A COMPARATIVE STUDIES ON WITHDRAWAL TIMES OF SOME ANTIBIOTICS FROM TISSUES

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ABSTRACT

The present work was carried out to determine the concentrations of pefloxacin and tilimicosin in serum, liver, kidney and muscle of 120 apparently healthy, one day old unsexed Hubbard broiler chicks at different time intervals using microbiological assay method. Moreover, the effect of heat treatment on their residues in tissues was estimated. The chicks were allocated into three separated groups, 40 birds for each. The chicks of 1st group were kept as negative control (non-medicated), the 2nd group chicks were administered pefloxacin (10mg/kg.b.wt.) in drinking water for 3days, while of the 3rd group were administrated tilmicosin (10mg/kg.b.wt.) in drinking water for 3days. The obtained results reflected moderate effects of the heat treatment on the residues of pefloxacin and tilmicosin in tissues of treated chicks.

INTRODUCTION

Antimicrobial agents are widely used in veterinary medicine to overcome many infections in both poultry and animal farms. Among the well developed antibacterial that seems producing in veterinary medicine are pefloxacin and tilmicosin.

Pefloxacine is a recent fluoroquinolone which is active against a wide range of G+ ve and G-ve microorganisms. fluoroquinolones are the most important group of synthetic antibacterial agents since the discovery of sulphonamides. These drugs are absorbed well and are distributed extensively in tissues with high tissue/plasma ratio. These characters make these drugs suitable for the therapy of a wide range of infection. **(Horie et al, 1994)**.

Tilmicosin is a macrolide antibiotic formed from a chemical modification of tylosin. It is licensed for subcutaneous injection for the treatment of respiratory disease in sheep and cattle. It is also approved as a feed additive for the prevention and control of respiratory disease in swine. Tilmicosin has been tested and used in various other species including rabbits and poultry **(McKay, et al. 1996; Charleston, et al., 1998)**.

The present study was carried out to estimate the residues of pefloxacin and tilmicosin in tissue and organs of treated chicks. Moreover, the effect of heat treatment (boiling and freezing) on these residues was estimated.

MATERIALS AND METHODS

Drugs:

1 : Pefloxacin (Peflodada®): as 10% of Pefloxacin (as mesylate dehydrate (Dar ASI Dawa Veterinary and Agricultural Industrial co. Itd, Na' ur-Jordan).

2 : Tilmicosin (Advotil Ac®) as tilimicosin phosphate (Chemvet Co. Egypt).

Chicks:

One hundreds and twenty apparently healthy, one day old unsexed Hubbard broiler chicks were obtained from El-Kahera poultry company and were used in this study. The chicks were allocated into three separated groups, 40 birds for each which administration drug in one day old as following first group of chicks were kept as negative control (non-medicated) while the second group of chicks were administered pefloxacin (10mg/kg.b.wt.) **(Dalsgeard and Pjeregaad, 1991)** in drinking water for 3 successive days the third groups of chicks were administrated tilmicosin (10mg/kg.b.wt.) **(Thompson and laudert, 1994)** in drinking water for 3 successive days.

Sampling:

1- Blood sampling:

Blood sampling were collected at the end of 1st, 7th, 14th, 21st and 28th day post administration of the drugs from chicks of all group. Five birds from each group were sacrificed for collection of blood samples in clean and dry tubes. Two blood samples were collected from 5 birds of each group; the 1st blood sample was collected without anticoagulant, for separation of clear serum for biochemical analysis, while the 2nd blood sample was collected in centrifuge tubes, left in slope position to clot at room temperature. Serum was carefully separated and centrifuged at 1000 r.p.m. for 10 minutes. Clear serum sample were transferred carefully in clean dry kits and kept in frozen at -20°C till assayed microbiologically.

2- Tissue samples:

Tissue samples (liver, kidney and muscles) were obtained from five chicks of each group at 1st, 7th, 14th, 21st, 28th days post administration of drugs. Each sample was divided into 3 parts, 1st fresh raw part, 2nd cooked part and 3rd freezed part.

3- Extraction of drug from samples:

One ml of phosphate buffer (pH 7.2) was added to 1gm of each sample. Tissue samples were homogenized thoroughly using sterile mortar with pistol then centrifuged at 3000rpm for 10 minutes, then the supernatant was assayed microbiology.

Antimicrobial assay:

The collected samples (serum and tissues) were assayed for determination of pefloxacin and tilmicosin concentrations by the microbiological assay method according to **Bennett et al., (1966) and Arret et al. (1971)** using Bacillus subtitis (ATCC 6633) as a tested organism.

Statistical analysis:

Data obtained in this study were statistically analyzed for variance (ANOVA), and least significant difference (LSD) as described by **Snedecor and Cochoran (1981)** using SPSS computer program version 10.0 (1999).

RESULTS

A- Standard curve of pefloxacin :

Standard curves of pefloxacin in antibacterial free chick's serum, muscle, liver and kidney using Bacillus subtilis (ATCC6633) as a tested organism. The diameters of inhibition zones were proportionally related to the concentration of pefloxacin. The diameter of inhibition zones (mm) were linear when plotted against the logarithm of the tested drug concentrations ($\mu g/ml^{-1}$) as shown in Table (1) and Figures (1-4)

A-1:Pefloxacin concentrations in serum

The mean concentration of pefloxacin in serum (μg/ml) and tissues (liver, kidney and muscle) (μg/gm) after 3days oral administrations at dose of (10 mg/kg) in chicks were recorded. The obtained data showed that the maximum serum concentration of pefloxacin was 2.30±0.04μg/ml on the 1st day post dosing, then declined up to 0.41±0.04μg/ml on the 28th day post dosing, Table (2), Table (1) showed in: The corrected reading of inhibition zones (mm) for the standard curve of pefloxacin in serum of chicks.

A-2: Pefloxacin residues in tissues

The mean concentrations of pefloxacin in raw tissues (liver, kidney and muscle μg/gm) after 3 days oral administrations in chicks at dose of 10 mg/kg were recorded.

