	Sun Pharma, Wardha
A^2	Cifran	Marketed	500 mg	Ranbaxy, Wardha
A^3	Cifran	Marketed	500 mg	Sun Pharma, Wardha
A^4	Cifran	Marketed	500 mg	Ranbaxy, Wardha
A^5	Cifran	Marketed	500 mg	Sun Pharma, Wardha

Table 2: Details of branded Ciprofloxacin HCl tablets used in study (Brand B).

Code	Brand Name	Sample	Label Strength	Manufactured by
B	Zoxan	Control	500 mg	FDC Pharma, Mumbai
B^1	Zoxan	Marketed	500 mg	FDC Pharma, Wardha
B^2	Zoxan	Marketed	500 mg	FDC Pharma, Wardha
B^3	Zoxan	Marketed	500 mg	FDC Pharma, Wardha
B^4	Zoxan	Marketed	500 mg	FDC Pharma, Wardha
B^5	Zoxan	Marketed	500 mg	FDC Pharma, Wardha

Table 3: Evaluation parameter for strip of generic tablet Cifran.

Sr. No.	Parameter	A	A^1	A^2	A^3	A^4	A^5
1	Foil Matching	+	+	-	+	-	+
2	Text matter matching	+	+	+	+	+	+
3	Font size of brand	+	+	+	+	+	+
4	Brand symbol	+	+	-	+	-	+
5	Examination of front size of strip	+	+	+	+	+	+
6	Length (cm)	10 ±0.05	9.9 ±0.07	9.9 ±0.04	10 ±0.010	10 ±0.05	10 ±0.09
7	Width (cm)	3.9 ±0.05	4 ±0.04	4 ±0.012	3.9 ±0.07	4 ±0.015	3.9 ±0.05

Where, + matches, - not matches, each value represent mean ±SD (*n*=3)

Table 4: Evaluation parameter for strip of Branded tablet Zoxan.

Sr. No.	Parameter	B	B^1	B^2	B^3	B^4	B^5
1	Foil Matching	+	+	+	+	+	+
2	Text matter matching	+	+	+	+	+	+
3	Font size of brand	+	+	+	+	+	+
4	Brand symbol	+	+	+	+	+	+
5	Examination of front size of strip	+	+	+	+	+	+
6	Length (cm)	7 ±0.010	7.1 ±0.041	6.9 ±0.015	7 ±0.05	7.1 ±0.019	7 ±0.05
7	Width (cm)	4.9 ±0.01	5.1 ±0.014	5.1 ±0.05	5 ±0.04	5 ±0.05	4.9 ±0.07

Where, + matches, - not matches, each value represent mean ±SD (*n*=3)

Disintegration, Dissolution, Microbiological study. The details of generic and branded tablet of Ciprofloxacin HCl and their manufacturer as shown in Table 1 and 2.

Preliminary Test[1,2]

i) Packaging Checking: Specification of the marketed Strip was observed under magnifying glass in both generic and Branded and evaluation parameter shown in Table 3, 4 and Figure 1 and 2.

ii) Visual Inspection[3,4]

The different brands of tablets were examined by visually like shape, size, and color of which was obtained from respective manufacturer shown in Table 5 and 6.

Figure 1: Strips Examination of front and back side of generic Ciprofloxacin HCl tablets (Cifran).

Uniformity of Weight[5-8]

Tablets (20) of each brand were weighed individually using a digital analytical balance. The average weight was determined and the percentage (%) deviation of the

Figure 2: Strips Examination of front and back side of branded Ciprofloxacin HCl tablets (Zoxan).

Table 5: Visual inspection of Ciprofloxacin HCl generic tablet of Cifran.

Sr. No.	Visual Inspection	Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	Colour	White	White	White	White	White	White
2	Shape	Round	Round	Round	Round	Round	Round
3	Strip colour (Front side)	Silver	Silver	Silver	Silver	Silver	Silver
4	Strip colour (Back side)	Pink	Pink	White and red	Pink	White and red	Pink

Table 6: Visual inspection of Ciprofloxacin HCl branded tablet of Zoxan.

