PHARMACOKINETICS AND BIOAVAILABILITY OF DOXYCYCLINE IN AFLATOXICATED BAIJIN DUCKLINGS WITH REFERENCE TO ITS EFFECTS ON BODY WEIGHT AND SERUM LIVER ENZYMES

ELBARAWY, A.M.A. AND Y. EL KATTAN

Mnofia province laboratory, Animal Health Research Institute,ARC, Ministry of Agriculture, Dokki – Giza - Egypt

(Manuscript received 4 May 2008)

Abstract

The pharmacokinetic behaviour and bioavailability of doxycycline were determined in experimentally B_1 aflatoxicated Baijin ducklings and in healthy ones following a single intravenous (i.v) , intramuscular (i.m) and oral administration of 20 mg/Kg bodyweight of doxycycline hyclate . Tissue residues of the tested drug after an oral dose of 20mg/Kg bodyweight given twice daily for 5 consecutive days were also estimated . Moreover, its effects on body weight and serum liver enzymes were also studied . B_1 aflatoxicosis resulted in a significant decrease in doxycycline serum concentration in aflatoxicated Baijin ducklings than those recorded in healthy ones following a single i.v , i.m and oral administration. Following a single i.v injection, the concentration time curve was fitted to follow the three compartments open model with elimination half lives ($t_{0.5\ \beta}$8.24± 0.04 and 7.32± 0.07 hours) in healthy and aflatoxicated Baijin ducklings , respectively. Higher volume of distribution at steady state (Vd_{ss}) and total body clearance (Cl_{tot}) were recorded in aflatoxicated Baijin ducklings (2.22±0.10 L/Kg and 0.25±0.001L/h/kg) than healthy ones (1.5±0.36L/kg and 0.14±0.008L/h/Kg). Lower values of systemic bioavailability were observed in aflatoxicated Baijin ducklings (72.7±2.1 %and 45.93±3.2%) than healthy ones (92.5±4.0%and 50.3±4.1%) after oral and intramuscular administration, respectively. After single oral administration , the absorption half life ($t_{0.5kel}$) and elimination half life ($t_{0.5kel}$)were longer in healthy ducklings (0.64±0.01 and 11.09±0.84hour) than in aflatoxicated ones (0.45±0.03 and 7.73±0.87hour). The maximum serum concentration of the drug was higher in healthy ducklings than aflatoxicated ones. The highest concentrations of doxycycline were present in kidney and liver, and the lowest concentrations were present in heart and muscles. The drug was completely disappeared from all edible tissues 7 days after the last dose of repeated oral administration. So, the administration of the drug must be discontinued for at least 7 days before slaughter .

INTRODUCTION

Doxycycline (α- deoxy- 5- hydroxytetra- cycline) is a tetracycline derivative with broad spectrum activity against Gram positive and Gram negative aerobic and anaerobic bacteria. Spirochetes, Mycoplasma , Chlamydia and Rickettsia species also demonstrate high susceptibility . It has advantages over the older tetracyclines, higher lipid solubility ,

complete absorption , good tissue distribution , longer elimination half-life and lower affinity for calcium (Dorrestein *et al.* ,1991).

Aflatoxins, a group of extremely toxic chemicals, are produced by certain species of fungi in the genus *Aspergillus*, and often appear as natural contaminants in poultry feed . The major types of aflatoxins are B_1,B_2,G_1,G_2in addition to two metabolic products $M_1$and M_2. Aflatoxicosis is of great concern as it causes hepatotoxicity, nephrotoxicity and gastroenteritis (Calnek, 1997). Occurrence of infection is a major concern during aflatoxicosis resulting in large economic losses to poultry industry worldwide. The inflammation of the different organs affects the absorption, distribution, metabolism and excretion of drugs. *(Baggot, 1980).*

Several authors have studied the pharmacokinetics of doxycycline in healthy chickens *(Laczay et al., 2001).* However, no published information is available on the effect of aflatoxicosis on disposition kinetics of doxycycline in ducklings . Thus, the aim of the present work was to investigate the pharmacokinetics of doxycycline in aflatoxicated Baijin ducklings, as well as its residues in their different tissues. Its effects on body weight and serum liver enzymes were also estimated

METERIALS AND METHODS

Drug

Doxycycline was obtained as capsules of 100 mg doxycycline hyclate from Pfizer Pharmaceutical Company, Cairo, Egypt . The drug was dissolved in sterile saline or distilled water to a volume of 0.5 or 2 ml prior to injection or oral administration.

