BIOEQUIVALENCE EVALUATION OF NORFLOXACIN TABLETS BASED ON *IN VITRO – IN VIVO* CORRELATION

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ABSTRACT

Present study was designed to establish in-vitro and in-vivo correlation (IVIVC) of two immediate release tablet formulations of 400mg Norfloxacin [Drug A as test and Drug B as reference].

Dissolution study was conducted in 0.1 N HCl using USP apparatus II. In-vivo evaluation was carried out in 18 healthy humans according to a single dose, two-sequence, and cross-over randomized with a wash-out period of one week. After dosing, serial blood samples were collected for a period of 10 hours. Plasma harvested from blood, was analyzed for norfloxacin by a sensitive, reproducible and accurate HPLC method. Various pharmacokinetic parameters were determined from plasma concentrations for both the formulations.

Non-significant difference was found for test/reference ratio of these parameters and the value of F was found to be 0.99 which is in good agreement with the limits given in FDA and WHO guidelines for such parameters.

Difference factor (f_1), similarity factor (f_2) and level A IVIVC were evaluated showing that drug A is bioequivalent to drug B.

Keywords: Norfloxacin, bioavailability, pharmacokinetics, HPLC, IVIVC.

INTRODUCTION

According to *in vitro/in vivo* correlation (IVIVC) guidance of Food and drug Administration, *in vitro* and in-vivo correlation is a mathematical predictive tool that explains the association between iv-vitro evaluation (generally dissolution) of a formulation and its in-vivo behavior (bioavailability). The application of IVIVC is specific to the nature of a specific drug product as tested in present study involving the bioequivalence evaluation of Norfloxacin [Drug A relative to reference formulation Drug B] in human. IVIVC is considered as a surrogate for bioavailability/ bioequivalence studies. Two formulations are considered to be bioequivalent if their dissolution profiles fall within the specified limits (± 10 % deviation from mean dissolution profile) (FDA, 1997; Leeson, 1995). The dissolution profiles can be compared by model independent approaches i.e. pair wise procedures. Pair wise procedures include the difference factor (f_1) [Eq. (1)] and the similarity factor (f_2) [Eq. (2)]. According to the FDA guidance, values of f_1 between zero and 15 and of f_2 between 50 and 100 ensure sameness or equivalence of the two dissolution profiles. In both equations, R_t and T_t represent the dissolution measurements at P time points of the reference and test, respectively (Polli *et al*., 1996).

$$f_1 = \{[\sum_{i=1}^{P} |R_t - T_t|]/[\sum_{i=1}^{P} R_t]\} \quad (1)$$

$$f_2 = 50 \log \{[1 + (1/P)\sum_{i=1}^{P} (R_t - T_t)^2]^{-1/2} * 100\} \quad (2)$$

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Quinolones comprise an interesting group of antibacterial which are primarily used for the treatment of urinary tract infections. Fluorinated derivatives such as ciprofloxacin, norfloxacin, levofloxacin, and ofloxacin have greatly improved antibacterial activity compared with nalidixic acid and achieve bactericidal levels in blood and urine. Norfloxacin is a new broad-spectrum antibacterial agent Norfloxacin exhibits greater antibacterial activity against gram-positive and gram-negative bacteria than other nalidixic acid analogs. Norfloxacin exerts its effects by inhibition of bacterial enzyme DNA gyrase so the synthesis of DNA is inhibited and is bactericidal. A 30-40 % of oral dose of Norfloxacin is absorbed through G.I.T. It is eliminated through metabolism, biliary excretion and renal excretion (Merck company product information, 2001; Catherine *et al*., 2002). Also numerous studies prove the effect of milk and dairy products, antacids, sucralfate, iron in delaying the absorption. The potential usefulness of Norfloxacin in the treatment of urinary tract infections and against gastrointestinal pathogens justifies its in-depth pharmacokinetic studies (Khalid *et al*., 2001; Venkata and Brain, 1982).

MATERIALS AND METHODS

Study products

Test product – Drug A–Norfloxacin 400 mg tablet, Batch No. 6391, Date of Expiry 05.2009.