It was found that, raw liver has the highest concentration (2.7±0.11μg/gm) followed by freezed liver (2.10±0.11 μg/gm) but cooked liver (2.02±0.09 μg/gm) showed the lowest concentration in medicated chicks the result were recorded in (Table. 3). Moreover, our data reflected that, the treatment of liver tissue by cooking and freezing significantly decreased the concentrations of pefloxacin on the 7th day (1.88±0.08 & 2.00±0.08 & 2.47±0.11) in cooked, freezed and raw liver respectively. These values were declined gradually till reached (0.41± 0.08 & 0.42 ± 0.06 and 0.6 ± 0.07μg/gm) in cooked, freezed and raw liver of treated chicks on the 28th days post treatment, respectively.

Our data reflected that, the treatment of kidney tissue by cooking and freezing significantly decreased the concentrations of pefloxacin on the 1st day (1.14±0.04 & 1.23±0.03 & 1.46 ± 0.02) in cooked, freezed & raw kidney respectively in medicated chicks the result were recorded in (Table.4). These values were declined gradually till reached (0.24±0.06 & 0.41 ± 0.06 and 0.57±0.04 μg/gm) in freezed, cooked and raw kidney of treated chicks on the 28th days post treatment, respectively.

Our data reflected that , the treatment of muscle tissue by cooking and freezing significantly decreased the concentrations of pefloxacin on the 1st day (2.12±0.06 & 2.62±0.06 & 3.27 ± 0.08) in freezed , cooked & raw muscle respectively in medicated chicks (Table 5). These values were declined gradually till reached (0.78±0.07 & 0.60±0.07and 0.98±0.07μg/gm) in freezed, cooked and raw muscle of treated chicks on the 28th days post treatment, respectively.

B- Standard curve of tilmicosin:

Standard curves of tilmicosin in antibacterial free chick's serum, muscle, liver and kidney using Bacillus subtilis (ATCC6633) as a tested organism. The diameters of inhibition zones were proportionally related to the concentration of Tilmicosin. The diameters of

inhibition zones (mm) were linear when plotted against the logarithm of the tested drug concentrations (µg/ml) as shown in Table (6) and Fig. (5-8).

B-1:Tilmicosin concentrations in serum:

The mean concentration of tilmicosin in serum (µg/ml) and tissues (liver, kidney and muscle) (µg/gm) after 3 days oral administrations at dose of (10mg/kg) in chicks were recorded. The obtained data showed that the maximum serum concentration of tilmicosin was 2.45 ± 0.09µg /ml on the 1st day post dosing, then declined to 0.95 ± 0.06µg / ml on the 28th day post dosing, table (7) and fig (5).

B-2: Tilmicosin residues in tissues:

The mean concentrations of tilmicosin in raw tissues (liver, kidney and muscle µg/gm) after 3 days oral administrations in chicks at dose of 10 mg/kg were recorded.

Our data reflected that, the treatment of liver tissue by cooking and freezing significantly decreased the concentrations of tilmicosin on the 1st day (1.21±0.05 & 1.25±0.06 & 1.59 ± 0.06) in cooked, freezed and raw liver respectively in medicated chicks the result were recorded in (Table.8).

These values were declined gradually till reached (0.17±0.03 & 0.20±0.05 and 0.42±0.04µg/gm) in freezed, cooked and raw liver of treated chicks on the 28th days post treatment, respectively.

Our data reflected that, the treatment of kidney tissue by cooking and freezing significantly decreased the concentrations of tilmicosin on the 1st day (1.27±0.06 & 1.59±0.08 & 1.74 ± 0.13) in cooked, freezed and raw kidney respectively in medicated chicks the result were recorded in (Table 9).

These values were declined gradually till reached (0.32±0.04 & 0.44±0.06 and 0.63±0.04µg/gm) in freezed, cooked and raw kidney of treated chicks on the 28th days post treatment, respectively.

Our data reflected that, the treatment of muscle tissue by cooking and freezing significantly decreased the concentrations of tilmicosin on the 1st day (0.94±0.03 & 1.05±0.06 & 1.17 ± 0.06) in cooked, freezed and raw muscle respectively in medicated chicks the result were recorded in (Table.10).

These values were declined gradually till reached (0.12±0.02 & 0.19±0.06 and 0.37±0.06µg/gm) in freezed, cooked and raw muscle of treated chicks on the 28th days post treatment, respectively.

DISCUSSION

The present study was carried out to estimate the residues of pefloxacin and tilmicosin in tissues and organs of treated chicks after administration of the therapeutic dose . More over, an investigation was undertaken to see if cooking or cold storage would destroy or decrease the level of biologically active pefloxacin and tilmicosin in tissues and organs of treated chicks.

A- Pefloxacin

Pefloxacin is one of several recently developed fluoroquinoloe antimicrobial agents. the primary target of all fluoroquinolones is DNA-

gyrase, an essential bacterial enzyme that maintains super helical twist in DNA causing irreversible chromosome damage and fragmentation, thus result in rapid cell death **(Einstein et al, 1994)** .

A-1:Pefloxacin concentrations in serum

It was found that the maximum serum concentration of pefloxacin (2.30 ± 0.04 µg / ml) on the 1st day post dosing. This finding was confirmed by **Montay et al., (1984)** who reported that pefloxacin was well absorbed rapidly after oral administration to mice, rat and dog. Also **Lynch et al., (1990)** found that a concentration of 0.43 and 0.21 mg/ml were obtained in lung and plasma, during the period of administration of danofloxacin (5mg/kgb.wt) per day for 3 days group of male 18 day old broiler chickens. The half life of the drug was 4.9 hr in plasma and 5.8 in lung. In addition **Giles et al. (1991)** recorded that, danofloxacin was rapidly absorbed after I.M and S.C injection to cattle. Moreover **Raemdonck et al., (1994)** recorded that, administration of danfloxacin to broilers had a pharmacokinetic profile that included rapid absorption following oral administration, good tissue penetration and a relatively long half life. Further more **Pant et al., (2005)** investigated the pharmacokinetics of pefloxacin and its active metabolite norfloxacin in chicken after a single oral administration at a dosage of 10 mg/kg. The authors recorded that the elimination half life, maximum plasma drug concentration, time to reach the maximum plasma drug concentration and mean residence time of pefloxacin were 8.74 ± 1.48hr, 3.78 ± 0.23 µg/ml, 3.3±0.21hr and 14.32 ± 1.94 hr, respectively, where as the respective values of these variables for norfloxacin were 5.66±0.81 hr, 0.8 ± 0.07 µg/ml, 3.67 ± 0.21 hr and 14.44 ± 0.97 hr.

