Veterinary Medical Journal -Giza (VMJG), Vol. 60(1), 17-31, June 2014
http://www.vetmedjcu.com/
ISSN 1110-1423

Influence of Some Acidifiers on Pharmacokinetics and Tissue Residues of Amoxicillin in Healthy and Experimentally *E. coli* Infected Broiler Chicken

Mohammed, A.M. M.[a*], Youssef, S.A.H.[b] and El-Banna, H. A.[b]

[a] Residues Analysis Unit, Reference Laboratory For Veterinary Quality Control On Poultry Production, Animal Health Research Institute, PO Box 12618 , Dokki, Giza, Egypt; [b] Pharmacology Department, Faculty of Veterinary Medicine, Cairo University, PO Box 12211, Giza, Egypt.

**Email: mohammedsaleh85_doctor@msn.com*

Received on November 10, 2013 and accepted on December 9, 2013

Abstract

This work investigated the influence of some acidifiers (Gallimix) on the disposition kinetics and tissue residues of β-lactam antibiotic (Amoxicillin) in healthy and experimentally infected broiler chicken with pathogenic *E. Coli* O 78.Thebacterial colony count was also investigated in experimentally infected broiler chickens in the presence of acidifier alone as well as in the presence of acidifier and Amoxicillin together. The concentrations of Amoxicillin in serum were measured using reversed phase high performance liquid chromatography (HPLC) on samples collected at frequent intervals after drug administration.

There was no significant increase in serum concentrations of Amoxicillin at 24 hours post administration however there was very high significant increase in serum concentrations at 48 hours in the group of birds treated with Gallimix as compared with the group given Amoxicillin alone in normal healthy broiler chicken. Amoxicillin was somewhat rapidly absorbed in infected chickens ($t_{1/2ab}$ 1.605 ± 0.05 h) as compared with treated only with Amoxicillin ($t_{1/2ab}$ 1.622 ± 0.04 h) and treated with Gallimix ($t_{1/2ab}$ 1.682 ± 0.05h).

There was no significant increase in Amoxicillin concentration in examined tissues when compared with values at corresponding time intervals in normal healthy broiler chickens received acidifier (Gallimix). There is a gradual decrease in the colony forming unit (CFU) in infected chickens that was treated with Amoxicillin orally (single and multiple doses (20 mg/kg b.wt.) and supplemented by the acidifier (Gallimix) as compared with infected non-treated control group.

Keywords: Acidifier, Amoxicillin, HPLC, kinetics, residue.

Introduction

Amoxicillin is β-lactam antibiotic that belong to the group of penicillin's. It is extremely active against both gram-positive and gram-negative organisms. Amoxicillin is widely used in veterinary medicine because it has good absorption and penetration into tissues and rapid bactericidal activity as described by Kung and Wanner (1994). The antibacterial spectrum of Amoxicillin is including different species of *Escherichia coli, Salmonella, Proteus* and *Klebsiella* (Anadon et al., 1996).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 favourable for multiplication of some useful microorganism, such as lactic acid bacteria (Simeanu 2004; Stan and Pop 1997; Stan and Simeanu, 2005).

Generally, *E. coli* affects poultry of all ages, although young birds are more sensitive. The infection is considered to be one of the leading causes of economic loss in the poultry industry. Different experimental *E. coli* infection has been described as septicemia, enteritis, granulomas, omphalitis, sinusitis, air sacculitis, arthritis, synovitis, peritonitis, pericarditis, cellulitis, swollen head syndrome, etc. More frequently, *E. coli* disease occurs as a consequence of the adverse influence of factors such as ammonia, moisture, dust, hormones or infectious agents such as viruses and mycoplasmas (Gross, 1990; Leitner and Heller, 1992). The aim of the present study was to investigate the influence of some acidifiers (Gallimix) on the disposition kinetics and tissue residues of β-lactam antibiotic (Amoxicillin) in healthy and experimentally infected broiler chickens with pathogenic *E. coli*.

Material and Methods

Drugs and chemicals:

Amoxicillin tri-hydrate is water soluble semi synthetic broad spectrum penicillin. The drug was obtained as a pure powder from the laboratory research of Pfizer pharmaceutical co., Animal Health Division, Cairo, Egypt. The drug is white powder for oral use and diluted in drinking water prior to administration at a dose of 20 mg/kg b.wt. Gallimix is encapsulated feed additive obtained from MG2Mix Company, France. The micro encapsulation technically consists of active ingredients [organic acids (Fumaric acid, Sorbic acid, DL malic acid and citric acid), essential oils (Aroma substances)] in a vegetable hydrogenated triglyceride matrix (Palm oil). It was added into

feed at a concentration of 0.4 gm/Kg feed. The solvents (Baker Inc., Phillipsburg, NJ, USA) used during the chromatographic analysis of the drug were HPLC grade.

