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Influence of Acidifiers on Pharmacokinetics And Tissue Residues of Lincomycin in Healthy Broiler Chickens

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Abstract

In this study we investigated the influence of acidifiers (Gallimix) on the disposition kinetics and tissue residues of Lincomycin following single i.v and oral administrations (20 mg/kg b.wt). Lincomycin serum concentration was determined by microbiological assay method. Following i.v injection, Lincomycin serum concentration versus time curve was best fitted a 2-comparment open model.

It is clear that there is no significant differences in the values of distribution rate constant (α) and distribution half-life ($t_{½\alpha}$) of Lincomycin following single oral administration of Lincomycin in chickens fed acidifiers containing ration (1ppm), the peak concentration (C_{max}) was 5.63±1.42 mg/ml and was achieved at T_{max} (0.62±0.23) which is significantly lower (C_{max}) and shorter T_{max} than chickens fed on free acidifiers.

The calculated bioavailability (F %) was 54.99±7.54% which is significantly lower than the corresponding one (80.13±4.68%) in chickens fed on acidifiers free ration. The average value of protein binding percentage of Lincomycin to chicken's serum proteins was 14.5±1.26%.

Following residue studies the obtained results revealed that Lincomycin was found widely distributed in chickens fed acidifiers free ration. In conclusion: concomitant administration of Lincomycin and Gallimix in broiler chickens must be not recommended as the interaction between them significantly reduces Lincomycin blood concentration and tissue distribution which consequently decreases its therapeutic efficacy.

Keywords: Acidifier, Lincomycin, Kinetics, Residues, Bioavailability.

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Introduction

All over the world, there is no doubt that poultry is considered as one of the meat important sources of animal. In our Arab world there is a continuous increasing demand for poultry meat with the rapid progressive expansion of poultry industry to meet this increasing demand.

Lincomycin is one of Lincosamide antibiotics isolated from *Streptomyces Lincolnensis* (Manson et al., 1962) that has a bacteriostatic effect against Gram Positive bacteria and *Mycoplasma Spp.* It has been improved a good therapeutic effect in treatment of many poultry diseases including CRD (Chaleva et al., 1994), necrotic enteritis caused by *E. coli* (Hamdy et al., 1983).

The pharmacokinetics of Lincomycin has been determined in humans (Fass, 1981) and for a variety of animals including calves (Burrows et al., 1983), pigs (Chaleva and Nguyen, 1987); chickens (Soback et al., 1987; Aziza et al., 2005) and goats (Abo El-Sooud et al., 2004). Lincomycin is extensively metabolized in liver into N-desmethyl Lincomycin, and Lincomycisulfoxide and approximately 40% of the administered dose is excreted in the urine as unchanged Lincomycin and N-desmethyl Lincomycin in pigs (Hornish et al., 1987).

Acidifiers are organic acids and its salts (acetic acid, propionic acid, citric acid, phosphoric acid, formic acid, lactic acid and furamaric acid etc....) make water acidification to a pH of 3.5 or less will selectively promote gut colonization with good healthy bacteria while suppressing *Salmonella* in the crop, thus organic acids in water improve the total gut health, which help in absorption of nutrients and overall performance of the birds. Acidifier usage in animal nutrition is mainly based on reducing pH value in digestive tract that could prevent multiplication of some pathogen germs such as *Salmonella, Clostridium, Staphylococcus* or *E. coli* and being favorable for multiplication of some useful microorganism, such as lactic acid bacteria (Stan and Pop 1997; Stan and Simeanu, 2005).

Persistence of the drug for long intervals (after the last dose) in food producing animals poses serious problems for human beings. Because broiler chickens are reared chiefly for food purposes, the tissue residues of these drugs need investigation. The aim of the present work was to investigate the influence of Gallimix as commercial acidifier on kinetic disposition; tissue distribution; withdrawal time and tissue residues of Lincomycin following its oral administration in broiler chicken.

