

TIAMULIN RESIDUES IN TARGET TISSUES, IN PIGS AFTER INTRAMUSCULAR INJECTION

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Tiamulin (Squibb Dynamulin) is a pleuramulin derivative, 14-deoxy-14 (2-diethylaminoethyl) mercapto-acidoxymulin hydrogen fumarate which has also been synthesized in the base form. It has been shown to be active against a variety of Gram positive bacteria, mycoplasmas and treponemes of clinical importance (Drews et al 1975, Taylor 1976, Kitai et al 1979, Goodwin 1979). Particularly noteworthy is the high activity demonstrated by this antibiotic against *Treponema hyodysenteriae* and *M. hyopneumoniae*, the organisms associated with swine dysentery and swine enzootic pneumonia respectively. The studies described were carried out to determine the active concentrations of drug in pig tissues, particularly target tissues i.e. intestine and lungs, after injection, relative to the two diseases.

The first study was undertaken as a siting experiment involving a single pig. The animal was fed weaner ration and water ad lib over the duration of the trial. Tiamulin base in an oily vehicle was injected to yield a dose equivalent to 15 mg Tiamulin hydrogen fumarate/kg IM over 5 days. Blood samples were collected prior to injection and at several periods up to 24 hours post injection. On the fifth day the pig was sacrificed and samples of lung, small intestine and colon were stored at -20°C until assayed for Tiamulin. Serum samples and tissue samples were assayed by a microbiological method using *Sarcina lutea* ATCC 9341 as the test organism. The limit of detection by this method was found to be 0.05 mcg/ml in serum and 0.05 mcg/g in tissue. Results from this study showed some interesting data particularly the elevated lung residues and prompted a more comprehensive study.

The second study was carried out on four male and four female, twelve week old pigs of the Large White type, averaging 25 kg in weight. They were divided into four groups each containing one male and one female and housed in groups in a controlled environment "Danish type" piggery. They were fed a pig weaner ration in meal form offered at 1.0 kg per animal per day, with water ad lib. Injections of Tiamulin base in an oily vehicle were given at doses equivalent to 10 mg or 15 mg Tiamulin hydrogen fumarate by IM injection (hind leg) for 5 consecutive days.

Bodyweights were recorded two weeks and one week prior to injection and at slaughter, along with daily records of food consumption. Venous blood samples were taken on several occasions from each animal and sera separated and stored at -20°C until assayed. Two to four hours after the last treatment on day 5, animals were sacrificed by electrical stunning, followed by exsanguination. Tissue samples were collected, each organ being divided into three portions, double wrapped in plastic bags, labelled and stored at -20°C until assayed.

Results

In the first study blood levels for Tiamulin indicated a peak blood level of 0.65 mcg/ml at about 4 hours in the first 24 hours of medication, with levels ranging from 0.23 mcg/ml at 0.5 hours to 0.18 mcg/ml at 24 hours. Analysis for Tiamulin-like activity gave results of 23.3 mcg/g in the lung and 4.8 mcg/g in the colon, samples of colon wall and content assayed separately giving no significantly different results.

Tiamulin serum levels obtained in the second study involving eight pigs are shown in Fig. 1 and Tiamulin tissue residues are shown in Tables 1 and 2.

FIG. 1
P/G SERUM TIAMULIN LEVELS AFTER IM INJECTION

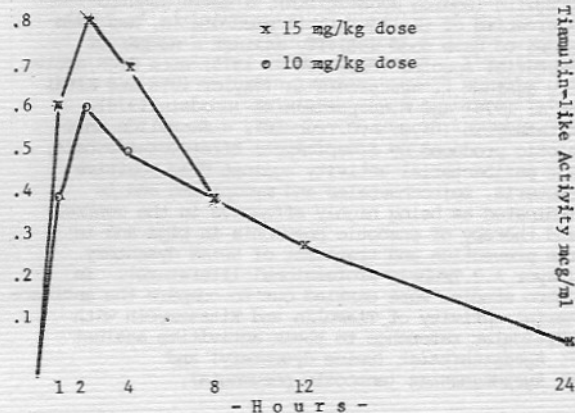


Table 1 Tiamulin Tissue Residues (mcg/g or mcg/ml for Bile)

Pig No.	Dose Given mg/kg	Liver	Kidney	Lung	Colon	Muscle	Bronch. Epith.	Bile
1	10	1.49	2.85	17.2	0.62	0.44	4.1	3.7
2	10	3.35	4.05	12.4	0.42	0.41	1.5	2.9
3	10	2.20	2.89	16.8	0.30	0.54	7.9	3.7
4	10	1.67	2.47	13.0	0.21	0.23	7.5	2.3
5	15	1.80	2.79	16.7	0.22	0.46	6.5	3.4
6	15	2.28	3.57	14.5	0.50	0.42	5.5	3.6
7	15	3.46	2.43	18.0	2.11	0.24	3.4	3.0
8	15	2.51	2.48	13.5	1.53	0.46	-	7.6

Table 2 Mean Tiamulin Residues in Target Tissues (mcg/g)

Tissue	10 mg/kg	15 mg/kg
Lung	14.9	15.7
Bronchial Epithelium	5.3	5.1
Colon	0.5	1.1

Discussion

High 'Tiamulin-like' activity was demonstrated in lungs of pigs injected with Tiamulin for 5 consecutive days in both studies. Levels of 23.3 mcg/g in one study and a mean of 15.7 mcg/g in lungs from eight pigs in a second study indicated a high affinity of this antibiotic for lung tissue, compared to other organs, further substantiated by the mean level of 5.3 mcg/g in bronchial epithelium. The concentrations demonstrated in lung and bronchial epithelium far exceed the M.I.C. values for *M. hyopneumoniae* of 0.031 mcg/ml (Drews et al 1975), the causative organism of swine enzootic pneumonia. Similarly the antibiotic activity levels demonstrated in gut tissue of 2.8 mcg/g in small intestine and 4.8 mcg/g in colon in the first trial and a mean of 1.1 mcg/g in eight pigs in a second trial once again are greatly in excess of M.I.C. of 0.05 mcg/ml obtained against *T. hyodysenteriae* the causative organism of swine dysentery (Taylor 1976) and confirm the usefulness of this antibiotic in these two diseases.

References: Drews, J., et al Antimicrobial Agents and Chemotherapy 7, 507-517, 1975. Taylor, D.J., International Pig Veterinary Society Congress, Ames, Iowa, U.S.A. 22-24 June, 1976. Kitai, K., et al Antimicrobial Agents and Chemotherapy 15, 392-395, 1979. Goodwin, R.F.W., Vet Record 104, 194-195, 1979.