Experimental birds:

Eighty three healthy Hubbard broiler chickens of 18 days old and weighting 900 gm were obtained from a private poultry farm (SPF) and fed on poultry feed free from any antibiotics or acidifiers and water ad libitum.

Organism:

Enteropathogenic *E. coli* O78 obtained from Bacteriology Department, Animal Health Research Institute, Dokki, Giza, Egypt with serial dilution 3×10^8 CFU/ ml.

Experimental design:

The chickens were divided into seven groups. Group (1): 11 birds were given single oral dose of Amoxicillin directly into the crop using a thin plastic tube attached to a syringe (20mg/kg b.wt) (Lashev and Semerdzhiev, 1983), blood samples (1ml) were taken at different time intervals. Group (2): 13 birds were given multiple oral doses of Amoxicillin for five days and different tissue samples were taken after 1st, 3rd, 6th and 9th days from stopping of drug administration (three birds were slaughtered every time). Group (3): 11 birds were given Gallimix (0.4 gm/kg feed) prior to single oral dose of Amoxicillin and blood samples were taken at different time intervals. Group (4):13 birds were given Gallimix prior to multiple oral doses of Amoxicillin for five days and different tissue samples were taken. Group (5): 11 birds were given Gallimix, then infected with *E. coli* and treated with single dose of Amoxicillin. Blood samples were taken at different time intervals also bacterial colony count was studied. Group (6): 13 birds were given Gallimix, then infected with *E. coli* and treated with multiple oral doses of Amoxicillin then different tissue samples were taken also bacterial colony count was studied. Group (7): 11 birds were divided into control group that infected with *E. coli* without treatment and another group taken Gallimix alone and infected with *E. coli* to study the effect of acidifier alone on *E. coli* colony count.

Analytical methods:

Serum concentrations of Amoxicillin were measured using HPLC method previously reported by Foulstone and Reading, 1982. The HPLC

system was performed using Agilent Series 1050 quaternary gradient pump, Series 1050 auto sampler, Series 1050 UV Vis detector, and HPLC 2D Chemstation software (Hewlett-Packard, Les Ulis, France). Five hundred µl aliquot of each serum sample was transferred to a 1.5 ml polypropylene tube then 500µl of 5% perchloric acid was added and mix by vortex mixer for 15 seconds. Centrifugation at 1000 Xg for 2 minutes. The clear supernatant was then injected directly into HPLC system after filtration with 0.45 µm acrodisc. The HPLC separation was performed using a reversed-phase C_{18} column (Extend-C_{18}, Zorbax column, 5 µm, 4.6 X250 mm, Agilent Co.), with an injection volume of 20 µL. The mobile phase for serum consisted of a mixture of 0.01 M Phosphate solution (PH 3.2): methanol 94: 6 (v/v), using an isocratic form with a flow rate of 2.0 ml/ min. The UV detection was performed at 227 nm. The mobile phase for tissues consisted of a mixture of 0.05 M KH_2SO_4 solutions (6.8 g/L) and adjust pH to 5.6 with 1M KOH solution. Mix 800 mL phosphate solution with 200 mL acetonitrile, filter through 0.45 mm pore nylon filter and degas. Tissue concentrations of Amoxicillin were measured using HPLC method previously reported by Luo and Catharina (2000). Under these chromatographic conditions, the limit of detection (LOD), limit of quantification (LOQ) and average recoveries were 0.04, 0.1 µg/gm and 95.3%, respectively for serum.

Sample Fortification:

Fortify 5 g samples with 250, 500, or 1000 µL of 100 µg/mL standard solutions to yield final concentrations of 5, 10, or 20 mg/kg, respectively then allow fortified samples to equilibrate at room temperature (23°C) for 30–60 min before initial extraction.

Sample preparation for Solid Phase Extraction (SPE):

For initial extraction, add 20 mL 0.01M phosphate buffer solution (pH 4.5). Homogenize mixture at 8000 Xg for 90 seconds. Centrifuge 10 min at 3600 Xg and decant supernatant into another 50 mL centrifuge tube. Homogenize residue with another 20 mL buffer solution, centrifuge as before, and combine supernatant with first extract. Filter through glass wool plug. Add 1 mL TCA solution (75%) into filtrate and mix 30 seconds. Centrifuge 20 min at 3600 Xg and filter supernatant through a filter paper.

