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Pharmacokinetics of Chloroquine in Rabbit: Effect of Fasting

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Chloroquine is an important drug in the tropics and subtropics for the treatment of malaria. There had been some reports on the effect of food on the pharmacokinetics of chloroquine [1], but as at now, there seems to be no published data on the effect of fasting on the pharmacokinetics of chloroquine. As a result of this, the present study has reported some pharmacokinetic parameters obtained from the urinary excretion level of fasted rabbits.

The difference in the parameters in the fed and fasted rabbits. ($P \leq 0.05$) implies that fasting has a significant effect on the pharmacokinetic of chloroquine in rabbits.

Chloroquine phosphate was a gift from Walter Reed, Washington, USA, the hydrochloric acid (BDH), diethyl ether and other buffer materials were of analar grade. The pH of all the buffer solutions prepared was checked with a Pye Unicam pH-meter and adjusted to appropriate value (if necessary) with 0.1 M NaOH solution. A Perkin Elmer spectrofluorimeter model 204 was used for fluorescence measurement.

Male albino rabbits weighing between 1.8 - 2.2 kg were used for the study.

Two groups of rabbits were used whereby one set of 6 rabbits was fasted and another set of 6 rabbits was allowed to have normal feeding. For the first group, the rabbits were kept in metabolic cages and allowed to get adaptation with the environment; they were fed normally. The second group kept in metabolic cages was also allowed to get adaptation to the environment but were not fed but allowed to drink water *ad libitum*.

Chloroquine phosphate was dissolved in normal saline and administered into the rabbits through stomach tube at a dose of 10 mg/kg. Before the administration, urine was collected to serve as the zero hour sample. After the administration, urine samples were collected between the following time intervals, 0-12, 12-24, 24-48, 48-72 and 72-96 hrs. The total volume of urine collected at these time intervals were noted. The urine at each interval was collected and stored in glass containers containing 0.5 ml of 5 M HCl and the samples were kept in the refrigerator until analysed.

Chloroquine in the urine samples was analysed by a modified fluorimetric method described previously [2].

From the values of the chloroquine concentration obtained in the study, the urinary excretion rate (dxu/dt) of chloroquine was determined and plotted against time on a semi-log paper from which the pharmacokinetic parameters were analysed according to the modified equation of Rowland and Tozer [3].

$$\frac{dxu}{dt} = \frac{K_e K_a F X_0}{(K_a - K_e)} \left(e^{-kt} - e^{-kat} \right) - 1$$

where dxu/dt is the excretion rate, Ke is the elimination rate constant, Ka is the absorption rate constant, F is the fraction of the drug absorbed and Xo is the dose administered.

The pharmacokinetic parameters obtained in the two sets of the experiments are presented in Table 1.

TABLE 1. PHARMACOKINETIC PARAMETERS OF CHLOROQUINE UPON ORAL ADMINISTRATION IN FED AND FASTED RABBITS.

*Parameter	Fed Rabbits	Fasted Rabbits
$K(h^{-1})$	0.069 ± 0.006	0.041 ± 0.005
$K(h^{1})1$	1.25 ± 0.12	0.83 ± 0.09
$t_{1/2}$ a(hr)	0.82 ± 0.07	1.08 ± 0.09
Ke (h^{-1})	0.015 ± 0.001	0.029 ± 0.003
$t_{1/2}$ el (hr)	12.5 ± 0.40	15.1 ± 0.52
T_{max} (h)	2.10 ± 0.11	3.80 ± 0.21
T_{lag} (h)	0.52 ± 0.08	0.73 ± 0.06

Each value is the mean of 6 determination ± S.E.M.
*K = elimination rate constant; *Ka =absorption rate constant;
Ke = urinary excretion rate constant; $t_{1/2}$ = half-life of absorption;
$t_{1/2}$ =half-life of elimination; T_{max} = time to reach maximum concentration;
T_{lag} =time between administration of the drug and when absorption begins.

The results were compared using the student's t-test at 0.05 significant level. It was found that the values of these pharmacokinetic parameters from the urinary excretion data for the fed rabbits are significantly different from the values obtained from the fasted rabbits ($P \leq 0.05$). The time for the absorption and the elimination of the drug is reduced in the fasted rabbits ($P \leq 0.01$) while the time to reach the maximum excretion rate in the fasted rabbits is higher than the time required in the normal rabbits ($P \leq 0.05$).

In this study, it has been demonstrated that the pharmacokinetics of chloroquine is greatly altered by fasting.

Though this study has been conducted in experimental animals and it is usually difficult to extrapolate animal studies to studies carried out in man, but the present investigation has indicated the need to carry out such study in man. The values obtained from such study will help in making the necessary dosage regime adjustments in chloroquine administration.

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Key words: Chloroquine, Pharmacokinetics, Fasting, Rabbits.

References

1. A. Turple and K. Krishnaswamy, Eur. J. Clin. Pharmacol., **23,** 271 (1982).
2. S.A. Adelusi and L.A. Salako, J. Pharm. Pharmac.,**32,** 711, (1980).
3. M. Rowland and T.N. Tozer, *Clinical Pharmacokinetics: Concepts and Applications* (Lea and Febiger, Philadephia, 1980), pp. 293-296.