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STUDIES ABOUT THE COMPATIBILITY OF ANTIBIOTICS IN RABBITS AFTER ORAL APPLICATIONS

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The use of antibiotics in the prophylaxis and treatment of animal diseases is spreaded and very effective in the control of bacterial diseases. In rabbits there are some problems in the oral application of antibiotics, because some of these have toxic effects with consequences on health and life for the treated animals, i.e. Ampicillin (Schatzmann et al. 1977) and Lincomycin (Fesce, 1977), which cause enteritis with high mortality.

To check the compatibility of various antibiotics effective against bacterias, which are known as causitive agents of infectious diseases in rabbits like Pasteurella multocida, Brodetella bronchiseptica, E. coli, Staphylococcus aureus, Clostridium perfringens, we have studied the influence from some of these antibiotics in normal growing rabbits after oral applications in therapeutic dosages.

Material and methods:

Animals: Rabbits of the New Zealand and Californier race and its cross-breeds, free from Pasteurella spec., Salmonella spec., Listeria spec., and Eimeria stiedae and from enteral helminthics were taken. The age of the animals at the beginning of experiments was - in average - between 8 and 12 weeks.

Housing system: Cages with wire network bottom, selfdrinking and feedin system (ad lib.), 2 until 3 rabbits per cage.

Feeding: Allmash feed with 16,0 % rough protein, 2.5 % fat, 16,0 % rough fibre, fortified by vitamins and minerals.

Antibiotic drugs:

ß-Lactamring antibiotics:

Penicillin V, Ampicillin, Cephalexin

Tetracycline:

Chlortetracycline, Doxicycline

Aminoglycosid-antibiotics:

Spectinomycine

Chloramphenicol:

Macrolite-antibiotics:

Erythromycine,Oleandomycine, Spiramycine, Tylosine

Lincomycine - Clindomycine group:

Lincomycine.

The antibiotics were given by oral route for 7 days. To prove the sensibilisation effect, the antibiotic applications were repeated after 12 days break with the same or with higher dosages.
The control of treatment effect was done by the following measurements:

- The body weight development,
- the external visible clinical symptoms,
- the composition of fecal and intestinal microflora respectively in treated and not treated control rabbits.

Results:

The oral application of ß-Lactamring antibiotics: Penicillin, Ampicilline and Cephalexine over 7 days in therapeutic effective dosages induced in the most treated animals distinct clinical symptoms. In the Penicillin group skin lesions with small bleedings and hairlosses were the predominant clinical consequences of the treatment. Diarrhoe occured in few cases only. No death was observed. - In the Ampicilline treated rabbits diarrhoe, skin lesions and loss of weight arose in connection with the 7 days application of this antibiotic. None of the treated animals were died. - Cephalexine application caused in all treated rabbits considerable weight losses, but no diarrhoe or skin lesions were stated.

From the tested makrolide-antibiotic group only the Spiramycine and Tylosine showed toxic effects with clinical consequences in the treated rabbits. By Spiramycine application skin lesions in the same manner as in connection with Penicilline or Ampicilline application were observed in the treated rabbits. Tylosine applications induced diarrhoe only in some of the treated rabbits. Diarrhoe occured also after treatment of rabbits with the Lincomycine. Additionally Tylosine and Lincomycine caused also distinct retardations of body growing in the rabbits.
No clinical symptoms were observed after the 7 days oral application by Chlortetracycline, Doxycycline, Spectinomycine, Chloramphenicol, Erythromycine and Oleandomycine. The growth of rabbits treated with these antibiotics was not influenced negatively in any way.