Solid-Phase Extraction (SPE):

Attach C18 SPE cartridges to vacuum manifold. Condition each cartridge with 5mL methanol then wash cartridge with 2mL water and 2

mL TCA solution (2%). Transfer sample filtrate onto cartridge and adjust flow to 1–2 mL/min. After all filtrate passes through, wash cartridge with 2 mL TCA (2%), wait until all TCA solution passes through cartridge, and then wash cartridge with 2mL water. Discard all effluent collected. Apply 2.0 mL of elution solution (50% acetonitrile in water) to cartridge and control flow rate to 0.7 mL/min. Collect all elute into 15 mL screw-capped glass centrifuge or culture tube. Store elute under refrigeration overnight.

Derivatization and Extraction:

Add 0.2 mL TCA solution (20%) and mix on Vortex mixer for 15 seconds. Add 0.2 mL formaldehyde solution and mix for 30 seconds. Heat in boiling water bath for 30 min, and then cool to room temperature in cold water bath. Add 0.5 g NaCl and mix briefly. Extract fluorescent Amoxicillin derivative with 3 mL ethyl ether 3 times. Mix for 1 min, centrifuge for 3 min at 1600 Xg, and remove ether layer each time. Combine ether extracts in 15 mL glass tube and evaporate tube contents to dryness under stream of nitrogen using an N-evaporator with water bath set at 40°C. Reconstitute by adding 0.5 mL mobile phase to each tube and mix thoroughly then injected into HPLC system (The injection volume is 50 µL). The flow rate is 1.0 mL/min and increased to 1.5–2 mL/min after 10 min. The fluorescence detector is set at 358 nm for excitation and 440 nm for emission).The limit of detection (LOD), limit of quantification (LOQ) and average recoveries were 0.05, 0.2 µg/gm and 81.7 to 82.9%, respectively for tissues.

Amoxicillin standard curve:

Serum and tissues standard samples (7 Amoxicillin concentrations between 0.04 and 12.5 µg/mL) were prepared using blank chicken serum and tissues samples that did not contain Amoxicillin for determination of standard curves. Standard curves were determined by plotting the Amoxicillin peak areas versus known concentrations. The standard curve equation was determined by use of the least squares method with linear regression. The standard curve for Amoxicillin in chicken serum and tissues samples was linear (range of values, 0.0.04 to 12.5 µg of Amoxicillin/mL). The values of the correlation coefficients(r) were > 0.98.

Pharmacokinetic analysis

A computerized curve-stripping program (R Strip, Micromath Scientific Software, Salt lake City, UT and USA) was used for data analysis for each bird after administration of Amoxicillin.

Bacterial colony count in fecal matters:

Bacterial colony count was studied in fecal matters as described by (Laboratory Manual For The Isolation And Identification Of Avian Pathogens, 1998).

Results

Tabulated data (Table.1) showed non-significant increased levels of serum concentrations of Amoxicillin at 0.25, 0.5, 1, 2, 4, 6, 8, 10, 12 and 24 hours however there was very high significant increased level of serum concentration at 48 hours in group of birds treated with Gallimix as compared with group given Amoxicillin alone in normal healthy broiler chicken as described also in fig.1 and 2.

Tabulated data revealed non-significant increased levels of serum concentrations for 24 hours post administration but there is very high significant increased level of serum concentration at 48 hours in infected group treated with Gallimix as compared with group given Amoxicillin alone in normal healthy broiler chicken as described also in fig.2 and3.

Amoxicillin was somewhat rapidly absorbed in infected chickens ($t_{1/2ab}$1.605 ± 0.05 h.) as compared with treated only with Amoxicillin ($t_{1/2ab}$ 1.622 ± 0.04 h.) and treated with Gallimix ($t_{1/2ab}$ 1.682 ± 0.05h.).

Table 1. Pharmacokinetic parameters of Amoxicillin following a single oral administration in a dose of 20 mg/kg b.wt alone and in presence of Gallimix in normal healthy broiler chickens and in experimentally infected broiler chickens with pathogenic *E. coli* O 78

Parameter	Unit	Mean ± SE		
		Amoxicillin alone conc. (µg/ml)	Amoxicillin with Gallimix conc. (µg/ml)	Amoxicillin with Gallimix conc. (µg/ml) after infection
A	µg/ml	14.84 ± 2.43	20.02 ± 3.47	15.62 ±1.5
K_{ab}	h^{-1}	0.43 ± 0.01	0.41 ± 0.01	0.44 ± 0.01
$t_{1/2ab}$	h	1.62 ± 0.04	1.68 ± 0.05	1.61 ± 0.05
C_{max}	µg/ml	2.04 ± 0.06	2.07 ± 0.07	2.20 ± 0.09
T_{max}	h	2.99 ± 0.04	3.03 ± 0.04	2.96 ± 0.06
B	µg/ml	14.84 ± 2.43	20.02 ± 3.47	15.62 ± 1.51
$t_{1/2el}$	h	2.48 ± 0.06	2.40 ± 0.09	2.40 ± 0.05
K_{el}	h^{-1}	0.28 ± 0.007	0.30 ± 0.02	0.29 ± 0.01
$Vd_{(B)}$	L/kg	1.53 ± 0.15	1.27 ± 0.21	1.37± 0.14
AUC_{oral}	µg/ml/h	16.25 ± 0.54	16.46 ± 0.54	17.10 ± 0.69
MRT	h	5.92 ± 0.09	5.89 ± 0.12	5. 78 ± 0.12