Ducklings

Eighty, eight weeks old (1.5–2 kg weight) Baijin ducklings were obtained from a private farm . The system of light, temperature and humidity were adjusted as recommended for ducklings production. Birds were fed on antibacterial and aflatoxin free balanced ration, and water was offered *ad-libitum.*

Grouping of Ducklings

The ducklings were classified into two main groups (40 ducklings each). The first group was fed on a balanced ration free from antibacterials and aflatoxins, and the second one was kept on ration contaminated with aflatoxin B_1 equivalent to 20µg/kg ration according to Allcroft (1965) for two weeks before the experiment, and this continued until the termination of experiment. Body weight in grams and activity of serum aspartate aminotransferase (AST) termination serum alanine aminotransferase (ALT) according to White *et al. (1970)* were recorded through this time of aflatoxin exposure.

Experimental design

Single dose study

Twenty ducklings from each group (healthy and aflatoxicated) were injected intravenously into the left wing vein with a single dose (20 mg/Kg b.wt.) of doxycycline (Davis *et. al.,* 2006) . Blood samples were collected from the right wing vein at 5,10,15 and 30 minutes, and 1,2,4,6,8,12 hours post-injection . The birds were left for two weeks to ensure complete excretion of the drug from their bodies.The ducklings in each group were divided into two subgroups of 10 ducklings each . The first two subgroups were injected intramuscularly with a single dose (20 mg/Kg b.wt.) of doxycycline. Blood samples were collected from each bird as mentioned above . Sera were separated by centrifugation and stored at – 20 °C until assayed for doxycycline concentrations.

Multiple dose study

Two groups of 20 ducklings each were given doxycycline orally at a dose of 20 mg Kg b.wt. twice daily for five consecutive days . Three ducklings from each group were slaughtered at 12 hours , 1,2,3,5 and 7 days after the last dose . Blood and tissue samples (liver, kidney, lung, spleen, heart, and breast muscles) were collected from each carcass and stored at – 20 °C until assayed for determination of doxycycline concentrations.

Assay of samples

Doxycycline concentrations in serum and tissues were assayed by microbiological method (Arret *et al.,* 1971) using Muller Hinton medium (Difco Laboratories , Detroit, MI,USA) and *Bacillus cereus* Var mycoides (ATTCC,11778) as test organism . Six wells of 100µl volume were cut at equal distances into a standard Petri-dish (120 mm) containing 25ml of seeded agar. The minimum inhibitory concentration which can be determined using this test organism is 0.25-8 µg /ml.

Pharmacokinetic analysis

The pharmacokinetic parameters were analyzed according to *Baggot (1978).* The coefficients (A, B) and rate constants (α, β) were calculated from the experimental data by least squares regression analysis. They were used to calculate the actual pharmacokinetic rate constants (K_{12}, K_{21}, and K_{e1}).

Vc = Apparent volume of central compartment. It was obtained from the equation:

$$Vc = \frac{\text{Dose (µg/ kg)}}{C^{\circ}\ (\mu g./ml)} = (mg/\ kg)$$

Where C°is the drug concentration at zero time (immediately) after intravenous dose.

Clearance of drug, which may be considered in terms of the volume of blood, cleared of the drug by the various elimination processes (biotransformation and excretion) per unit time, which represents the sum of all clearance processes.

$$\text{Bioavilability (F \%)} = \frac{\text{AUC (oral or i.m) X 100}}{\text{AUC i.v}}$$

where AUC is the area under the serum concentration time curves

Statistical analysis

The results obtained were statistically analyzed as explained by Petri and Watson (1999) and using SPSS ver. 15 computer program.

RESULTS

Table 1. Pharmacokinetic parameters of doxycycline in healthy and aflatoxicated Baijin ducklings following a single i.v dose of 20 mg/Kg body weight (n=20).

