

## Pharmacokinetics of ciprofloxacin in layer chicks

B.A.Al - Khafaji , A.A.Al-Khayyat , O.M.S.Al-Shaha.

Department of physiology , college of Vet. Med. University  
of Baghdad , Baghdad , Iraq.

### Abstract

Pharmacokinetics parameters of ciprofloxacin were calculated from constructed plasma disappearing curves (PDC) after oral or i.v. injection of 5mg / kg in two -week old hybrid layer . The i.v. PDC indicated a first order biphasic kinetic . The distribution phase was too short to be considered . The parameters of the elimination phase indicated that the biological half - life (  $t_{1/2}$  ) was 3.7 hours and the volume of distribution (Vd) was 1.7 l/kg .

The oral PDC indicated a first order kinetic with a peak plasma level (PPL) of 3.0 ug / ml achieved after 1.75 hours , a  $t_{1/2}$  of 2.9 hours and a Vd of 1.7 l/kg . Bioavailability value was  $84 \pm 9.7\%$  . Binding of ciprofloxacin to chicken plasma protein was estimated to be  $25.4 \pm 1.3\%$ .

### Introduction

Respiratory affections in poultry are considered among the most important problem that is facing poultry industry in Iraq . In one study , the ratio of these diseases was estimated to be 37% of total diseases of broiler and that are caused by *E.coli* was 18.6% (1) .

Ciprofloxacin was recently introduced among other fluoroquinolones for the treatment of these diseases. In addition to its bactericidal effect , it is also active against some resistant Gram - ve bacteria and mycoplasma (2) , this drug also known to achieve higher concentration in the respiratory organs (3,4) .

This study was done to evaluate some important pharmacokinetic parameters including Bioavailability,  $t_{1/2}$ ,  $V_d$ , and the ratio of plasma protein binding, in chickens, which may be of benefit to estimate the required dosage in poultry.

### **Materials and Methods**

A group (39) two – week old hybrid breed chicks was given ciprofloxacin (Pure, Vapco. Co., Jordan) at the recommended dose of 5mg /kg, orally. Another similar group was given the same dose through the wing vein after it was dissolved in 0.1 N NaOH. Blood samples before and at planned intervals after administration were taken in order to construct the plasma disappearance curve. Three chicks were used for collection of blood sample through heart puncture for each interval.

Samples were analyzed by a microbiological assay using *E. Coli* ATCC 25922 as the test organism based on (5).

Parameters of pharmacokinetic were calculated from the plasma disappearance curve according to (6). Binding of ciprofloxacin to chicken plasma protein was done by the equilibrium dialysis methods described by (7).

### **Results**

The PDC after oral administration (Table 1) indicates a first order kinetic with PPL of 2.1 ug / ml after 1.75 hours of administration, the elimination  $t_{1/2}$  was 2.9 hours and the  $V_d$  was 1.7 l/kg. The elimination PDC after i.v. route indicates also a first order kinetic and a biphasic curve. The elimination  $t_{1/2}$  was 3.7 hours and  $V_d$  was 1.7 l/kg. Bioavailability of ciprofloxacin was  $84 \pm 10\%$  (Table 1). Binding of the drug with plasma protein ranged between 18.0 – 30.8% (Table 2).

**Table 1:** Pharmacokinetic parameters of ciprofloxacin after a single dose of 5 mg/kg B. W. in chicks

Parameter <sup>(1)</sup>	Oral Mean ± SE	Intravenous Mean ± SE
Slope minute <sup>-1</sup>	- 0.0040	- 0.0034
Drug concentration at zero time (µg/ml)	2.86 ± 0.18 a <sup>(2)</sup>	2.89 ± 0.30 a
Biological half-life (t½, hour)	2.90 ± 0.24 a	3.70 ± 1.00 a
Volume of distribution (Vd, l/kg)	1.70 ± 0.24 a	1.70 ± 0.20 a
Area under curve (AUC, µg/kg.min)	6.90 ± 0.15 a	5.80 ± 0.70 b
Bioavailability (F%)	84 ± 9.7	

(1) All parameters represent the elimination phase.

