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Efficacy and Tissue Reside Depletion of Florfenicol (Water Soluble Formulation) in Healthy and *E. coli* Infected Broiler Chickens

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Abstract: Efficacy and tissue residue depletion and withdrwal period of water soluble formulation of florfenicol was studed in control healty and experimently *E. coli* infected broiler chickens. Florfenicol given orally in drinking water with atherapeutic dose (30 mg kg^{-1} body weight, twice daily) for 5 cosequetive ds. Florfenicol administration for 5 successive ds 30 mg kg^{-1} twice daily was highly efficacious in the control of the disease induced by *E. coli*. These finding indicated by the decreasing of mortality %, pm lesions and bacterial reisolation from birds treated with 30 mg kg^{-1} b wt twice daily for 5 ds as compared with group treated with 20 mg kg^{-1} b wt twice daily for 5 d. Florfenicol residue depletion from tissues of healthy chickens was faster than from tissues of infected ones. Oral administration of florfenicol twice daily for 5 consecutive ds in *E. coli* infected chickens resulted in a higher tissues concentration of the drug at different time interval after stopping the drug medication as compared with values recorded in healthy birds. Bile had the highest concentration of florfenicol followed by liver and kidney, while the lowest concentration was determined in fat and brain in both healthy and infected birds. Florfenicol was still detected in serum, bile and all tested tissues on the 6th d after discontinuation of medication in both healthy and infected birds, while all tissues of slaughtered healthy and infected birds could be considered drug free except liver of infected birds which had a concentration of 0.11±0.01 ug g^{-1} at 7th d after stopping of drug administration. A withdrwal period >6 ds in healthy chickens and >7 ds in infected ones is satisfactory.

Key words: Efficacy, tissue reside, florfenicol, depletion, *E. coli*

INTRODUCTION

Florfenicol, a structural analogue of thiamphenicol, possessing a wide spectrum of activity against both Gram-negative and Gram-positive bacteria (Syriopoulou *et al*., 1981). Florfenicol was reported to have a greater activity than chloramphenicol and thiamphenicol especially against Pasteurella, *Salmonella*, *E. coli* and *Staphylococcus aureus*. The mechanism of antibacterial activity of florfenicol is Similar to that of chloramphenicol and thiamphenicol, through inhibition of bacterial protein synthesis at the 50 S ribosomal subunit (Cannon *et al*., 1990). Thiamphenicol and florfenicol are different from chloramphenicol in that the para-nitro group attached to the benzene ring is replaced by a sulfomethyl group, that make florfenicol more safe, as the presence of para-nitro group in chloramphenicol prohibited its use for the treatments of food-producing animals as it induced 2 types of adverse toxic effect on bone marrow-derived cells (A dose-related reversible suppression on erythropoiesis due to inhibition of mitochondrial protein synthesis (Brest, 1967) and a rare dose-independent idiosyncratic response resulting in aplastic anaemia (Yunis and Bloombery, 1964; Yunis, 1969, 1973). In addition, replacement of -OH at C-3 site by Fluorine atom florfenicol prevent the bacterial enzymatic acetylation at this site by Chloramphenicol Acetyltransferase (CAT) which present in resistant organisms (Sams, 1995). Consequently florfenicol show a greater safety and efficacy over thiamphenicol and chloramphenicol so it is supposed to be an ideal replacement of these drugs in treating many infectious diseases caused by chloramphenicol-resistant or thiamphenicol-resistant strains. Florfenicol firstly introduced in the markets as injectable solution for treatment of respiratory diseases in cattle and now it introduced in some countries as oral solution for the treatment of several poultry diseases.

The aims of the present resaerch is to: Study the efficacy of florfenicol against *E. coli* infected broiler chickens and determined tissue depletion pattern of a

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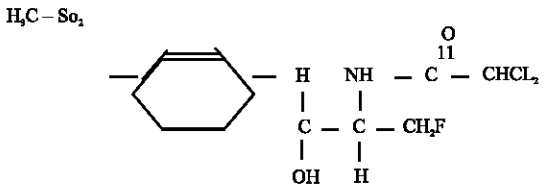
newly water soluble formulation of florfenicol administered orally at therapeutic dosage, in varius tissues of healthy and *E. colin* infected broiler chickens.