Sr. No.	Visual Inspection	Zoxan					
		B	B^1	B^2	B^3	B^4	B_5
1	Colour	White	White	White	White	White	White
2	Shape	Oval	Oval	Oval	Oval	Oval	Oval
3	Strip colour (Front side)	Silver	Silver	Silver	Silver	Silver	Silver
4	Strip colour (Back side)	Blue	Blue	Blue	Blue	Blue	Blue

individual tablets from the mean was determined shown in Table 7 and 8.

Hardness Test[5-8]

The crushing strength of the tablets was determined using Erweka (Heusenstamm, Germany) hardness tester. Sample tablets (10) of each brand were taken, a tablet was placed between the spindle of the Erweka hardness tester machine until the tablet breaks and the pressure required tobreak the tablet was then read off the machine and recorded shown in Table 9 and 10.

Thickness[5-8]

Thickness of tablets can be fluctuate without any change in its weight because of variation in the granules density, pressure and speed of tablet machine. Tablets thickness

Table 7: Uniformity of Weight of Ciprofloxacin HCl generic tablet Cifran.

Sr. No.	Parameter	Generic Tablet Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	Uniformity of Weight (gm)	0.65	0.69	0.75	0.73	0.77	0.75
2	SD	0.12	0.02	0.18	0.08	0.04	0.07

Each value represent mean ±SD (n=3)

Table 8: Uniformity of Weight of Ciprofloxacin HCl Branded Tablet Zoxan.

Sr. No.	Parameter	Branded Tablet Zoxan					
		B	B^1	B^2	B^3	B^4	B^5
1	Uniformity of Weight (gm)	0.75	0.76	0.7	0.68	0.75	0.75
2	SD	0.01	0.07	0.1	0.09	0.15	0.15

Each value represent mean ±SD (n=20)

Table 9: Hardness of Ciprofloxacin HCl generic tablets (Cifran).

Sr. No.	Parameter	Generic Tablet Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	Hardness (kg/cm^2)	2.72	1.95	2.32	3.25	4.84	2.45
2	SD	0.37	0.17	0.14	0.08	0.39	0.47

Each value represent mean ±SD (n=3)

Table 10: Hardness of Ciprofloxacin HCl branded tablet of Zoxan.

Sr. No.	Parameter	Branded Tablet Zoxan					
		B	B^1	B^2	B^3	B^4	B^5
1	Hardness (kg/cm^2)	1.79	1.53	4.98	1.75	1.89	3.43
2	SD	0.28	0.34	0.49	0.35	0.52	0.52

Each value represent mean ±SD (n=3)

was determined by Model No-C-WWTDH500N Campbell Electronics, (Germany), measured the thickness in millimeters. Allowed limit is ±5% depending on the size of tablets shown in Table 11 and 12

Diameter[5-8]

Diameter of tablet was measured by using Model No. C-WWTDH500N Campbell Electronics, (Germany). Five tablets from each batch were randomly selected and diameter was measured and average diameter was calculated shown in Table 13 and 14

Friability Test[5-8]

Six tablets of each brand were weighed and subjected to abrasion using a Roche friabilator at 100 revolutions

Table 11: Thickness of Ciprofloxacin HCl generic (Cifran) and Branded (Zoxan) tablets.

Sr. No.	Parameter	Generic Tablet Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	Thickness (mm)	4.8	4.5	4.58	4.62	4.6	4.39
2	SD	0.1	0.15	0.09	0.08	0.8	0.17

Each value represent mean ±SD (*n*=3)

Table 12: Thickness of Ciprofloxacin HCl Branded (Zoxan) tablets.

Sr. No.	Parameter	Branded Tablet Zoxan					
		B	B^1	B^2	B^3	B^4	B^5
1	**Thickness (mm)**	5.39	5.57	5.27	5.75	5.62	5.63
2	**SD**	0.04	0.28	0.45	0.31	0.21	0.24

Each value represent mean ±SD (*n*=3)

Table 13: Diameter of generic Ciprofloxacin HCl (Cifran) tablets.

