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Pharmacokinetics and bioavailability of spectinomycin after i.v., i.m., s.c. and oral administration in broiler chickens

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A pharmacokinetic and bioavailability study of spectinomycin was conducted in healthy broiler chickens following administration of a single (50 mg/kg bw) intravenous (i.v.), intramuscular (i.m.) and subcutaneous (s.c.) dose and oral doses of 50 and 100 mg/kg bw. Following i.v. administration, the elimination half-life ($t_{1/2\beta}$), mean residence time (*MRT*), volume of distribution at steady-state ($V_{d(ss)}$), volume of distribution based on the terminal phase ($V_{d(z)}$) and total body clearance (Cl_B) were 1.46 ± 1.10 h, 1.61 ± 1.05 h, 0.26 ± 0.009 L/kg, 0.34 (0.30–0.38) L/kg and 2.68 ± 0.017 mL/min/kg respectively. After i.m. and s.c. dosing, the C_{max} was 152.76 ± 1.08 and 99.77 ± 1.04 μg/mL, achieved at 0.25 (0.25–0.50) and 0.25 (0.25–1.00) h, the $t_{1/2\beta}$ was 1.65 ± 1.07 and 2.03 ± 1.06 h and the absolute bioavailability (*F*) was 136.1% and 128.8% respectively. A significant difference in C_{max} (5.13 ± 0.10, 14.26 ± 1.12 μg/mL), $t_{1/2\beta}$ (3.74 ± 1.07, 8.93 ± 1.13 h) and Cl_B/F (22.69 ± 0.018, 10.14 ± 0.018 mL/min/kg) were found between the two oral doses (50 and 100 mg/kg bw respectively), but there were no differences in the t_{max} [2.00 (2.00–4.00), 2.00 (2.00–2.00) h] and $V_{d(z)}/F$ [6.95 (6.34–9.06), 7.98 (4.75–10.62) L/kg). The absolute bioavailability (*F*) of spectinomycin was 11.8% and 26.4% after oral administration of 50 and 100 mg/kg bw respectively.

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INTRODUCTION

Spectinomycin is a bacteriostatic aminocyclitol antibiotic prescribed in veterinary medicine for the treatment of respiratory and enteric bacterial infections (Burrows, 1980; Holloway, 1982; Jeff *et al.*, 2002). It has broad spectrum activity against Gram-negative aerobic bacteria (e.g. *Mannheimia haemolytica*, *Pasteurella multocida*, *Escherichia coli*), facultative anaerobes (e.g. *Actinomyces bovis*) (Bakker, 1992; Guerin-Faublee *et al.*, 1993; Schwarz *et al.*, 2004) and against different species of Mycoplasma (Bakker, 1992; Burrows *et al.*, 1993; Jordan *et al.*, 1998). The successful therapeutic use of spectinomycin requires knowledge of its pharmacokinetics and pharmacodynamics (PK/PD). For this purpose, the area under the plasma concentration–time curve (*AUC*), the maximum plasma concentration (C_{max}) and the time to reach C_{max} (t_{max}) are the major useful PK parameters, and the minimum inhibitory concentration (*MIC*) is the most useful PD parameter. Spectinomycin is considered to be a bacteriostatic antibiotic. However, there are no published data to demonstrate if spectinomycin is a concentration-dependent, time-dependent or co-dependent antibiotic. Nevertheless, the efficacy of bacteriostatic antibiotics is considered to be correlated with the time that concentrations are one to five times above the *MIC* (time >*MIC*) of the susceptible micro-organisms (Burrows, 1980; Holloway, 1982; Jeff *et al.*, 2002).