(2) Similar letter indicates absence of statistical significance to a degree of 99% of confidence.

Table 2: Percentage of binding of ciprofloxacin to chicken plasma protein.

Original conc. of ciprofloxacin in plasma µg/ml	Protein conc. In chicken plasma sample g/dl	Percentage of binding <sup>(1)</sup>
0.50	4.60	19.39
0.50	4.60	17.15
1.00	4.20	30.90
1.00	4.20	24.74
2.00	4.30	31.94
2.00	4.30	30.59
4.00	4.20	28.35
4.00	4.20	24.10
10.00	5.00	22.83
10.00	5.00	24.08
Mean:	4.46	25.40

(1) Results were corrected to protein concentration in each sample.

### **Discussion**

The elimination of ciprofloxacin from the plasma as can be seen from the PDC of i.v. and oral group follow first order kinetic . This result is expectable , as the same results were seen with other species ( 8 , 9) .

The PDC of i.v. route indicates a biphasic type of elimination . The first phase which represents the disposition took place within the first hour following treatment where as the rest of the curve represents the elimination phase. Such result was noticed in man (14) and dogs (11).

Peak plasma levels , after oral or i.v. were less than that seen in man (14) but more than that seen in dogs (11) . This could be explained on basis of species variation factor . The biological half - life ( $t_{1/2}$ ) of the drug was 2.9 and 3.7 hour for oral and i.v. route respectively. However , this difference was not significant statistically as expected from first order kinetic , but it is found to be close to that described in rat , after i.v. route (12) and longer than that described in calves (13) and dogs (11). This can be attributed to difference in biotransformation among species.

The Vd of ciprofloxacin after either route was higher than the volume of body water despite the presence of moderate percentage of plasma protein binding. This indicates cellular concentration which is a beneficial property of the drug when treatment of respiratory affection is taken into consideration , as the drug is known to achieve adequate concentration in the respiratory tissues (3 , 4) .

The drug showed a relatively high percentage of Bioavailability (84%) which was higher than what was seen in man (14) .

The mean percentage of plasma protein binding was 25% which is considered as a moderate one when systemic treatment is taken in consideration , and slightly lower than that reported in adult chickens (15).

In conclusion most of parameters of pharmacokinetic in chicks are slightly different or similar to man or other species of animals or adult poultry.

## **References**

- 1-Ibrahim , H.M.(1982) . Survey on diseases of chickens in Baghdad for the year 1981 – 1982. MSc. Thesis , college of veterinary Medicine , University of Baghdad.
- 2-Label, M.(1988) . Ciprofloxacin chemistry , machanism of action , resistance , antimicrobial spectrum, pharmacokinetic , clinical trails & adverse reactions. Pharmacotherapy. 8: 3 – 33.
- 3-Dan, M., Torossian, K., Weissberg, D. & Kitzes, R.(1993). The penetration of ciprofloxacin into bronchial mucosa, lung parenchyma and pleural tissue after intravenous administration . Eur. J. Clin. Pharmacol. 44 : 101- 102 .
- 4-Stutman, H.R.; Shalit ,I.; Marks, M.I.; Greenwood, R.; Chartrand, S.A.& Hilman, B.C. (1987) . Pharmacokinetic of two dosage regimens of ciprofloxacin during a two-week therapeutic trail in patients with cystic fibrosis. A.J.M. 82: 142 – 145.
- 5-Grove, D.C. & Randel, W.A. (1955) assay methods of antibiotic . Antibiotic Monograph No.2 Medical encyclopedia, Inc.New York.
- 6-Shargel, L. & Andrew , B.C.(1984) . Applied biopharmaceutics and pharmacokinetics . Appleton – Century – Croftss / New York.
- 7-Davis, B.D. (1943) . The binding of sulfonamide drugs by plasma proteins, a factor in determining the distribution of drug in the body . J.Clin. Invest. 22: 753.
- 8-Bergan, T.; Thorsteinsson, S.B.; Solberg , R.; Bjornsen, L.; Kolstad, M.I. & Johnsen, S. (1987). Pahamacokinetics of ciprofloxacin: intravenous and increasing oral doses.AJM.82(supp 4 A) : 97 –102.

