The Effect of Soya bean (*Glycine max*) on Pefloxacin Absorption in Rats

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Abstract

The study was to investigate the effect of soya bean on the absorption of pefloxacin when given by oral route in rats. The first group of animals feeding on standard pellet feeds was given pefloxacin (8 mg/kg, p.o), while the second and third groups were also given the drug at the same dosage level but were fed with 50 % and 100 % soya bean respectively. Plasma samples were collected at different time intervals following drug administration. The concentrations of pefloxacin in plasma were determined using spectrophotometric method. Feeds with 50 % and 100 % soya bean respectively, gave significant increase ($P<0.05$) in the mean maximum plasma concentration (C_{max}), mean area under the plasma concentration-time curve (AUC) compared to those obtained for standard pellet feeds alone. No significant change in the mean time to reach maximum concentration (T_{max}) was observed in all the tests. The results suggest an increase in the total absorption of pefloxacin by soya bean.

Keywords: Soya bean, *Glycine max*, Pefloxacin absorption, Bioavailability, Rats

Introduction

The rate and extent to which an orally administered drug is absorbed depend on its physicochemical properties as well as various interactions between the drug and the gastrointestinal tract (Gibaldi and Feldman, 1970; Levy, 1972; Chasseaud and Taylor, 1974). Food components can act on the release from dosage form as well as on the absorption of drugs. Potentially, food may interfere with tablet disintegration, drug dissolution and drug transport through the gastrointestinal tract. Several studies have reported the influence of standard meals or food components on drug absorption (Levine, 1970; Welling, 1977; Toothaker and Welling, 1980; Kirk, 1995; Jefferson, 1998; Leibovitch *et al*., 2004). Pefloxacin,1,4-dihydro-7-(4-methylpiperazinyl)-4-oxo-3-quinoline carboxylic acid is a second generation fluoroquinolone antibacterial agent. It acts by inhibiting DNA synthesis through cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and type iv topoisomerase, resulting in rapid bacterial death (Hooper, 1999). Pefloxacin absorption, metabolism and mechanism of renal elimination in animals and humans have been reported to be influenced by food and antacid (Montay *et al*., 1984; Ulrich *et al*., 1994). Soya bean (*Glycine max*), in various preparations serves as an important source of protein in diets to various peoples of the world. Locally, soya bean serves as an ingredient in preparing foods for diabetic patients and as a good beverage for many households. In this investigation, the influence of soya bean on pefloxacin absorption was studied. Soya bean was chosen because of the reasons already cited and literature review has shown little or no study on its effect on pefloxacin absorption. Pefloxacin was chosen for the study, because it is used for various disease states such as infections of the respiratory and urinary tracts, skin and soft tissue, gastrointestinal tract as well as severe systemic infections.

Materials and Methods

Materials: Pefloxacin mesylate was obtained from Fidson Healthcare Ltd, Nigeria while soya bean was purchased from Nsukka central market in Enugu State, Nigeria. All other chemicals were of analytical grade.

Methods

Preparation of samples: Pefloxacin mesylate was prepared by suspending in 0.25 % w/v carboxymethyl cellulose while soya bean was prepared by drying in an oven at 50 ^{o}C and pulverizing with a mill.

Pharmacokinetic study: In-house bred albino rats of either sex, weighing between 180-250 g were utilized for the study. The animals were housed in polypropylene cages and allowed access to food and water. In one group of rats (n=4) feeding on standard pellet diet (poultry growers feed), pefloxacin (8 mg/kg, p.o) was administered orally. The other group of rats- 2nd and 3rd groups, (n=4) were fed on 50 % (standard pellet diet: soya bean, 1:1) and 100 % soya bean respectively, and also received pefloxacin at the dosage level as the 1st group of animals. Blood samples (0.5 ml) were collected in tubes containing 1 mg of ethylene diamine tetra acetic acid sodium (EDTA sodium) through microcapillary technique from retro-orbital plexus (Sorg and Buckner, 1964) under light ether anesthesia before treatment with pefloxacin and thereafter at 0.5, 1.0, 1.5, 2.0, 3.0, 4.0, 6.0, 8.0, 10.0, 12.0 and 24.0 h after oral administration of

pefloxacin. Plasma samples after centrifugation (10 min, 3000 rev/min), were deproteinized with acetonitrile. The plasma/acetonitrile mixture was allowed to stand for 10 min before centrifuging at 5000 rev/min for 10 min. The upper layer was separated and used for the determination of pefloxacin levels.

Determination of plasma pefloxacin concentration: The plasma concentrations of pefloxacin were determined by ultra violet spectrophotometric method at maximum wavelength of 280 nm. The standard curve constructed using deproteinized plasma was linear in the range of 0.5-10 µg/ml. Quantification of pefloxacin in rat plasma was done by reading the analyte response against the calibration curve.