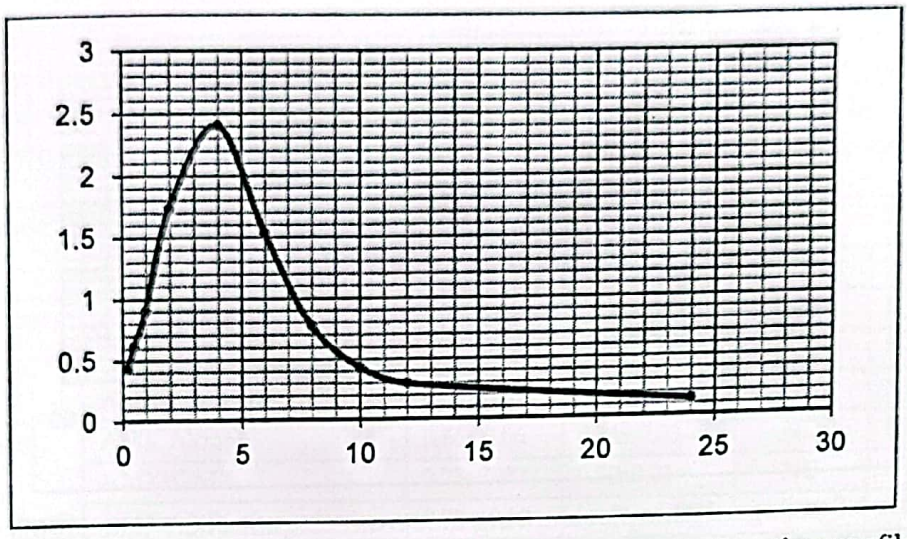

Figure 1. Semilogarthimic plot showing the serum concentration–time profile of Amoxicillin following a single oral administration in a dose of 20 mg/kg b.wt alone in normal healthy broiler chickens.

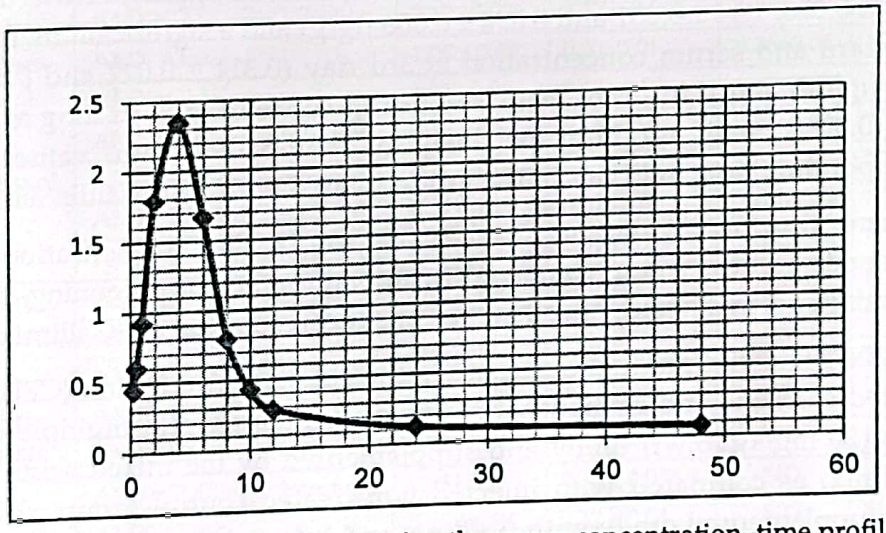

Figure 2. Semilogarthimic plot showing the serum concentration–time profile of Amoxicillin following a single oral administration in a dose of 20 mg/kg b.wt in presence of Gallimix in normal healthy broiler chickens.