Reference product – Drug B –Norfloxacin 400 mg tablet, Batch No. N150, Date of Expiry 12.2009.

Dissolution study

The dissolution test was conducted in 0.1 N HCl at 37 ± 0.5°C using USP dissolution apparatus II at 50 rpm. Sufficient quantity of samples was extracted at pre-determined time points and same quantity of dissolution medium was added.

Subjects and experimental design

Eighteen healthy adult male volunteers participated in this comparative study at the Islamia University of Bahawalpur according to a single dose, two-sequence, and cross-over randomized with a wash-out period of one week as given below:

Group	Periods	
	I	II
1	Drug A (Norfloxacin 400 mg Tablet)	Drug B (Norfloxacin 400 mg Tablet
2	Drug B (Norfloxacin 400 mg Tablet	Drug A (Norfloxacin 400 mg Tablet)

Their age was from 18-40 years and body weight in the range of 50-70 kg. On the basis of medical history, clinical examination and laboratory investigation (hematology, blood biochemistry, and urine analysis), no subject had a history of hepatic, renal, gastrointestinal or hematologic diseases or drug allergy. No milk or dairy products were served during the study. Informed consent was obtained from the subjects after explaining the nature and purpose of the study.

Sample collection

A 20-gauge venous cannula was inserted into forearm for collection of blood samples. A blood sample was collected before drug was given (zero time) and then at 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8 and 10 hours after dosing of Norfloxacin. 5 ml blood sample was collected each time. Blood Samples were centrifuged at 3000 rpm for 10 minutes and plasma was separated. The plasma samples were then frozen at -20°C in refrigerator until assay.

Chromatographic conditions

HPLC (Agilent 1200) with fluorescence detector and Reverse phase C_{18} column was employed. The mobile phase consisted of 14 % acetonitrile in buffer solution. The aqueous phase was prepared by mixing 2 g of citric acid, 2 g sodium acetate and 1 ml of triethylamine in 1 L of Milli-Q water (Khalid *et al*., 2001). The mobile phase was filtered through a 0.45 µm membrane filter before use. The mobile phase was then degassed by passing nitrogen gas for about 2-3 minutes until complete degassing of mobile phase was ensured. The mobile phase was eluted at flow rate of 1.2 ml/min and effluent was monitored at excitation and emission wavelengths of 330 and 440 nm.

Extraction procedure

A 200 µl plasma sample was taken in a glass-stoppered tube and 500 µl of acetonitrile was added to precipitate the plasma proteins; the mixture was shaken for 1 min and centrifuged at 4000 rpm for 15 min. The supernatant was transferred to a 1.5 ml micro-centrifuge tube and evaporated to dryness at 40°C under a nitrogen stream. The residue was reconstituted with 200 µl of mobile phase followed by vortex mixing for 30 second; a 20 µl aliquot was then injected to column and peak areas were recorded (Khalid *et al*., 2001).

Level A correlation establishment

Level A correlation is a point to point correlation with highest efficiency. It is evaluated by plotting a graph between drug released (%) and drug absorbed (%). Drug absorbed (%) was measured using Wagner-Nelson equation (Leeson, 1995):

$$\text{Percent Drug Absorbed} = \frac{\{(C\,(t) / Ke + AUC_{(0\text{-}t)}}{AUC_{(0\text{-}8)}} \times 100 \qquad (3)$$

Pharmacokinetic analysis

Pharmacokinetic analysis was performed by using non-compartmental method of analysis and MS Excel Windows professional XP. Maximum concentration of Norfloxacin in plasma (C_{max}) and time to reach maximum concentration (T_{max}) were determined by visual inspection of plasma concentration vs. time profiles. The area under concentration time curve ($AUC_{0\text{-}\infty}$) was calculated by linear trapezoidal rule.

STATISTICAL METHOD

Paired t-test was used to calculate the difference whether significant or non-significant between the values of the bioparameters of the two different brands of Norfloxacin i.e., Drug B and Drug A.