A-2: Pefloxacin residues in tissues

The obtained results revealed that, pfloxacin concentration in liver was 2.7±0.11µg/gm, in kidney was 1.46±0.02 µg/gm and in muscle was 3.27±0.08 µg/gm post dosing in raw chick samples, and then the concentrations were gradually decreased. On the other hand the concentrations in cooked tissue samples were 2.02±0.09, 1.14±0.04 and 2.62±0.06 µg/gm respectively, where concentrations were 2.1±0.11, 1.23±0.03 and 2.12±0.06µg/gm respectively, in freezed tissue samples. The concentrations in freezed liver samples were 2.1± 0.11, 2±0.08, 1.39±0.05 on the 1st, 7th and 14th day post treatment. These finding showed that, the effect of cooking and cold storage on the biological activity of pefloxacin residues were minimal. These results were agree with those of **Al-Mustafa and Al-Ghamdi (2000)** who estimated the antibiotic residues by microbiological assay in samples of market-ready chicken muscle and liver from 32 local broiler farms. The antibiotic residues positive muscles and livers from 22 farms were further analyzed for norfloxacin (NFX) residues by high performance liquid chromatography. NFX was detected in 35.0% and 56.7% of raw antibiotic residue positive muscles and livers, respectively. The NFX-positive muscles and livers were respectively obtained from 11 (50.0%) and 14 (63.6%) of the 22 antibiotic-residue-positive farms. Since the maximum residue limit (MRL) for NFX has not yet been fixed, the MRL for enrofloxacin was used in the study. All NFX-positive farms had mean raw tissue levels, which were 2.7-to 34.3-fold higher than the MRL. Although

cooking markedly reduced NFX tissue concentrations, mean detectable levels remained above MRL in large proportions of NFX-positive samples and farms.

In addition **Pant et al., (2005)** who investigated the residue of pefloxacin and its active metabolite norfloxacin in chickens after oral administration once daily at a dosage of 10 mg/kg for 4 days. The concentrations of pefloxacin (microg/g) 24 h after the fourth dose of the drug were declined in the following order: liver (3.20 +/- 0.40) > muscle (1.42 +/- 0.18) > kidney (0.69 +/- 0.04) > skin and fat (0.06 +/- 0.02). Norfloxacin was also detectable in all the tissues analyzed except muscle. No drug and/or its metabolite were detectable in tissues except skin and fat 5 d after the last administration. The concentrations of pefloxacin and norfloxacin in skin and fat 10 d after the last dose of pefloxacin were 0.04 +/- 0.02 and 0.03 +/-0.01 microgram/g, respectively.

Moreover, **Lolo et al., (2006)** studied the effect of different cooking processes (microwaving, roasting, boiling, grilling and frying) on naturally incurred enrofloxacin residues in chicken muscle. Enrofloxacin and its metabolite, ciprofloxacin, were analysed using a validated LC-MS method with limits of detection (LOD) and quantification (LOQ), respectively, of 2 and 5 ng g^{-1} quinolones in muscle samples. The method was shown to be linear over the range 5-500 ng g^{-1}. Mean intra-day relative standard deviation (RSD) at a concentration of 50 ng g^{-1} (n = 6) was 6%; inter-day RSD was 12%. A recovery study demonstrated that 65-101%, of the drug and metabolite could be recovered from the tissue.

The RSD with naturally incurred roasted chicken breast was 9.18% at a concentration of 11 +/- 1.01 ng g-1 (n = 6). In water, enrofloxacin remained stable for 3 h when heated at 100 degrees C.

B- Tilmicosin

Tilmicosin is a macrolide antibiotic formed from a chemical modification of tylosin. It is recommended for treatment and prevention of pneumonia in cattle, shep and pig, associated with Pasteurella hemolytic, P.multocida, Actinobacilus pleusopneumonia, mycoplasma species and other microorganisms. It has also been tested and used in various other species including rabbits and poultry **(McKay, et al. 1996 and Charleston et al, 1998)**.

B-1: Tilmicosin concentrations in serum

The results recorded in table (13) showed that the maximum serum concentration of tilmicosin (2.45±0.09µg/mL) was reached at 1st day post dosing. Similar finding in serum recorded by **Thomson (1989) in calves, Patel et al (1991)** in sheep and **Tonkinson et al., (1993)** in swine. These results were related to those of **Thompson and Lawrence (1994)** who stated that oral absorption of macrolides is dependant on it may being protected during passage through the stomach as tylosin, azithromycin and clarithromycin are well absorbed from the gastrointestinal tract and do not require enteric coating since **Prescott (2000)** found that tilmicosin is formulated as both a phosphate and tart rate. Difference are observed in the absorption may be related to the severe inflammatory reaction that occurs at the site of injection.

B-2 : Tilmicosin residues in tissues:

Regarding the presence of tilmicosin in tissues of treated chicks, it was found that tilmicosin concentration in liver was (1.59 ± 0.06) µg/gm, in kidney was (1.74 ± 0.13) µg/gm and in muscle was (1.17 ± 0.06) µg/gm at 1st day post dosing in non treated chicks which then gradually decreased. Our results were in accordance with many authors. **Giera et al, (1986)** observed that, residues of tilmicosin were similar in liver and kidney tissues of steer at days (36.0 and 39.2 mg/kg, respectively), but were higher in liver at longer withdrawal period. **Patel et. al (1992)** found that, residues of tilmicosin were distributed throughout tissues assayed in sheep sacrificed at day 3 through 28, with highest levels found in liver at day 28. Also, the results were agree with **Zhang et al., (2004)** who showed that residue depletion of tilmicosin in broiler chickens after dosing over a 5 days period by incorporation of the drug into drinking water at 37.5 and 75.0 mg/kg. tilmicosin concentrations in liver and kidney were highest on day 3 of medication and on day 5 in muscle, in both low- and high-dose groups. The residue levels in both groups were significantly higher in liver than in kidney or muscle. A minimum withdrawal time of 9 days was indicated for residue levels in muscle, liver, and kidney tissues below the maximum residue level (MRL).

