



## Live Performance and Processing Yields of Broilers Fed Diets With Tiamulin and Salinomycin Combinations

### ■ Author(s)

Vieira SL<sup>1</sup>  
Favero A<sup>2</sup>  
Berres J<sup>2</sup>  
Freitas DM<sup>2</sup>  
Martinez JEP<sup>2</sup>  
Mayorga ME<sup>2</sup>  
Coneglian JLB<sup>2</sup>

- <sup>1</sup> Associate Professor, Departamento de Zootecnia, Universidade Federal do Rio Grande do Sul - UFRGS. Porto Alegre, RS.
- <sup>2</sup> Aviário de Ensino e Pesquisa da UFRGS. Porto Alegre, RS.

### ■ Mail Address

Sergio Luiz Vieira  
Av. Bento Gonçalves, 7712  
91.540-000. Porto Alegre, RS, Brazil

E-mail: slvieira@ufrgs.br

### ■ Keywords

Antibiotic, broiler, ionophores, salinomycin, tiamulin.

### ABSTRACT

A study was conducted with the objective of evaluating the combined application of tiamulin (TIA) and salinomycin (SAL) in broiler diets fed from 1 to 42 d of age. One thousand and two hundred Cobb x Cobb 500 male broilers were housed in 48 floor pens and fed corn-soybean meal diets containing 66 ppm of SAL combined or not with TIA at 30 or 20 and 20 or 15 ppm, respectively, in the starter (1-21 d) and grower feeds (22-42 d); however, TIA was withdrawn from the feeds 7 days before slaughter. The experimental design was completely randomized with 3 treatments and 16 replicates of 25 birds each. Broilers were weekly evaluated for live performance whereas carcass yield, abdominal fat and commercial cuts were assessed at 42 d using 6 birds randomly taken from each pen. Results obtained at the end of the study demonstrated that body weight gain was not affected ( $P > 0.05$ ) by the treatments, whereas feed intake was reduced ( $P < 0.05$ ) and feed conversion was improved ( $P < 0.05$ ) for birds on diets containing TIA at 30/20 and 20/15 ppm, respectively. Carcass yield, abdominal fat, and commercial parts were not affected ( $P > 0.05$ ) by the treatments. Live performance and post-slaughter yields data obtained in this study did not indicate that combinations of TIA with SAL could be detrimental. In fact, an improvement in feed conversion was observed at the lowest dose of TIA.

### INTRODUCTION

Ionophores have been added to broiler feeds with the objective of preventing coccidiosis for a long time. These compounds are divided into two general groups based on the mode of ion transfer across the cell membrane; channel formers or ion carriers (Kart & Bilgili, 2008). Commercially grown animals generally use ion-carrier ionophores, which move ions across the membrane releasing them afterwards inside de cell. The protective effect of these drugs against coccidia is associated with their ability to change its ionic balance (Augustine *et al.*, 1992). Ionophores are generally safe and effective if used at recommended levels; however, ionophore toxicity might occur due to accidental overdoses, misuse, feed mixing errors as well as when combined factors lead to liver incapacity to fully metabolize them (Chapman, 2001; Nebbia *et al.* 1999).

Tiamulin (TIA) is a semi-synthetic antibiotic derived from pleuromutilin, which is recommended for the treatment of mycoplasmosis of poultry (Chapman & Johnson, 2002). It has been used for animals for a long time, but its use in broilers has been frequently avoided due to reported incompatibilities with ionophores (Witkamp *et al.* 1995; Schuhmacher *et al.* 2006). Ataxia, leg weakness, and myopathy have been found in chickens and turkeys following the simultaneous administration of



monensin and TIA (Horrox, 1980; Uchimura *et al.* 1978; Umemura *et al.* 1984). Inhibition of P450 3A enzyme isoform by TIA, which is responsible for the oxidation metabolism of monensin, was demonstrated, leading to accumulation of monensin in animal tissues (Chapman, 2001; Nebbia *et al.* 1999). It has been observed that toxic symptoms due to TIA and monensin combinations are identical to those produced by single overdoses of monensin (Hanrahan, 1981; Van Vleet *et al.* 1987).

