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AN EXPERIMENTAL STUDY ON THE TOLERABILITY OF AMINOSIDINE SULPHATE GIVEN ORALLY TO THE RABBITS

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In a early work was found a favorable influence of aminosidine sulphate on rabbit's growth and health, when administered at the dose level of 140 ppm in the diet, for several weeks, after weaning (Tocchini and Tardani, 1975).

Enteric and respiratory diseases in rabbit are now attributed to multifactorial causes (Morisse, 1986).

Expecially factors contributing to perturb intestinal ecology of the rabbit were investigated (Bourget et al., 1987; Peeters et al., 1986).

The experimental use of antibiotics is enumerated too (Fesce et al., 1977).

Moreover, usefulness of antibiotics prophylaxis and therapy of enzootic diseases in commercial rabbits production were debated (Löliger et al., 1984; Lumeij et al., 1987; Maiers and Mason, 1984; Popoff, 1986).

Consequently we wanted to verify anew the safety of aminosidine sulphate in young rabbits after experimental supply via drinking water and food.

We also intended to investigate about the presence of residues in organs and tissues of the treated animals.

MATERIALS AND METHODS

Aminosidine sulphate in water.

63 rabbits, aged 48 days, male and female, all belonged to the same breeding, with an average weight of 1225 g were divided into 6 homogeneous groups.

Five groups were treated with aminosidine sulphate at 10% in soluble support (Gabbrocol Vetem S.p.A.) administered at different dose levels in drinking water and one group was used as control, as reported in TAB. 1.

The rabbits were fed ad libitum with unmedicated pelletted feed.

Aminosidine sulphate in pelletted feed.

91 little rabbits aged 30 days, male and female, with an average weight of 629 g, all belonged to the same breeding, were divided into 8 groups as reported in TAB. 2. The animals were given pelletted feed integrated with aminosidine sulphate at 10% in soluble support.

All the rabbits grew in metallic grating cages in a building of zinced plate cohibited.

The following remarks were carried out on the experimental animals:

Ingested feed: the ingested feed has been estimated weekly during the whole period of antibiotics supply and up to one week later, relatively to each group.

Animals weight: during all Gabbrocol's supply period and for some further weeks all animals have been individually weighted weekly.

Feed conversion rate: during the supply of medicated water feed and for the next weeks, the feed conversion rate has been estimated for each group weekly.

Animal's health control: all animals have been controlled daily.

Mortality: all animals died during the trial have been registered and weighted (for the calculation of feed conversion rate) and submitted to necroscopic and microbiological tests.

To determine the aminosidine sulphate residues, only from some groups three rabbits were sacrificed as follows:

- One the last day of treatment;
- One 2 days after the end of treatment;
- One 7 days after the end of treatment.

From each animals the following samples were taken: serum, kidneys, liver, muscle, spleen.

The above samples were frozen and stored at -30°C till the microbiological determination of antibiotic.

As already stated (Tiecco et al., 1988) the assessment of the residues was carried out for organs, tissues and serum.

Comparison among the groups treated with different antibiotic's dose level and control were effected on average weight, mean weight gain and conversion rate by regression analysis with parallel lines test.

RESULTS

The aminosidine sulphate's supply (as medicated int. rator) in feed and via drinking water to rabbits' groups aged within 30 .nd 48 days has given the following results:

- absence of specific mortality;
- absence of clinical signs and peculiar behaviours referable to antibiotic's supply up to 1800 ppm in feed;
- excellent palatability in both the supply's methods.

Aminosidine sulphate in water.

Mean weight gain (TAB. 3) and conversion rate (TAB. 4) are not significant among groups.

Average weights (TAB. 5) on the contrary is significant: (TABS. 6-7-8) the 5th group (450g/100 liter) treated for 7 days gave better results than the other treated groups and control.

Aminosidine sulphate in feed.

Mean weight gain (TAB. 9) and conversion rate (TAB. 10) are not significant among groups.

Average weights (TAB. 11) are statistically significant among groups: the second group (150 g/100 kg) shows a lower average weight than other groups. Groups which expressively differ from the control group are No. 5,6 and 7 that received high doses of antibiotic, of 600 ppm, 900 ppm, 1800 ppm, for 7 days respectively. These animals show higher average weights (TABS. 12-13-14).

As far as the positive presence of residues in rabbits treated with A.S. in water is concerning, see TAB. 15.

All other organs, tissues of rabbits examined showed no presence of residues.

Among sacrificed rabbits after treatment with aminosidine sulphate in feed, one animal of group 3a immediately sacrificed after treatment showed a residue of 0.36 mcg/g in kidneys. All other rabbits examined showed no evidence of residues in organs and tissues examined.

The obtained results on residues allow us to draw the following conclusions:

a) aminosidine sulphate administered per os, also at relatively high dosages is not absorbed by the enteric tract, as previously reported (Tiecco et al., 1988).

b) in few cases the antibiotic passed into the blood stream and its presence has been found only in serum and kidneys of those rabbits which received high doses of antibiotic and killed immediately after treatment.

c) the maximum concentration of residues was observed in kidneys.

d) aminosidine sulphate, in positive samples, was always extremely low.