MATERIALS AND METHODS

Drug: Florfenicol: Florfenicol, structurally analogous to thiamphenicol, is a new antibiotic possessing a wide spectrum of activity against both Gram-negative and Gram-positive bacteria. Florfenicol was kindly obtained as oral solution (10%) from pharmaswede Egypt under trade name *Aviflor*. The pure powdered form of the drug was obtained also from pharmaswede Egypt and dissolved in propylene glycol then diluted with a sterile deionized water for intravenous injection.



Structure of florfenicol

(Varma *et al.*, 1986)

Birds and housing: One hundred and eighty six clinically healthy Hubbard chicks unsexed one day old were obtained from a private commercial hatchery. The birds were reared on floor pens within an environmental controlled research unit. Birds were housed in cages, fed on antibacterial-free balanced rations *ad-libitum* with free access for water

Antibacterial activity *in vitro* (Minimum inhibitory concentration): Determination of Minimum Inhibitory Concentration (MIC) by using broth dilution method. MIC was determined for *E. coli* O_{78}.

- It was tested according to Cruick Shank *et al.* (1975).

Experimental infection with *E. coli* O_{78}: One hundred and twenty Hubbard chicks, 23 days old and their body weights ranged from 575 to 600 g were experimentally infected with *E. coli* (strain N°. O_{78}) which was kindly obtained from Bacterial toxins unite Animal health Research Institute, Dokki, Giza.

Experimental infection: The method described by Shen *et al.* (2002) was applied in which *E. coli* (O_{78}) was inoculated into a beef infusion broth and cultured for 24 h at 37°C and then on MacConkey agar for 24 h at 37°C. Broiler chickens of all groups except the control one (non-infected healthy) group were infected by intraperitoneal injection with 0.2 mL of the inoculum with a concentration 6.7×10^9 CFU (Colony Forming Units) *E. coli* mL. The infected birds were used for studying the efficacy of florfenicol in treating infection with *E. coli* O_{78} as well as for studying the tissues distributiondrawal period of watersolublr formulation of of florfenicol.

Antibacterial activity of florfenicol on *E. coli*, *in vivo* (Efficacy studies)

Grouping and treatments: One hundred and fifty (23-day old) broiler chickens were divided into 5 equal groups (30 birds of each) and floor reared in a separate units. One hunderd and tweenty broiler chickens were exprimentally infecected with *E. coli* (strain N°. O_{78}). The broiler chickens were immediately treated with drugs in drinking water post infection as follows:

Group I: Was left as control without treatment (non infected-non treated).

Group II: Experimentally infected with *E. coli* and non treated. it was retained to observe clinical signs and mortality.

Group III: Experimentally infected with *E. coli* and treated with florfenicol (20 mg kg^{-1} b wt) for 5 successive days.

Group IV: Experimentally infected with *E. coli* and treated with florfenicol (30 mg kg^{-1} b wt) for 5 successive days.

Group V: Experimentally infected with *E. coli* and treated with enrofloxacin (10 mg kg^{-1} b wt) for 5 Successive days All chickens were left under observation during the experimental period to record the clinical symptoms and mortality.

Clinical symptoms of Colibacillosis: Experimentally infected birds showed sever diarrhea, Lack of appetite and ruffled feathers.

Mortality rate: The number of dead birds in the infected non treated and infected treated groups was recorded and calculated as the percentage of mortality.

Post mortem examination of slaughtered birds: Three birds from each group were taken and slaughtered and subjected to postmortem lesions affecting their organs (Liver-Heart-Air sacs) from the next day following last dose of treatments and for 5 Successive days (6, 7, 8, 9, 10th day post stop medication).

Bacterial re-isolation: The slaughtered birds which were examined for post-mortem lesions were also used for bacterial re-isolation (*E. coli* strain O_{78}) form liver, heart, kidneys and bile.

Tissue distribution and residual content: Two groups (18 healthy and 18 *E. coli* infected) broiler chickens were used for studying tissue distribution and determining the withdrawal time of florfenicol using microbiological assay technique. The birds of both groups were given florfenicol (30 mg kg^{-1} body. Weight) orally twice daily for 5 successive days.

Three chickens from each group were randomly selected for slaughtering 2 h after stopping of the drug administrations then at 1st, 2nd, 4, 6 and 7th day. Blood, bile and tissue samples (liver, kidney, lung, heart, spleen, brain, fat, thigh muscle and breast muscle) were taken from all slaughtered birds till the disappearance of the drug residues from their tissues for estimation of the drug concentration.