Sr. No.	Parameter	Generic Tablet Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	Diameter (mm)	13	13.1	13.1	13.1	13.1	13.1
2	SD	0.04	0.01	0.07	0.02	0.05	0.04

Each value represent mean ±SD (*n*=3)

Table 14: Diameter of Branded Ciprofloxacin HCl (Zoxan) tablets.

Sr. No.	Parameter	Branded Tablet Zoxan					
		B	B^1	B^2	B^3	B^4	B^5
1	**Diameter (mm)**	17.8	17.8	17.8	17.5	17.7	17.7
2	**SD**	0.03	0.34	0.28	0.29	0.15	0.21

Each value represent mean ±SD (n=3)

Table 15: Diameter of generic Ciprofloxacin HCl (Cifran) tablets.

Sr. No.	Parameter	Generic Tablet Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	**Friability (%)**	0.12	0.29	0.18	0.14	0.25	0.23
2	**SD**	0.001	0.004	0.001	0.002	0.003	0.001

Each value represent mean ±SD (*n*=3)

Table 16: Diameter of Branded Ciprofloxacin HCl (Zoxan) tablets.

Sr. No.	Parameter	Branded Tablet Zoxan					
		B	B^1	B^2	B^3	B^4	B^5
1	**Friability (%)**	0.09	0.16	0.33	0.35	0.32	0.27
2	**SD**	0.001	0.004	0.003	0.001	0.002	0.001

Each value represent mean ±SD (*n*=3)

Table 17: Disintegration Test of generic tablets Ciprofloxacin HCl (Cifran).

Sr. No.	Parameter	Generic Tablet Cifran					
		A	A^1	A^2	A^3	A^4	A^5
1	**Disintegration Test (min:sec.)**	3:00	3:50	4:30	4:00	3:00	4:55
2	**SD**	0.07	0.19	0.05	0.36	0.07	0.26

Each value represent mean ±SD (*n*=3)

Table 18: Disintegration Test of branded tablets Ciprofloxacin HCl (Zoxan).

Sr. No.	Parameter	Branded Tablet Zoxan					
		B	B^1	B^2	B^3	B^4	B^5
1	**Disintegration Test (min:sec.)**	3:00	3:00	5:30	4:20	3:30	4:00
2	**SD**	0.07	0.05	0.15	0.15	0.12	0.05

Each value represent mean ±SD (n=3)

for 4 min. The tablets were deducted and weighed again then percent of weight loss was recorded Table 15 and 16. The friability of the tablets were then calculated using the following expression

$$\% \text{ Friability} = \left[\frac{(\text{Initial weight} - \text{Final weight})}{\text{Initial weight}}\right] \times 100$$

Disintegration Test[5-8]

Tablet disintegration was determined at 37°C ±0.2% using disintegration test apparatus. The disintegration time of randomly selected six tablets of each brand was determined in distilled water. The disintegration time was taken to be the time no granule of any tablet was left on the mesh shown in Table 17 and 18

In vitro Dissolution Test[1,5-8]

The tablets were evaluated for *in vitro* drug release using USP dissolution apparatus II DT600 dissolution apparatus. The dissolution was carried out in 900 ml of citrate phosphate buffer pH 6.8 with rotating peddle at 100 rpm and at 37 ± 0.5°C. After every one hour, aliquot of 1 ml was removed from each flask, filtered by whatman filter paper 42 and diluted up to 10 ml with buffer. The sample was analyzed for the quantity of drug released at 270.40 nm using UV visible double beam spectrophotometer (Shimadzu, UV1701, Japan). The dissolution medium was replenished with an equal volume of the fresh medium after each removal.

Microbial Assay Method[9-17]

The antimicrobial activity of Branded and Generic marketed tablet was evaluated against *E. coli (*NCIM 2256) and *Staphylococcus aureus* (NCIM 2901). *E. coli* was grown microbial slant of nutrient agar medium at 37°C for 24 hr. Further aliquots of required strength of the test organism suspension were prepared in 0.9% saline solution. Solutions of known concentrations of Ciprofloxacin HCl (10µg/ml) was evaluated in Petri dishes (135×21mm) containing growth medium for antibiotic assay inoculated with *Staphylococcus aureus* (NCIM 2901) and *Escherichia coli* (NCIM 2256) in the proportion of 5.0%. 20 tablets of Ciprofloxacin HCl were weighed accurately (control and marketed tablets) to obtain the average tablet weight, the tablets were crushed and triturated in a mortar and amount of the powder equivalent to one tablet (10mg) was weighed accurately and taken into a 10ml volumetric flask. The powder was dissolved in 10 ml 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 1 ml was pipette out and diluted upto 10 ml 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* (NCIM 2901) and *Escherichia coli* (NCIM 2256) in the proportion of 5.0% in incubator at 37°C for 48 hr.