Recovery: Recovery of pefloxacin from plasma was obtained using 1.0-5.0 µg/ml concentrations by comparing absorbance of spiked deproteinized standards with those of corresponding concentration in acetonitrile.

Analysis of data: The area under the plasma concentration-time curve (AUC) to the last sampling time was estimated by the linear trapezoidal method. The maximum concentration (C_{max}) and maximum time (T_{max}) were obtained directly from the generated data. The elimination constants (k) and terminal half-lives were calculated from the log-linear part of the slope. The differences between the three respective treatment groups were analyzed for significance using student's t-test. P values equal to or less than 0.05 were considered significant.

Results and Discussion

The regression equation describing the absorbance versus concentration relationship is A = 0.113C + 0.062 (r = 0.9934). The recovery analysis (Table 1) shows that the solvent was effective in extracting pefloxacin from the spiked plasma.

Table 1: **Recovery of pefloxacin from the plasma samples**

Concentration of pefloxacin (µg/ml) (n= 3)	% Recovery (Mean ± SD)	% CV
1.0	91.51 ± .008	0.008
2.0	99.35 ± 0.127	0.128
3.0	94.90 ± .060	0.634
4.0	87.90 ± 0.093	0.106
5.0	90.21 ± 0.1513	0.168

The relative extent of bioavailability of pefloxacin in the presence of 50 % and 100 % soya bean respectively, was significantly ($p<0.05$) greater than that of pefloxacin in the presence of standard pellet feeds (Fig. 1).

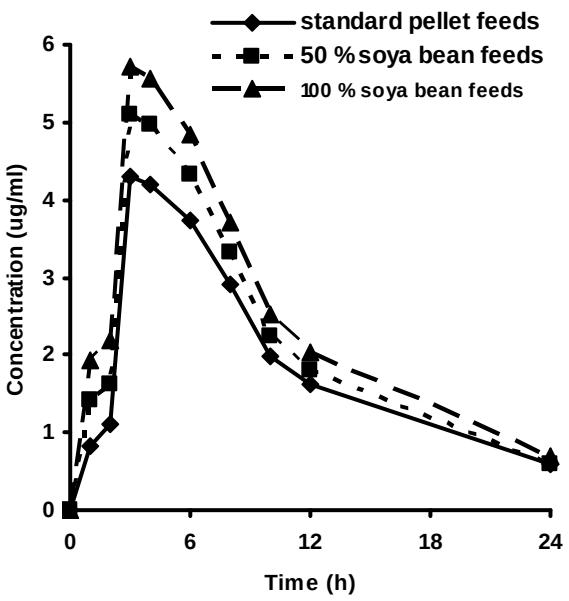

Fig. 1: Plasma level-time profile for standard pellet feed, 50 % soya bean feed and 100 % soya bean feed. Each point represents the mean ± SD of four observations

This was reflected by a mean increase of 25 % and 31 % in area under the curve ($AUC_{0\rightarrow24}$) when pefloxacin was given with 50 % and 100 % soya bean respectively. It was also noted that the pefloxacin peak plasma concentration was increased by 23 % when given with 50 % soya bean or by 28 % when given with 100 % soya bean. There was no significant change in the time to reach peak plasma concentration, a rough estimate of absorption rate. The rest of the pharmacokinetic parameters are presented in Table 2.

Any co-administered treatment influencing the rate of gastric emptying of orally administered drug should be considered as potentially affecting the rate of absorption. Although, food has been found as a factor modifying drug absorption by delaying the gastric emptying rate (Melander, 1978), soya bean may not have modified pefloxacin absorption by this mechanism since the time to peak concentration was not significantly affected in the study. The probable mechanism of action could either be the formation of aggregates that could associate with and solubilize pefloxacin molecules, or reduction in the contact angle between the drug and the gastrointestinal fluids by increasing the effective surface area of pefloxacin particles. Another probable mechanism could be a change in the pH of the environment of the dissolved drug.

Conclusion: Pefloxacin absorption was significantly increased in rats fed with soya bean. The results of this investigation would suggest that the extent of pefloxacin absorption could be increased by as much as 31 % in the presence of soya bean.

Table 2: Plasma pharmacokinetic parameters of pefloxacin (8 mg/kg, p.o) administered alone or together with soya bean in rats

Parameter	Standard pellets feeds (Treatment group I)	50 % soya bean feeds (Treatment group II)	100 % soya bean feeds (Treatment group III)
C_{max} (µg/ml)	4.31 ± 0.404	5.63 ± 0.658	5.73 ± 0.568
T_{max} (h)	2.9 ± 0.513	2.7 ± 0.532	3.0 ± 0.462
AUC $_{0\rightarrow24}$(µg.h/ml)	31.73 ± 0.661	42.27 ± 0.878	46.12 ± 0.649
$t_{1/2}$ (h)	14.6 ± 1.907	14.4 ± 0.847	14.3 ± 1.553

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