Analytical procedure: Florfenicol in serum, bile and tissue samples was determined by the microbiological assay technique described by Arret *et al.* (1971) using *Bacillus subtilis* (ATCC 6633) as test organism. Standard curves were constructed using antibacterial-free sera collected from either healthy or infected-duck. Triplicates of 100 μL from either standards or unkown samples were added to wells in the assay dish. The lower detectable limit of the florfenicol assay was 0.050 μg mL^{-1}.

RESULTS

Antibacterial activity *in vitro*: The *in vitro* activities of florfenicol, thiamphenicol and enrofloxacin against *E. coli* (serotype, O_{78}) as determined by serial dilution tube technique was 2, 4 and 0.03 ug mL^{-1}, respectively.

Efficacy of florfenicol against induced colibacillosis
Clinical observation: Inoculation with *E. coli* (O_{78}) induced a sever colibacillosis on non medicated birds characterized by depression, diarrhea, congestion of mucous membrane, gasping and respiratory manifestation. These signs appeared 2-3 days after inoculation.

Medication with either florfenicol (20, 30 mg kg^{-1} b wt) or enrofloxacin 10 mg kg^{-1} b wt greatly reduced the prevalence and severity of clinical signs.

Mortality rates: Mortality rates was recorded throughout the experiment in each group and calculated a percent. High mortality rate by *E. coli* infected (33.33%) occurred in non treated birds. Medication with florfenicol reduced

Table 1: Effect of medication on mortality percent

Group	Dose mg kg^{-1}	Number of dead birds/day 1st d	2nd d	3rd d	4th d	5th d	Total mortality: Total N^5 of mortality / Total N^5 of group	(%)
I-Control non infected and non treated	-	0	0	0	0	0	0/30	00.00
II-Infected and non treated	-	4	3	1	1	1	10/30	33.33
III-Infected and treated with florfenicol	20	3	2	1	0	0	6/30	20.00
IV-Infected and trated with florfenicol	30	2	2	1	0	0	5/30	16.67
V- Infected and treated with enrofloxacin	10	2	1	1	0	0	4/30	13.33

Total number of each group = 30 birds

Table 2: Effect of medication on percentage of birds with post- mortum lesion (Perihepatitis, pericarditis and airsaculitis)

Group	Dose mg kg^{-1}	Lesions	Number of positive 1st d	2nd d	3rd d	4th d	5th d	Total N^5 of tve / Total N^5 examined	(%)
I-Control non infected non treated	-	Perihepatitis	0	0	0	0	0	0/15	0.0
		Pericarditis	0	0	0	0	0	0/15	0.0
		Airsacculitis	0	0	0	0	0	0/15	0.0
II-Infected non treated	-	Perihepalitis	3	3	3	2	2	13/15	86.6
		Pericarditis	3	3	3	3	2	14/15	93.33
		Airsacculitis	3	3	3	3	3	15/15	100.0
III-Infected treated with florfenicol	20	Perihepatitis	2	1	1	0	0	4/15	26.67
		Pericarditis	2	1	1	0	0	4/15	26.67
		Airsacculitis	2	2	1	0	0	5/15	33.33
IV-Infected treated with florfenicol	30	Perihepatitis	2	0	0	0	0	2/15	13.33
		Pericarditis	2	0	0	0	0	2/15	13.33
		Airsacculitis	2	1	1	0	0	4/15	26.67
V-Infected treated with enorfloxacin	10	Perihepatitis	2	1	0	0	0	3/15	20.0
		Pericarditis	2	1	0	0	0	3/15	20.0
		Airsacculitis	2	2	0	0	0	4/15	26.67

* Number of examined birds from each group per day = 3 birds, *post-mortem lesions (Pericarditis, perihepatitis and airsaculitis)*

