Research Article

Generic Vs. Branded: A Comparative Dissolution Study of Some Commercially Available Levofloxacin Hemihydrate Film Coated Tablets and their Pharmacoeconomic Evaluations

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ABSTRACT

The main objective of the present study was to conduct a comparative study of various branded dosage forms and generic dosage form todetermine whether all the formulations were equivalent. Five different brands of marketed product of Levofloxacin Hemihydrate (250mg) (A, B, C, D, E) and one product of generic formulation (F) were purchased and were analysed. The results showed that all the branded and generic product of Levofloxacin Hemihydrate film coated tablets met the pharmacopoeial specifications. Further, all the tablets passed the hardness, thickness, length, diameter, depth, weight variation tests, disintegration time and dissolution study as per pharmacopoeia. Disintegration time for generic product was found to be 15.1 ± 1.153 minutes which was higher than all the branded products. The dissolution study data of all the formulations passed the test as per the pharmacopoeia. Further, it was observed from the dissolution data that of the five branded products; three of these released the drug in 15 minutes and the remaining two in 20 minutes while the generic product released the drug in 30 minutes. Hence it may be conclude that all the branded products and the generic form of Levofloxacin Hemihydrate film coated tablets (250mg) were found to be equal, hence generic product should be prescribed by health care professionals as the cost of generic product is comparatively less to an extent of 30-50 % of the branded products which may reduce the cost of medication to the patients.

Keywords: Levofloxacin hemihydrate, generic product, branded product, dissolution

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INTRODUCTION

Rationale

Levofloxacin Hemihydrate is one of the most widely prescribed drugs for gram positive bacterial infection. The main rationale of this work was to comparethe dissolution study of generic and branded products. Generic form of the drug should be widely prescribed to reduce the medication cost and make the treatment economical to the patients.

One of the most debated issues in health care today concerns the difference between brand name (also called branded, innovator, and pioneered) drugs and their generic versions. Evolution of every drug starts from a research laboratory and ends in a medical shop [1].

Antibiotics are among the most frequently prescribed medications in modern medicine, they cure disease by killing or Inhibiting bacteria. With the increasing number of available antibiotics, prescribing these drugs has become a challenge. Levofloxacin is the optical S- (-) isomer of Ofloxacin. Ofloxacin is a racemic mixture, but the S-isomer has antibacterial activity 32- to 128-fold more potent than the R-isomer – hence most of the antibacterial activity of Ofloxacin is due to the S-isomer. Levofloxacin has been developed to take advantage of this antibacterial potency while requiring only about half the usual dose of Ofloxacin to achieve similar efficacy, but potentially with an improved toxicity profile. Levofloxacin is rapidly and essentially completely absorbed after oral administration. Therapeutically it is used for urinary tract infection, sinusitis, and chronic bronchitis [2].

MATERIAL AND METHODS

Materials

Levofloxacin Hemihydrate (pure drug) was a kind gift sample from Saga Laboratory Ahmedabad. Generic formulation and five different brands of Levofloxacin Hemihydrate film coated tablet were obtained from different retail pharmacies of Bardoli (Gujarat) market.

Table 1: Details of Levofloxacin Hemihydrate film coated tablets (marketed and generic products)

Tablet Code	A	B	C	D	E	F
Brand Name	LIVEBEST 250	GLEVO 250	LEVOFLOX 250	LEON 250	ZILEE 250	Generic 250
Manufacturer	Abbott Health Pvt. Ltd.	Glenmark Pharma-ceuticals	Cipla Ltd.	Dr.Reddy's Lab. Ltd.	FDC Limited	-
Shape	Oval shape	Round shape	Capsule shape	Round shape	Round shape	Oval shape
Description	Each film coated tablet contains Levofloxacin Hemihydrate IP equivalent to Levofloxacin ....250 mg Excipients……..……q.s.					
Colour	Titanium dioxide IP	Red dioxide of iron & titanium dioxide	Red dioxide of iron & titanium dioxide	Titanium dioxide IP	Red dioxide of iron & TiO_2	-
Dosage	As prescribed by the physician					
Storage	Store in dry place, protect from light.					
Mfg. Lic. no.	MNB/06/394	MNB/05/182	MNB/05/109	MNB/09/780	656	-
Mfg. date	July 2013	April 2012	April 2013	June 2013	July 2012	-
Exp. date	June 2016	March 2014	March 2016	May 2016	June 2014	-
Price (PER 10 TABLETS)	43.55/-	58.00/-	46.00/-	46.80/-	38.50/-	34.00/-