RESULTS

The dissolution profiles of both formulations (fig. 1) were found similar to each other. Ninety percent drug release was observed from both formulations in 12.8 hours. The dissolution rate constant for Drug B was little greater than Drug A. The release profiles of Drug B and Drug A were taken as reference and test dissolution data points and f_1 and f_2 were less than 5 (f_1 = 4.11) and greater than 90 (f_2 = 83.65), respectively for both of the formulations indicating similarity between both release profiles. Norfloxacin was well tolerated by the subjects; unexpected incidents that could have influenced the outcome of study did not occur. Analysis of norfloxacin in plasma was conducted using a modified method of Khalid *et al*., (2001). All volunteers who started the study continued to the end and were discharged in good health. Both formulations were readily absorbed from the gastrointestinal tract in nearly all volunteers. Plasma

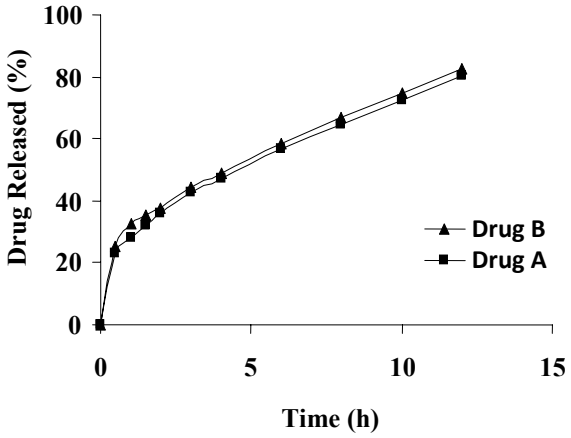

Fig. 1: Dissolution profiles of Drug B and Drug A.

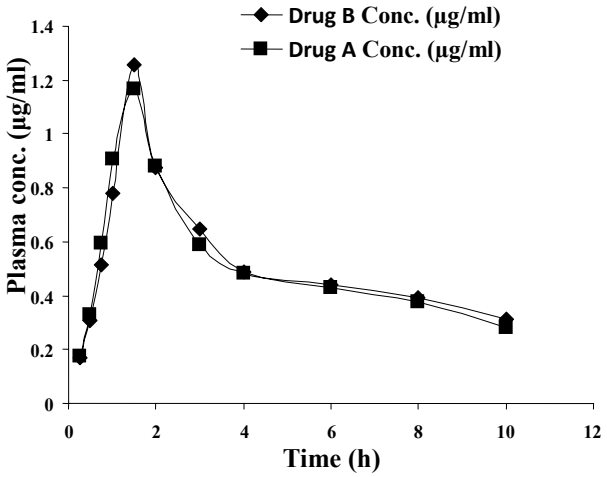

Fig. 2: Comparison of plasma concentration vs. time profile of Drug B and Drug A plotted on rectangular co-ordinate graph, administered in the oral dose of 400 mg in 18 subjects.

concentration-time curves (fig. 2) were also identical of both compared formulations. Good IVIVC (figs. 3 and 4) were observed for both of the formulations. Plasma concentration verses time profiles of Drug A and Drug B administered in the oral dose of 400mg in 18 healthy human volunteers are shown in tables 1 and 2. The bioavailability and pharmacokinetic parameters of Drug A and Drug B in normal subjects administered in the oral dose of 400mg are given in tables 3 and 4. Pharmacokinetic parameters of both norfloxacin tablets are compared in table 5.

DISCUSSION

Standard curve was constructed in the range of 0.156-20 µg/ml and the value of $R^2 = 0.99$ was observed. Drug B and Drug A were compared statistically by using student t-test to observe the difference between plasma concentrations of two brands (table 5).

Both profiles appeared almost similar and are indicative of rapid drug absorption after dosing. The numerical values of pharmacokinetic and bioavailability parameters obtained with Drug B and Drug A is shown in Tables 3, 4 and 5. $AUC_{0-\infty}$ and T_{max} are indicative of respective extent and rate of drug absorption where as peak plasma concentration (C_{max}) related to both processes. The extent of absorption is key characteristic of drug formulation. The $AUC_{0-\infty}$ is an important parameter for analysis in bioavailability study. However, the two other parameters, namely C_{max} and T_{max} are also important features of the plasma level profile that are related to therapeutic use of many drugs and hence, are also considered in the present analysis. According to previous studies, following single oral dose of norfloxacin 400mg, mean maximum serum concentration of 1.29 to 1.58µg/ml have been achieved within 1 to 2 hours (Seth *et al*., 1995). In the present study, mean maximum serum concentration was 1.421 ±