Table 3: Effect of medication on E. coli re-isollation rates

Group	Dose mg kg^{-1}	Orgarn	Number of positive 1st d	2nd d	3rd d	4th d	5th d	Total N^5 of tve / Total N^5 examined	(%)
I-Control non infected non treated	-	Liver	0	0	0	0	0	0/15	0.00
		Heart	0	0	0	0	0	0/15	0.00
		Kidney	0	0	0	0	0	0/15	0.00
		Bile	0	0	0	0	0	0/15	0.00
II-Infected non treated	-	Liver	3	3	3	3	3	15/15	100.0
		Heart	3	3	3	3	3	15/15	100.0
		Kidney	3	3	3	3	3	15/15	100.0
		Bile	3	3	3	3	3	15/15	100.0
III-Infected treated with florenicol	20	Liver	3	3	2	0	0	8/15	53.3
		Heart	3	3	2	2	1	11/15	73.3
		Kidney	3	2	2	1	0	8/15	53.3
		Bile	3	2	1	0	0	6/15	40.0
IV-Infected treated with florfenicol	30	Liver	3	2	1	0	0	6/15	40.0
		Heart	3	3	1	0	0	7/15	46.67
		Kidney	3	2	1	0	0	6/15	40.0
		Bile	2	1	0	0	0	3/15	20.0
V-Infected treated with Enrofloxacin	10	Liver	3	2	1	1	0	7/15	46.67
		Heart	3	2	2	1	0	8/15	53.3
		Kidney	3	2	1	1	0	7/15	46.67
		Bile	2	1	1	0	0	4/15	26.67

* Number of examined birds from each group per day = 3 birds

Table 4: Mean serum, bile and tissues concentrations of florfenicol (ug mL^{-1} or ug g^{-1}m) assayed microbiologically, in healthy broiler chickens following oral administration of 30 mg kg^{-1} b wt twice daily for 5 consecutive days. n = 3

Tissue	Time of slaughter after the last dose: 2 h	1st day	2nd day	4th day	6th day	7th day
Serum	6.8±0.49	3.08±0.32	1.36±0.05	0.69±0.03	0.27±0.04	-
Liver	7.77±0.36	3.98±0.37	1.82±0.37	0.48±0.13	0.32±0.03	-
Spleen	4.81±0.23	3.46±0.49	1.68±0.34	0.72±0.09	0.35±0.05	-
Kidney	7.19±0.25	4.35±0.10	1.43±0.09	0.76±0.05	0.28±0.04	-
Heart	4.25±0.36	2.49±0.58	1.06±0.11	0.41±0.03	0.26±0.04	-
Lung	5.95±0.31	3.25±0.36	1.52±0.04	0.48±0.04	0.16±0.05	-
Fat	3.62±0.79	2.32±0.58	1.16±0.11	0.30±0.06	0.19±0.01	-
Brain	3.51±0.69	2.75±0.35	1.38±0.55	0.40±0.23	0.20±0.03	-
Breast ms	3.92±0.27	1.82±0.32	1.42±0.07	0.79±0.06	0.26±0.03	-
Thigh ms	3.01±0.0.37	1.58±0.49	1.40±0.36	0.32±0.17	0.18±0.04	-
Bile	8.85±0.57	3.20±1.06	2.59±0.51	1.17±0.12	0.50±0.15	-

-Undetectable

Table 5: Mean serum, bile and tissues concentrations of florfenicol (ug mL^{-1} or ug g^{-1}m) assayed microbiologic ally in *E. coli* infected broiler chickens following oral administration of 30 mg kg^{-1} b.wt twice daily for 5 consecutive days. n = 3

Tissue	Time of slaughter after the last dose: 2 h	1st day	2nd day	4th day	6th day	7th day
Serum	2.07±0.09	1.18±0.11	0.78±0.10	0.28±0.02	0.14±0.01	-
Liver	9.98±0.31	4.87±0.07	2.68±0.06	1.29±0.04	0.44±0.07	0.11±0.01
Spleen	4.90±0.45	3.89±0.07	2.52±0.04	0.98±0.03	0.50±0.08	-
Kidney	8.15±0.45	5.31±0.23	1.78±0.03	0.88±0.03	0.38±0.04	-
Heart	5.73±0.27	3.40±0.07	1.52±0.04	0.76±0.03	0.39±0.02	-
Lung	6.0±0.87	3.67±0.57	1.98±0.15	0.63±0.04	0.27±0.04	-
Fat	4.35±0.68	2.59±0.62	1.75±0.12	0.45±0.03	0.24±0.01	-
Brain	4.14±0.31	2.68±0.06	1.41±0.03	0.56±0.03	0.35±0.01	-
Breast ms	4.15±0.73	1.98±0.15	1.52±0.04	0.98±0.04	0.29±0.02	-
Thigh ms	4.68±0.99	1.85±0.33	1.81±0.07	0.54±0.03	0.35±0.01	-
Bile	9.53±0.53	4.67±0.52	3.10±0.40	1.67±0.19	0.68±0.09	-

-Undetectable

mortality to 20.0% when used at 20 mg kg^{-1} b wt and to 16.67% when used at 30 mg kg^{-1} b wt compared to 13.33% recorded in group treated with enrofloxacin 10 mg kg^{-1} b wt (Table 1).