RESULTS AND DISCUSSION

Fourier-transform infrared spectroscopy

The potassium bromide containing drug substance was prepared to record the spectrum in the range of 4000-400cm^{-1} by using FTIR spectrophotometer as shown in Figure 3.

In vitro drug release study

Drug release of five strip generic and branded drug of Ciprofloxacin HCl tablet in 55 min were in the succeeding order of cifran: Generic $A^5 > A^2 > A^1 > A^3 > A^4$ whereas Zoxan: Branded in the $B^2 > B > B^1 > B^4 > B^5 > B^3$. The best result showed Batch A^5 in generic tablet purchased from marketed wardha manufactured by sun pharma in 55 min as compared with control tablet purchased from Sun Pharma, Mumbai. In case of branded tablet B^2 showed better result from marketed tablet Wardha manufactured by FDC Pharma, Wardha in 55 min as compared with control tablet manufactured by FDC Pharma, Mumbai shown in Tables 19-20 and Figures 4-5.

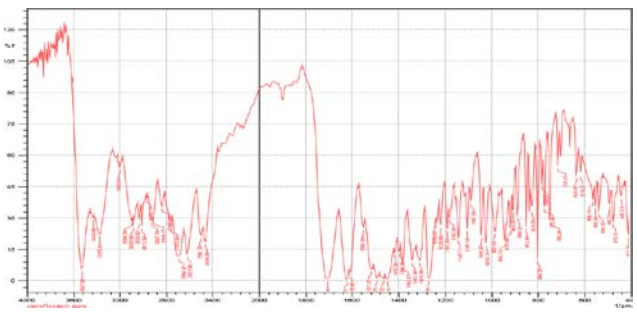

Figure 3: FTIR of Pure Ciprofloxacin HCl.

Antimicrobial Study

The zone of inhibition of all (Generic and Branded) marketed samples as well as control sample tablets

Table 19: *In-vitro* dissolution of Ciprofloxacin HCl generic tablets Cifran.

Time	% Drug Released					
(min.)	A	A^1	A^2	A^3	A^4	A^5
0	0	0	0	0	0	0
5	11.25	11.55	14.4	11.5	11.6	11.1
10	20.97	20.11	20.18	21.06	22.41	20.46
15	28.51	30.68	31.63	25.68	35.28	34.43
20	36.81	44.31	44.22	37.26	45.87	44.47
25	49.55	54.51	50.37	49.5	56.97	69.52
30	66.01	65.77	63.82	60.75	63.29	77.74
35	75.78	77.3	70.79	70.91	67.7	85.48
40	86.42	82.23	84.52	80.75	74.37	91.48
45	92.21	85.52	90.67	86.84	77.79	95.88
50	95.61	91.82	96.62	90.59	84.28	99.63
55	100.87	98.02	100.67	97.79	89.96	101.14
60	100.87	98.02	100.67	97.79	89.96	101.14

Table 20: *In-vitro* dissolution of Ciprofloxacin HCl branded tablet Zoxan.

Time	% Drug Released					
(min.)	B	B^1	B^2	B^3	B^4	B^5
0	0	0	0	0	0	0
5	14.4	11.55	11.1	11.45	11.55	11.5
10	20.18	20.11	20.46	16.56	20.11	21.06
15	31.63	30.68	34.43	27.43	30.68	25.68
20	44.22	44.31	44.47	36.96	44.31	37.26
25	50.37	54.51	69.52	48.7	54.51	49.5
30	63.82	65.77	77.74	59	65.77	60.75
35	70.79	77.3	85.48	62.52	77.3	70.91
40	84.52	82.23	91.48	67.19	82.23	80.75
45	90.67	85.52	95.88	72.91	85.52	86.84
50	96.62	91.82	99.63	80.49	91.82	90.59
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60	100.67	98.02	101.14	89.23	98.02	97.79