Oral water medication is the most common route used to administer antimicrobials in the chicken industry. Few studies have targeted the disposition kinetics of spectinomycin in domestic animals (Ziv & Sulman, 1973; Caputo, 1995; el-Sayed *et al.*, 1995; Cameron, 1997), and there is no information currently available about the pharmacokinetic profile of spectinomycin in chickens after oral and subcutaneous (s.c.) administration. Furthermore, there has not been a single comprehensive study conducted to compare the PK of spectinomycin in chickens following intravenous (i.v.), intramuscular (i.m.), subcutaneous (s.c.) and oral administration. It should be recognized that the accurate determination of spectinomycin concentration levels in chicken plasma following

administration by different routes is of interest as it provides a precise and broad-outlook that permits maximal optimization of dosage regimens. Accordingly, the current study was designed to calculate the single-dose PK and bioavailability of spectinomycin after i.v., i.m., s.c. and oral administration in broiler chickens.

MATERIALS AND METHODS

Chickens

Fifty healthy broiler chickens (Hubbard×Hubbard), 45–50 days old, weighing 1.8–2.2 kg were used. These chickens were purchased from a local poultry farm and placed in the Animal House at Jordan University of Science and Technology. The chickens were allowed 14 days for acclimatization prior to study. The Animal House temperature was maintained at 25 ± 2 °C and humidity at 45–65%. All chickens had free access to water and antibacterial-free food.

Drug administration

Spectinomycin hydrochloride (assigned potencies 650 μg/mg) (Provimi Jordan Ltd., Amman, Jordan) was dissolved in water for injection to a total volume of 25 mL, to give a final concentration of 100 mg/mL prior to administration.

Experimental design

The chickens were blocked by weight into 10 groups of five. Within each block, animals were then randomly assigned to one of five equal study groups (10 chickens/group). A parallel study design was used. Chickens of groups 1–4 were given a single dose of spectinomycin (50 mg/kg bw) by i.v., i.m., s.c. and oral administration respectively. Spectinomycin was given in the right brachial vein, pectoralis muscle, neck and directly into the crop using a thin plastic tube attached to a syringe for i.v., i.m., s.c. and oral administration respectively. Chickens of group 5 were given a single oral dose of spectinomycin (100 mg/kg bw). Feed was withheld 12 h before and until 6 h after drug administration. Water was provided *ad libitum*. Blood samples (1.0–1.5 mL) were collected from the left brachial or cutaneous ulnar veins into heparinized tubes immediately before and at 0.08, 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24 and 48 h after drug administration. All blood samples were centrifuged directly at approximately 1000 ***g*** for 5 min to obtain clean plasma and stored at −20 °C until assayed.

High-performance liquid chromatography system

A high-performance liquid chromatography (HPLC) system was used to determine the concentrations of spectinomycin in chicken plasma. The HPLC system (Shimadzu, Kyoto, Japan) consisted of LC-10A DVP HPLC pump, SIL-10A DVP auto injector, SPD-10 AVP UV-vis detector, SCL-10 AVP system controller, DGV-12 A degasser and Shimadzu class-VP software Ver 6.12 SP4. Chromatographic separation was performed using Chromolith RP-18e column (4.6 mm i.d. × 50 mm length, macropore 2 μm, mesopore 2 nm; Merck, Germany).

Chromatographic condition

The HPLC method and extraction procedures were modified from a previously published method (Burton *et al.*, 1991). Spectinomycin was eluted with a mobile phase prepared from HPLC-grade solvents that contain acetonitril (A) and water-acetonitril (4:1 v/v) (B). A gradient solvent programme with following conditions was applied: (i) 0–2 min (A–B, 45:55 v/v); (ii) 2–3 min (A–B, 45–95:55–5 v/v); (iii) 3–5 min (A–B, 95:5 v/v); (iv) 5–6 min (A–B, 95–45:5–55 v/v); (v) 6–9 min (A–B, 45:55 v/v). The mobile phase was filtered using a 0.45 μm membrane filter and degassed. The flow rate was performed at 2.0 mL/min and the UV detector was set at a wavelength of 405 nm. The volume of injection was 50 μL.