The in-vitro studies described the effects of boiling and freezing on tilmicosin residues on muscle and organs showed that, tilmicosin concentration in boiled tissues (liver, kidney and muscle) were (1.21 ± 0.05 & 1.27 ± 0.06 and 0.94 ± 0.03µg/gm respectively) where it was (1.25 ± 0.06 & 1.59±0.08 and 1.05 ± 0.06µg/gm) respectively, in free zed samples.

The obtained results Concerned with the effect of cooking or freezing on tilmicosin residues reflected a moderate effects on the heat treatment on there residues. This finding was supported by the results obtained by **O'Brien et al (1981)** who stated that the effect of cooking and cold storage on the biological activity of the residues of ampicillin, chloramphenicol, oxytetetracycline, streptomycin and sulphadimidine were varied in the same instance the effects were minimal, on other nil.

CONCLUSION

It could be concluded from this investigation that, the effect of heat treatment (cooking or freezing) on residues of pefloxacin and tilmicosin should be considered before data obtained from measurement on raw tissues are used for consumer exposure estimate and dietary intake calculations.

Table (1): The corrected reading of Inhibition zones (mm) for the standard curves of pefloxacin in serum and tissues of chicks.

Concentration ($\mu g/ml^{-1}$)	Inhibition zone (mm)			
	Serum	Liver	Kidney	Muscle
50	30	24	39.7	33
25	17	13.7	22	18
12.50	12.5	9.5	13	13
6.25	10	8	8	7.5
3.12	7	7	6	6
1.5	5.5	4.5	4	4
0.78	4	3	2.5	2.5

Table (2): The concentration of pefloxacin in serum of treated chicks . Mean±S.E n=5

Time of sample	M ± SE
1 day	2.30 ± 0.04
7 day	1.73 ± 0.05
14 day	1.23 ± 0.04
21 day	0.83 ± 0.04
28 day	0.41 ± 0.04

P<0.05

Table (3): The concentration of pefloxacin in liver of treated chicks. Mean±S.E n=5

Time of sample	Raw liver	Cooked liver	Freezed liver
1 day	2.7 ± 0.11^{a}	2.02 ± 0.09^{b}	2.10 ± 0.11^{a}
7 day	2.47 ± 0.11^{a}	1.88 ± 0.08^{c}	2.00 ± 0.08^{b}
14 day	1.70 ± 0.09^{a}	1.41 ± 0.06^{b}	1.39 ± 0.05^{b}
21 day	1.28 ± 0.09^{a}	0.91 ± 0.07^{b}	0.86 ± 0.06^{c}
28 day	0.6 ± 0.07^{a}	0.41 ± 0.08^{b}	0.42 ± 0.06^{b}

P<0.05

Table (4): The concentration of pefloxacin (μg/gm) in kidney of treated chicks.

Mean±S.E n=5

Time of sample	Raw kidney	Cooked kidney	Freezed kidney
1 day	1.46 ± 0.02^{a}	1.14 ± 0.04^{c}	1.23 ± 0.03^{c}
7 day	1.29 ± 0.03^{a}	1.06 ± 0.04^{b}	1.11 ± 0.03^{c}
14 day	1.02 ± 0.06^{a}	0.8 ± 0.02^{b}	0.93 ± 0.05^{a}
21 day	0.75 ± 0.04^{a}	0.72 ± 0.04^{a}	0.67 ± 0.04^{b}
28 day	0.57 ± 0.04^{a}	0.41 ± 0.06^{b}	0.24 ± 0.06^{c}

$P<0.05$

Table (5) : The concentration of pefloxacin (μg /gm) in muscle of treated chicks.

Mean±S.E n=5

Time of sample	Raw muscle	Cooked muscle	Freezed muscle
1 day	3.27 ± 0.08^{a}	2.62 ± 0.06^{b}	2.12 ± 0.06^{c}
7 day	2.17 ± 0.08^{a}	2.06 ± 0.08^{b}	1.75 ± 0.07^{c}
14 day	1.42 ± 0.05^{a}	1.13 ± 0.04^{b}	1.1 ± 0.06^{b}
21 day	1.16 ± 0.05^{a}	0.93 ± 0.06^{b}	0.97 ± 0.06^{b}
28 day	0.98 ± 0.07^{a}	0.60 ± 0.07^{b}	0.78 ± 0.07^{c}

$P<0.05$

Table (6): The corrected reading of Inhibition zones (mm) for the standard curves of tilmicosin in serum and tissues of chicks.

Concentrations (μg/ml)	Inhibition zone (mm)			
	Serum	Liver	Kidney	Muscle
50	24.5	34.5	33	34.7
25	14	20.5	18.5	20.25
12.5	8.7	17	11.2	16
6.25	7.8	11	10	12
3.12	7	6.9	8	6.55
1.5	4	6	4.6	5.44
0.78	2.5	4.6	2	3

Table (7): The concentration of tilmicosin in serum of treated chicks. Mean±S.E n=5

Time of sample	M± SE
1 day	2.45 ± 0.09
7 day	1.77 ± 0.08
14 day	1.53 ± 0.09
21 day	1.31 ± 0.06
28 day	0.95 ± 0.06

P<0.05

Table (8): The concentration of tilmicosin (µg/gm) in liver of treated chicks. Mean±S.E n=5

Time of sample	Raw liver	Cooked liver	Freezed liver
1 day	1.59 ± 0.06^{a}	1.21 ± 0.05^{b}	1.25 ± 0.06^{b}
7 day	1.53 ± 0.04^{a}	1.01 ± 0.08^{b}	1.06 ± 0.03^{b}
14 day	0.81 ± 0.05^{a}	0.66 ± 0.14^{b}	0.45 ± 0.03^{b}
21 day	0.72 ± 0.04^{a}	0.52 ± 0.05^{b}	0.39 ± 0.10^{c}
28 day	0.42 ± 0.04^{a}	0.20 ± 0.05^{b}	0.17 ± 0.03^{c}

