Arch. Pharm. Res. **15**(3), 208-210 (1992)

Relative Bioavailability Studies on Two Tablet Preparations of Ofloxacin

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(Received March 19, 1992)

Abstract □ Comparative bioavailability of two tablet dosage forms of ofloxacin (either as Hoechst (India) or Ranbaxy preparation) was investigated. In a randomized cross-over study, eight healthy human volunteers received single 200 mg dose of film coated ofloxacin in fasting state. The concentrations of ofloxacin in the collected saliva and serum samples were measured by high performance liquid chromatography. No significant difference in bioavailability of both preparations was judged from various serum and saliva pharmacokinetic parameters such as peak concentration, time to peak concentration and area under the curves. Intersubject variation was also found to be insignificant.

Keywords □ Ofloxacin, comparative bioavailability.

Ofloxacin, is a recently developed fluoroquinolone carboxylic acid derivative, structurally related to nalidixic acid and is claimed to exert excellent antibacterial activity against a wide spectrum of organisms[1]. The pharmacokinetic properties of ofloxacin have been investigated by various workers. Kalager *et al*[2] investigated the pharmacokinetics of drug in serum and skin blisters. Okhamafe and Akerele[3] investigated the effect of food and sex of individuals on availability of the drug.

Ofloxacin is reported to be completely absorbed after oral administration. It has a long half-life and more than 90% is excreted unchanged *via* kidneys.

Variation in drug availability may result when a drug is administered in different formulations, resulting in therapeutic inequivalence[4]. The aim of the present study is to investigate comparative bioavailability of two tablet dosage forms of ofloxacin after oral administration to human volunteers.

EXPERIMENAL METHODS

Eight healthy young volunteers participated in the study. Their mean age was 23 years (21-25 years) and mean weight was 60.2 kg (58-62 kg). None of the subjects had a history of cardiac, renal or gastro-intestinal disease and showed normal haematological data. The subjects were informed of the scope of the study and written consent was obtained from them. They were non-smokers and had not taken any medication a week prior to the study.

All subjects were fasted overnight and provided standard lunch 4h after administration of 200 mg film coated ofloxacin tablet. The study was carried out using a random cross over design. Four subjects received the Hoechst (India) product [Tarivid^R, (formulation A)] and remaining four received Ranbaxy Product [Zanocin^R, (formulation B)] (treatment I). After a wash out period of one week the alternate formulations were administered (treatment II).

Venous blood samples were drawn into heparinized tubes at different time intervals i.e. 0, 0.5, 1, 2, 4, 6, 9, 12 and 24h thereafter. The serum was separated and stored frozen at $-20^{\circ}C$ until analysed. Saliva samples were also collected from each individual at 0, 0.5, 1, 2, 4, 6, and 9h in clean test tubes and frozen till analysis. Serum and saliva levels of ofloxacin were determined by high performance liquid chromatography using method of Chan and co-workers[5].

Biological fluid (0.1 m*l*) was treated with pipemi-

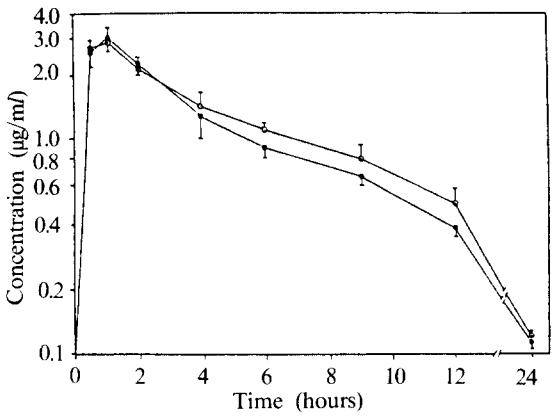

Fig. 1. Serum ofloxacin concentrations folloing adminstration of formulation A (—○—) and formulation B (—●—). Bars at data points indicate± S.D. (n=8).

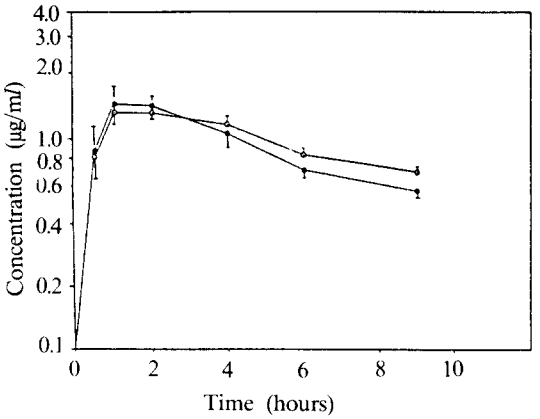

Fig. 2. Saliva ofloxacin concentrations folloing administration of formulation A (—○—) and formulation B (—●—). Bars at data points indicate± S.D. (n=8).

dic acid which served as an internal standard and mixed with 1.0 M $HClO_4$ (0.1 m*l*) at 55℃ for 15 min. After centrifugation (10,000g for 5 min), the supernatant solution (10 to 50 μ*l*) was analysed on a column (30 cm×3.9 mm) of μ-Bondapak C-18 (10 μm) with acetonitrile: 0.4 M citric acid (1 : 5) as a mobile phase (1 m*l*/min) and detection was performed at 275 nm.