- 9-Hoffken, G.; Lode, H.; Prinzing, G.; Borrel, K. & Koeppe, P. (1985) Pharmacokinetic of ciprofloxacin. Second communication: Distribution to and elimination from tissue and organs following single or repeated administration of C<sub>14</sub> . Ciprofloxacin in albino rats. *Arzneim – Forsch*, 36 : 1503 – 1510.
- 10-Munoz, M.J.; Lioveria, P.; Santos, M.P.; Abadia, A.R.; Aramayona, J.J. & Bregante , M.A. (1996) . Pharmacokinetics of ciprofloxacin in sheep after single intravenous or intramuscular administration . *Vet. Quart.* 18 : 45-48.
- 11-Abadia, A.R.; Bregante, M.A.; Saez, M.P.; Aramayona, J.J.; Garcia, M.A. & Fraile, L. (1994) . Interspecies variation pharmacokinetics of enrofloxacin . *Methods & Finding in Experimental & clinical pharmacology* . 16:159.
- 12-Siefert, H.M.; Maruhn, D. & Scholl, H. (1986). Pharmacokinetics of ciprofloxacin. Second communication: Distribution to and elimination from tissue and organs following single or repeated administration of C<sub>14</sub> - ciprofloxacin in rats . *Arzneim – Forsch*, 36: 1503 – 1510.
- 13-Nouws, J.F.M.; Merius, D.J.; Vree, T.B.; Baars, A.M. & Laurensen , J. (1988). Pharmacokinetics, renal clearance and metabolism of ciprofloxacin following intravenous and oral administration to calves & pigs . *Vet. Quart* 10: 211 – 216 .
- 14-Drusano, G.A.; Standiford, H.C.; Plaisance, K. & Forrest, A. (1986). Absolute oral bioavailability of ciprofloxacin. *Antimicrob. Agents. Chemoth.* 30: 444 – 446.



15-Villa R.; Prondini,E.; Calami,F. & Canli, S.(1997).Serum protein binding of some sulphonamides, quinolones and fluoroquinolones in farm and domestic animals. J veterinary pharmacol. Therap. 20: 34 – 35.

## دراسة الحركية الدوائية للسبروفلوكساسين في افراخ الدجاج البياض

بتول امين الخفاجي ، علي عزيز الخياط ، عروبة محمد سعيد الشاها

فرع الفلسفة والادوية ، كلية الطب البيطري ، جامعة بغداد

بغداد - العراق

### الخلاصة

تم قياس معايير الحركية الدوائية للسبروفلوكساسين من منحنى اختفاء الدواء من بلازما الدم بعد إعطائه عن طريق الفم او عن طريق الوريد بجرعة 5 ملغم / كغم في افراخ الدجاج البياض المهجن وبعمر اسبوعين . اظهر منحنى الاختفاء بعد طور الانتشار سريع مما يتعذر حساب معاييرها وكان عمر النصف لطور الاطراح 3.7 ساعة وحجم الانتشار الظاهري 1.7 لتر / كغم واظهر منحنى الاختفاء بعد إعطاء الدواء عن طريق الفم نفس الطراز من الحركية الدوائية وكان اعلى تركيز للدواء هو 1.2 مكغم / مل تحقق بعد 1.75 ساعة وكان عمر النصف 2.9 ساعة وحجم الانتشار الظاهري 1.7 لتر / كغم . قدرت قيمة التوفر الحيوي ب  $84 \pm 9.7\%$  .

قدرت نسبة اتحاد السبروفلوكساسين ببروتينات بلازما الدجاج ب  $1.3 \pm 25.4\%$  .