P<0.05

Table (9): The concentration of tilmicosin (µg/gm) in kidney of treated chicks. Mean±S.E n=5

Time of sample	Raw kidney	Cooked kidney	Freezed kidney
1 day	1.74 ± 0.13^{a}	1.27 ± 0.06^{b}	1.59 ± 0.08^{c}
7 day	1.53 ± 0.08^{a}	1.14 ± 0.04^{b}	1.17 ± 0.06^{b}
14 day	1.23 ± 0.08^{a}	1.01 ± 0.09^{b}	0.97 ± 0.04^{c}
21 day	1.08 ± 0.07^{a}	0.58 ± 0.05^{b}	0.68 ± 0.02^{c}
28 day	0.63 ± 0.04^{a}	0.44 ± 0.06^{b}	0.32 ± 0.04^{c}

P<0.05

Table (10) : The concentration of tilmicosin (µg/gm) in muscle of treated chicks. Mean±S.E n=5

Time of sample	Raw muscle	Cooked muscle	Freezed muscle
1 day	1.17 ± 0.06^{a}	0.94 ± 0.03^{b}	1.05 ± 0.06^{c}
7 day	1.11 ± 0.03^{a}	0.86 ± 0.12^{b}	0.95 ± 0.04^{c}
14 day	0.92 ± 0.03^{a}	0.54 ± 0.04^{b}	0.69 ± 0.05^{b}
21day	0.69 ± 0.05^{a}	0.34 ± 0.06^{b}	0.33 ± 0.03^{b}
28day	0.37 ± 0.06^{a}	0.19 ± 0.04^{b}	0.12 ± 0.02^{c}

P<0.05

Fig. (1): The corrected reading of inhibition zones (mm) for standard curve of pefloxacin in serum of chicks.

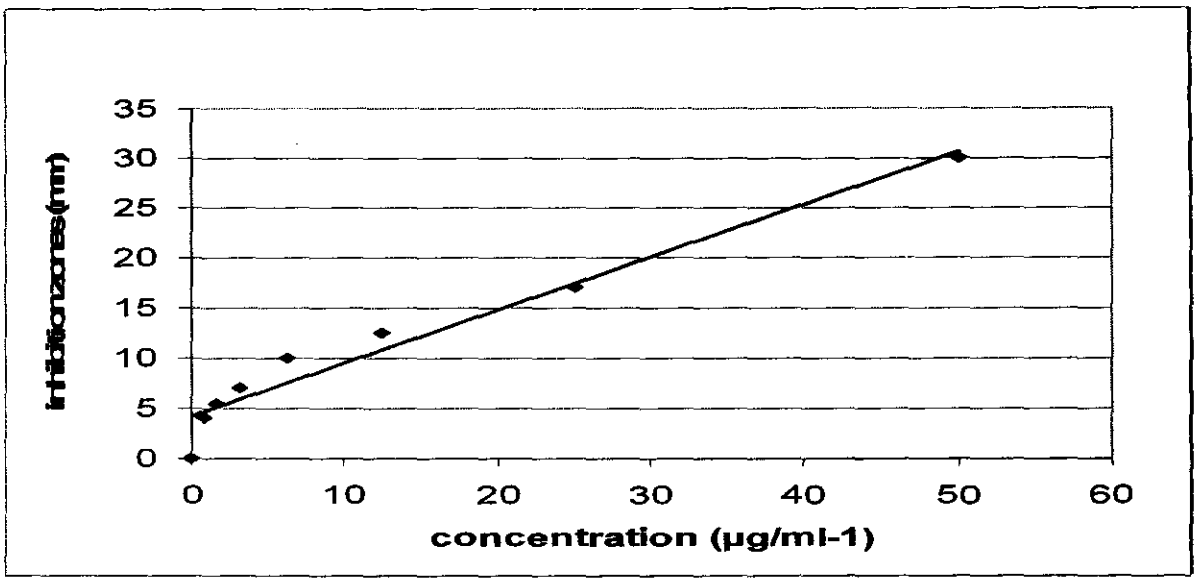


Fig. (2): The corrected reading of inhibition zones (mm) for standard curve of pefloxacin in liver of chicks.

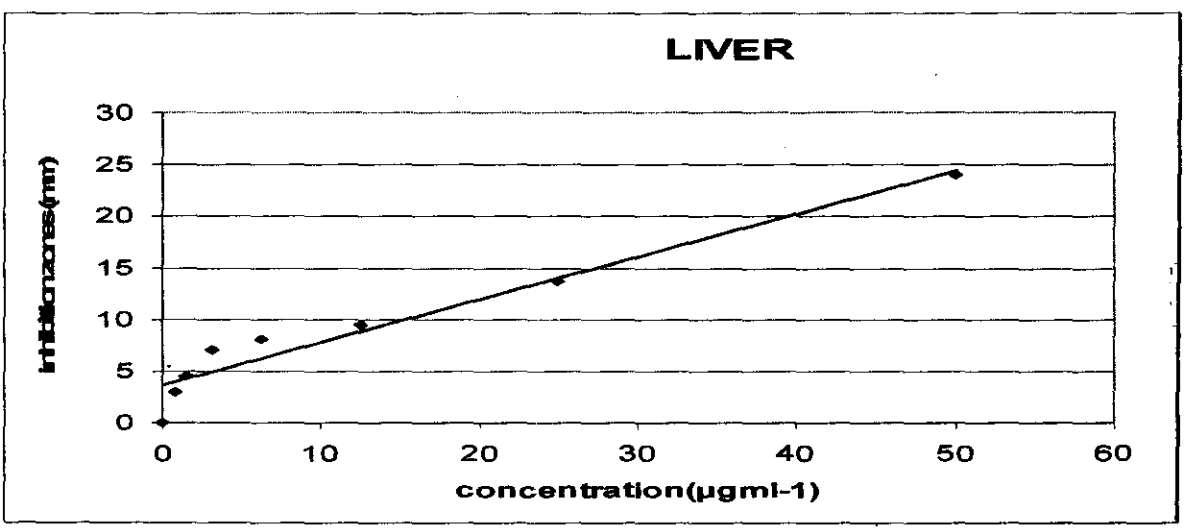


Fig (3): The corrected reading of inhibition zones (mm) for standard curve of pefloxacin in kidney of chicks.