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Material and Methods

A- Drugs :

1- Lincomycin

Lincomycin hydrochloride was obtained from V.M.D, Belgium as soluble powder in concentration of 40%

2- Gallimix (acidifiers)

Gallimix is encapsulated feed additive obtained from MG2MIX Company, France.

B- Birds:

Forty six clinically healthy broiler chickens (Hubbard breed) forty five days old, weighing between 1.5 and 2.1 kg, were obtained two weeks before the start of the study from a commercial farm. During acclimatization period the birds were fed antibacterial-free, balanced, commercial rations and drinking water was freely available.

C- Experimental design :

1- Pharmacokinetic studies

16 broiler chickens were individually weighed before drug administration and doses were calculated precisely. The broiler chickens were allocated to four equal groups of 4 each. Birds in group one and three were kept on free Gallimix medicated ration and given a single I.V and oral dose of Lincomycin at 20 mg/kg into the left brachial vein and into the crop by means of a feeding tube and a syringe, respectively. Birds in other groups were offered a Gallimix medicated ration for five consecutive days. At the 5th day, Lincomycin was intravenously and orally administered as mentioned before at the same previous dose to chickens of both groups.

Blood samples:

One ml blood samples from all previous groups were collected from the right brachial vein of each chicken by puncture method in tubes just before and at 15 and 30 min. and 1, 2, 4, 6, 8, 10 and 12 h after administration of Lincomycin.

All the blood samples were centrifuged at 3000 rpm for 15 min to separate the serum. The serum samples were collected and frozen at -20°C until assayed for Lincomycin concentration.

2-Tissue residue study:

30 broiler chickens were divided into two equal groups of 15 birds each. The chickens in the 1st group were left to feed non-medicated ration, while those in the 2nd one offered Gallimix medicated ration in the same previous

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concentration for 5 consecutive days. At the 5th day, Lincomycin was given at a dose of 20 mg/kg once daily for 5 consecutive days through oral route. Three broiler chickens were killed at 1, 2, 3, 4 and 5 day post Lincomycin administration. Blood and tissue samples (liver, kidney, lung, thigh muscle, breast muscle and intestine) were taken and stored at -20°C until assayed for Lincomycin concentration.

Analytical procedures:

Concentrations of Lincomycin in serum and tissues were determined by a microbiologic agar diffusion assay (Arret et al., 1971) using *Sarcina lutea* (ATCC 9341) as the test organism. The limit ofquantitation by this method was 0.156 µg/ml in serum and tissues. The response of Lincomycin was linear over the range of concentration between 0.156 and 20µg/ml. The mean correlation coefficient (r^2) of the standard curves was found to be 0.99. The recovery from spiked tissue samples and serum was ranged from 88 to 96 %, respectively, and the intra-day coefficient of variation (CV) was 8 %.

Tissues samples: One gram of tissue (liver, kidney, lung, thigh muscle, breast muscle and intestine) was homogenized in 10 ml of distilled water and the homogenate was centrifuged at 3000 rpm for 20 min. The supernatant was directly added to the culture plate to measure Lincomycin concentrations.

Estimation of protein binding to the tested antibiotic:

The free unbound antibiotic is only capable to diffuse through agar. The protein binding of the tested antibiotic was estimated by dilution the drug in buffer solution or in control sample of serum to obtain concentrations of 5.0, 2.5, 1.25, 0.625, 0.313 and 0.156 µg/ml of Lincomycin.

The difference in the diameter of zone of inhibition between the solution of antibiotic in buffer and serum were used in calculation of the percentage of protein binding of the antibiotic by the following formula according to Craig and Suh, 1991.

$$\text{Binding \%} = \frac{\text{Zone of inhibition in buffer} - \text{Zone of inhibition serum}}{\text{Zone of inhibition in buffer}} \times 100$$

Statistical analysis:

The mean serum pharmacokinetic variables and tissues concentrations for Lincomycin were statistically compared by nonparametric analysis, using the Mann–Whitney test and Instant version 3.00 (GraphPad Software, San Diego, CA, USA). Mean values were considered significantly different at $P < 0.05$, $P < 0.01$ and $P < 0.001$. Pharmacokinetic variables and concentrations in tissues are reported as mean ± SD.