METHODS

UV spectroscopy

A solution of Levofloxacin Hemihydrate (10µg/ml) was prepared in 0.1N HCl. The UV spectrum of Levofloxacin Hemihydrate was recorded using double beam UV-Visible Spectrophotometer (Shimadzu, UV 3092) in the range of 200-400nm. The wavelength of maximum absorption was found to be 293 nm in the solvent which complies with Pharmacopoeial standards (IP 2010).

Preparation of Standard Curve in 0.1 N HCl

Levofloxacin Hemihydrate (10 mg) was dissolved in 100 ml of 0.1N HCl to get stock solution (100 µg /ml). Aliquots of 0.2, 0.4, 0.6, 0.8 and 1.0 ml were serially diluted with 0.1N HCl up to 10 ml to get 2, 4, 6, 8 and 10 µg/ml concentration of Levofloxacin Hemihydrate. The absorbance of the solution was measured at 293 nm against a reagent blank solution (0.1N HCl). Calibration curve was prepared by plotting

absorbance on Y-axis and respective concentrations on X-axis.

Weight variation test

Twenty tablets were selected at random, weighed individually and the average weightwas calculated from total. Then percentage deviation from the average weight was then calculated.According to IP standards, not more than two of the individual weight deviates from the average weight by more than the percentage shown below and none deviatesby more than twice that percentage.

Thickness, Diameter, Length and Depth

The thickness, diameter (round tablets), length (oval/oblong tablets), depth (oval/oblong tablets) of three tablets from each batch was determined using Vernier calliper.

Hardness Test

Tablet requires a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked from each batch to measure hardness. The standard value of hardness for film coated tablet is 8-12Kg/cm^2.

RESULTS & DISCUSSION

UV Spectroscopy

Disintegration Test

For determination of disintegration time, one tablet was placed in each tube and basket rack was positioned in a beaker of water at 37 ± 2^0 C. The baskets containing the tablets were moved up and down. According to the test, the tablet must disintegrate and all particles must pass through the 10 mesh screen in the specified time.The standard value of disintegration time for film coated tablet is within 30 minutes.

Dissolution study

Apparatus: USP apparatus type I (basket)

Temperature: 37°C ± 0.5°C

RPM: 100

Dissolution medium: 0.1 N HCl

Volume of medium: 900 ml

Sampling interval: 5, 10, 15, 20, 25 and 30 min

10 ml of the sample withdrawn was filtered through whatmann filter paper. Appropriate dilutions were made to get the absorbance in linearity range of medium. The absorbance of the samples was determined at wavelength of 293 nm in 0.1 N HCl UV spectrophotometer against 0.1 N HCl. The amount of drug present in the filtrate was calculated from the calibration curve equation and cumulative percent of drug release was calculated.