Parameter	unit	H	A
CP^o	$\mu g.ml^{-1}$	71.69±0.27	45.36±0.25***
A	$\mu g.ml^{-1}$	60.68±1.3	38.81±0.11***
α	h^{-1}	4.57±0.35	3.21±0.14**
$T_{0.5\alpha}$	h	0.15±0.005	0.21±0.01***
B	$\mu g.ml^{-1}$	11.01±1.00	6.54±0.35***
β	h^{-1}	10.33±0.98	6.24±0.42**
$T_{0.5\beta}$	h	8.24±0.04	7.32±0.07***
K_{12}	h^{-1}	3.39±0.22	2.20±0.10***
K_{21}	h^{-1}	0.77±0.03	0.54±0.01***
K_{el}	h^{-1}	0.48±0.07	0.56±0.03
V_C	$L.kg^{-1}$	0.28±0.003	0.44±0.01***
Vd_{ss}	$L.kg^{-1}$	1.50±0.36	2.22±0.10
Clb_{tot}	$L.h^{-1}.kg^{-1}$	0.14±0.008	0.25±0.001***
$AUC_{(0\text{-last})}$	$\mu g.ml^{-1}h^{-1}$	90.67±3.5	53.41±0.12***
$AUC_{(0\text{-inf})}$	$\mu g.ml^{-1}h^{-1}$	140.97±2.4	79.82±0.24***
MRT	h^{-1}	11.42±1.08	10.24±0.19

**Sig. at P ≤ 0.01 ***Sig.t at P ≤ 0.001

H: Healthy A : Aflatoxicated

Table 2. Pharmacokinetic parameters of doxycycline in healthy and aflatoxicated Baijin ducklings following a single i.m dose of 20 mg/Kg body weight (n=10).

Parameter	unit	H	A
K_{ab}	h^{-1}	0.89±0.08	1.02±0.07
$t_{0.5(ab)}$	h	0.78±0.05	0.68±0.03
$t_{0.5(k\ el)}$	h	4.03±0.2	3.37±0.05**
C_{max}	$\mu g.ml^{-1}$	5.02±0.70	3.26±0.20*
T_{max}	h	2.29±0.06	1.97±0.05**
$AUC_{(0\text{-}last)}$	$\mu g.ml^{-1}.h^{-1}$	63.48±3.3	33.75±2.4***
$AUC_{(0\text{-}inf)}$	$\mu g.ml^{-1}.h^{-1}$	71.04±2.6	36.67±1.5***
MRT	h^{-1}	5.82±0.45	5.05±0.12
F	%	50.39±4.1	45.93±3.2

*Sig.t at $P \leq 0.05$ **Sig.t at $P \leq 0.01$ ***Sig.t at $P \leq 0.001$

H: Healthy A : Aflatoxicated

Table 3. Pharmacokinetic parameters of doxycycline in healthy and aflatoxicated Baijin ducklings following a single oral dose of 20 mg/Kg body weight (n=10).

Parameter	unit	H	A
K_{ab}	h^{-1}	1.07±0.05	1.55±0.51
$T_{0.5(ab)}$	h	0.64±0.01	0.45±0.003***
$t_{0.5\ (kel)}$	h	11.09±0.84	7.73±0.87**
C_{max}	$\mu g.ml^{-1}$	6.09±0.3	4.64±0.06***
T_{max}	h	2.81±0.07	1.95±0.03***
$AUC_{(0\text{-}last)}$	$\mu g.ml^{-1}.h^{-1}$	71.18±2.42	37.95±2.33***
$AUC_{(0\text{-}inf)}$	$\mu g.ml^{-1}.h^{-1}$	130.43±5.36	58.04±3.56***
MRT	h^{-1}	15.66±1.22	11.36±1.8
F	%	92.5±4.00	72.70±2.1**

**Sig. at $P \leq 0.01$ ***Sig.t at $P \leq 0.001$

H: Healthy A : Aflatoxicated

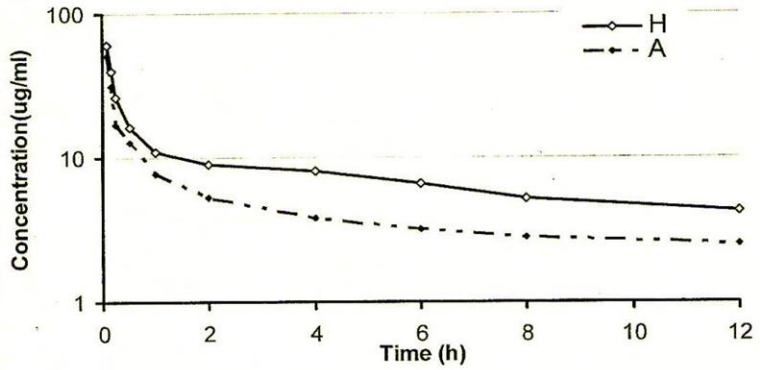

Fig. 1. Semi-logarithmic graph depicting the time-concentration course doxycycline in healthy and aflatoxicated ducklings following single i.v dose of 20mg/kg b.w.