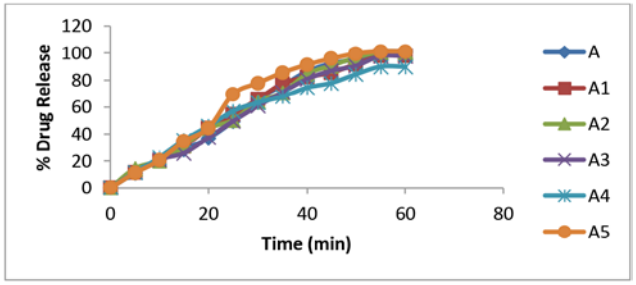

Figure 4: Comparative drug released profile for Ciprofloxacin HCl generic tablets Cifran.

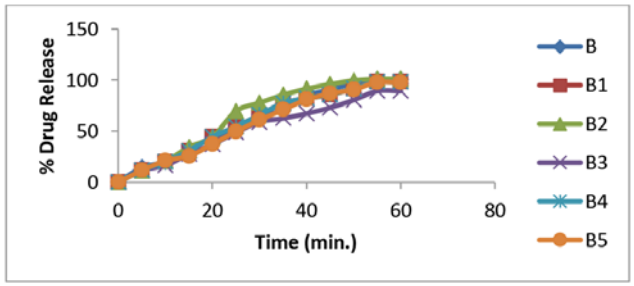

Figure 5: Comparative drug released profile for Ciprofloxacin HCl branded tablets Zoxan.

Table 21: Zone of inhibition of generic tablet Ciprofloxacin HCl of *Staphylococcus aureus.*

Sr. No.	Parameter	A	A_1	A_2	A_3	A_4	A_5
1	Zone of inhibition (cm)	3.8	3.8	4.4	5.5	5.2	4.8

Table 22: Zone of inhibition of branded tablet Ciprofloxacin HCl of *Escherichia coli.*

Sr. No.	Parameter	A	A_1	A_2	A_3	A_4	A_5
1	Zone of inhibition (cm)	5.8	5.8	5.3	5.5	5.7	6

Table 23: Zone of inhibition of generic tablet Ciprofloxacin HCl of *Staphylococcus aureus.*

Sr. No.	Parameter	B	B_1	B_2	B_3	B_4	B_5
1	Zone of inhibition (cm)	4.7	5.2	4.8	4.9	5.7	5.5

Table 24: Zone of inhibition of branded tablet Ciprofloxacin HCl of *Escherichia coli.*

Sr. No.	Parameter	B	B_1	B_2	B_3	B_4	B_5
1	Zone of inhibition (cm)	4.9	4.8	5.2	5.1	4.7	4.5

was shown results in 3.8 - 6. But generic tablet A, A^1 branded tablet B^1 shows minimum zone of inhibition 3.8 and generic tablet A^5 shows the maximum zone of inhibition 6 as shown in Tables 21-24 and Figures 6-9. Hence, the anti-microbial activity of marketed

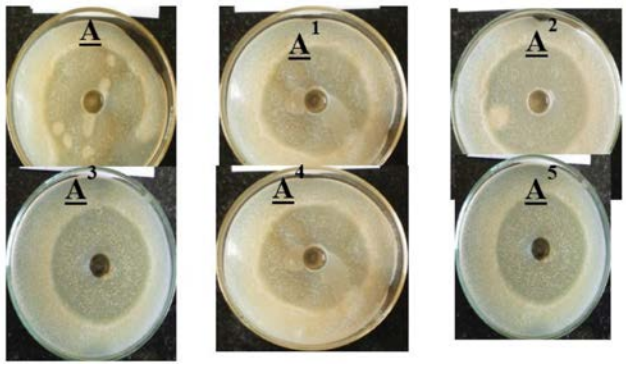

Figure 6: Zone of inhibition of generic tablet Ciprofloxacin HCl of *Staphylococcus aureus.*