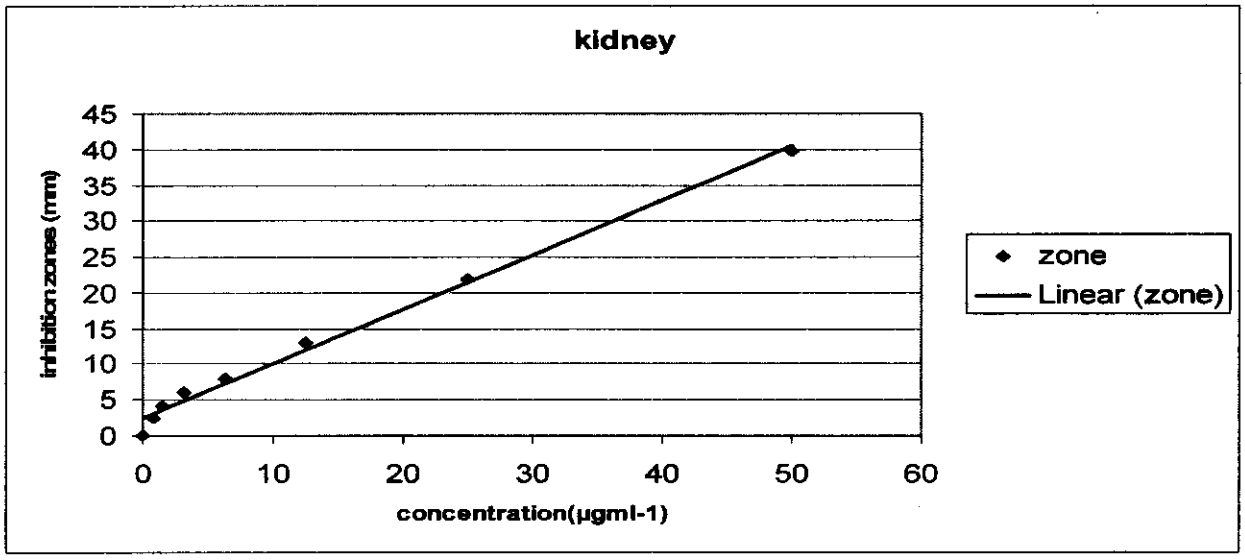


Fig (4): The corrected reading of inhibition zones (mm) for standard curve of pefloxacin in muscles of chicks.

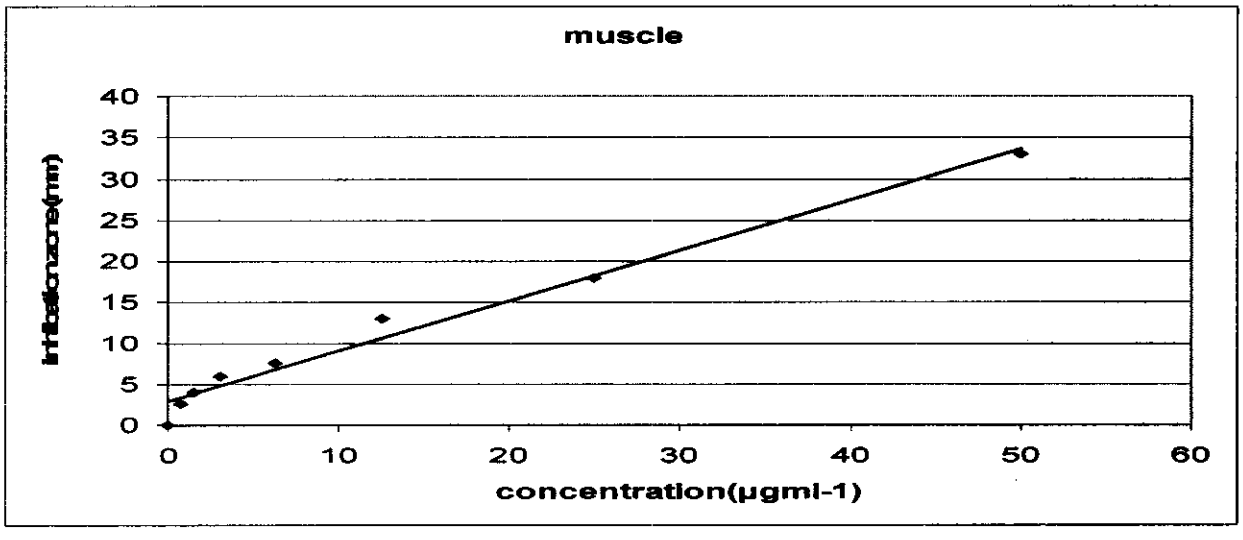


Fig (5): The corrected reading (mm) of inhibition zones for standard curve of tilmicosin in serum of chicks.