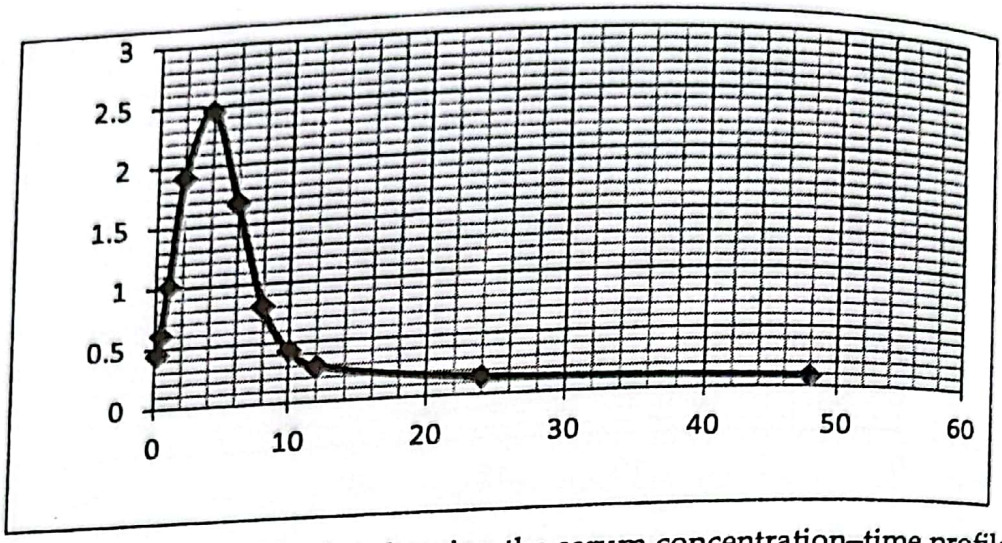

Figure 3. Semilogarthimic plot showing the serum concentration–time profile of Amoxicillin following a single oral administration in a dose of 20 mg/kg b.wt in presence of Gallimix in experimentally infected broiler chickens with pathogenic *E. Coli* O78.

Table 2 revealed a significant increase of Amoxicillin concentration in kidney, breast muscle and serum at 1th day after stopping of the drug (2.118 ± 0.026, 1.14 ± 0.031 and 0.594 ± 0.006 µg/g) and a significant increase in gizzard and serum concentration at 3rd day (0.314 ± 0.027 and 0.41 ± 0.007 µg/ml) and significant increase of drug concentration in lung at 6th day (0.32 ± 0.012µg/gm),respectively as compared with values at corresponding time intervals in the group treated with Amoxicillin alone.

There was no significant increase in Amoxicillin concentration in examined tissues when compared with values at corresponding time intervals in normal healthy broiler chickens received acidifier (Gallimix).

Table 3 showed gradual decreases in the colony forming unit (CFU) in infected chickens and treated with Amoxicillin (single and multiple oral doses (20 mg/kg. b.wt) orally and supplemented by the mixed acidifiers (Gallimix) as compared with infected non-treated control group. Birds were supplemented orally with Gallimix and infected with *E. coli* showed a significant gradual decrease in CFU of *E. coli* and reached only 458 ± 12.02 CFU in samples collected 4 days after infection as compared with chickens treated with Amoxicillin (single and multiple doses) and supplemented with Gallimix (1500 ± 86.602 CFU and 500 ± 11.547 CFU, respectively) and non-treated infected group (6050 ± 11.54CFU).

Table 2. The concentration of Amoxicillin in tissues of slaughtered chickens at various intervals following the oral administration (20 mg/kg b.wt once daily for 5 consecutive days) alone and in presence of Gallimix in normal healthy broiler chicken and in presence of Gallimix in experimentally infected broiler chickens with pathogenic *E. coli*)O 78 (n=3)

Tissue	The concentration (µg/gm) Mean ± SE				
		1st	3rd	6th	9th
Serum	AMX Alone	0.5 ± 0.02	0.26 ± 0.04	ND	ND
	AMX+GMX	0.58± 0.03	0.39± 0.003*	ND	ND
	AMX+GMX after infection	0.59 ±0.01*	0.41 ± 0.007*	ND	ND
Liver	AMX Alone	0.66± 0.06	0.24± 0.03	ND	ND
	AMX+GMX	0.71± 0.07	0.30±0.01	ND	ND
	AMX+GMX after infection	0.71 ± 0.02	0.347 ±0.027	ND	ND
Lung	AMX Alone	0.97± 0.06	0.62± 0.03	0.25±0.02	ND
	AMX+GMX	1.02±0.07	0.67± 0.03	0.29±0.02	ND
	AMX+GMX after infection	1.04± 0.037	0.68± 0.009	0.32±0.01*	ND
Kidney	AMX Alone	1.98± 0.02	1.44± 0.16	0.68± 0.08	ND
	AMX+GMX	2.03± 0.05	1.54± 0.05	0.75±0.07	ND
	AMX+GMX after infection	2.12 ±0.03*	1.57 ± 0.047	0.79±0.02	ND
Spleen	AMX Alone	1.08 ± 0.09	0.6 ± 0.01	0.26±0.04	ND
	AMX+GMX	1.11± 0.06	0.65± 0.03	0.37±0.02	ND
	AMX+GMX after infection	1.16 ± 0.11	0.66 ± 0.04	0.37±0.02	ND
Gizzard	AMX Alone	0.41 ± 0.09	0.166 ±0.03	ND	ND
	AMX+GMX	0.51± 0.08	0.22± 0.06	ND	ND
	AMX+GMX after infection	0.52±0.04	0.31 ± 0.027*	ND	ND
Heart	AMX Alone	0.83 ± 0.09	0.59 ±0.006	0.17±0.03	ND
	AMX+GMX	0.99± 0.06	0.596± 0.01	0.20±0.03	ND
	AMX+GMX after infection	1.04±0.034	0.61 ±0.019	0.21±0.02	ND
Thigh muscle	AMX Alone	0.67 ± 0.04	0.214 ±0.03	ND	ND
	AMX+GMX	0.72± 0.06	0.30± 0.03	N D	ND
	AMX+GMX after infection	0.73± 0.02	0.31 ± 0.036	ND	ND
Breast muscle	AMX Alone	0.96 ± 0.04	0.42 ± 0.04	ND	ND
	AMX+GMX	1.07± 0.09	0.52± 0.03	N D	ND
	AMX+GMX after infection	1.14 ± 0.03*	0.548 ± 0.03	ND	ND
Skin and fat	AMX Alone	0.87 ± 0.13	0.407 ±0.14	ND	ND
	AMX+GMX	0.97± 0.10	0.58± 0.100	N D	ND
	AMX+GMX after infection	0.99 ± 0.066	0.62 ± 0.046	ND	ND