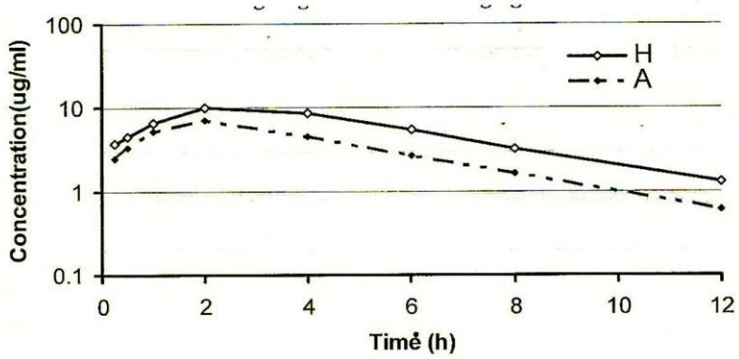

Fig. 2. Semi-logarithmic graph depicting the time - concentration course of doxycycline in healthy and aflatoxicated ducklings following single i.m dose of 20mg/kg b.w.

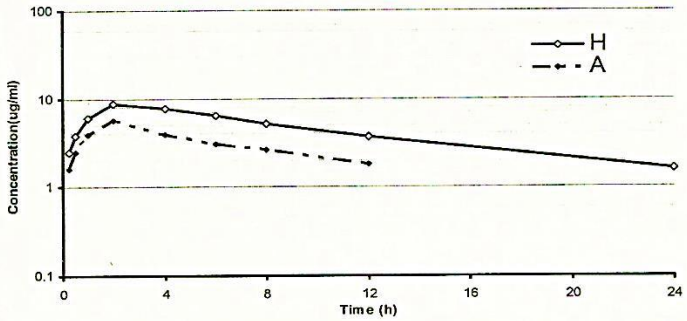

Fig. 3. Semi-logarithmic graph depicting the time - concentration course of doxycycline in healthy and aflatoxicated ducklings following single oral dose of 20mg/kg b.w.

Table 4. Tissue concentrations of doxycycline (µg/gm) in healthy and aflatoxicated Ducklings after multiple doses of 20mg/kg b.wt. twice daily for 5 consecutive days. Mean ±SE (n=3)

Tissue		Time of slaughter after the last dose					
		12 h	1st day	2nd day	3rd day	5th day	7th day
Serum	H	4.80 ±0.12	2.90±0.13	1.80±0.10	1.10±0.07	0.66±0.05	ND
	A	* 2.90±0.25	** 1.90±0.07	* 0.98±0.11	** 0.76±0.03	* 0.50±0.03	ND
Liver	H	6.81±0.13	5.62±0.18	2.56±0.25	1.70±0.04	0.88±0.05	ND
	A	** 4.10±0.15	** 3.30±0.20	** 1.80±0.07	** 1.10±0.06	** 0.56±0.03	ND
Heart	H	3.60±0.11	0.90±0.06	ND	ND	ND	ND
	A	** 2.10±0.12	** 0.60±0.03	ND	ND	ND	ND
Kidney	H	9.74±0.32	6.64±0.40	3.70±0.09	1.95±0.20	1.10±0.07	ND
	A	** 6.22±0.20	** 4.40±0.15	* 3.10±0.13	** 1.33±0.06	* 0.70±0.05	ND
Lung	H	5.30±0.50	3.68±0.09	1.98±0.08	1.20±0.07	ND	ND
	A	** 3.60±0.15	** 2.80±0.10	** 1.40±0.07	** 0.90±0.03	ND	ND
Muscle	H	4.66±0.30	2.50±0.09	1.30±0.09	0.86±0.06	ND	ND
	A	** 2.30±0.13	** 1.30±0.10	** 0.80±0.06	** 0.50±0.04	ND	ND