Pharmacokinetic analysis:

A computerized curve-stripping program (R Strip; Micromath Scientific Software, Salt Lake City, UT, USA) was used to analyze the concentration–time curves for each individual bird after the administration of Lincomycin by different routes. For the intravenous data, the appropriate pharmacokinetic model was determined by visual examination of individual concentration-time curves and by application of Akaike's Information Criterion (AIC) (Yamaoka et al., 1978).

This program also calculated non-compartmental parameters using the statistical moment theory (Gibaldi and Perrier, 1982).

Results

The present work was performed to study the influence of mixed acidifier (Gallimix) on the disposition kinetic and tissue residues of antibiotic Lincomycin in broiler chickens.

No clinical abnormalities of all birds were detected during the study. No local signs of pain or soft tissue swelling at injection sites or systemic adverse reactions to Lincomycin were detected in birds after i.v or p.o administration. Results of the Akaike's information criterion test indicated that a 2-compartment open model best represented the serum concentration-versus-time data following I.V and p.o administration of Lincomycin in Semi-logarithmic plot of mean Lincomycin concentrations in serum vs. time following single i.v and oral administrations in the absence and presence of Gallimix in broiler as shown in Fig. 1 and 2.

The pharmacokinetic parameters describing the disposition of Lincomycin after single I.V and p.o administration of 20 mg/kg b.wt in the absence and presence of Gallimix are given in Table 1 and 2.

The effect of acidifiers on tissue residues of Lincomycin in broiler chickens was studied following its oral administration in a dose 20 mg/ kg b.wt once daily for 5 successive days was presented in Table 3 and 4.

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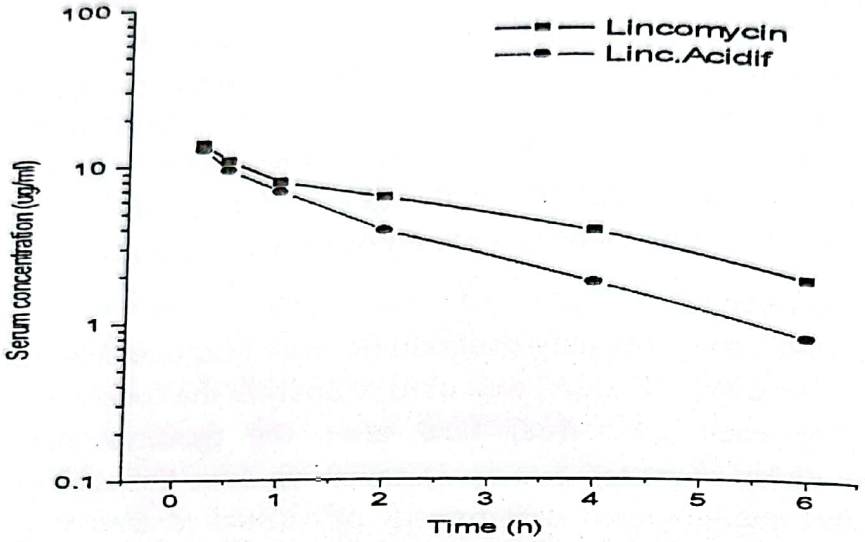

Figure 1. Semilogarithmic graph depicting the time concentration of Lincomycin inserum of chickens after a single intravenous injection (20 mg/kg b.wt) in Lincomycin and Lincomycin +Acidifiers chickens.