Sample preparation

The plasma samples were subjected to derivatization using precolumn 2,4-dinitrophenyl hydrazine (2,4-DNPH) as derivatizing agent as described by Burton *et al.* (1991). Briefly, frozen plasma samples were thawed at room temperature and then 100 μL of plasma was added to 400 μL of trifluoroacetic acid (TFA) (3% TFA in acetonitrile) in a clean glass tube. After centrifuging (1000 ***g*** for 3 min), 250 μL of clear supernatant was transferred to a clean glass tube and 200 μL of 2,4-DNPH (5 mg/mL in acetonitrile) was added. The mixture was shaken and then heated at 70 °C for 60 min. After heating, the samples were cooled on ice for 2 min. After cooling, 30 μL of acetone was added to the mixture. Additional mixing was applied and then another heating (70 °C, 10 min) was performed. After cooling, the samples were centrifuged at approximately 1000 ***g*** for 5 min and the clear supernatant was directly injected into the HPLC system using special glass vials.

Calibration curve

Daily fresh calibration curves were prepared by dissolving standard spectinomycin powder in HPLC-grade water to obtain a concentration of 1 mg/mL. This solution was used to prepare standards of 0.5, 1, 2, 5, 10, 50, 100, 200 and 300 μg/mL in HPLC-grade water or drug-free chicken plasma. The calibration curves were obtained by plotting the peak area as a function of the respective spectinomycin concentrations and the linear regression was calculated.

The HPLC method was validated by assessing the inter- and intra-day reproducibility at a concentration of 8, 80 and 160 μg/mL and the extraction efficiency. The calculated limit of detection was 0.25 μg/mL based on a signal-to-noise ratio of 3:1, whereas the limit of quantitation was 0.5 μg/mL based on a signal-to-noise ratio of 6:1. Standard curves were linear over the range of 0.5–300 μg/mL ($r^2 > 0.999$). The mean percentage analytical

recovery of spectinomycin in plasma was 97.5%. The intra-day and inter-day assay coefficients of variations was <15%.

Pharmacokinetics and statistical analysis

The PK analysis of the data was performed using noncompartmental analysis based on statistical moment theory according to the method described by (Gibaldi & Perrier, 1982), with the help of the commercially available software program WinNonlin® (Pharsight Corporation, Cary, NC, USA). The area under plasma concentration–time curve (*AUC*) was calculated using the trapezoidal rule with extrapolation to infinity. The maximum concentration (C_{max}) and the corresponding peak time (t_{max}) were determined by the inspection of the individual drug plasma concentration–time profiles. The slope of the terminal phase of the semi-log time–concentration curve was determined by linear regression and converted to an elimination half-life by multiplying the reciprocal by 0.693. The absolute bioavailability (F) was calculated using equation 1. The other pharmacokinetic parameters [total body clearance (Cl_B), volume of distribution based on the terminal phase ($V_{d(z)}$) and volume of distribution at steady-state ($V_{d(ss)}$)] were calculated according to well-established equations (Baggot, 1977).

$$F = \frac{AUC_{ev} \times Dose_{iv}}{AUC_{iv} \times Dose_{ev}}. \quad (1)$$

The data were statistically analysed using analysis of variance (ANOVA) (for those pharmacokinetic parameters that were normally distributed following log-transformation) or the Kruskal–Wallis ANOVA on ranks (for those that were not normally distributed). The multiple comparisons of means were performed using Fisher's Least Significant Difference Test (ANOVA) or the Tukey test (ANOVA on ranks). The differences were considered significant when $P < 0.05$. These calculations were performed using commercially available software (SYSTAT, version 10; Systat Software Inc., Bangalore, India). Data were summarized as mean ± SE (normally distributed) or median, 25th and 75th percentile (not normally distributed).