Post-mortum lesions: Post-mortum lesions (preicarditis, perihepatitis and airsaculitis) typical of *E. coli* infection were found in 86.6 to 100% of the infected non treated group. Medication with florfenicol significantly reduced

the incidence of lesions (Table 2) to 26.67 and 33.33% when used at 20 mg kg^{-1} b wt and to 13.33 and 26.67% when used at 30 mg kg^{-1} b wt compared to 20.0 and 26.67% for enrofloxacin (10 mg kg^{-1} b wt).

Bacterial re-isolation: *E. coli* was cultured from all organs of examined un-medicated birds (100%), non infected birds showed no bacterial re-isolation. Medication with florfenicol (20 mg kg^{-1} b wt) significantly reduced the frequency of isolation (Table 3) of *E. coli* to 40.0 and 73.3%. In addition, treatment with florfenicol in a dose of 30 mg kg^{-1} b wt reduced the isolation to 20.0 and 46.0% compared to 26.67 and 53.3% for birds treated with enrofloxacin (10 mg kg^{-1} b wt).

Tissues distribution and withdrawal time: The concentrations of florfenicol in serum, bile and tissues of slaughtered healthy as well as *E. coli* infected broiler chickens at various intervals (2 h, 1st, 2nd, 4, 6 and 7th days) following the dosage regimen (30 mg kg^{-1} b wt twice daily for 5 consecutive days) are presented in Table 4 and 5. The obtained data showed that the drug was distributed in serum, bile and tissues tested (Liver, spleen, kidney, heart, lung, fat, brain, breast muscle and thigh muscle). Oral administration of florfenicol twice daily for 5 consecutive days in *E. coli* infected chickens resulted in a higher tissues concentration of the drug at different time interval after stopping dosage regimen as compared with values recorded in healthy birds. Bile had the highest concentration of florfenicol followed by liver and kidney, while the lowest concentration was determined in fat and brain in both healthy and infected birds.

Using the microbiological assay technique, florfenicol was still detected in serum, bile and all tested tissues on the 6th day after discontinuation of medication in both healthy and infected birds, while all tissues of slaughtered healthy and infected birds could be considered drug free except liver of infected birds which had a concentration of 0.11±0.01 ug g^{-1} (Table 5) at 7th day after stopping of drug administration.

DISCUSSION

Antibacterial activity *in vitro*: The obtained results showed that the Minimum Inhibitory Concentration (MIC) of florfenicol, thiamphenicol and enrofloxacin against *E. coli* (O_{78}) was found to be 2, 4 and 0.03 ug mL^{-1}, respectively using serial dilution tube technique. These values was lower than those recorded previously by Sarah and Jeffery (2002) as they found that, the MIC for florfenicol against *E. coli* was 4 ug mL^{-1}. In addition, Yang *et al.* (2002) reported that the MIC against *E. coli* (O_{78}) is 6 ug mL^{-1}. The variations in these results may be attributed to the density of the microorganism used. In this respect Bradbury *et al.* (1994) mentioned that, the inoculum density is a critical factor for determining the results of MIC on Mycoplasma. On the other hand, the reported MIC for florfenicol against other organisms is 0.5 ug mL^{-1} against *Shigella dysenteriae* and *Salmonella typhi* (Syriopolou *et al.*, 1981) 1.25 mg $liter^{-1}$ against *Mycoplasma gallisepticum* (Pu *et al.*, 2002) 0.5 ug mL^{-1} against *Vibrio anguillarum* (Samuelsen *et al.*, 2003) and 1 ug mL^{-1} against *Riemerella anatipestifer* (Wang and He, 2004).

Efficacy against induced colibacillosis: Inoculation of birds with *E. coli* (O_{78}) induced a typical severe colibacillosis with respiratory signs and high mortality in nonmedicated birds. Florfenicol administration for 5 successive days 30 mg kg^{-1} twice daily was highly efficacious in the control of the disease induced by *E. coli*. These finding indicated by the decreasing of mortality %, pm lesions and bacterial reisolation from birds treated with 30 mg kg^{-1} b wt twice daily for 5 days as compared with group treated with 20 mg kg^{-1} b wt twice daily for 5 days. In addition enrofloxacin 10 mg kg^{-1} b wt twice daily for 5 days also significantly reduced mortality %, pm lesions and bacterial reisolation. Florfenicol has been reach high concentrations in chickens organs following the oral dose (Afif and EL-Sooud,1997; Shen *et al.*, 2002) and enrofloxacin is considered to be bactericidal in their mode of action against gram positive and negative bacteria (Bauditz 1987; Jenkins and Friedlander, 1988). These properties would contribute to the marked reduction of mortality, clinical signs seen in infected birds following the medication with either florfenicol or enrofloxacin. The decrease in the frequency of bacterial reisolation that occurred following the administration of 30 mg kg^{-1} florfenicol as compared when used at a dose 20 mg kg^{-1} body weight indicate that a dose of 20 mg kg^{-1} is considered sub-therapeutic.