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CONCLUSIONS

Consequently we can think that aminosidine sulphate is also perfectly tolerated by both weaning and growing rabbits at high dosages.
Residues in tissues and organs are low and no longer detectable after 2 days since the experimental treatment ended.
On the basis of results achieved, it is necessary to define the therapeutic role of Aminosidine both in the prophylaxis and treatment of enzootic diseases in rabbits and in particular in the enteritis-complex of commercial rabbits.

TABLE 1 - Aminosidine sulphate (A.S.) 10% via drinking water in rabbits

group n°	A.S. 10% g/100 lt	n° animals	n° days of treatment
1	50	9	21
2	100	9	21
3	150*	12	21
4	300*	12	21
5	450	9	7
6	control	12	21

* In the above groups three animals were treated with A.S. 10% for only seven days and than sacrified for residue determination

TABLE 2 - Aminosidine sulphate 10% in rabbits feed

group n°	A.S. 10% g/100 kg	n° animals	n° days of treatment
1a	75	9	21
2a	150	9	21
3a	300	12*	21
4a	450	12*	21
5a	600	9	7
6a	900	9	7
7a	1800	9	7
8a	control	12	21

* In the above groups three animals were treated with A.S. 10% for only seven days and than sacrified for residue determination

TABLE 3 - Weekly mean weight gains expressed in g in various groups of rabbits aged at start 48 days after supply of aminosidine sulphate (A.S.) into the drinking water for 3 consecutives weeks in different dosages.

Group n°	g of A.S. 10% in 100 lt of H20	Treatment period				
		start	1° week	2° week	3° week	4° week
1	50	--	276	198	198	208
2	100	--	267	159	209	91
3	150	--	297	171	225	168
4	300	--	274	184	205	151
5	450*	--	335	310	--	--
6	control	--	327	125	218	114

* Treated for only one week

TABLE 4 - Weekly average feed conversion rate in the various groups of rabbits aged at start 48 days treated with aminosidine sulphate (A.S.) in different dosages into the drinking water for 3 consecutives weeks.

Group n°	g of A.S. 10% in 100 lt of H20	Average feed conversion rate				
		start	1° week	2° week	3° week	4° week
1	50	--	3.13	3.04	4.58	4.46
2	100	--	3.29	3.97	4.53	5.89
3	150	--	2.40	3.58	4.18	5.20
4	300	--	2.74	3.42	4.57	6.04
5	450*	--	2.60	2.62	--	--
6	control	--	2.04	3.2	4.12	3.96

* Treated for only one week

TABLE 5 - Average weight in g of the various groups of rabbits aged at start 48 days treated with aminosidine sulphate (A.S.) in different dosages, into the drinking water.

Group n°	g of A.S. 10% in 100 lt of H20	Treatment period				
		start	1° week	2° week	3° week	4° week
1	50	1234	1531	1730	1929	2151
2	100	1210	1477	1637	1847	1956
3	150	1235	1532	1698	1923	2094
4	300	1222	1497	1698	1905	2077
5	450*	1207	1563	1840	--	--
6	control	1245	1532	1692	1917	2019

* Treated for only one week

TABLE 6 - Statistical analysis of groups of rabbits treated with Aminosidine sulphate 10% in the drinking water

dependent variable	regression analysis with parellel lines assay
average weight	P = 0.017*
average increase	P = 0.9338
average conversion rate	P = 0.2089

* P 0.05 see TAB. 7 and 8

TABLE 7 - Valued and corrected mean for independent variable of age days

Treatment group n°	A.S. 10% g/100 lt	Means
1	50	1691.08571
2	100	1606.45000
3	150	1673.80357
4	300	1657.10714
5	450	1819.25595
6	control	1660.28929

TABLE 8 - Probability of the comparison test (t) between the extimated and corrected mean (at probability 0.05 there are significative difference)

Group n°	1	2	3	4	5	6
1	.	0.0047	0.5173	0.2114	0.0053	0.2553
2			0.0186	0.0653	0.0001	0.0518
3				0.5314	0.0021	0.6117
4					0.0009	0.9045
5						0.0010
6						.

TABLE 9 - Weekly mean weight gains expressed in g in various groups of rabbits aged at start 30 days after supply of aminosidine sulphate (A.S.) in feed in different dosages.

Group n°	g of A.S. 10% in 100 kg	Treatment period				
		start	1° week	2° week	3° week	8° week
1a	75	--	177	189	257	550
2a	150	--	170	202	111	566
3a	300	--	216	260	88	583
4a	450	--	190	182	177	540
5a	600	--	214	288	200	546
6a	900	--	265	272	260	450
7a	1800	--	326	222	233	423
8a	control	--	208	202	293	466

TABLE 10 - Weekly feed conversion rate in the various groups of rabbits aged at start 30 days treated with aminosidine sulphate (A.S.) in feed in different dosages.