RESULTS

All tested chickens were clinically healthy throughout the period of the study. There were no identifiable adverse reactions recorded after administration of the drug by all routes and therefore, unexpected incidents that could have influenced the outcome of the study did not occur. The mean plasma concentration–time profile of spectinomycin (50 mg/kg bw) after a single i.v., i.m. and s.c. administration are shown in Fig. 1 and Table 1. Spectinomycin was not detected at 12 h post drug administration for all parenteral routes in all chickens. The pharmacokinetic parameters are shown in Table 2. The plasma spectinomycin concentration reached a peak (C_{max}) of 152.76 ± 1.08 and 99.77 ± 1.04 μg/mL at 0.25 (0.25–0.50) and 0.25 (0.25–1.00) h (t_{max}) after a single i.m. and s.c. injection (50 mg/kg bw) respectively. The absolute bioavailability (F) of spectinomycin after i.m. and s.c. administration was 136.1% and 128.8% respectively (Table 2).

The mean plasma concentration–time curve and the pharmacokinetic parameters for spectinomycin (50 and 100 mg/kg bw) after a single oral administration are shown in Fig. 1 and Table 2. Spectinomycin was detected at 12 and 24 h after oral administration at a dose of 50 and 100 mg/kg bw respectively. The mean value of the peak concentration (C_{max}) of spectinomycin at a dose of 100 mg/kg bw was approximately three times higher than in chickens given 50 mg/kg bw (14.26 ± 1.12 vs. 5.13 ± 0.10 μg/mL). The absolute bioavailability (F) of spectinomycin after oral administration at a dose level of 50 and 100 mg/kg bw were 11.8% and 26.4% respectively (Table 2).

DISCUSSION

Spectinomycin is used in chickens either alone or in combination with other antibiotics (e.g. lincomycin-spectinomycin) for the treatment of air-sacculitis caused by either *M. synoviae* or *M. gallisepticum* and complicated chronic respiratory disease

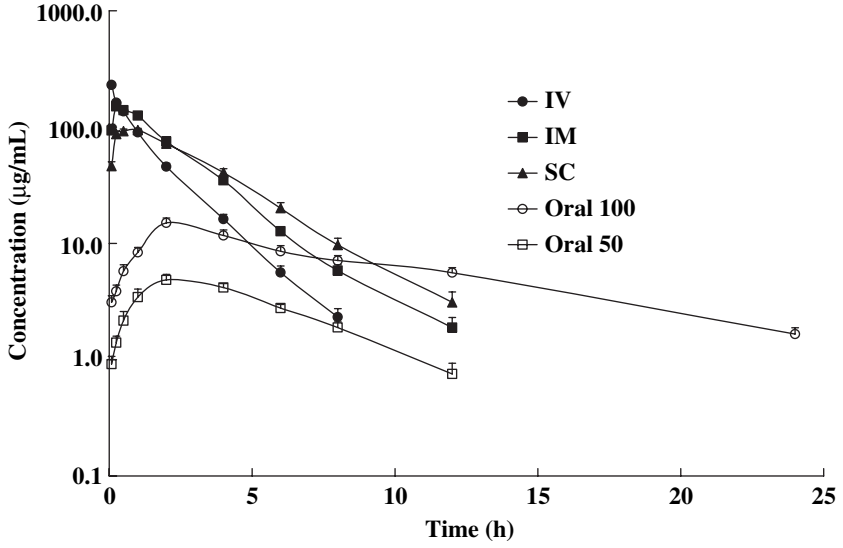

Fig. 1. Semilograthimic plot showing the plasma concentration–time profile of spectinomycin after intravenous (i.v.), intramuscular (i.m.) and subcutaneous (s.c.) administration at a dosage of 50 mg/kg bw and oral administration at a dosage of 50 and 100 mg/kg (oral 50 and 100) as determined by HPLC method. Values are mean ± SE ($n = 10$).