The bacteriological investigation of feces in the antibiotic treated rabbits showed in comparison to the not treated control animals distinct changes in the compound of the fecal microflora mainly by increase of compound E. coli (table 2). By treatment with the ß-lactamring antibiotics, particularly Penicilline and Ampicilline an increase of aerobic bacterias mainly E. coli and a decrease of anaerobic bacterias, mostly lactobacilli and bacteroides spec. in the feces became obviously accompaigned. A slight increase of E. coli in the feces was also seen after treatment with Spiramycine and Lincomycine.
All other tested antibiotics did not show distinct effects on the bacterial compound in the feces of the treated rabbits.
In most cases of increase of E.coli compound in the feces as well as in the ingestum of caecum and colon a shifting of the pH from slight acid (pH 6,3-6,8) to slight alcalic reaction (pH 7,5-8,5) could be observed. The shifting of pH was particularly to state after treatment with the ß-lactamring antibiotics Penicilline, Ampicilline and Cephalexine and after application of Lincomycine. The changing of pH in feces and caecum was not seen after application of Spiramycine and Tylosine, which induced skin lesions and diarrhoes in the rabbits.

After repetition of all the treatments with the same or twofold dosages 12 days after the end of the first treatment period no sensibilisation effect in the pretreated animals could be observed. The clinical symptoms of those antibiotics, which have shown toxic effect in the first passage

were the same also in the treatment repetition. Only the clinical symptoms were more severe than after the first treatments. Antibiotics without toxic effects and clinical symptoms did not develope toxic effects after its repetition, too.

Summary:

Experimental studies resulted that Chlortetracycline,Doxycycline, Chloramphenicole, Spectinomycine, Erythromycine and Oleandomycine are well compatible for rabbits in the therapeutic use by oral application. The compatibility is also given after treatment repeat and if the dosage is increased on the twofolds.In contrast to this the ß-lactamring antibiotics Penicilline, Ampicilline and Cephalexine as well as the macrolide antibiotics Spiramycine and Tylosine and the antibiotic Lincomycine can develope toxic effects in the treated rabbits, sometimes with deadly exit. The use of these anitbiotics for therapeutic treatment of rabbits by oral application can not be recommended.

Untersuchungen über die Verträglichkeit von Antibiotika bei oraler Behandlung von Kaninchen

Zusammenfassung:

Experimentelle Untersuchungen ergaben, daß Chlortetracyclin, Doxycyclin, Chloramphenicol, Spectinomycin, Erythromycin und Oleandomycin in der therapeutischen Anwendung bei oraler Eingabe für Kaninchen gut verträglich sind. Die gute Verträglichkeit bleibt auch bei Wiederholungsbehandlungen in doppelter Dosierung bestehen. Im Gegensatz dazu zeigen die ß-Lactamring Antibiotika Penicillin, Ampicillin und Cephalexin wie auch die Makrolid Antibiotika Spiramycin und Tylosin sowie das Antibiotikum Lincomycin toxische Wirkungen bei den behandelten Kaninchen, gelegentlich mit tödlichem Ausgang. Die Anwendung dieser Antibiotika zur oralen Behandlung von Kaninchen kann daher nicht empfohlen werden.

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Investigaciones sobre la tolerabilidad de los antibióticos en el tratamiento oral de los conejos

Las investigaciones experimentales han dado por resultado que la clorotetraciclina, doxiciclina, cloranfenicol, spectinomicina, eritromicina y oleandomicina son bien toleradas en sus aplicaciones terapéuticas a los conejos por via oral. La buena tolerabilidad se mantiene aun en los tratamientos repetidos con dosis duplicada. Por el contrario, los antibióticos lactámicos beta: penicilina, ampicilina, y cefalexina, así como también los antibióticos macrolídicos spiramicina y tilosina, así como el antibiótico lincomicina, producen efectos tóxicos en los conejos con ellos tratados, en ocasiones incluso la muerte. No puede por lo tanto recomendarse la aplicación de esos antibióticos al tratamiento de conejos por vía oral.

Studi sulla tollerabilità di antibiotici nel trattamento orale dei conigli

Da studi sperimentali si è tratto il risultato che gli antibiotici Chlortetracyclin, Doxycyclin, Chloramphenicol, Spectinomycin, Erythromycin e Oleandomycin vengono ben tollerati nell 'applicazione terapeutica sui conigli, se somministrati per via orale. Il buon grado di tollerabilità persiste anche nel caso di applicazioni continuate in dose doppia. Al contrario, i ß-Lactamring antibiotici penicillina, ampicillina e cephalexina, come pure i Macrolid-antibiotici spiramicina e tilosina ed infine l'antibiotico lincomicina sviluppano effetti tossici sui conigli sottoposti a trattamento, a volte con esito letale. E' quindi da sconsigliarsi l'applicazione di questi antibiotici nel trattamento orale dei conigli.