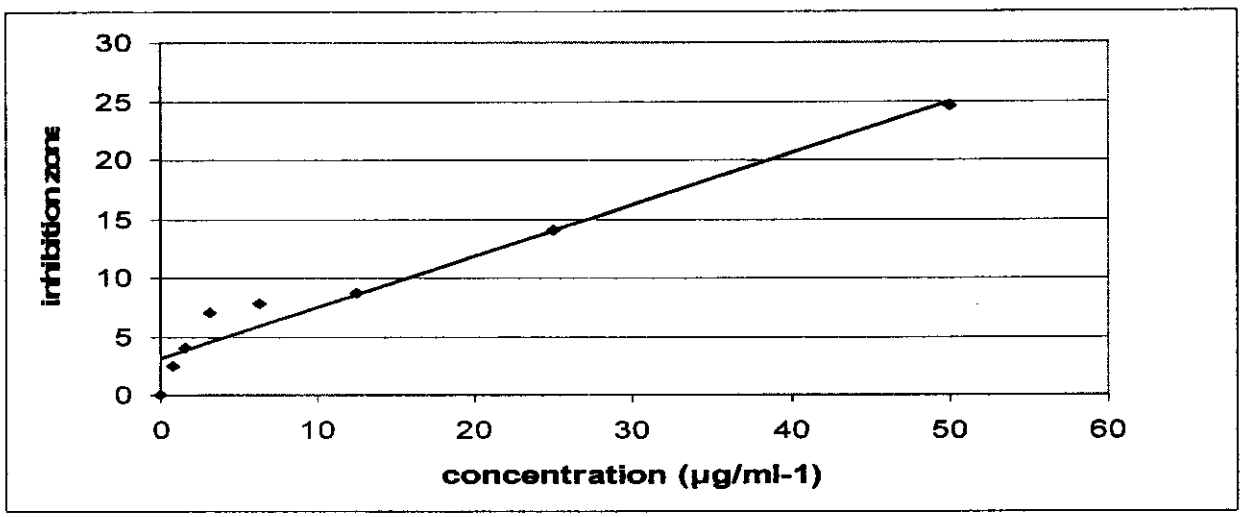


Fig (6): The corrected reading of inhibition zones (mm) for standard curve of tilmicosin in liver of chicks.

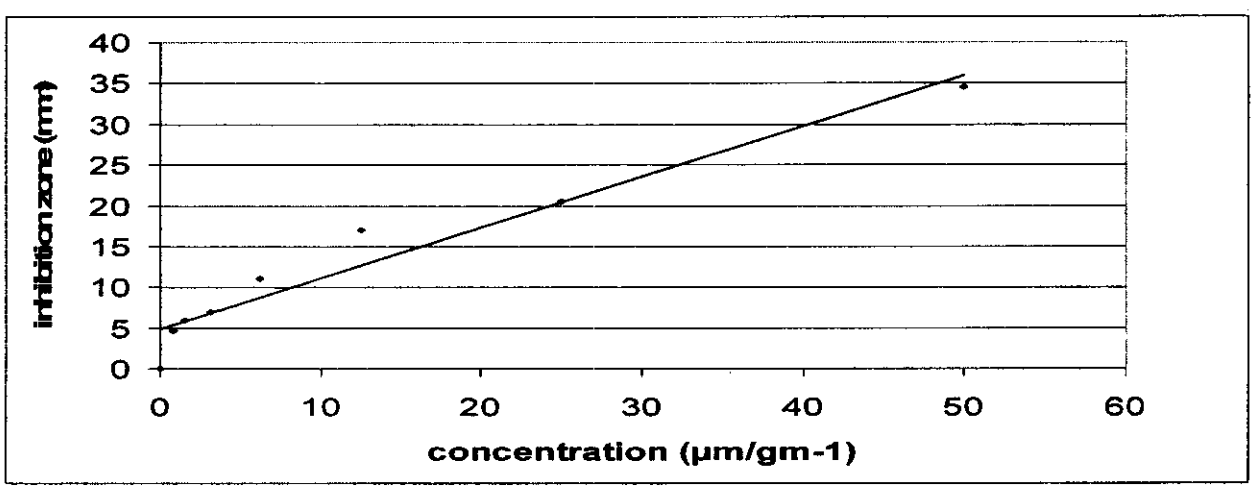


Fig (7): The corrected reading of inhibition zones (mm) for standard curve of tilmicosin in kidney of chicks.

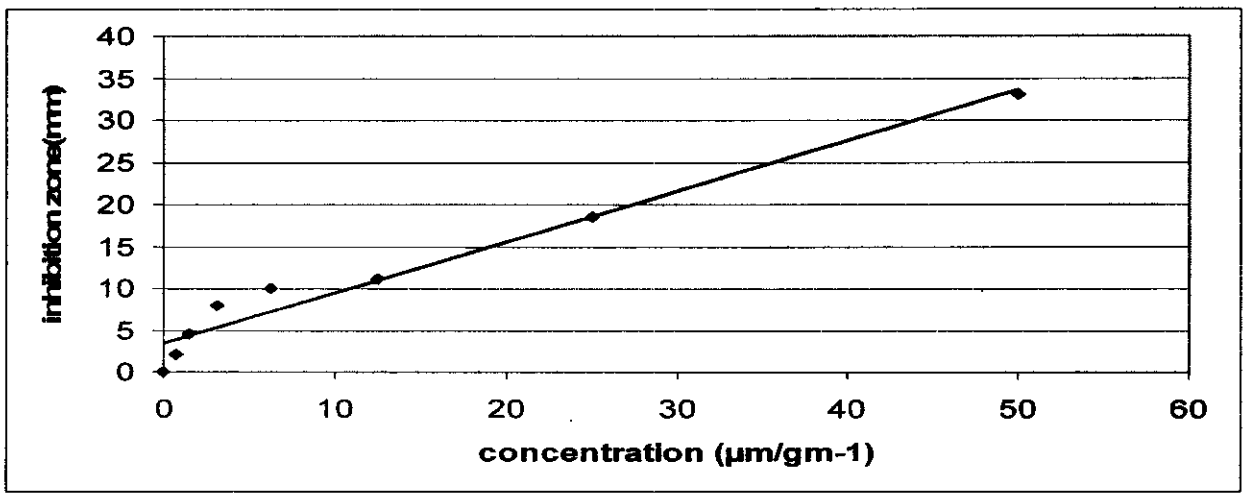
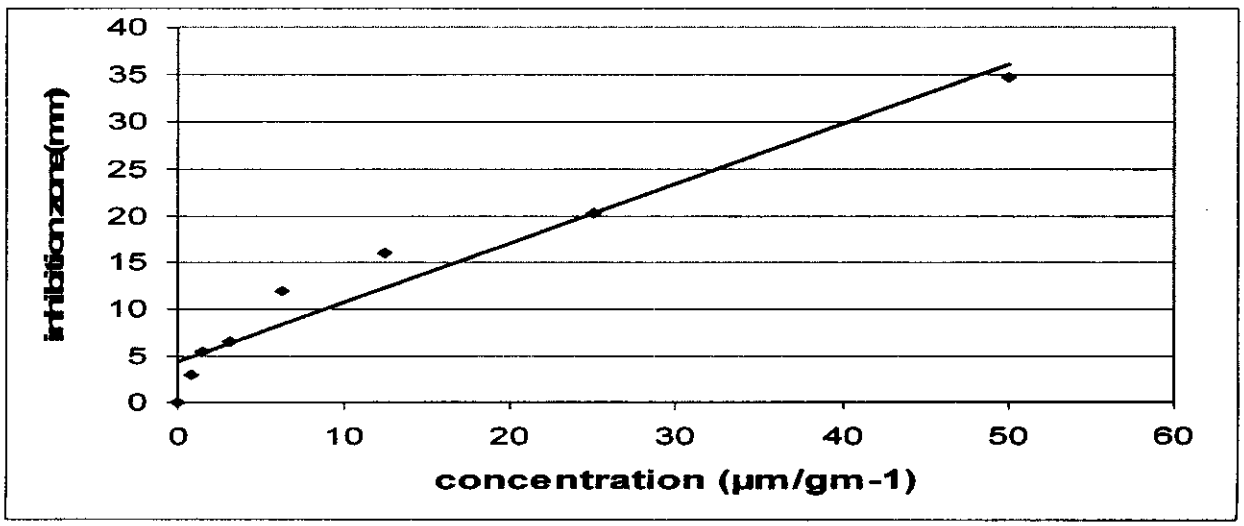