Table 1. Spectinomycin plasma concentrations (μg/mL) in chickens after intravenous (i.v.), intramuscular (i.m.), subcutaneous (s.c.) and oral administration at a dosage of 50 mg/kg bw and after a single oral administration at a dosage of 100 mg/kg bw. Values are mean ± SE ($n = 10$)

Time (h)	i.v.	i.m.	s.c.	Oral (50 mg/kg bw)	Oral (100 mg/kg bw)
0.083	230.7 ± 9.17	93.56 ± 11.95	46.11 ± 4.22	0.92 ± 0.15	3.12 ± 0.44
0.25	162.6 ± 6.95	150.76 ± 12.89	87.23 ± 5.56	1.40 ± 0.195	3.87 ± 0.51
0.5	136.9 ± 5.5	139.67 ± 8.69	92.25 ± 4.01	2.16 ± 0.43	5.76 ± 0.80
1	90.1 ± 1.98	125.8 ± 7.08	94.32 ± 3.29	3.45 ± 0.6	8.37 ± 0.88
2	45.7 ± 3.16	75.32 ± 5.148	72.08 ± 3.53	4.86 ± 0.57	13.83 ± 1.19
4	16.2 ± 1.58	34.80 ± 2.39	40.80 ± 3.05	4.17 ± 0.34	12.86 ± 1.84
6	5.6 ± 0.77	12.73 ± 0.69	20.11 ± 2.33	2.78 ± 0.21	8.53 ± 1.03
8	2.33 ± 0.4	5.85 ± 0.71	9.69 ± 1.40	1.89 ± 0.22	7.11 ± 0.75
12	ND	1.89 ± 0.42	3.10 ± 0.71	0.75 ± 0.18	5.6 ± 0.59
24	ND	ND	ND	ND	1.66 ± 0.22
48	ND	ND	ND	ND	ND

ND, not detected.

Table 2. Pharmacokinetics parameters of spectinomycin in chickens after intravenous (i.v.), intramuscular (i.m.), subcutaneous (s.c.) and oral administration at a dosage of 50 mg/kg bw and after a single oral administration at a dosage of 100 mg/kg bw

Parameters	Units	i.v.	i.m.	s.c.	Oral (50 mg/kg bw)	Oral (100 mg/kg bw)
$t_{1/2\beta}$	h	1.46 ± 1.10[a]	1.65 ± 1.07[a,b]	2.03 ± 1.06[b,c]	3.74 ± 1.07[c]	8.93 ± 1.13[d]
MRT	h	1.61 ± 1.05[a]	2.42 ± 1.04[b]	3.21 ± 1.04[c]	6.32 ± 1.06[d]	11.94 ± 1.09[e]
V_{dz}/F	L/kg	0.34 (0.30–0.38)[a]	0.30 (0.25–0.33)[a]	0.38 (0.33–0.40)[a]	6.95 (6.34–9.06)[b]	7.98 (4.75–10.62)[b]
$V_{d(ss)}$	L/kg	0.26 ± 0.009	–	–	–	–
Cl_B/F	mL/min/kg	2.68 ± 0.017[a]	1.97 ± 0.017[b]	2.08 ± 0.018[b]	22.69 ± 0.018[d]	10.14 ± 0.018[e]
C_0	μg/mL	276.13 ± 13.82	–	–	–	–
C_{max}	μg/mL	–	152.76 ± 1.08[a]	99.77 ± 1.04[b]	5.13 ± 0.10[c]	14.26 ± 1.12[d]
t_{max}	h	–	0.25 (0.25–0.50)	0.25 (0.25–1.00)	2.00 (2.00–4.00)	2.00 (2.00–2.00)
AUC_{0-t}	μg·h/mL	305.49 ± 1.04[a]	418.79 ± 1.05[b]	391.74 ± 1.05[b]	30.41 ± 1.09[c]	141.58 ± 1.11[d]
$AUC_{0-\infty}$	μg·h/mL	311.17 ± 1.04[a]	423.64 ± 1.05[b]	400.87 ± 1.06[b]	36.73 ± 1.09[c]	164.44 ± 1.11[d]
F	%	–	136.1	128.8	11.8	26.4

Values are mean ± SE or median (25th–75th percentile) ($n = 10$). Within a row, parameters that do not have the same superscript letters are significantly different.

caused by *E. coli* and *M. gallisepticum*. However, few studies are available on the PK and bioavailability of spectinomycin in animals including poultry. Therefore, the current study was designed to investigate the PK and bioavailability of spectinomycin in broiler chickens after administration by different routes.