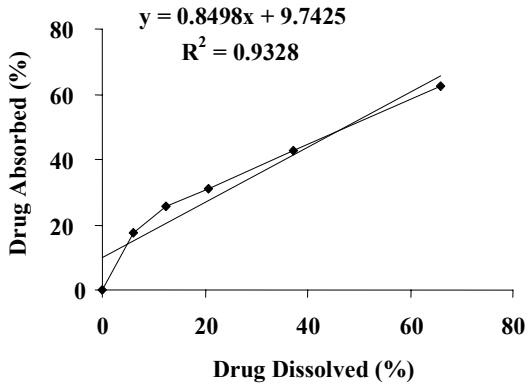

Fig. 3: A rectangular coordinate plot between drug absorbed (%) and drug dissolved (%) for Drug B.

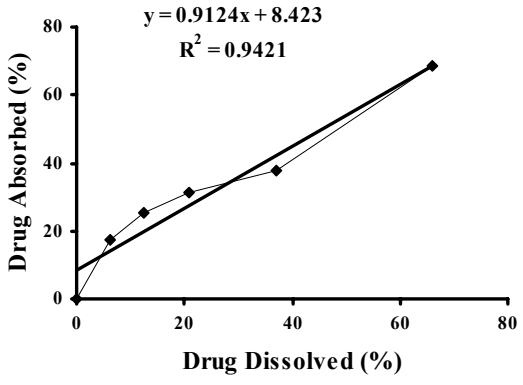

Fig. 4: A rectangular coordinate plot between drug absorbed (%) and drug dissolved (%) for Drug A.

Table 1: Plasma concentration verses time profile of Drug A administered in the oral dose of 400mg in 18 healthy human volunteers.

No.	Time (h)	Volunteers																				
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Mean	SD	SEM
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.000	0.000
2	0.25	0.16	0.21	0.16	0.26	0.16	0.16	0.16	0.26	0.16	0.16	0.16	0.16	0.16	0.18	0.16	0.17	0.17	0.21	0.175	0.029	0.008
3	0.5	0.32	0.35	0.33	0.54	0.33	0.21	0.21	0.54	0.21	0.23	0.33	0.32	0.31	0.51	0.21	0.32	0.29	0.35	0.328	0.104	0.030
4	0.75	0.59	0.45	0.69	0.74	0.69	0.68	0.68	0.74	0.45	0.54	0.69	0.36	0.41	0.92	0.68	0.61	0.69	0.45	0.596	0.162	0.047
5	1	0.68	0.56	0.90	1.47	0.90	1.41	1.41	1.47	0.76	0.64	0.90	0.62	0.69	1.22	1.41	0.81	1.09	0.56	0.905	0.317	0.092
6	1.2	1.41	0.97	1.35	0.94	1.35	0.79	0.79	0.94	1.25	0.79	1.35	1.41	1.51	0.88	0.79	1.29	1.39	0.97	1.165	0.266	0.077
7	2	0.79	1.49	0.48	0.79	0.48	0.73	0.73	0.79	1.06	1.33	0.48	0.69	0.79	0.78	0.73	0.98	0.59	1.49	0.878	0.293	0.085
8	3	0.58	0.86	0.45	0.58	0.45	0.64	0.64	0.58	0.78	0.66	0.45	0.41	0.59	0.51	0.64	0.59	0.39	0.86	0.586	0.139	0.040
9	4	0.49	0.62	0.41	0.49	0.41	0.55	0.55	0.49	0.51	0.51	0.41	0.39	0.41	0.49	0.55	0.46	0.41	0.62	0.480	0.066	0.019
10	6	0.41	0.51	0.39	0.45	0.39	0.51	0.51	0.45	0.41	0.45	0.39	0.39	0.39	0.43	0.51	0.43	0.39	0.51	0.433	0.043	0.012
11	8	0.41	0.38	0.35	0.39	0.35	0.44	0.44	0.39	0.39	0.34	0.35	0.34	0.36	0.39	0.44	0.34	0.36	0.38	0.376	0.031	0.009
12	10	0.39	0.17	0.29	0.29	0.29	0.22	0.22	0.29	0.32	0.29	0.29	0.29	0.31	0.29	0.22	0.17	0.31	0.17	0.282	0.063	0.018

Table 2: Plasma concentration verses time profile of Drug B administered in the oral dose of 400mg in healthy human volunteers.