RESULTS AND DISCUSSION

The minimum detectable levels of ofloxacin were 50 ng/m*l* when analysed both in plasma and saliva. The average serum levels of ofloxacin folloing ad-

Table I. Serum pharmacokinetic parameters of ofloxacin after single oral doses of 200 mg tablet

Pharmacokinetic parameter	Hoechst preparation (Formulation A)	Ranbaxy* preparation (Formulation B)
1. Peak serum concentration, C_{max}, (μg ml^{-1})	2.94± 0.55	3.02± 0.31
2. Time to peak serum concentration t_{max} (h)	0.86± 0.26	0.92± 0.62
3. AUC (0-24) ug ml^{-1} h^{-1}	15.10± 2.05	13.29± 1.66
4. Serum half life of elimination $t_{1/2}$ (h)	6.42± 1.71	7.06± 1.81

Results are shown as mean± s.d., n=8

*The differences are insignificant (all parameters) ($p \leq 0.05$, Student t-test).

Table II. Salivary pharacokinetic parameters of ofloxacin after single oral doses of 200 mg tablet

Pharmacokinetic parameter	Hoechst preparation (Formulation A)	Ranbaxy* preparation (Formulation B)
1. Peak salivar concentration, C_{max}, (μg ml^{-1})	1.35± 0.41	1.43± 0.33
2. Time to peak salivar concentration t_{max} (h)	1.34± 0.21	1.25± 0.37
3. AUC (0-9) μg ml^{-1} h^{-1}	10.20± 1.15	8.55± 2.10
4. Saliva half life of elimination $t_{1/2}$ (h)	5.90± 1.55	6.37± 2.08

Results are shown as mean± s.d., n=8

*The differences are insignificant (all parameters) ($p \leq 0.05$, Student t-test).

minstration of formulation A and B are illustrated in Fig. 1. The relevant pharmacokinetic parameters C_{max}, t_{max}, AUC_{0-24} and $t_{1/2}$ are recorded in Table I. The various pharmacokinetic parameters were tested for significant difference using Student's t-test. No significant differences were recorded in all the parameters for both the treatments ($p<0.05$).

The results were fairly consistent as the inter-subject variation folloing both treatments was found to be insignificant ($p<0.05$, ANOVA). No significant difference in the relevant pharmacokinetic parameters indicated equivalent bioavailability of ofloxacin folloing both treatments.

The saliva levels of ofloxacin folloing treatments I and II are shown in Fig. 2 and derived pharmacokinetic parameters are recorded in Table II. The difference in pharmacokinetic parameter was insignificant as found with serum data ($p<0.05$). The intersubject variation was also noted to be insignificant ($p<0.05$, ANOVA). The saliva profiles were found to be closely parallel to the serum profiles. The results were in agreement with the findings of Uematsu *et al*[6].

In conclusion, both the tablet dosage forms seemed to be bioequivalent as judged by various pharmacokinetic parameters. The intersubject variation was also found to be insignificant folloing their administration.

ACKNOWLEDGEMENT

The authors wish to thank, Prof. N.K. Jain, Head, Department of Pharmaceutical Sciences, Dr. Harisingh Gour Vishwavidyalaya, Sagar (M.P.) India for providing necessary facilities.

LITERATURE CITED

1. Wittenberger R.: *Ofloxacin versus pipemidsaure und cotrimoxazole.* Infection, **14** (Suppl. 1), 93 (1986).
2. Kalager, T., Digranes, A., Bergan, T. and Rolstad, T.: *Pharmacokinetics of ofloxacin in serum and skin blister.* In: Proceedings of the 14th, International Congress on Chemotheraphy, Kyoto, pp. 1765-66 (1985)
3. Okhamafe, A. O. and Akerele, J. O.: *Some aspects of the bioavailability of orally administered ofloxacin in healthy human volunteers. Int. J. Pharm.,* **50**, 83 (1989).
4. Greenblatt, D. J., Smith, T.W. and Koch-wester J., *Bioavailability of drugs: the digoxin dilemma. Clin. Pharmacokin.* **1**, 36 (1976).
5. Chan, C. Y., Lam, A. W. and French, G. L.: *Rapid HPLC assay of fluoroquinolones in clinical specimens. J. Antimicrob. Chemother.* **23**, 597 (1989).
6. Uematsu, M., Morihana, T., Sekiguchi, T., Imoto, T. and Sasaki, J.: The pharmacokinetics and saliva penetration of ofloxacin, norfloxacin, enoxacin and pipemidic acid. In. Proceedings of 14th International Congress on Chemotherapy, Kyoto, pp. 1891-92 (1985).