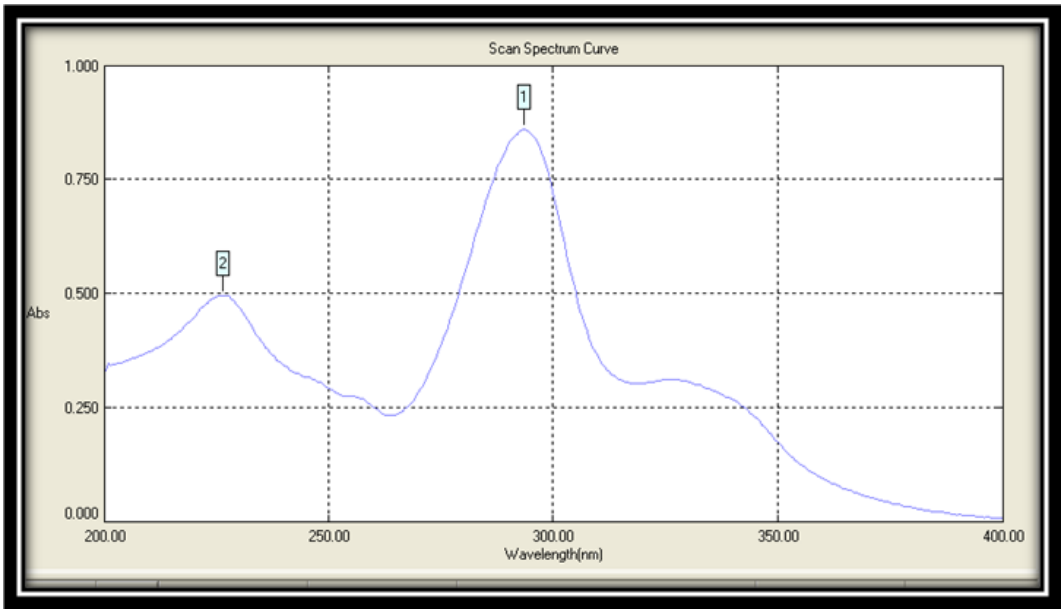

Figure 1: UV spectra of Levofloxacin Hemihydrate in 0.1N HCl

Standard Curve in 0.1 N HCl

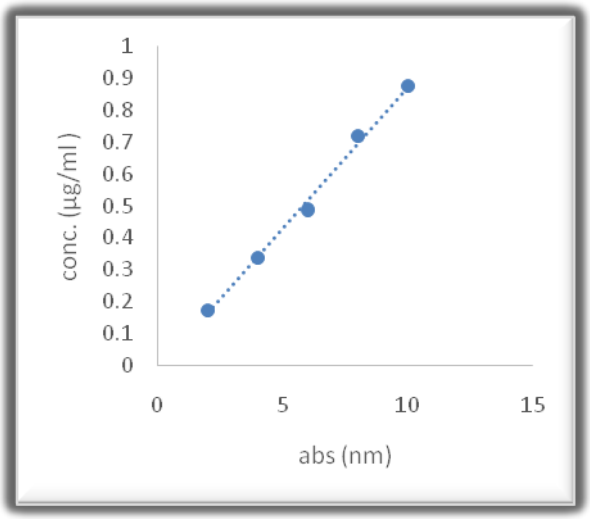

Fig. 2: Calibration curve of Levofloxacin Hemihydrate in 0.1N HCl

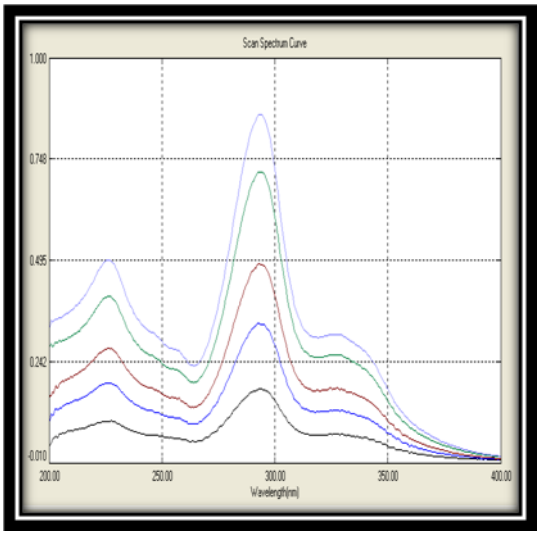

Fig. 3: UV spectra of Levofloxacin Hemihydrate in 0.1N HCl (2-10 µg/ml)

Table 2: Calibration data of Levofloxacin Hemihydrate in 0.1N HCl at ʎmax=293nm

Sr. No.	Concentration (µg/ml)	Absorbance			Average Absorbance (n=3, Mean ±SD)
1.	2	0.173	0.172	0.173	0.174±0.0005
2.	4	0.335	0.340	0.339	0.338±0.0026
3.	6	0.418	0.485	0.495	0.487±0.0072
4.	8	0.713	0.715	0.726	0.718±0.0070
5.	10	0.858	0.870	0.894	0.874±0.0183
			$y = 0.089x - 0.0158$		
			$R^2 = 0.995$		

Evaluation Of Levofloxacin Hemihydrate Film Coated Tablets

Physical properties such as weight variation, thickness, hardness, diameter, length, depth were measured and results are shown in (**Table 3**).

