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STUDY ON THE EFFECT OF UNRIPE PLANTAIN (*MUSA PARADISISACA*) ON PEFLOXACIN ABSORPTION IN RATS

MBAH C. J, UBOH K. H.

Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka. Enugu State, Nigeria

E-mail of Corresponding Author: cjmbah123@yahoo.com

ABSTRACT

The present study was carried out to investigate the effect of unripe plantain (*Musa paradisisaca*) on pefloxacin absorption in rats. Pefloxacin (20mg/kg), was administered orally to three groups of albino rats fed on standard pellet feeds, 50 % and 100 % unripe plantain respectively. Blood samples were taken at pre-application and 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 post-application from retro-orbital plexus of the animal using micro-capillary technique. Ultraviolet spectrophotometric method was used to determine pefloxacin concentration in plasma samples. Feeds with 50 % and 100 % unripe plantain respectively, gave significant increase ($P<0.05$) in the mean maximum plasma concentration (C_{max}), mean area under the plasma concentration-time curve (AUC) as 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 that the total absorption of pefloxacin could be enhanced by unripe plantain.

Keywords: Unripe plantain, pefloxacin, bioavailability.

INTRODUCTION

Pefloxacin, 1,4-dihydro-7-(4-methylpiperazinyl)-4-oxo-3-quinoline carboxylic acid is a second generation fluoroquinoline antibacterial agents. Its mechanism of action like most fluoroquinolones, involves the inhibition of DNA synthesis by promoting cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and
type iv topoisomerase, resulting in rapid bacterial death[1]. Clinically, the drug is used in the treatment of various disease states such as respiratory and urinary tract infections, skin and soft tissue infections, gastrointestinal tract infections, severe systemic infections. Food can influence absorption of drugs by interfering with tablet disintegration, drug dissolution and its transport through the gastrointestinal tract. A number of studies have reported on the influence of standard meals or food components on drug absorption [2,3,4,5,6,7]. Plantain (*Musa paradisisaca*), ripe or unripe in various preparations serves as an important source of food to various peoples of the world. In this part of the world, ripe or unripe plantain could be served either as a sauce or eaten as roasted or boiled plantain usually with palm oil. Locally, the unripe plantain serves as: (i) good carbohydrate source for diabetic patients (ii) anti-motility agent for those suffering from gastrointestinal disorders such as diarrhoea or dysentery (iii) readily source of food for workers in offices as well as buyers and sellers in open markets. It is against the background that local patients on pefloxacin could

feed on unripe plantain while in offices or markets that the present study investigated the effect of unripe plantain on pefloxacin absorption in rats. Furthermore, literature review has shown little or no study on the effect of plantain on pefloxacin absorption.

MATERIALS AND METHODS

Pefloxacin mesylate (Fidson Healthcare Ltd, Nigeria), carboxymethyl cellulose (Aldrich-Sigma, USA), unripe plantain (Nsukka, Nigeria) was dried in an oven at
50 ^{o} C and pulverized. All other chemicals were of analytical grade.

Pharmacokinetic study:

In house bred albino rats of either sex weighing between 200-250 g were used for the study. The animals were housed in polypropylene cages and allowed access to food and water. The ethical clearance was obtained from the ethics committee of the Faculty of Veterinary Medicine, University of Nigeria, Nsukka. In one group of rats (n=4) feeding on standard pellet diet (poultry growers feed), pefloxacin (20mg/kg) was administered orally. The second and third groups of rats (n=4) feeding on
50 % (standard pellet diet: unripe plantain, 1:1) and 100 % unripe plantain respectively, also received pefloxacin at the dosage level as the first group of animals. Blood samples (0.5 ml) were collected in tubes containing 1 mg of EDTA sodium through microcapillary technique from retro-orbital plexus[8] 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 separated by centrifugation (10 min, 3000 rev/min) were deproteinated with acetonitrile. The plasma and 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 concentrations:

Ultraviolet spectrophotometric method was used to quantify pefloxacin concentrations in plasma samples. Determination of pefloxacin was performed at a maximum wavelength of 280 nm. The standard curve constructed using deproteinized plasma was linear in the range of 1.0 -10 µg/ml. Deproteinized plasma was used as the blank.

Accuracy and precision:

To determine the intra-day and inter-day accuracy and precision, the concentrations of pefloxacin present in five replicates of deproteinized plasma spiked with 1.0, 2.0 and 3.0 ug/ml respectively was determined within a day or on three consecutive days. Accuracy of 85-100 % and coefficient of variation values < 5 % were considered acceptable.