Group n°	g of A.S. 10% in 100 kg	Average feed conversion rate				
		start	1° week	2° week	3° week	8° week
1a	75	--	2.98	3.32	2.49	3.03
2a	150	--	2.89	2.96	6.70	3.34
3a	300	--	2.69	2.67	6.75	3.70
4a	450	--	3.07	3.19	4.58	3.18
5a	600	--	2.45	2.14	--	--
6a	900	--	2.10	2.46	--	--
7a	1800	--	1.79	3.13	--	--
8a	control	--	2.58	2.97	3.02	3.57

TABLE 11 - Average weight in g in the various groups of rabbits aged 30 days at start treated with aminosidine sulphate (A.S.) in feed in different dosages.

Group n°	g of A.S. 10% in 100 kg	Treatment period				
		start	1° week	2° week	3° week	8° week
1	75	653	831	1020	1277	2693
2	150	583	753	938	1048	2443
3	300	593	810	1064	1153	2793
4	450	643	833	975	1153	2665
5	600	643	857	1134	1356	2833
6	900	603	868	1130	1405	2703
7	1800	686	1013	1217	1450	2533
8	control	627	835	1002	1284	2603

TABLE 12 - Statistical analysis of groups of rabbits treated with Aminosidine sulphate 10% in the drinking water

dependent variable	regression analysis with parellel lines assay	
average weight	P = 0.005	P 0.01*
average increase	P = 0.5393	P 0.05
average conversion rate	P = 0.9814	P 0.05

* Significant, see TAB. 13 and 14

TABLE 13 - Value and corrected mean for independent variable of age days

Treatment group n°	A.S. 10% g/100 kg feed	Means
1a	75	1467.85714
2a	150	1302.71429
3a	300	1443.85714
4a	450	1408.71429
5a	600	1544.14286
6a	900	1527.42857
7a	1800	1532.14286
8a	control	1442.00000

TABLE 14 - Probability of the comparison test (t) between the extimated and corrected mean (at probability < 0,05 there are significative difference)

Group n°	1a	2a	3a	4a	5a	6a	7a	8a
1a	.	0.0001	0.5207	0.1182	0.0460	0.1156	0.0903	0.4892
2a			0.0005	0.0067	0.0001	0.0001	0.0001	0.0005
3a				0.3484	0.0099	0.0296	0.0220	0.9603
4a					0.0007	0.0027	0.0019	0.3742
5a						0.6543	0.7477	0.0087
6a							0.8994	0.0264
7a								0.0195
8a								.

TABLE 15 - Aminosidine sulphate in organs of sacrificed rabbits immediately after the last day of treatment (7 or 21 days) with A.S. 10% in drinking water.

Group n°	A.S. 10% g/100 lt	7 day treatment mcg of A.S. x g/ml kidney	7 day treatment mcg of A.S. x g/ml serum	21 day treatment mcg of A.S. x g/ml kidney	21 day treatment mcg of A.S. x g/ml serum
1	50	n.d.	n.d.	-	-
2	100	n.d.	n.d.	-	-
3	150	-	-	-	-
4	300	1.02	0.16	1.0	0.16
5	450	1.68	0.20	n.d.	n.d.
6	0	-	-	-	-

n.d. = not done
- means absolutely no reaction to the microbiological test (sensibility 0.16 mcg g/ml).

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ABSTRACT

AN EXPERIMENTAL STUDY ON THE TOLERABILITY OF ORALLY GIVEN AMINOSIDINE SULPHATE IN THE RABBITS.

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The tolerability of aminosidine sulphate in rabbits of different ages was studied. The antibiotic have been give orally by means of drinking water (for twentyone days at dosesof 50 , 100 , 150 , 300 ppm or for seven days at 450 ppm) or added in the feed (for twentyone days at dosesof 75 , 150 , 300 , 450 ppm or seven days at 600 , 900 , 1800 ppm).
The antibiotic administration did not cause mortality,suffering or particular behaviours in rabbits whose weight gain and feed efficiency were unaffected.
Finally , this study showed an optimal antibiotic tolerability.

RICERCHE SPERIMENTALI NEL CONIGLIO SULLA TOLLERABILITA' DEL= L'AMMINOSIDINA SOLFATO SOMMINISTRATA PER VIA ORALE.

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Gli AA. hanno valutato la tollerabilità di un integratore me= dicato con amminosidina solfato in conigli di varia età.
L'antibiotico è stato somministrato per via orale nell'acqua da bere (per 21 giorni alle dosi di 50 , 100 , 150 e 300 ppm e 7 giorni a 450 ppm) e addizionato al mangime (per 21 giorni alle dosi di 75 , 150 , 300 e 450 ppm e 7 giorni alle dosi di 600 , 900 e 1800 ppm).
Il consumo dell'antibiotico non ha causato mortalità né compar= sa di manifestazioni di sofferenza di ordine generale ed atteg= giamenti particolari riferibili al trattamento ;non ha influen= zato significativamente l'incremento ponderale e l'indice di conversione alimentare.
In conclusione la sua tollerabilità si può ritenere ottimale.