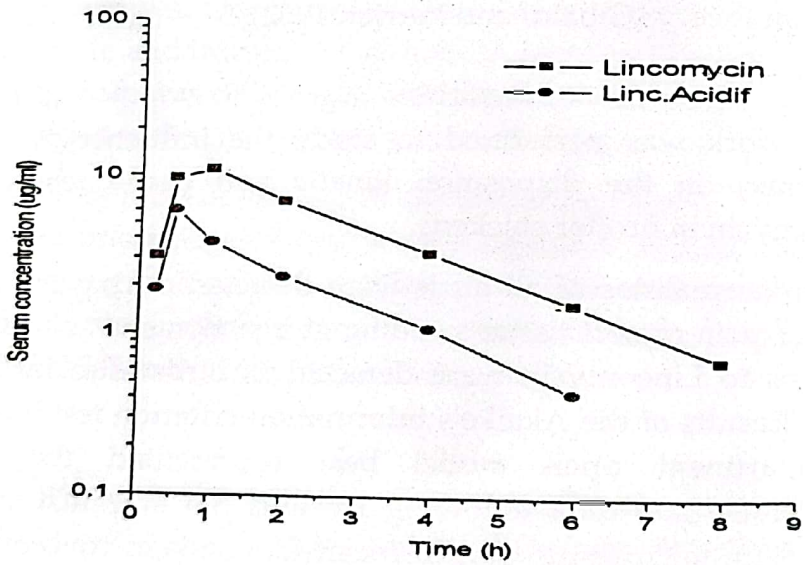

Figure2. Semilogarithmic graph depicting the time concentration of Lincomycin in serum of chickens after a single oral administration (20 mg/kg b.wt) in Lincomycin and Lincomycin +Acidifiers chickens.

The obtained results were revealed that Lincomycin is found widely distributed in chickens fed acidifiers free ration, particularly in liver, kidney, intestine and lungs, respectively. The lowest concentration was found in serum and breast muscles.

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As shown in Table (4) Lincomycin was detected in tissue of chickens fed on acidifiers containing ration (0.4g/kg feed), concentrations significantly lower than that in chickens fed on acidifiers free ration, particularly on the 2nd and 3rd days after stopping of its administration. In addition the withdrawal time for all examined tissues was 3 days after the last dose.

Table 1. Pharmacokinetic parameters of Lincomycin following a single intravenous injection (20 mg/kg b.wt) in Lincomycin and Lincomycin acidifiers chickens (Mean ±SD, n=4)

Parameters	Unit	Lincomycin	Lincomycin +Acidifiers
B	µg/ml	9.93 ± 0.51	10.51 ± 0.41
A	µg/ml	12.07 ±2.3	11.79 ± 5.46
α	h-1	4.67 ± 0.78	5.24 ± 1.72
t1/2α	h	0.16 ± 0.028	0.14 ± 0.041
β	h-1	0.25 ± 0.18	0.52 ± 0.013***
t1/2β	h	2.79 ± 0.198	1.31 ± 0.036***
K12	h-1	2.12 ± 0.32	2.045 ± 1.2
K21	h-1	2.278 ± 0.570	2.718 ± 0.409
K12/ K21	Ratio	0.930±0.08	0.752±0.07
VC	L/kg	0.912 ± 0.073	0.935 ± 0.215
Vdss	L/kg	1.80 ± 0.05	1.52 ± 0.08
Cltot	L/h/kg	0.477 ± 0.015	0.875 ± 0.017***
AUC	µg.h/ml	41.93 ± 1.548	22.85 ± 0.502***
AUMC	µg.h2/ml	160.50 ± 14.55	38.24 ± 1.16***
MRT	h	3.775 ± 0.207	1.728 ± 0.057***

B&A: zero time serum drug concentration intercepts of elimination and distribution phase, respectively; α: distribution rate constant; t1/2α: distribution half-life; β: elimination rate constant; t1/2β: elimination half-life, K12 and K21 first-order rate constants for drug distribution between the central and peripheral compartments, Vc: the apparent volume of central compartment; Vdss: volume of distribution; Cltot: total body clearance; AUC: area under the curve from zero to infinity by the trapezoidal integral; AUMC: total area under the first moment curve; MRT: mean residence time. * P<0.05, **P<0.01, ***P<0.001.