Table 3: Evaluation parameter of Levofloxacin Hemihydrate film coated tablets

Tablet Code	Weight Variation(mg) (n=20, Mean ± SD)	Thickness (mm)	Hardness (kg/cm³) (n=3, Mean ± SD)	Diameter (cm)	Length (cm)	Depth (mm)
A	341.25 ± 1.357	4	6.4 ± 0.057	-	1.2	8
B	396.55 ± 1.288	4	4.5 ± 0.1	1.1	-	-
C	332.45 ± 1.195	4	10.3 ± 0.288	-	1.3	6
D	370.55 ± 1.298	4	7.3 ± 0.288	1.1	-	-
E	419.8 ± 2.811	4	6.4 ± 0.057	1.1	-	-
F	388.95 ± 1.087	5	11.1 ± 0.288	-	1.2	8

Disintegration time of Levofloxacin Hemihydrate film coated tablets

All the formulations were evaluated for disintegration time. The data of disintegration time of batch A to F are shown in (**Table 4**).

Table 4: Disintegration time of Levofloxacin Hemihydrate film coated tablets

Tablet Code	A	B	C	D	E	F
Disintegration Time (min) (n= 3, mean ± SD)	10.27 ± 0.025	2.21 ± 0.030	9.29 ± 0.005	2.25 ± 0.01	6.38 ± 0.02	15.1± 1.153

All batches show disintegration in not more than 30 minutes (film coated) as reported in Table 4. It was observed that the hardness of F-tablet (generic tablet) is higher; hence the time taken for disintegration is longer i.e, 15 minutes as compared to A to E-tablets (marketed tablets) which are in the range of 2-10 minutes. The entire tablets were found to be in the official limits as per the I.P. for disintegration test.

Dissolution study of Levofloxacin Hemihydrate film coated tablets

All the formulations were evaluated for *in-vitro* drug release study. The data of *in vitro* release study are shown in table 5 and figure 4. *In Vitro* release study of A to F-tablets in 0.1N HCl shown in (**Table 5 and Figure 4**).

Table 5 Percentage drug release of Levofloxacin Hemihydrate film coated tablets

Time (min)	% Drug release (n= 3, mean ± SD)					
	A	B	C	D	E	F
5	56.61±1.25	49.75±0.51	37.30 ± 1.90	66.55±1.20	77.26±2.05	38.38±0.90
10	95.93±1.36	83.76±1.85	66.35 ± 0.85	73.78±1.39	86.35±1.03	41.79±1.05
15	102.91±2.71	99.36±0.63	76.36±1.04	100.66±2.10	91.74±1.99	77.21±0.93
20	-	-	100.33±1.30	-	100.74±1.32	85.99±1.40
25	-	-	-	-	-	95.10±1.70
30	-	-	-	-	-	101.6±0.64