Apparently, other ionophores may cause negative responses when used in combination with TIA for broilers, but the resulting effects depend on the type of ionophore and also on TIA levels (Meingassner *et al.*, 1979). This has been the case of salinomycin and narasin; however, lasalocid has shown no negative effects when combined with TIA and fed to turkeys (Lodge *et al.*, 1988). Semduramycin also seems not to interact with TIA probably due to a detoxification mechanism different from that of monensin (Schuhmacher *et al.*, 2006).

Recently, TIA at 20 ppm has been reported to be safe when used along with SAL (Islam *et al.*, 2008a), the interest in field applications of TIA in broilers. The objective of this study was to evaluate the effects of the combined supplementation of SAL with TIA on broiler live performance and carcass and commercial cuts yields. (Islam *et al.*, 2008a) which has renewed the interest for field applications of TIA in broilers.

## MATERIAL AND METHODS

One thousand and two hundred one-day-old Cobb X Cobb 500 (Cobb-Vantress Brasil Ltda) male broilers vaccinated for Marek's disease, were housed in 1,65 x 1,70 floor-pen boxes, 25 birds in each. Chicks originated from broiler breeders previously tested and confirmed as free of *Mycoplasmosis*. Although placement was done only three days after removal of the previous flock, management was performed to maintain temperature within the comfort range. Live performance was weekly determined by pen group evaluations of body weight, feed intake, and feed conversion. Mortality was daily recorded, and the weight of dead birds was used to correct the feed conversion and evaluated via *post mortem* examination for the cause of death. Females eventually found were removed at 21 d of age. Broiler carcass evaluation was performed at 42 days of age on 6 birds randomly taken from each pen. Birds were individually weighed, and slaughtered using electrical stunning at 45V. Eviscerated carcasses without feet and heads were

chilled in slush ice for 2 h, allowed to drip for 2 min, and were then weighed. Carcasses were cut into commercial parts by trained processing plant personnel and the following cuts were produced: breast fillets, tenders, thighs, drumsticks, wings, and abdominal fat. All cuts were individually weighed and their yields were expressed as percentage of the carcass.

Corn-soybean meal mash feeds were formulated using a two-phase feeding program: starter from 1 to 21 d and grower from 22 to 42 d (Table 1). Energy and nutrients were similar to those used in Brazilian integrations. Group 1 comprised the negative control birds, which were fed a diet containing 66 ppm SAL (Coxistac<sup>®</sup> 12%, Phibro Animal Health) only, whereas Groups 2 and 3 were given SAL at 66 ppm and also TIA (Denegard<sup>®</sup> 10%, Novartis Animal Health) at 30 and 20 ppm or 20 and 15 ppm from 1 to 21 d and 21 - 42 d, respectively. All drugs were continuously administered via their respective feeds and diet. All feeds were assayed for TIA and all were found to contain the appropriate level of drug. Mean drug concentration of SEM-containing feeds was 66 ppm. No other antibiotic was used in the feeds and TIA was removed from the feeds 7 days before slaughter.