Tests sur la tolérance des antibiotiques pour le traitement oral de lapins

Des analyses expérimentales ont eu pour résultat que la tolérance des antibiotiques Chloretetracycline, Doxycycline, Chlore-amphenicole, Spectinomycine, Erythromycine et Oleandomycine est bonne dans la thérapeutique des lapins en l 'administrant par voie orale. Cette tolérance periste même en répétant le traitement au double dosage. Contrairement à ces produits les antibiotiques ß-Lactamring Pénicilline, Ampicilline et Céphalexine ainsi que les antibiotiques Makrolid Spiramycine et Tylosine et l 'antibiotique Lincomycine produisent des effets toxiques sur les lapins traités, parfois avec résultat mortel.Il n'est donc pas à recommander d'administrer ces antibiotiques pour le traitement oral des lapins.

Table 1

Influence of 7-days oral application of antibiotic on body weight development and clinical symptoms in rabbits

antibiotic daily dosage/ kg body weight	total body weight (average) in g				clinical symptoms
	before treatment		12 days after last treatment		
	treatment	control	treatment	control	
Penicillin 7x120 000 IU	1530	1610	1947 +417	1950 +340	skin lesions (diarrhoe)
Ampicillin 7x20 mg	2495	2510	2438 -57	2834 +324	skin lesions (diarrhoe)
Cephalexin 7x100 mg	2012	1900	1805 -216	2303 +403	emaciation
Chlortetracyclin 7x40 mg	1389	1410	1831 +442	1859 +449	no symptoms
Doxycyclin 7x35 mg	1575	1590	2042 +467	2078 +468	no symptoms
Spectinomycin 7x150 mg	2044	2005	2193 +149	2397 +392	no symptoms
Chloramphenicol 7x50 mg	1789	1810	2194 +405	2260 +450	no symptoms
Erythromycin 7x15 mg	1415	1425	1870 +455	1889 +464	no symptoms
Oleandomycin 7x75 mg	1552	1565	2022 +470	1990 +425	no symptoms
Spiramycin 7x20 mg	2467	2445	2762 +295	2774 +329	skin lesions
Tylosin 7x30 mg	1521	1515	1554 +33	1837 +322	diarrhoe
Lincomycin 7x50 mg	1816	1800	1860 +44	2138 +338	diarrhoe

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Table 2a

Influence of 7-days oral application of antibiotic on the compound (in percentage) of aerobic and anaerobic bacterias in the faeces of rabbits