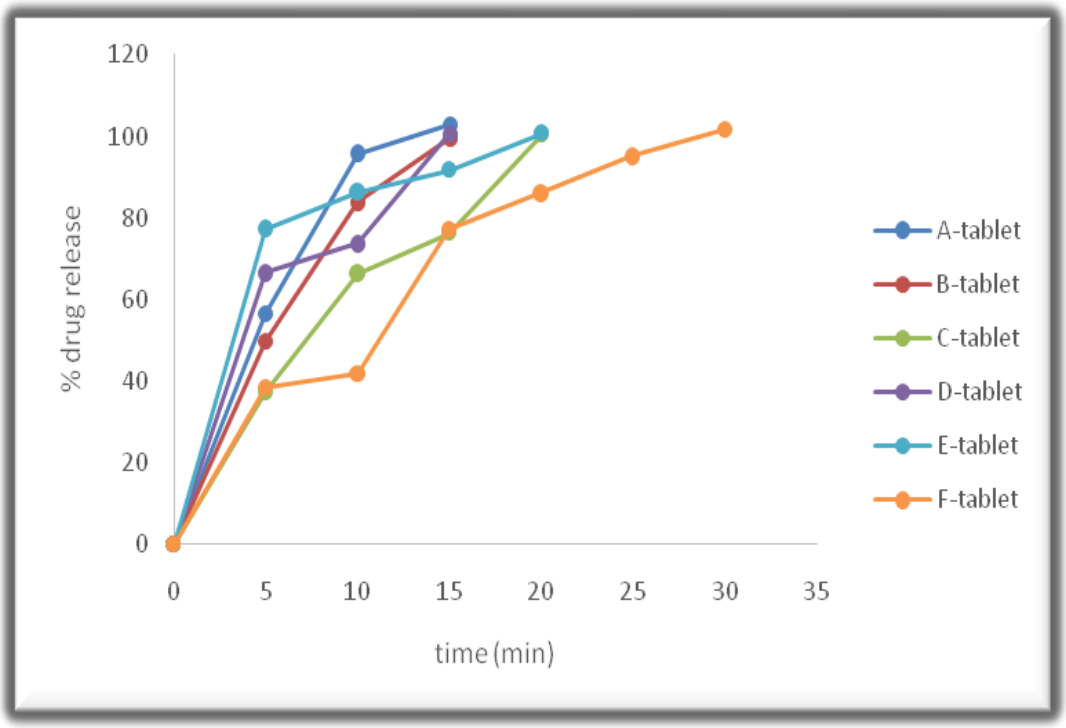

Figure 4: Percentage drug release of Levofloxacin Hemihydrate film coated tablets

A dissolution study gives an idea of the amount of drug available for absorption after oral administration. The in vitro dissolution profiles were found to be varying for each tablet but within the prescribed limit.Time taken for 40 – 70 % of drug release was found to be in 5 minutes for all the tablets. Drug release of A, B and D-tablets were found to be 102.91 %, 99.36 % and100.66 % respectively in 15 minutes. Drug release of C and E-tablets were found to be 100.33 % and 100.74 % respectively in 20 minutes. The drug release of F-tablet was found to be 101.6 % in 30 minutes which is comparatively higher than the other tablets.The dissolution study reveals that all the tablets had released the drug within the limits as per I.P.

Cost Minimization Analysis (CMA)

The cost of the all tablet formulations were evaluated for cost minimization analysis and were compared with each other. Results for CMA are shown in Table 10. from the data it is observe that generic formulation (F-tablet) has lower cost as compared to other marketed products (A to E-tablets).The cost of tablet 'B' was highest at Rs.58.00/- per 10 tablets as compared with that of tablets D,C,A and E at Rs.46.80/-, Rs.46.0/- Rs.43.55/- and Rs.38.50/- respectively for 10 tablets each. The cost of tablet 'F' tablet was the lowest amongst all the tablets at Rs.34.00/- for 10 tablets.

Table 6: Cost Minimization Analysis of Levofloxacin Hemihydrate film coated tablets

Tablet code	A	B	C	D	E	F
Price (per 10 tablets)	43.55/-	58.00/-	46.00/-	46.80/-	38.50/-	34.00/-

CONCLUSION

In this study, an attempt was made to compare dissolution study of different brands and generic product of Levofloxacin Hemihydrate 250 mg film coated tablets. The physical properties of tablets such as hardness, thickness, diameter, length, depth and disintegration time of the products assessed were within the pharmacopoeial specifications. Disintegration time of all the branded and generic tablet were found in the pharmacopoeial limit with generic tablet showing higher disintegration time (15.1 ± 1.153) comparatively. Significant difference was observed in dissolution release of branded and generic tablet. Drug release of generic tablet (F-tablet) was found to be 101.6 % in 30 minutes which is comparatively higher than the branded tablets (15-20 min) which showed drug release within 20 minutes. Hence, it can be concluded that the comparative dissolution study of branded vs. generic of Levofloxacin Hemihydrate 250 mg film coated tablets were all found to be within the limits and bioequivalent. Further, the study suggests that generic form of the drug should be widely prescribed to reduce the medication cost and make the treatment economical.

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