* Significant at $P \leq 0.05$

Table 3. Mean ± SE of *E. coli* count (CFU) in fecal samples collected for 4 successive days in control infected non-treated chickens group, treated with Amoxicillin (single and multiple oral doses and supplemented with Gallimix) groups and group supplemented only with Gallimix (n=3)

Days	Control (infected non-treated group)	*E. coli* count(Amoxycillin single oral dose with Gallimix)	*E. coli* count (Amoxicillin multiple oral doses with Gallimix)	*E. coli* count (Gallimix alone)
1st day	4080±52.0	4250±144.3***	4500±16.7***	2250±132.3***
2nd day	5000±145.3	3000±115.5***	2500±101.4***	900±60.6***
3rd day	5540±92.38	2250±125.8***	2000±136.4***	790±5.8***
4th day	6050±11.5	1500±86.6***	500±11.5***	458±12.0***

Discussion

The pharmacokinetics of Amoxicillin in chicken were similar to that described previously in calves (Archimbault and Boutier, 1981), buffaloes (Khanikor et al., 1986), foals (Baggot, 1988), mares (Wilson et al., 1988), dogs (Tenet al., 1990), sheep and goats (Craigmill et al., 1992) and broilers (Atef et al., 1995; Carceles et al., 1995a,b and Dorota and Cezary, 2010).

The pharmacokinetic showed that C_{max} (2.04± 0.06µg/ml) was lower than (41.90 ± 5.59 µg/ml) obtained by (Bhar et al., 2010) at 1 hr in broiler chickens and lower than (160.40 ± 4.67 µg/mL) obtained by (Anadon et al., 1996) and (3.50 ± 0.30 µg/ml) obtained by (Abo El- Sooud et al., 2004) and these differences could be related to the selected dose in this study, species and age variations which could affecting the degree of protein binding of the drug and/or due to the difference in the method used for assaying of the drug.

This peak concentration achieved at a time T_{max} of (2.998± 0.04 h) was higher than (0.49 ± 0.76h) reported by Abo El-Sooud et al.(2004) and (1.00 ± 0.06h) reported by Anadon et al.(1996).

Apparent volume of distribution ($Vd_{(B)}$) value of healthy chicken was higher compared to those reported by Abo El-Sooud et al. (2004), Anadon et al. (1996) and Bhar et al. (2010). $Vd_{(B)}$ values of healthy birds was 1.527 ± 0.152 L/Kg, while that reported by Anadon et al. (1996) was 0.054 ± 0.003 L/Kg and that reported by Bhar et al.(2010) was 0.87 ± 0.12 L/Kg and that reported by Abo El-Sooud et al. (2004) was 1.12 L/Kg.

Residues of Amoxicillin were highest in kidney, lung, breast muscle and liver. No Amoxicillin residues detected in tissues and plasma after 9 days of stopping of drug administration. Amoxicillin concentration in normal healthy broiler chickens was significantly higher in Gallimix treated group than non-treated ones in serum only at 3rd day withdrawal (0.39± 0.003 µg/ml).

The results showed that a pre-slaughter withdrawal time more than 6 days as the drug is still detected in kidney, lung, spleen and heart till the 6th day is needed to ensure that the drug is eliminated from tissues. Similar findings of high therapeutic concentrations of Amoxicillin in different tissues of broiler chickens were reported by Bhar et al. (2010).