*Sig. at P ≤ 0.05 **Sig. at P ≤ 0.01 ***Sig.t at P ≤ 0.001

H: Healthy A : Aflatoxicated ND:Not detected

Table 5. Mean value of body weight , serum AST and serum ALT in B1 in aflatoxicated (20µg/kg ration daily for 14 days) and nonaflatoxicated Baijin ducklings (Mean± S.E, n= 40)

Age / Group	1st day			1st week			2nd week		
	B.wt. (gm)	AST (µ/l)	ALT (µ/l)	B.wt. (gm)	AST (µ/l)	ALT (µ/l)	B.wt. (gm)	AST (µ/l)	ALT (µ/l)
Non- aflatoxicated	70 ± 4.5	10.80 ± 0.13	10.2 ± 0.35	120.8 ± 6.23	10.3 ± 0.19	10.6 ± 0.65	320 ± 6.5	11 ± 0.24	9.8 ± 0.28
Aflatoxicated	68 ± 3.5	10.5 ± 0.25	9.8 ± .0.35	90.5 ± 3.93 **	78.2 ± 0.80 ***	18.5 ± 0.15 ***	210 ± 5.13 ***	85 ± 1.5 ***	19.5 ± 0.90 ***

**Sig. at P ≤ 0.01 ***Sig.t at P ≤ 0.001

Following i.v administration of the drug at a dose of 20 mg/ Kg body weight, the drug serum concentrations declined in a biphasic pattern that can be described by a two-compartments, open model (Fig.1). The kinetic parameters (Table 1) showed shorter elimination half life ($t_{0.5\ \beta}$) in aflatoxicated ducklings (7.32± 0.07 h) than in healthy ones (8.24± 0.04h). A higher volume of distribution at steady state (Vd_{ss}) was found in aflatoxicated birds (2.22 ±0.10 L kg^{-1}) than in healthy ones (1.5 ±0.36L kg^{-1}).

Significantly, lower maximum serum concentrations (C_{max}) and shorter elimination half life ($t_{0.5(kel)\ \beta}$) were observed in aflatoxicated birds than in healthy ones. Following i.m administration (Table 2 & Fig.2) or oral (Table 3 & Fig.3, Fig.1), significantly lower systemic bioavailability percent was determined after i.m administration (45.93±3.2 %) or oral dosing (72..70±2.1 %) in aflatoxicated ducklings compared with healthy ones (92.5±4.0 and 50.39±4.1 %) , respectively.

Repeated oral administration of the drug at a dose of 20 mg/Kgbody weight twice daily for 5 consecutive days resulted in significant lower serum and tissue concentrations of doxycycline in aflatoxicated ducklings than in healthy ones (Table 4).

The significant highest concentrations of doxycycline residues were found in kidney and liver, and the lowest concentrations were present in heart and muscles. . No residues could be detected in serum and tissues 7 days after cessation of oral administration in healthy and aflatoxicated ducklings .

Administration of aflatoxin B_1 (20 µg/Kg ration)to ducklings for 14 days resulted in significant decrease in body weight and significant increase in serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) activities (Table 5). The clinical signs of living aflatoxicated birds showed off-food, depression ,ruffled feathers , anorexia and constant diarrhoea.

DISCUSSION

The pharmacokinetic parameters of doxycycline in healthy Baijin ducklings reported in our study following a single i.v , i.m and oral administration of 20 mg/Kg body weight were similar to other findings in chickens (Laczay *et al.,* 2001 and Atef *et al.,* 2002) .

The obtained results following i.v injection of doxycycline showed significant lower serum concentration of the drug in aflatoxicated ducklings than in healthy ones. This finding was consistent with that previously reported for florofenicol in infected ducks (EL-Banna, 1998), and for doxycycline in aflatoxicated chickens (Atef *et al* , 2002). Additionally , the lower serum concentrations of doxycycline in aflatoxicated ducklings than in healthy ones were a reflection of large volume of distribution (V_{ss}, 2.22±0.10 L/kg versus 1.5±0.36 L/kg),rapid total body clearance (Cl_{tot} ,0.25±0.01 L/h/kg versus0.14±0.08 L/h/kg), as well as shorter elimination half life ($t_{0.5\beta}$, 7.32±0.07 hours versus 8.24±0.04 hours)in aflatoxicated ducklings comparable to healthy ones.