After a single i.v. administration of spectinomycin (50 mg/kg bw), the elimination half-life ($t_{1/2\beta}$) expresses the overall rate of drug elimination and can be used to predict drug accumulation for multiple-dose regimens. The mean value of $t_{1/2\beta}$ (1.46 h) was similar to those reported in cattle (1.52 h) and sheep (1.62 h) (Ziv & Sulman, 1973) but different from another reported study in chickens (3.28 h) (el-Sayed *et al.*, 1995). This dissimilarity may be attributable to differences in the pharmacokinetic model that was used (noncompartmental vs. a classical three-compartment model) and the period of time for which concentration data were collected (24 vs. 8 h). However, the Cl_B of 2.68 mL/min/kg obtained in the present study was similar than the value reported in chickens previously (3.62 mL/min/kg) (el-Sayed *et al.*, 1995).

The volume of distribution based on the terminal phase ($V_{d(z)}$) (0.34 L/kg) would suggest that the distribution of spectinomycin is limited to the extracellular fluid. The value calculated in our study is higher than the value previously reported for the chicken (0.14 L/kg) (el-Sayed *et al.*, 1995), but similar to the values for the cow (0.3 L/kg) and sheep (0.3 L/kg) (Ziv & Sulman, 1973). The $V_{d(ss)}$ (0.26 L/kg) was similar to those reported in chickens (0.35 L/kg) (el-Sayed *et al.*, 1995).

Following i.m. administration, spectinomycin was rapidly absorbed with a C_{max} of 152.76 μg/mL achieved at 0.25 h (t_{max}). The calculated $t_{1/2\beta}$ (1.65 h) obtained in the present study was similar to those reported in cattle (1.0 h) (Caputo, 1995), sheep (1.10 h) (Craigmill *et al.*, 1995) and humans (1.85 h) (Novak *et al.*, 1990) and lower than those reported in chickens (3.27 h) (el-Sayed *et al.*, 1995). The short elimination half-life suggests that spectinomycin was rapidly eliminated from the body. We calculated the absolute bioavailability (F) as being 136.1% after i.m. administration. This is in agreement to those reported in cattle (118%) and sheep (104%) (Caputo, 1995; Craigmill *et al.*, 1995) but different from the value reported for chickens (3.72%) (el-Sayed *et al.*, 1995). This sizeable difference in calculated bioavailability for chickens is unlikely to be attributable to differences in the assay for determination of spectinomycin concentrations and we are unable to provide a reasonable explanation for this observation.

Following s.c. administration, spectinomycin was rapidly absorbed with a C_{max} of 99.77 μg/mL reached at 0.25 h (t_{max}). The $t_{1/2\beta}$ (2.03 h) was higher than the respective value after i.v. and i.m. administration (1.46 and 1.65 h respectively) indicating absorption rate-dependant elimination. The Cl_B/F and $V_{d(z)}/F$ were 2.08 mL/min/kg, 0.38 L/kg, with no significant differences to the respective values after i.m. administration (2.68 mL/min/kg and 0.30 L/kg respectively). The *MRT* was significantly different between s.c. and i.m. administration (3.21 and 2.42 h respectively). The bioavailability of spectinomycin following s.c. administration was 128.8%. Our results are similar to those reported in cattle (120%) (Caputo, 1995). It is interesting that the calculated bioavailabilities for both the i.m. and s.c. routes in our study were >100%. This may be attributable to differences in the average clearance between the study groups, as a cross-over design was not used (Toutain & Bousquet-Melou, 2004).