Tissue distribution and withdrawal period: The present study demonstrated that florfenicol has the tendency to accumulate in the blood and tissues either in healthy or infected broiler chickens after its oral administration for of 30 mg kg^{-1} twice daily for 5 consecutive days. This may be attributed to the ability of the drug to bind with plasma or tissue proteins at various PH media (Abou El-Makarim *et al.*, 1967) and secondly to the reabsorption of the free fraction from the renal tubules.

Florfenicol was found to be distributed in all tissues of healthy and *E. coli* infected broiler chickens and relatively higher concentrations were detected in tissues of infected chickens than normal ones. These finding are consistent with the higher value of volume of distribution in infected birds than in normal ones.

The highest concentrations of florfenicol were present in kidney, bile, liver, lung. These observation supports those of Adams *et al.* (1987), Afifi and El-Sooud (1997). Concentrations of florfenicol were similar to or higher the corresponding serum concentrations. This indicated that, the penetration of florfenicol into these tissues were good. The high volume of distribution and relatively low protein binding capacity of this drug in chickens is reflected by its persistence in tissues for prolonged period. The high florfenicol concentrations in the kidney and lung indicated that florfenicol may be an excellent drug for treating urinary and respiratory tract infection caused by susceptible organism. The drug may be of value for controlling of CRD affected broilers and turkeys as florfenicol is effective against gram-positive and gram negative bacteria. In addition Pu *et al.* (2002) found that, the MIC of florfenicol 1.25 μg mL^{-1} against *Mycoplasma gallisepticum*. On the basis of the high concentration of florfenicol in bile and its good absorption, the drug may undergo some degree of enterohepatic recirculation and be eliminated through bile and urine. These Finding supported its value for controlling *E. coli* infection in poultry. Lower concentrations of the drug were found in brain and fat, indicating that florfenicol can cross blood brain barrier to limited extent and that it has a low affinity for fat-containing tissues. Similar findings were previously reported in poultry by Afifi and El-Sooud (1997) and in ducks (El-Banna, 1998). No florfenicol residues were found in tissues after 6 days in healthy birds while it still detected in liver of infected birds. These findings represented a long withholding time of florfenicol in infected chickens (7 days) as compared with healthy birds (6 days). In this respect (EMEA, 1999) mentioned that 7 days after the end of the treatment with florfenicol in broilers, the concentrations of florfenicol amine (microbiologically active metabolites) were below the limit of quantification for liver (less than 461 μg kg^{-1}) and could be still measured in kidney (136 μg kg^{-1}). The variation in the withdrawal time recorded for healthy chickens (7 days) and infected ones (8 days) may be attributed to the high rate of drug distribution in infected chickens than healthy ones (Pennington *et al.*, 1975). Furthermore Baggot (1980) reported that infection caused a significant change in the rate of drug biotransformation and this may alter both excretion and metabolism in infected cases.

Oral formulation of florfenicol is suitable for treating systemic infections with *E. coli* when given twice a day at 30 kg^{-1} to maintain its therapeutic concentrations.

- A withdrawal period of 8 days should be elapsed before slaughtering.

It is recommended to adjust the dosage regimen of florfenicol according to the type of the microorganism as l (30 mg kg^{-1} twice daily for 5 days).

CONCLUSION

It must be emphasised that it would be unwise to overgeneralise the findings of this study in relation to all poultry diseases; becausethere is a wide range in the sensitivity of the drug against different bacteria (0.5-6 ug mL^{-1}). Serum and tissues florfenicol concentrations for 30 mg kg^{-1} twice daily dosage ulation following the oral administration of water soluble formwere suitable to maintain its therapeutic concentration for controlling poultry colibacillosis. In addition, florfenicol should be withdrawn at least 7 days before marketing to ensure that the drug is completely eliminated from tissues.

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