Similar results of large Vd_{ss} and Cl_{β} values and shorter elimination half life ($t_{0.5\beta}$) were previously reported for doxycycline in aflatoxicated chickens (Atef *et al.,* 2002). The large volume of distribution reported in aflatoxicated ducklings may be attributed to high penetration power of the drug to diseased tissues (Baggot, 1980). The diseases increase the Vd_{ss} of the drugs by an enhanced capacity for penetration of cellular membranes . These findings were also confirmed by results of Miller and Wyatt (1985) who reported that aflatoxicosis lowers the serum concentrations of chlorotetracycline as a result of decreased binding of chlorotetracycline to serum proteins and a significant hypoproteinemia in aflatoxicated chickens . The drug was completely disappeared from all edible tissues 7 days after the last dose of repeated oral administration .

Aflatoxicosis affects the vital organs of the birds as liver, kidney and gastrointestinal tract resulting in hepatitis, nephritis and gastroenteritis . The significant increases in the activities of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are indicators of hepatotoxic effect of aflatoxin B_1 due to their release from the damaged liver cells into circulation . The obtained results were in agreement with those previously reported by Harvey *et al.* (1991) in lambs.

Despite pharmacokinetic and pharmacodynamic relationships are well established for tetracyclines as antibacterial agents (Agwuh, and MacGowan, 2006). The inflammation of the different organs of aflatoxicated ducklings affects the absorption , distribution and excretion of the drug. Serum concentration of the drug becomes lower than MIC of the most infective agents, and the medication failure is the consequent result . . Hence, 12-hourly dosing of doxycycline in the murine model (Kevin *et. al.,* 2007) is not enough dosing regime as anti-infective agent in aflatoxicated ducklings . The administration of the drug in healthy and aflatoxicated ducklings must be discontinued for at least 7 days before slaughter.

REFERENCES

1. Agwuh, K. N. and A. MacGowan. 2006. Pharmacokinetics and pharmacodynamicsof the tetracyclines including glycylcyclines. J. Antimicrob. Chemother., 58:256–265.
2. Allcroft,R. 1965. Aspects of aflatoxicosis in farm animals.Mycotoxines in food stuffs BN.Wogan, Mit.Press., Cambridge,Massachusetts,pp.163-173.
3. Anadon,A., M.R. MartinezLarranaga, M.J. Diaz, P. Bringas, M.C. Fernandez,- M.L. Fernandez-Cruz, J. Iturbe and M.A. Martinez. 1994. Pharmacokinetics of doxycycline in broiler chickens.Avian Patholog,23,79-90.
4. Arret.B., D.P. Johnson and A. Kirshbaum. 1971. Outline of details of microbiological assay of antibiotics .J. pharmacy, Sci., 60,1690-1694.
5. Atef,M., S.A.H. Youssef, H.A. El-Banna and A.A. El Maaz. 2002. Influence of aflatoxins B_1on the disposition kinetics, systemic bioavailability and tissue residues of doxycycline in chickens . Brit poul. Sci.,43:528-532.
6. Baggot,J.D. 1978. Some aspects of clinical Pharmacokinetics in veterinary Medicine . J. Vet. Pharm. thera.,1:5-18.
7. Baggot,J.D. 1980. Distribution of antimicrobial agents in normal and diseased animals. J. Am. Vet. Med.. Assex,176:1085-1090..
8. Calnek,B.W.1997. Diseases of poultry. Ioth end.IowaUniv Press,USA.
9. El-Banna,H.A. 1998. Pharmacokinetics of florofenicol in normal and pasteurella-infected Muscuvy ducks. Brit. poul. Sci.,39:492-496.
10. Davis JL, J.H. Salmon, M.G. Papich. 2006. Pharmacokinetics and tissue distribution of doxycycline after oral administration of single and multiple doses in horses. Am J. Vet. Res. 67(2):310-6.