Fig (8): The corrected reading (mm) of inhibition zones for standard curve of tilmicosin in muscles of chicks.



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الملخص العربى

دراسات مقارنة عن فترات سحب بعض المضادات الحيوية من الأنسجة

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أجريت هذه الدراسة على عدد 120 كتكوت عمر يوم واحد لدراسة بقايا البيفلوكساسين والتيلموكوزين فى مصل الدم والأنسجة الحية (الكبد، الكلى والعضلات) بطريقة القياس الميكروبولوجى، وقد أعطى الدواء عن طريق مياه الشرب لمدة ثلاث أيام متتالية، قسمت الكتاكيت فى هذه الدراسة إلى ثلاث مجاميع متساوية كل يحتوى على 40 طائر :

المجموعة الأولى : أعطيت هذه المجموعة عقار البيفلوكساسين عن طريق ماء الشرب بجرعة علاجية قدرها 10مجم / كيلوجرام من الوزن الحى يومياً لمدة ثلاث أيام متتالية.

المجموعة الثانية : أعطيت هذه المجموعة عقار التيلموكوزين عن طريق ماء الشرب بجرعة علاجية قدرها 10مجم / كيلوجرام من الوزن الحى يومياً لمدة ثلاث أيام متتالية.

المجموعة الثالثة : وهى المجموعة الضابطة ولم يتم إعطاء أدوية لها فى مياه الشرب.

١- البيفلوكساسين : وقد أوضحت الدراسة أن أعلى تركيز لعقار البيفلوكساسين فى مصل الكتاكيت المستخدمة قد سجل بعد 24 ساعة من إنتهاء الجرعة المستخدمة فى الكتاكيت وكانت 2.30±0.04 ميكروجرام / ميلليتر قد قل التركيز تدريجياً حتى وصل إلى .41±0.04 ميكروجرام / ميلليتر بعد 28 يوم من إنتهاء الجرعة العلاجية، وقد بينت الدراسة أن بقايا عقار البفلوكساسين فى الأنسجة الطازجة بعد ثلاث أيام علاج متتالية كانت أنسجة العضلات قد أعطت أعلى تركيز(3.27±0.08 ميكروجرام / جرام) ثم الكبد (2.7±0.11 ميكروجرام / جرام) وأقلهم الكلى (1.46±0.02 ميكروجرام / جرام)، هذه النتائج قلت تدريجياً إلى أن وصلت (0.98±0.07 ، 0.56±0.07 و 0.56±0.04 ميكروجرام / جرام) فى العضلات والكبد والكلى فى الكتاكيت المعالجة فى اليوم الـ28 من إنتهاء العلاج، بالترتيب.

أوضحت الدراسة أن معاملة أنسجة الكبد والكلى والعضلات بالطهى أو بالتجميد قد أحدث إنخفاضاً معنوياً لبقايا عقار البفلوكساسين مقارنة بالأنسجة الطازجة وذلك عند اليوم الأول بعد وحتى اليوم 28 بعد إيقاف العلاج.

٢- التيلميكوزين :

أوضحت النتائج أن أعلى تركيز لعقار التيلموكوزين فى مصل الكتاكيت المستخدمة قد سجل أعلى تركيز بعد 24 ساعة من إنتهاء الجرعة المستخدمة فى الكتاكيت وكانت 2.45±0.09 ميكروجرام / ميلليتر والتى تناقصت تدريجياً حتى وصلت إلى 0.95±0.06 ميكروجرام / ميلليتر بعد 28 يوم من إنتهاء الجرعة الدوائية، كما أظهرت النتائج أن بقايا عقار التيلميوكوزين فى الأنسجة الطازجة

(بعد ثـلاث أيـام عـلاج متتـالية) سجلت أن أنسجة الكلى قـد أعطـت أعلـى تركيز (1.74±0.13 ميكروجرام / جرام) ثم أنسجة الكبد (1.59±0.06 ميكروجرام / جرام) وأقلهـم العضـلات (1.17±0.06 ميكروجرام / جرام)، هـذه النتائـج قلت تدريجـياً إلى أن وصلت 0.63 .0+0.04 ، 0.42±0.04 و 0.37±0.06 ميكروجرام / جرام في الكلى والكبد والعضلات فى الكتاكيت المعالجـة فى اليوم الـ28 من إنتهاء العلاج، بالترتيب.

تبين من النتائج أن معاملة أنسجة الكبد والكلى والعضلات بالطهى أو بالتجميد قد أحدث إنخفاضاً معنوياً لبقايا عقار التيلموكوزين مقارنة بالأنسجة الطازجة وذلك عند اليوم الأول بعد وحتى اليوم 28 بعد إيقاف العلاج.