No.	Time (h)	Volunteers																				
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Mean	SD	SEM
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.000	0.000
2	0.25	0.16	0.16	0.16	0.17	0.162	0.16	0.16	0.25	0.16	0.15	0.12	0.16	0.17	0.17	0.16	0.16	0.16	0.15	0.17	0.02	0.01
3	0.5	0.31	0.32	0.31	0.32	0.32	0.31	0.24	0.54	0.32	0.22	0.24	0.31	0.32	0.23	0.32	0.27	0.31	0.25	0.30	0.08	0.02
4	0.75	0.59	0.88	0.41	0.48	0.79	0.63	0.3	0.74	0.88	0.31	0.3	0.41	0.47	0.31	0.79	0.39	0.63	0.27	0.51	0.21	0.06
5	1	0.69	1.45	0.52	0.55	1.08	0.77	0.51	1.47	1.44	0.71	0.51	0.51	0.54	0.37	1.08	0.77	0.77	0.45	0.78	0.36	0.10
6	1.2	1.41	0.97	1.39	1.45	1.30	1.40	1.40	0.93	0.97	1.67	1.40	1.38	1.44	1.42	1.30	0.94	1.40	0.73	1.25	0.28	0.08
7	2	0.79	0.81	0.75	0.69	0.68	0.83	0.48	0.79	0.80	0.88	0.48	0.74	0.69	0.99	0.68	1.42	0.83	1.32	0.87	0.26	0.07
8	3	0.58	0.59	0.52	0.52	0.59	0.74	0.46	0.57	0.59	0.73	0.46	0.51	0.52	0.79	0.59	0.84	0.74	0.79	0.64	0.12	0.03
9	4	0.49	0.42	0.49	0.52	0.51	0.51	0.41	0.49	0.41	0.51	0.41	0.49	0.51	0.41	0.51	0.65	0.51	0.41	0.48	0.07	0.02
10	6	0.43	0.41	0.42	0.46	0.47	0.51	0.39	0.45	0.41	0.45	0.39	0.42	0.45	0.39	0.47	0.51	0.51	0.39	0.44	0.04	0.01
11	8	0.41	0.41	0.37	0.34	0.41	0.41	0.35	0.39	0.40	0.41	0.35	0.37	0.34	0.39	0.41	0.45	0.41	0.34	0.39	0.03	0.01
12	10	0.39	0.29	0.28	0.28	0.29	0.41	0.29	0.28	0.29	0.32	0.29	0.28	0.28	0.27	0.29	0.31	0.41	0.29	0.32	0.04	0.01

Table 3: Bioavailability and pharmacokinetic parameters of Drug B in normal subjects administered in the oral dose of 400mg