11. Dorrestein,G.M., J.J.D. Bruijne and A. Vulto. 1991. Bioavvailability of doxycycline injectable formulation in pigeons .Acta vet. Scandinavica,87:291-292.
12. Harvey,R.B., L.F. Kubena, J.D. Phlillips, D.E. Corrier, M.H. Elissalde and W.E. Huff. 1991. Diminution of aflatoxins toxicity to growing lambs by dietry supplementation with hydrated sodium calcium aluminosilicate. Am.J.Vet.Res., 52,152-156.
13. Kevin, T. Batty, S. F. Law Angela, Verity Stirling and R. Moore Brioni. 2007. Pharmacodynamics of Doxycycline in a Murine Malaria Model_ Antimicrob. & Chemother., 51, (12):4477–4479.
14. Lacazy, P., G. Semjen, J. Lehel and G. Nagy. 2001. Pharmacokinetics and Bioavvailability of doxycycline in fasted and nonfasted broiler chickens.Acta Veterinaria Hunngarica, 49:31-37.
15. Miller, B.L. and R.D. Wyatt. 1985. Effect of dietary aflatoxins on uptake and elimination of chlorotetracycline in broiler chickens. Brit. Poul. Sci., 64:1637-1643
16. Petri, A. and P. Watson. 1999. Statistics for Veterinary and Animal Science .1st Ed.,pp90-99 ,The blachwell Science Ltd,UK
17. White,B.A., M.M. Erickson and S.C. Stevens. 1970. Chemistry for Medical technologists.3rd edn.C.V. GOT and GP

المسار الحركي والإتاحة الحيوية للدوكسيسيكلين في البط البكيني المسمم بالأفلاتوكسين مع الإشارة لتأثيره على وزن الجسم وعلى مستويات إنزيمات الكبد بالمصل

عبد العظيم البراوي ، ياسر القطان

معهد بحوث صحة الحيوان – مركز البحوث الزراعية – وزارة الزراعة – الدقى – جيزة

تمت هذه الدراسة على عدد ٨٠ من البط البكيني عند عمر ٨ اسابيع (وزن ١,٥-٢كجم) وتم تقسيمه الى مجموعتين الأولى ضابطة أعطيت عليقة خالية من السموم الفطرية والأخرى تم اعطاؤها عليقة مسممة بالأفلاتوكسين(٢٠ميكروجرام /كجم من العليقة) و تم تتبع المسار الحركي والإتاحة الحيوية لعقار الدوكسيسيكلين (دوكسيسيكلين هليكات) بعد حقن جرعة واحدة (٢٠مجم /كجم من الوزن الحي) في الوريد أو في العضل أو عن طريق الفم في كلتا المجموعتين . وتم أيضا قياس بقايا الدواء في أنسجة الطائر المختلفة (بعد إعطاء نفس الجرعة عن طريق الفم مرتين يوميا لمدة خمسة أيام متتالية) في كلتا المجموعتين كما درس أيضا تأثيره على وزن الجسم وعلى مستويات إنزيمات الكبد بالمصل. أدى التسمم بالأفلاتوكسين الى نقص معنوي في تركيز الدواء في مصل البط المسمم بالمقارنة بالبط السليم بعد حقن جرعة واحدة من الدواء بالطرق المختلفة أو إعطائه عن طريق الفم . بعد حقن جرعة واحدة في الوريد كان منحنى تركيز الدواء متوافقا مع نموذج الثلاثة أقسام للمسار الحركي وكان نصف عمر الإخراج للدواء٠,٠٤ ±٨,٢٤ و ٠,٠٧ ±٧,٣٢ ساعة في البط السليم و المسمم على التوالي .كان حجم انتشار الدواء ومعدل التخلص الكلي للدواء أعلى في البط المسمم بالمقارنة بالبط السليم . و كانت الإتاحة الحيوية للدواء بعد الحقن العضلي والإعطاء عن طريق الفم في البط المسمم أقل منها في البط السليم . كان نصف عمر الامتصاص و الإخراج بعد إعطاء الدواء عن طريق الفم أطول في البط السليم عنه في مصل البط المسمم .كان أعلى متبقيات الدواء في أنسجة البط بعد الذبح في الكبد والكلى وكان أقل تركيز في القلب والعضلات . تم اختفاء الدواء نهائيا من كل الأنسجة بعد ٧ أيام من آخر جرعة مكرره ولذلك يجب وقف استخدام العقار نهائيا قبل سبعة أيام على الأقل من الذبح . كما وجد أن التسمم بالأفلاتوكسين يقلل وزن الجسم ويرفع مستويات إنزيمات الكبد بالمصل.