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Table 2. Pharmacokinetic parameters of Lincomycin following a single oral administration (20 mg/kg b.wt) in Lincomycin and Lincomycin acidifiers chickens (Mean ±SD, n=4)

Parameters	Unit	Lincomycin	Lincomycin +Acidifier
B	µg/ml	9.15 ± 0.68	9.50 ± 0.40
A	µg/ml	17.93 ± 0.56	17.35 ± 0.79
Kab	h-1	4.77 ± 0.45	4.22 ± 0.76
t1/2ab	h	0.15 ± 0.02	0.28 ± 0.24
Kel	h-1	0.39 ± 0.01	1.74 ± 1.25
t1/2el	h	1.74 ± 0.05	0.70 ± 0.61
AUC	µg.h/ml	33.51 ± 0.715	12.55 ± 1.572***
AUMC	µg.h2/ml	92.76 ± 3.84	14.99± 13.66***
MRT	h	2.73 ± 0.05	1.41 ± 0.83
Cmax	µg/ml	10.72 ± 0.22	5.63 ± 1.42*
Tmax	h	0.76 ± 0.02	0.62 ± 0.23
F	%	80.13 ± 4.68	54.99 ± 7.54*

B&A: zero time serum drug concentration intercepts of elimination and distribution phase, respectively; kab: absorption rate constant; t½ab: absorption half-life; kel: elimination rate constant; t½el: elimination half-life; AUC: area under the curve from zero to infinity by the trapezoidal integral; AUMC: total area under the first moment curve; MRT: mean residence time; Cmax: maximum plasma concentration;; F(%), bioavailability. * P<0.05, ***P<0.001.

Table 3. Mean ± SD serum and tissues concentrations of Lincomycin (µg/g or µg/ml) after oral doses of 20 mg/kg b.wt for 5 consecutive days in broiler chickens (n=3)

Tissue	Lincomycin Concentrations (µg/g or µg/ml)				
	Time after the last dose (days)				
	1	2	3	4	5
Liver	3.82±0.63	3.04±0.78	2.24±0.69	0.2±0.46	Nd
Kidney	3.65±0.71	2.95±0.75	1.82±0.54	0.91±0.11	Nd
Lung	3.28±0.41	2.88±0.65	1.24±0.53	0.22±0.06	Nd
Serum	2.43±0.17	1.83±0.15	0.97±0.25	Nd	Nd
Thigh Muscle	2.77±0.40	2.07±0.76	1.61±0.53	0.21±0.03	Nd
Breast Muscle	2.65±0.63	2.15±0.71	1.26±0.37	0.17±0.05	Nd
Intestine	3.36±0.76	2.96±0.62	1.18±0.21	0.17±0.08	Nd

Nd: Not Detected

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Table 4. Mean ± SD serum and tissues concentrations of Lincomycin (µg/g or µg/ml) after oral doses of 20 mg/kg b.wt concomitant with acidifiers for 5 consecutive days in broiler chickens (n=3).

Tissue	Lincomycin Concentrations (µg/g or µg/ml)				
	Time after the last dose (days)				
	1	2	3	4	5
Liver	3.22±0.63	2.15±0.41	0.98±0.21*	Nd	Nd
Kidney	2.63±0.27	1.83±0.15	0.84±0.16*	Nd	Nd
Lung	2.55±0.43	1.95±0.62	0.23±0.05*	Nd	Nd
Serum	2.32±0.15	1.57±0.06	0.53±0.12	Nd	Nd
Thigh Muscle	1.73±0.19	0.91±0.17	0.17±0.05*	Nd	Nd
Breast Muscle	1.69±0.25	0.59±0.07	0.14±0.02*	Nd	Nd
Intestine	1.72±0.14	0.56±0.10*	0.18±0.06*	Nd	Nd

Nd: Not Detected, *P<0.05,

Discussion

This present work was performed to investigate the effect of Gallimix as a commercial acidifier's product on the pharmacokinetics of Lincomycin in healthy broiler chickens.