Subjects	AUMC $_{(0-\infty)}$ ($\mu g.h^2/ml$)	AUC $_{(0-\infty)}$ ($\mu g.h/ml$)	C_{max} ($\mu g/ml$)	T_{max} (h)	MRT (h)	Ke (h^{-1})	$T_{1/2\beta}$ (h)	V_d (L/Kg)	(V_{SS}) (L/Kg)	CL (ml/h/kg)
1	23.32	5.18	1.78	1	4.49	0.22	3.11	346.97	17.14	77.13
2	23.17	4.72	1.01	1.5	4.91	0.20	3.40	416.08	17.25	84.74
3	26.12	5.47	1.44	1	4.76	0.21	3.30	348.20	15.31	73.02
4	28.10	5.84	1.67	1.5	4.80	0.20	3.33	328.61	14.23	68.38
5	23.46	4.61	1.41	1.5	5.08	0.19	3.524	440.75	17.04	86.67
6	25.10	5.11	1.38	1.5	4.91	0.20	3.40	384.15	15.93	78.23
7	27.05	5.64	1.30	1.5	4.79	0.20	3.32	339.44	14.78	70.84
8	24.98	5.18	1.32	2	4.81	0.20	3.33	371.40	16.01	77.11
9	25.10	5.11	1.38	1.5	4.91	0.20	3.40	384.15	15.93	78.23
10	28.10	5.84	1.67	1.5	4.80	0.20	3.33	328.61	14.23	68.38
11	23.17	4.72	1.00	1.5	4.91	0.20	3.40	416.08	17.25	84.74
12	23.46	4.6	1.40	1.5	5.08	0.19	3.52	440.75	17.04	86.67
13	25.02	5.16	1.44	1.5	4.84	0.20	3.36	375.59	15.98	77.47
14	25.84	5.36	1.42	1.5	4.81	0.20	3.33	359.30	15.47	74.57
15	27.05	5.64	1.30	1.5	4.79	0.20	3.32	339.44	14.78	70.84
16	30.63	6.42	1.42	2	4.76	0.21	3.30	296.48	13.05	62.22
17	31.14	6.15	1.40	1.5	5.05	0.19	3.50	328.76	12.84	64.98
18	24.98	5.18	1.32	2	4.81	0.20	3.33	371.40	16.01	77.11
MEAN	26.16	5.40	1.42	1.500	4.84	0.20	3.35	361.31	15.42	74.61
S.D.	2.65	0.54	0.19	0.302	0.15	0.01	0.10	39.69	1.47	7.28
SEM	0.76	0.15	0.05	0.087	0.04	0.01	0.03	11.45	0.42	2.10

0.055 µg/ml for Drug B and 1.376 ± 0.027µg/ml for Drug A and the T_{max} was 1.500 ± 0.087 h for Drug B and 1.458 ± 0.097 h for Drug A. In the previous studies of Norfloxacin, the AUC was found to be in the range of 6.2 to 6.7 µg.h/ml. The values of AUCs in this study are within the range (i.e. 5.409 ± 0.156 µg.h/ml of Drug B

Table 4: Bioavailability and pharmacokinetic parameters of Drug A in normal Subject administered in the oral dose of 400mg.

Subjects	$AUMC_{(0-\infty)}$ ($\mu g.h^2/ml$)	$AUC_{(0-\infty)}$ ($\mu g.h/ml$)	C_{max} ($\mu g/ml$)	T_{max} (h)	MRT (h)	Ke (h^{-1})	$T_{1/2\beta}$ (h)	V_d (L/Kg)	V_{SS} (L/Kg)	CL (ml/h/kg)
1	28.35	5.60	1.40	1.5	5.05	0.19	3.50	360.64	14.10	71.33
2	26.03	5.57	1.47	1.0	4.66	0.21	3.23	334.72	15.36	71.70
3	27.26	5.71	1.24	1.5	4.77	0.20	3.30	334.49	14.67	70.05
4	26.12	5.48	1.32	2.0	4.76	0.21	3.30	347.72	15.31	72.96
5	26.34	5.97	1.49	2.0	4.40	0.22	3.05	295.09	15.18	66.94
6	22.62	5.12	1.28	1.5	4.41	0.22	3.05	344.10	17.68	78.00
7	23.53	4.81	1.34	1.5	4.88	0.20	3.38	406.21	16.99	83.08
8	25.80	5.40	1.22	1.0	4.77	0.20	3.30	353.49	15.50	74.02
9	26.12	5.48	1.32	2.0	4.76	0.21	3.30	347.72	15.31	72.96
10	26.03	5.57	1.47	1.0	4.66	0.21	3.23	334.72	15.36	71.70
11	23.53	4.81	1.34	1.5	4.88	0.20	3.38	406.21	16.99	83.08
12	23.35	4.73	1.40	1.5	4.93	0.20	3.41	416.77	17.13	84.49
13	24.95	5.18	1.50	1.5	4.81	0.20	3.33	370.91	16.03	77.10
14	25.80	5.40	1.22	1.0	4.77	0.20	3.30	353.49	15.50	74.02
15	26.44	5.55	1.40	1.0	4.76	0.21	3.30	342.91	15.12	72.02
16	22.62	5.12	1.28	1.5	4.41	0.22	3.05	344.10	17.68	78.00
17	24.10	4.98	1.38	1.5	4.83	0.20	3.35	388.39	16.59	80.27
18	26.34	5.97	1.49	2.0	4.40	0.22	3.05	295.09	15.18	66.94
MEAN	25.41	5.34	1.37	1.4	4.75	0.21	3.29	357.95	15.80	75.16
S.D.	1.71	0.37	0.09	0.3	0.19	0.01	0.13	33.67	1.08	5.42
SEM	0.49	0.10	0.02	0.1	0.05	0.01	0.03	9.72	0.31	1.56