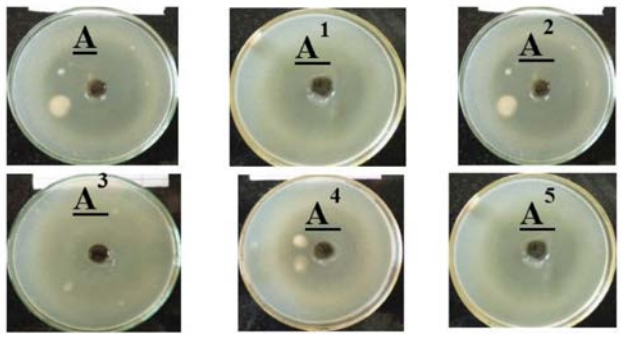

Figure 7: Zone of inhibition of branded tablet Ciprofloxacin HCl of *Escherichia coli.*

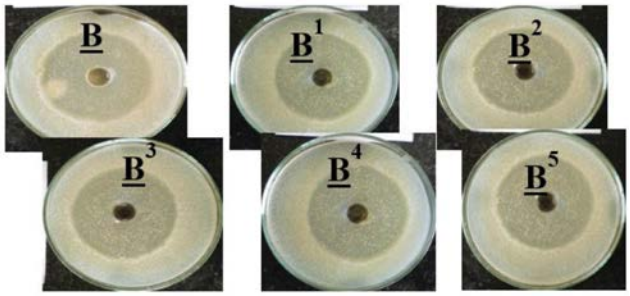

Figure 8: Zone of inhibition of generic tablet Ciprofloxacin HCl of *Staphylococcus aureus.*

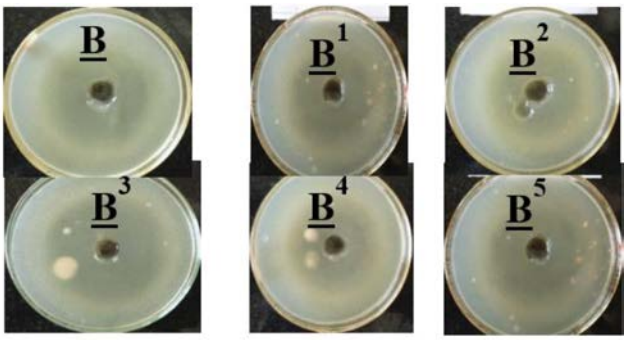

Figure 9: Zone of inhibition of Ciprofloxacin HCl (Brand B) of *Escherichia coli.*

and control sample was also shows satisfactory results against *Staphylococcus aureus* as compare to *Escherichia coli*, but *Staphylococcus aureus* was shows better microbiological assay response as compare to *Escherichia coli*.

CONCLUSION

The aim of the present study was to evaluate the quality of five generic and branded ciprofloxacin hydrochloride tablets available in Wardha district. This study revealed that all generic and branded ciprofloxacin tablets fulfilled the quality control parameters as per the Indian Pharmacopoeia specifications. Hence, generic and branded ciprofloxacin tablets available in the Wardha market meet the quality parameter to satisfy the therapeutic efficacy.

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Authors are thankful to Sun Pharma, Mumbai for providing the Ciprofloxacin HCl as gift samples.

CONFLICT OF INTEREST

All authors declare that there is no Conflict of Interest.

ABBREVIATIONS

FTIR: Fourier transform infrared spectroscopy.

SUMMARY

Quality of generic and branded drugs of ciprofloxacin HCl tablets in Wardha district was evaluated and checked the parameters such as Drug content, Hardness, Friability, Thickness, Diameter, Weight variation, Disintegration time. It was observed of all products used in the study were within specified limits as per Indian Pharmacopoeia. In case of identification of dimension of strip was measured by vernier caliper it was matches with respect to control sample but generic tablet batch A^2 and A^4 was observed its length 9.9 cm and branded tablet B and B^5 was observed its width 4.9 cm. finally, microbial study was shown satisfactory results against *Staphylococcus aureus* and *Escherichia coli*, but *Staphylococcus aureus* was shows better microbiological assay response as compare to *Escherichia coli*.

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