This study used the bioassay technique to determine the pharmacokinetics of Lincomycin in broiler chickens. The microbiological assay has been used in many studies, for measuring Lincomycin concentrations in serum and other biological matrices (Abo El-Sooudet al., 2004; Aziza et al., 2005).The reason that we selected the bioassay is that the microbiological assay cannot distinguish between active metabolites and the parent compound. However, active metabolites of Lincomycin have not been reported in swine, chicken, rats, and dogs, antimicrobial activity being mainly due to the parent drug (Hornish et al., 1987).

Following i.v injection, Lincomycin serum concentration follows a two-compartment open model in both the Lincomycin (non-medicated) and Gallimix medicated groups, indicating the presence of distribution and elimination phases and justifying the use of a two-compartment kinetic model for analyzing the data. This finding was also observed in human (Fass, 1981), calves (Burrows et al., 1983 and Burrows et al., 1986), goats

(Abo El-Sooud et al., 2004), broiler chickens (Aziza et al., 2005) and cats (Albarellos et al., 2012).

The drug was rapidly distributed when administered simultaneous with Gallimix that evidenced by a shorter distribution half-life ($t_{1/2\alpha}$) (0.14h) than when administered alone. It was also confirmed by the lower values for the distribution rate constant from central compartment to the peripheral one (k_{12}) and the ratio of distribution rate between compartments (K_{12}/K_{21}) in Gallimix medicated chickens (2.045 h^{-1} and 0.752 h^{-1}, respectively) than in Lincomycin control ones (2.12 h^{-1} and 0.930 h^{-1}, respectively). These values of (K_{12}/K_{21}) are inconsistent with that values obtained by Aziza et al., 2005 in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil) (0.36and 0.61L/Kg, respectively).

Lincomycin is widely distributed as reflected by the volume of distribution (V_{dss}) greater than the unit. In our study Lincomycin showed a high V_{dss} (1.80 and 1.52L/kg) in broiler chickens Lincomycin alone and concomitant Gallimix with Lincomycin, respectively. These values are close to that reported in goats (1.81± 0.60 and 1.68L/kg) by Abo El-Sooud et al., 2004 and higher than that reported in cats (1.24L/kg) by Albarellos et al., 2012.These values are inconsistent with that reported by Aziza et al., 2005 in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil) (1.38and 1.727 L/Kg, respectively), whereas in humans it is higher (102 to 139 L/Kg after administration of Lincomycin to volunteers weighting 71 to 94 Kg (Gwilt and Smith, 1986).

The elimination half-life ($t1/2\beta$) was shorter in Gallimix medicated chickens (1.31 ± 0.036 h) than in the Lincomycin control ones (2.79h).This revealed rapid Lincomycin elimination in presence of Gallimix, which might occurred due to enhancement of its metabolism by the active constituents of this compound. In this respect, sorbic acid has been improved inducing effect for sorboyl-CoA reductase and 2.4-dienoyl-CoA reductase enzymes in mouse liver (Nishimaki et al., 1991). Propionate also was found to have a great effect on the hepatocyte metabolism (Petitet et al., 1998). These values are consistent with that reported by Aziza et al., 2005 in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil) (1.27 and 0.95 h, respectively), while inconsistent with that reported by Abo El-Sooud et al., 2004 in goats when Lincomycin administered alone and concomitant with aspirin (1.17and 1.12 h, respectively). These differences might be due to different assay methods, different age of animals, or differences between species.