The average values of C_{max} (14.26 and 5.13 μg/mL) and $t_{1/2\beta}$ (8.93 and 3.74 h) were approximately two to three times higher, and the average value of $AUC_{0-\infty}$ (164.44 and 36.73 μg·h/mL) was approximately five times higher for the single oral dose of 100 mg/kg bw compared with the dose of 50 mg/kg bw respectively. This difference is higher than can be attributed merely to the doubling of the dose. Moreover, the value of Cl_B/F (10.14 and 22.69 mL/min/kg for the 100 mg/kg and the 50 mg/kg respectively) was lower for the higher dose. A possible explanation for these observations is that elimination processes are saturated at the higher dose, resulting in nonlinear PK. In contrast, the $V_{d(z)}/F$ (7.98 and 6.95 L/kg) and t_{max} (2.00 and 2.00 h) for spectinomycin at the doses of 100 and 50 mg/kg bw, respectively, were not significantly different. The calculated absolute bioavailability (F) of spectinomycin was 11.8% and 26.4% after a single oral administration of 50 and 100 mg/kg bw respectively. The greater calculated bioavailability (approximately two times) for the higher dose could be attributed to the lower calculated Cl_B for this dose (approximately 1/2), as the calculation of the bioavailability of a drug by comparing AUC's is based on the assumption that the average drug clearance is the same in both study groups (i.v. and extravascular) (Gibaldi & Perrier, 1982).

The lowest concentration of antimicrobials, which inhibit the growth of the target pathogen, is referred to as the *MIC*. The MIC_{90} refers to the concentration that will inhibit the growth of 90% of tested isolates. The reported *MIC*s for susceptible veterinary micro-organisms isolated from different species of animals that are susceptible to spectinomycin were 0.39–10, 0.39–6.25, 1–128, 8–32, 8–128, 1.56–25, 16–128 and 4 μg/mL for *M. gallisepticum*, *M. synoviae* (Valks & Burch, 2002), *P. multocida*, *Mannheimia haemolytica* (Laperle *et al.*, 1996; Schwarz *et al.*, 2004), *E. coli* (Wray *et al.*, 1993), *Haemophilus paragallinarum*, *Salmonella* spp. (Salmon & Watts, 2000) and *Helicobacter* spp. (Van den Bulck *et al.*, 2005) respectively. MIC_{90} values, although not reported for all these micro-organisms, were listed as 32 μg/mL for both *P. multocida* and *M. haemolytica*, 128 μg/mL for *E. coli*, 6.25 μg/mL for *H. paragallinarum* and 64 μg/mL for *Salmonella* spp.

The results of the current study showed that spectinomycin plasma concentrations in chickens were above the *MIC* for most susceptible micro-organisms after i.v., i.m. and s.c. administration (mean peak plasma concentrations of 276.13 ± 13.82, 152.76 ± 1.08 and 99.77 ± 1.04 μg/mL respectively). Spectinomycin was detected in chicken plasma at concentrations higher than *MIC* for most susceptible micro-organisms and Mycoplasma for 6 h following i.v. administration and 8 h after i.m. and s.c. administration. Therefore, parenteral spectinomycin given at a dose of 50 mg/kg bw seems to be a suitable therapeutic dose in broiler chickens. However, repeated doses are necessary to maintain spectinomycin plasma concentrations above the *MIC*s for most susceptible micro-organisms.

Single oral administration of 50 mg/kg bw in healthy chickens produced a maximum blood concentration of 5.13 ± 0.10 μg/mL at 2.00 (2.00–4.00) h postadministration. This concentration did not exceed the *MIC*s of spectinomycin for most susceptible bacteria and Mycoplasma. Whereas, single oral administration of 100 mg/kg bw in healthy chickens produced a maximum blood concentration of 14.26 ± 1.12 μg/mL at 2.0 (2.00–2.00) h postadministration. This concentration exceeds the *MIC*s of spectinomycin for Mycoplasma. Spectinomycin was detected in chicken plasma at concentrations higher than *MIC* for Mycoplasma for 12 h following single oral administration of 100 mg/kg bw administration. Nevertheless, spectinomycin at a dose of 50 and 100 mg/kg bw given orally can only be recommended for treatment of susceptible micro-organisms with *MIC* <0.5 μg/mL or <3 μg/mL respectively.

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