Recovery:

Recovery of pefloxacin from plasma was estimated using 1.0-5.0 µg/ml concentrations by comparing absorbance of spiked deproteinized plasma 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_{el}) and terminal half-lives ($t_{1/2}$) 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 calibration graph of pefloxacin was linear in the concentration range of

1.0-10 μg/ml. The regression equation describing the absorbance versus concentration relationship is A = 0.113C + 0.062 (r = 0.9934). The inter-day and intra-day estimation of pefloxacin reveals the reproducibility of the results (Table 1) irrespective of time and day. The recovery analysis (Table 2) shows that the solvent was effective to extract pefloxacin from the spiked plasma. The results indicate that the relative extent of bioavailability of pefloxacin in the presence of 50 % and 100 % unripe plantain respectively, was significantly ($p<0.05$) greater than that of pefloxacin in the presence of standard pellet feeds (Fig.1).

This was reflected by a mean increase of 23 % and 45 % in area under the curve ($AUC_{0\rightarrow24}$) when pefloxacin was given with 50 % and 100 % unripe plantain respectively. It was also noted that the pefloxacin peak plasma concentration was increased by 19 % when given with 50 % unripe plantain or by 30 % when given with 100 % unripe plantain. 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 reported in Table 3.

Although, food has been found as a factor modifying drug absorption by delaying the gastric emptying rate[9], unripe plantain 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. Furthermore, changes in pH of the environment of the dissolved drug or stimulation of the intestinal blood flow could also be probable mechanisms.

CONCLUSION

Pefloxacin absorption was significantly increased in rats fed with unripe plantain. Although, the present investigation was carried out in rats, the results could also be obtained in humans who feed on unripe plantains. Furthermore, the results of the present study would suggest that the extent of pefloxacin absorption could be increased by as much as 45 % in the presence of unripe plantain. Finally, as acetonitrile was able to extract the drug from the deproteinized plasma, the present method appears comparatively simple for plasma preparations.

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Table 1: Accuracy and Precision of the Method for estimating Pefloxacin concentration in plasma

Known Concentration, µg/ ml	Concentration found (Mean ± SD, µg/ ml	Accuracy (%)	Precision (% CV)
Intra day (n = 5)			
1.0	0.862 ± 0.11	86.2	1.20
2.0	1.852 ± 0.061	92.6	3.30
3.0	2.859 ± 0.087	95.3	3.04
Inter-day (n = 5)			
1.0	0.901 ± 0.019	90.1	2.06
2.0	1.914 ± 0.055	95.72	2.88
3.0	2.979 ± 0.098	99.3	3.29

Table 2: **Recovery of pefloxacin from the plasma samples**

Concentration of pefloxacin (µg/ml) (n= 3)	% Recovery (Mean ± SD)	% CV
1.0	97.64 ± 1.02	2.83
2.0	88.21 ± 3.12	3.54
3.0	94.70 ± 3.92	4.16
4.0	91.32 ± 2.74	3.00
5.0	96.4 ± 3.32	3.44

Mean ± SD: n = 3

Table 3: Plasma pharmacokinetic parameters of pefloxacin (20 mg/kg, p.o) administered alone or in the presence of unripe plantain

Parameter	Standard pellets feeds	50 % unripe plantain feeds	100 % unripe plantain feeds
C_{max} (µg/ml)	7.65 ± 1.32	9.48 ± 0.688	10.96 ± 0.568
T_{max} (h)	3.02 ± 0.513	2.94 ± 0.514	3.11 ± 0.416
AUC $_{0\rightarrow24}$ (µg.h/ml)	31.73 ± 2.46	41.25 ± 1.45	57.62 ± 3.15
K_{el}	0.075 ± 0.004	0.072 ± 0.002	0.069 ± 0.007
$t_{1/2}$ (h)	8.86 ± 0.414	9.86± 0.461	10.16± 0.607

Mean ± SD: n = 3

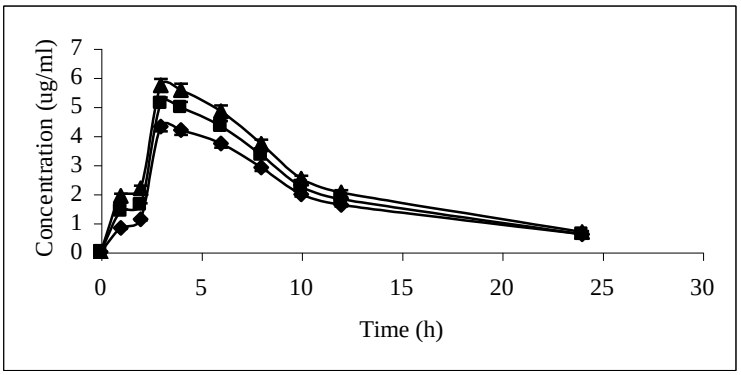

Fig. 1. Plasma level-time profile for standard pellet feeds (▪), 50 % unripe plantain feeds (■), 100 % unripe plantain feeds (▲) Each point represents the mean ± SD of four observations.