The rate of drug total body clearance (CL_{tot}) was higher in Gallimix medicated group than in Lincomycin control one. This is an expected result for its rapid elimination in presence of Gallimix. The acidic constituents of Gallimix might be perhaps deviating the pH of the renal tubules and the lower gut of Gallimix medicated chickens from the normal alkaline reaction (in normal broiler chickens) to the acidic side. Consequently, Lincomycin which is a basic drug with a PKa value of 7.6 (Ziv and Sulman, 1973) and mainly excreted via the bile and the urine (Rang and Dale 1991) will be more ionized in this acidic pH and so will be rapidly excreted (Harlod et al., 1998). The obtained values are lower than that reported by Aziza et al., 2005 in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil) (0.85 and 1.95 L/kg/h, respectively), goats (2.11 L/h/kg) by Abo El-Sooud et al., 2004, and similar to that reported in calves (0.486 L/h/kg) by Burrows et al., 1983.

Following oral dosing, the obtained values are consistent with that reported by Aziza et al., 2005 in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil). These obtained data revealed that Gallimix may affect the actual process of Lincomycin absorption via chicken's gut. Oral absorption of any drug is controlled by the pH partition hypothesis (Hogben et al., 1959). According this theory, basic drugs are less absorbed from the more acidic contents in the gut (Baggot, 2001). So the lowering in Lincomycin absorption that concomitantly administered with Gallimix might be correlated to the lowering in the pH of chickens gut in Gallimix medicated group to the acidic side, and so enhancing Lincomycin ionization and consequently decrease its absorption, meaning that Lincomycin might be inactivated, before its absorption, by the acidic constituents of Gallimix. In this respect, Dorrestein and Vanmiert, 1988 reported that oral administration in birds is greatly affected by the pH of the gut as reported in case of penicillin G and erythromycin which are inactivated by the strongly acidic reaction of the gastric contents.

The elimination half–life ($t_{1/2el}$) was shorter in Gallimix medicated group than in Lincomycin control one. These obtained data is consistent with that reported by (Aziza et al., 2005) in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil) (1.72 and 1.25 h, respectively). The main components of Gallimix compound exhibit some metabolizing stimulant effects (Nishimaki et al., 1991 and Petitet et al., 1998), which may enhance other drug metabolism and so shortened its

elimination half-life. In the same time the acidic constituents of Gallimix enhance Lincomycin excretion via the bile and the urine as previously discussed following i.v injection in this study.

The lowered systemic bioavailability (F) for Lincomycin in Gallimix medicated group than in Lincomycin control one is an expected result to the lowered AUC and the absorption rate constant (K_{ab}) for Lincomycin in Gallimix medicated chickens in comparison with control Lincomycin. The obtained data is consistent with that reported by Aziza et al., 2005 in broiler chickens when Lincomycin administered alone and concomitant with antifungal (toxy-nil) (73.25and 38.255%, respectively). Hornish et al., 1987reported that the bioavailability of Lincomycin in swine varied between (20 % and 50 %), they explained the low bioavailability not by low degree of absorption but by an extensive metabolism of the drug.

Our study showed that Lincomycin displayed a low level of binding to serum proteins. This finding was lower than that recorded for sheep (30-40%) (Zivand Sulman, 1973), humans (72%) (Fass, 1981), chickens (23% and 29.14%) (Soback et al., 1987; Aziza et al., 2005), for goats (50%) (Abo El-Sooud et al., 2004) and close to that reported in cats (11.24-17.68%) by Albarellos et al., 2012.

Lincosamides are well absorbed after oral administration and extensively distributed to edible tissues. Its use may produce residues in animal tissues and subsequently, the induction of allergic reaction in humans, as well as resistance in pathogen bacteria, which may results in health problems. Therefore, improper administration of these antibiotics may encourage the presence of their residues in food samples of animal origin. To ensure the safety of food for consumers, the European Union (EU) Commission and the Joint FAO/WHO Expert Committee on Food Additives have established a maximum residue limit (MRL) for residues of most antimicrobials in edible animal tissues. The residue tolerance for Lincomycin is varied from 50 µg/kg for fat to 1,500 µg/kg for kidney. Although only Lincomycin is approved as a veterinary drug in animal husbandry, there is also the risk the application of clindamycin, which is registered in human medicine (Kowalski et al., 2014).