number of animals: 3 each cage group, age: 8-12 weeks

antibiotic daily dosage/ kg body weight	group	bacterial compound (in percent) in faeces before(b) and after(a) treatment											
		aerobic		anaerobic		coccacea		E.coli		Lactobacilli		bacteroides	
		b	a	b	a	b	a	b	a	b	a	b	a
Penicillin 7x120 000 IU	1	54,9	77,6	45,1	22,4	0	44,9	0	0	37,4	20,4	7,6	2,0
	2	62,2	76,1	37,8	23,9	0	3,6	0,4	14,5	32,7	23,2	5,1	0,7
	3	51,4	55,4	48,6	44,6	0,8	10,3	0,9	0,5	40,0	41,0	8,2	3,6
Ampicillin 7x20 mg	1	57,9	81,5	42,1	18,5	1,8	3,7	1,2	22,3	34,2	7,4	7,9	11,1
	2	60,7	85,8	39,3	14,2	2,1	0	0,8	28,6	32,5	7,1	6,8	7,1
	3	50,0	90,7	50,0	9,3	0,1	0	0	34,2	38,8	0,8	11,2	7,7
Cephalexin 7x100 mg	1	51,8	58,3	48,2	41,7	0	0,2	3,1	29,4	37,2	34,1	11,0	7,6
	2	49,6	46,4	50,4	53,6	0	0,1	0	7,8	34,5	41,5	15,9	12,1
	3	51,0	78,7	49,0	21,3	0	0	0,9	38,4	37,1	12,4	11,9	8,9
Chlortetra-cyclin 7x40 mg	1	61,1	67,7	38,9	32,3	4,5	5,4	3,8	1,9	31,4	26,8	7,5	5,4
	2	57,3	81,7	42,7	18,3	6,5	16,5	1,9	5,4	35,6	15,3	6,9	3,0
	3	70,9	70,9	29,1	29,1	0,9	21,4	0,4	2,8	25,6	28,3	3,5	0,8
Doxycyclin 7x35 mg	1	48,5	47,9	51,5	52,2	0,3	0,9	0,1	0,2	39,7	43,2	11,8	8,9
	2	52,4	55,2	47,6	44,8	0	0,1	0,1	0,1	39,9	40,2	7,6	4,6
	3	43,0	46,9	57,0	53,1	0,4	5,6	3,2	0,8	41,2	40,2	15,6	12,9
Spectinomycin 7x150 mg	1	53,6	48,4	46,4	51,6	0	0	0,9	0,1	40,2	44,8	6,2	6,8
	2	62,9	50,6	37,1	49,4	0	0	0,1	0,2	31,1	42,2	6,0	7,2
	3	60,0	48,8	40,0	51,2	0	0	0,1	0	33,3	44,3	6,7	6,9
Chloramphenicol 7x50 mg	1	51,5	47,3	48,5	52,7	0,1	0	0,5	1,4	28,2	34,8	20,2	17,9
	2	54,1	55,0	45,9	45,0	0	0	2,0	2,9	29,8	22,9	15,9	22,1
	3	48,7	42,0	51,3	58,0	0	0,1	0,9	2,0	25,6	45,2	25,7	12,8
Erythromycin 7x15 mg	1	50,7	46,1	49,3	53,9	0,1	0,2	2,3	0,8	28,4	35,2	20,9	18,7
	2	46,8	42,2	53,2	57,8	0	0	0,9	1,4	33,4	42,2	19,8	15,5
	3	51,2	51,1	48,8	48,9	0,3	0	1,2	1,5	28,4	29,0	20,4	19,9

Table 2b

antibiotic daily dosage/ kg body weight	group	bacterial compound (in percent) in faeces before(b) and after(a) treatment											
		aerobic		anaerobic		coccacea		E.coli		Lactobacilli		bacteroides	
		b	a	b	a	b	a	b	a	b	a	b	a
Oleandomycin 7x75 mg	1	49,8	48,9	50,2	51,1	0	0	0,1	0,2	29,8	35,4	20,4	15,7
	2	49,2	50,5	50,8	49,5	0	0	0,3	0,2	35,7	27,7	15,1	21,8
	3	50,1	50,3	49,9	49,7	0	0	0	0,4	32,0	30,8	17,9	18,9
Spiramycin 7x20 mg	1	48,8	58,6	51,2	41,4	0,1	0,1	0,1	8,2	44,7	34,8	6,5	6,5
	2	50,2	55,2	49,8	44,8	0	0	0,4	6,1	42,8	37,4	6,9	7,2
	3	49,7	61,3	50,3	38,7	0,4	0	0,1	8,9	43,9	32,8	6,4	5,9
Tylosin 7x30 mg	1	48,8	51,4	51,2	48,6	0,1	0,1	0,8	1,2	44,0	41,7	7,2	6,9
	2	52,2	53,4	47,8	46,6	0	0	0,1	4,5	41,7	39,9	6,1	6,7
	3	50,8	50,7	49,2	49,3	0,2	0	0,5	1,9	42,7	42,2	6,5	7,1
Lincomycin 7x50 mg	1	51,3	53,8	48,7	46,2	0,9	2,1	1,9	12,7	42,2	40,3	6,5	5,9
	2	50,7	51,6	49,3	48,4	1,2	0,1	3,5	9,1	41,1	42,4	8,2	6,0
	3	53,5	56,8	46,5	43,2	0,7	1,1	1,2	15,8	42,4	35,1	4,1	8,1