Table 5: Pharmacokinetic parameters of Norfloxacin tablets

Parameters	Drug B (Mean ± SEM)	Drug A (Mean ± SEM)
Maximum plasma concentration (C_{max}, µg/ml)	1.421± 0.055	1.376 ± 0.027 ^{ns}
Time to reach maximum plasma concentration (T_{max}, h)	1.500 ± 0.087	1.458 ± 0.097 ^{ns}
Area under the plasma concentration-time curve (AUC, µg.h/ml)	5.409 ± 0.156	5.346 ± 0.109 ^{ns}
Area under first moment of plasma concentration-time curve (AUMC, $\mu g.h^2/ml$)	26.166 ± 0.766	25.412 ± 0.496 ^{ns}
Mean residence time (MRT, h)	4.840± 0.044	4.758 ± 0.055^{ns}
Elimination rate constant (K_e, h^{-1})	0.207 ± 0.002	0.211 ± 0.002 ^{ns}
Absorption half life ($t_{1/2\alpha}$, h)	3.354 ± 0.030	3.297 ± 0.038 ^{ns}
Apparent volume of distribution (V_d, L/kg)	5.162 ± 0.164	5.114 ± 0.139 ^{ns}
Volume of distribution at steady state (V_{SS}, L/kg)	15.423 ± 0.426	15.808 ± 0.313^{ns}
Total body clearance (Cl_{total}, $L.h^{-1}kg^{-1}$)	74.616 ± 2.103	75.168± 1.567 ^{ns}

and 5.346 ± 0.109 µg.h/ml for Drug A). Elimination half life of norfloxacin ranges from 3 to 5 hours in previous studies and in the present study the half life was 3.35 ± 0.030 h for reference and 3.29 ± 0.038 h for test product. Volume of distribution reported in previous study was 3.2 l/kg in western population whereas in the present study, V_d for reference was 5.162 ± 0.164 L/kg and 5.114 ± 0.139 L/kg for test product. In the present study it was increased as study was conducted in summer, consequently the basal metabolic rate (BMR) and drug solubility increases, so V_d increases whereas other parameters are within the range. As a result, it is observed that there was no significant difference in pharmacokinetic parameters between two brands of norfloxacin and the bioavailability of both preparations was comparable.

In vitro - in vivo correlation

A good correlation between the dissolution and pharmacokinetic data was observed. IVIVC was determined by drawing plots between drug absorbed (%) and drug dissolved (%) at same time points for all

formulations. A high value of determination coefficient (R^2 = 0.9328 and 0.9421 for Drug B (reference) and Drug A (test), respectively) suggested good correlation between in vitro and in vivo profiles. This correlation shows that dissolution profile can be utilized as a predictive tool for in vivo data. Similar results have already been described in literature (Leeson, 1995).

CONCLUSION

The Bioequivalence study was conducted on two brands of Norfloxacin i.e., Drug B (reference) and Drug A (test). The results of reference and test products showed that the brands posses almost same dissolution, bioavailability and pharmacokinetic assessment. The value of F was found to be 0.99, which is in good agreement with the limits given in FDA & WHO guidelines for such parameters. Therefore, on the basis of above mentioned values it can be concluded that both the brands are bioequivalent and

can be used as pharmaceutical substitute with each other. The present studies has been conducted in normal conditions, the assessment of bioavailability and pharmacokinetic parameters of the drugs can further explored while conducting these studies in real clinical conditions.

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