The tissue concentration following oral administration of Lincomycin alone at 20 mg/kg daily for 5 days or Lincomycin concomitant with Gallimix were high initially and then decreased over time. Concentrations of Lincomycin in tissues were similar to or higher than the corresponding

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serum concentrations. This indicates that the penetration of Lincomycin into these tissues was good. The high volume of distribution and low protein binding of this drug in broiler chickens is reflected by its persistence in tissues for longer periods. High Lincomycin concentrations in the liver, kidney, serum, lung intestine and muscle indicate that Lincomycin may be an excellent drug for treating septicemia, alimentary, urinary and respiratory tract infections caused by susceptible organisms. Our results showed that, for daily oral administration of Lincomycin at 20 mg/kg for 5 days, a pre-slaughter withdrawal time of more than 3 days and 4 days is needed to ensure that the drug is eliminated from the tissues in Lincomycin alone and Lincomycin concomitant with Gallimix, respectively. Indicating that concomitant administration of Gallimix with Lincomycin reduce the withdrawal time of Lincomycin in broiler chickens tissues and serum.

Conclusion

The concomitant administration of Lincomycin and Gallimix must be not recommended in broiler chickens, as the interaction between them decreases the blood concentration and tissue distribution of Lincomycin which consequently reduces its therapeutic efficacy.

A pre-slaughter withdrawal time in broiler farms must be at least 3 days and 4 days to ensure that the drug is eliminated from the tissues in Lincomycin alone and Lincomycin concomitant with Gallimix, respectively. Indicating that concomitant administration of Gallimix with Lincomycin reduce the withdrawal time of Lincomycin in broiler chickens tissues and serum.

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تاثير المواد المحمضة على المسار الحركى ومستبقيات الانسجة لعقار اللينكوميسين فى دجاج التسمين السليم

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استهدفت هذه الدراسة دراسة التداخل الدوائي لعقار اللينكوميسين وحيدًا وبعد إعطاء الجاليمكس (0.4 جم/كجم من العلف) (المواد المحمضة) معه و دراسة مستبقيات الأنسجة ومعدل الإتاحة الحيوية في دجاج التسمين بعد إعطاء اللينكوميسين بطرق مختلفة بجرعة منفردة 20 مجم/ كيلوجرام من وزن الدجاج عن طريق الفم والحقن في الوريد. وقد تم تعيين تركيزات اللينكوميسين في عينات السيرم والأنسجة باستخدام الطريقة الميكروبيلوجية. وأظهرت نتائج هذه الدراسة أنه بعد حقن اللينكوميسين عن طريق الوريد كانت فترة نصف العمر لإفرازه هي 2.79 و 1.31 ساعة وأن فترة نصف العمرلأنتشار الينكوميسين هي 0.16 و 0.14 ساعة, على التوالي. بعد إعطاء الينكوميسين عن طريق الفم بجرعة منفردة وجد أن فترة نصف العمر لإفراز الدواء هي 1.74 و 0.70 ساعة ومعدل الاستفادة الحيوية هي 80.13 و 54.99 % على الترتيب. كانت نسبة اتحاد اللينكوميسين ببروتينات السيرم معمليًا 14.5 %. وقد تم إعطاء اللينكوميسين بجرعة 20مجم/ كيلوجرام عن طريق الفم مرة واحدة يوميا لمدة خمسة أيام متتالية وذلك لدارسة توزيعه في الأنسجة المختلفة وكذلك مدة بقائه في هذه الأنسجة ومعرفة المدة اللازمة قبل التسويق للتخلص من الدواء. وتم استنتاج انه يجب ترك ثلاثة وأربعة أيام على الأقل كفترة سحب قبل التسويق أو الذبح للتخلص من مستبقيات اللينكوميسين في مزارع الدواجن إذا أعطي منفردًا أو مع الجاليمكس علي التوالي.

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