The present findings have revealed that *E. coli* colony count (CFU) was decreased following crop administration of the mixed acidifiers (Gallimix) in tested broilers. These findings are inconsistent with those reported by (Simeanu, 2004; Stan and Pop, 1997; Stan and Simeanu, 2005; Hashemi et al., 2005; Loddi et al., 2004 and Pelicano et al., 2005; Palenzuela, 2003; Lückstädt, 2003 and Lückstädt et al., 2004) who reported that the addition of acidifiers in poultry feed prevent and or inhibit enteric pathogenic germs in poultry like *Salmonella*, *E. coli* and *Clostridium*.

On the other hand, the obtained results showed that the oral administration of Amoxicillin with Gallimix has the same potential activity of Gallimix alone following oral administration of Amoxicillin for 5 consecutive days in broiler fed on poultry feed with added Gallimix.

Conclusion

Addition of acidifiers to poultry feed did not change pharmacokinetic pattern of Amoxicillin following its oral administration. Amoxicillin was rapidly absorbed in infected chickens as compared with those treated with Amoxicillin alone or Amoxicillin plus Gallimix. No Amoxicillin residues detected in tissues and plasma after 9 days of stopping of drug administration.

Acknowledgment

I have pleasure to insure my sincere gratitude and thanks to Dr. Mohammed Khalifa Hassan, Chief Researcher in Animal Health Research Institute.

References

Abo El-Sooud, K., Al-Tarazi, Y.H. and Al-Bataineh, M.M., 2004. Comparative pharmacokinetics and bioavailability of Amoxicillin in chickens after intravenous, intramuscular and oral administrations. Veterinary Research communications 28(7), 599-607.

Anadon, A., Martinez-Larranaga, M.R., Diaz, M.J., Bringas, P., Fernandez, M.C. et al.,, 1996. Pharmacokinetics of Amoxicillin in broiler chickens. Avian pathology 25(3), 449-458.

Archimbault, P., Boutier, C., 1981. Amoxycillin in the calf. Comparative bioavailability of injectable preparations. Revue de Medicine Veterinaire 132(1), 51-56.

Atef, M., Youssef, S.A.H. and El-Maaz, A.A., 1995. Influence of aflatoxin B1 on the pharmacokinetic profile of some antibiotics in broiler chickens. PhD Thesis, Vet. Pharmacology Department, Faculty of Vet. Medicine, Cairo University.

Baggot, J.D. 1988. Bioavailability and disposition kinetics of Amoxicillin in neonatal foals. Equine Veterinary Journal 20, 125-127.

Bhar, M.K., Datta, B.K., Patra, P.H., Dash, J.R., Sar, T.K. et al., 2010. Disposition kinetics of Amoxicillin in healthy, hepatopathic and nephropathic conditions in chicken after single oral administration. Veterinary Research Forum 1(3), 150–156.

Carceles, C.M., Escudero, E. and Baggot, J.D., 1995a. Comparative pharmacokinetics of Amoxicillin/clavulanic acid combination after intravenous administration to sheep and goats. Journal of Veterinary Pharmacology and Therapeutics 18(2); 132-136.

Carceles, C.M., Soledad Vicente M. and Escudero, E., 1995b. Pharmacokinetics of Amoxicillin/clavulanic acid combination after intravenous and intramuscular administration to turkeys and chickens. Avian pathology (24:4), 643-652.

Craigmill, A.L., Pass, M.A. and Wetzlich, S., 1992. Comparative pharmacokinetics of Amoxicillin administered intravenously to sheep and goats. Journal of Veterinary Pharmacology and Therapeutics 15(1), 72-77.

Dorota, K. and Cezary, J.K., 2010. Pharmacokinetic parameters of Amoxicillin in pigs and poultry. Acta Poloniae Pharmaceutica Drug Research 67(6), 729-732.

Foulstone, M. and Reading, C., 1982. Assay of Amoxicillin and clavulanic acid, the components of Augmentin, in biological fluids with high-performance liquid chromatography. Antimicrobial agents and chemotherapy 22(5), 753-762.

Gross, W.B., 1990. Factors affecting the development of respiratory disease complex in chickens. Avian Diseases 34, 607– 610.

Hashemi, S.R., Zulkifli, I., Davoodi, H., Hair-Bejo, M. and Loh, T.C., 2005. Effect of phytogenic and acidifier feed additives on meat Ph and vital organ size in broiler chickens. Faculty of Animal Science, Gorgan University of Agricultural Sciences and Natural Resources, Gorgan, Iran.

Khanikor, H.N., Srivastava, A.K., Paul, B.S. and Malik, J.K., 1986. Disposition of ampicillin and Amoxicillin in buffalo calves following repeated parentral administration. Acta Veterinaria, Yugoslavia 36(5/6), 295-300.

Kung, K. and Wanner, M., 1994. Bioavailability of different forms of Amoxicillin administered orally to dogs. Veterinary Record 135(3), 552-554.

Lashev, L. and Semerdzhiev, V., 1983. Absorption and distribution of Amoxicillin in fowls and mallard ducks. VeterinarnimeditsinskiNauki 20(5), 22-28.

Leitner, G. and Heller, E.D., 1992. Colonization of Escherichia coli in young turkeys and chickens. Avian Diseases 36, 211– 220.

Loddi, M.M., Maraes, V.M.B., Nakaghi, I.S.O., Tucci, F., Hannas, M.I. et al., 2004. Mannan oligosaccharide and organic acids on performance and intestinal morphometric characteristics of broiler chickens. In: proceedings of the 20th annual symposium. (Suppl. 1), pp. 45.

Lückstädt, C., 2003. Biotronic–solutions for modern livestock production. Biomin Newsletter 3, 1-4.

Luo and Catharina, Y.W., 2000. Determination of Amoxicillin Residues in Animal Tissues by Solid Phase Extraction and Liquid Chromatography with Fluorescence Detection. Journal of the Association of Official Agricultural Chemists International 83(1), 20-25.

Palenzuela, P.R., 2003. Los acidosorganicoscomo agents antimicrobianos. nutricion y alimentacion animal, Madrid.

Pelicano, E.R.L., Souza, P.A., Souza, H.B.A., Figueiredo, D.F., Boiago, M.M. et al., 2005. Intestinal mucosa development in broiler chicken fed natural growth promoters. RevistaBrasileira de CienciaAvicola, Campina.

Simeanu, D., 2004. BiostimulatoriînalimentaĠiapăVărilor. Editura Alfa, Iasi.

Stan, Gh. and Pop, I.M., 1997. Alimenta Ġiaúinutri Ġiaanimalelor. Editura. Junimea, Iaúi.

Stan, Gh. and Simeanu, D., 2005. NutriĠieanimală. Ed. Alfa, Iaúi.

Ten, G., Broeze, J., Hartman, E.G., VanGogh, H., 1990. The influence of the injection site on the bioavailability of ampicillin and Amoxicillin in beagles. Veterinary Quarterly 12, 73-79.

Analytical Communities International 83(1), 20-25.

Wilson, W.D., Spensley, M.S., Baggot, J.D., Hietala, S.K., 1988. Pharmacokinetics and estimated bioavailability of Amoxicillin in mares after intravenous, intramuscular and oral administration. American Journal of Veterinary Research 49(10), 1688-1694.

تاثير بعض المواد المحمضة على المسار الحركى ومستبقيات الانسجة لعقار الاموكسيسيللين فى دجاج التسمين السليم والمصاب معمليا بسلالة الايشريشيا كولاى المعدية

حسنى عوض البنا[2] ; صلاح الدين عبدالحميد يوسف[2] ; محمد احمد ماهر[1]

[1] وحدة تحليل المتبقيات – معهد بحوث صحة الحيوان, [2] قسم الأدوية

كلية الطب البيطري –جامعة القاهرة

استهدفت هذه الدراسة معرفة تأثير بعض المواد المحمضة (جاليمكس) على المسار الحركى للأموكسيسيللين فى الدجاج السليم والمصاب معمليا بسلالة الايشريشيا كولاى المعدية وكذلك على معدل توزيع المضاد الحيوى فى الأنسجة المختلفة. ولقد تم العد البكتيرى فى الدجاج المصاب معمليا فى وجود المواد المحمضة فقط وكذلك فى وجود كلا من المواد المحمضة والأموكسيسيللين معا. وقد تم قياس مستوى الأموكسيسيللين فى عينات الدم والأنسجة المختلفة وذلك بواسطة جهاز التحليل الكروماتوجرافى عالى الكفاءة. ومن هذه النتائج نستنتج سرعة امتصاص الاموكسيسيللين الى حد ما فى وجود العدوى مقارنة بالدجاج السليم. لاتوجد زيادة ملحوظة فى تركيز الأموكسيسيللين فى الدم والأنسجة المختلفة مقارنة بالدجاج السليم والمعالج بمادة الجاليمكس ومن هنا نستنتج أن مادة الجاليمكس لاتؤثر على توزيع الدواء وبقاياه فى الأنسجة المختلفة ولكن العدوى البكتيرية أحدثت تغييرات فى مدة رفع الدواء وبقاياه. وقد وجد انخفاض ملحوظ فى العد البكتيرى فى وجود الجاليمكس والأموكسيسيللين معا مقارنة بالدجاج المعدى فقط والغير معالج.