**Table 1** - Composition of basal diets for broilers from 1 to 21 and 21 to 42 days of age.

| Ingredients, %                                 | 1-21  | 22-42 |
|--|-------|-------|
| Corn   | 55.55 | 61.17 |
| Soybean meal 45,6% CP                          | 37.65 | 31.00 |
| Dicalcium phosphate                            | 1.83  | 1.57  |
| Limestone                                      | 0.59  | 0.48  |
| L-Lysine HCl                                   | 0.17  | 0.19  |
| Salt   | 0.31  | 0.34  |
| Choline chloride                               | 0.09  | 0.06  |
| DL - Methionine                                | 0.26  | 0.23  |
| Sodium bicarbonate                             | 0.32  | 0.01  |
| Soybean oil                                    | 3.00  | 4.72  |
| L-Threonine                                    | 0.06  | 0.06  |
| Vitamin and mineral premix <sup>1</sup>        | 0.17  | 0.17  |
| <b>Energy and Nutrients, % or as indicated</b> |       |       |
| ME, kcal/kg                                    | 3,025 | 3,240 |
| CP   | 22.00 | 19.42 |
| Ca   | 0.95  | 0.80  |
| Av. P  | 0.46  | 0.40  |
| K  | 0.92  | 0.81  |
| Na   | 0.23  | 0.16  |
| Cl   | 0.28  | 0.30  |
| Choline, mg/kg                                 | 1,800 | 1,500 |
| <b>Digestible aminoacids, %</b>                |       |       |
| Lysine   | 1.20  | 1.06  |
| Methionine + Cysteine                          | 0.85  | 0.76  |
| Threonine                                      | 0.78  | 0.69  |
| Tryptophan                                     | 0.24  | 0.20  |
| Valine   | 0.90  | 0.82  |
| Isoleucine                                     | 0.78  | 0.71  |

<sup>1</sup>Composition per kg of diet: A - 5,000 IU; D3 - 1,000 IU; E - 20 IU; K3 - 0.9 mg; B1 - 0.6 mg; B2 - 3 mg; B6 - 1 mg; B12 - 6 mcg; Niacin - 15 mg; Pantothenic acid - 7 mg; Biotin - 0.04 mg; Folic acid - 0.5 mg; Zn - 51 mg; Mn - 67.5 mg; Cu - 8 mg; Fe - 64 mg; I - 0.72 mg; Se - 0.28 mg.



The study was conducted according to a completely randomized design with 3 treatments of 16 replicates each. Resulting data was submitted to ANOVA and Tukey's (SAS Institute, 2001) test was used to separate the means when treatment differences were significant ( $P < 0.05$ ).

## RESULTS AND DISCUSSION

Live performance data are presented on Table 2. Analyzed feeds contained SAL and TIA levels that corresponded to expected inclusions. Broilers fed diets with SAL + TIA (30/20 ppm) showed lower feed intake and body weight gain ( $P < 0.05$ ) from 14 to 21 d as compared to the diet without TIA. During the overall period, reduced feed intake was observed in birds fed TIA (30/20 ppm); however, no effect was observed on body weight ( $P > 0.05$ ). Feed conversion significantly improved in birds fed TIA (20/15 ppm) during weeks corresponding to 14-21 and 35-42 d, as well as during the overall period. The use of TIA (30/20 ppm) promoted better results than the control treatment from 21 to 28 d ( $P < 0.05$ ). Overall bird mortality was low (grand mean = 2.36%), and was not affected by the treatments ( $P > 0.05$ ).

Carcass data resulting from processing (Table 3) did not show statistical significant differences among treatments ( $P > 0.05$ ). The present study evaluated the

animal responses that are usually measured in commercial environments. Therefore, discussions and conclusions from this study cannot provide further explanations regarding mode of action of SAL, TIA or their combination.

Results of the present investigation demonstrate that the continuous use of TIA (30 - 20ppm) in feeds containing SAL (66 ppm) were safe. No clinical signs of toxicity, such as high mortality, leg weakness, myopathy or any other muscle lesions were observed in live animals or carcasses. Reports that found incompatibilities between TIA and ionophores generally applied TIA at 150 ppm and 250 ppm in feed and water, respectively (Schuhmacher *et al.* 2006; Stipkovits *et al.* 1999) with the medicated feeds and water supplied for periods of 7 and 5 d, respectively. In those cases, some birds showed mild signs of incompatibilities characterized by reduced feed intake and body weight, but no mortality.

Medication programs with high TIA doses often lead to anorexia and live performance losses during the period of concurrent administration of TIA and ionophores. However, when TIA treatment was withdrawn, there were significant compensatory improvements in feed efficiency and differences in body weight could not be detected during the subsequent periods (Schuhmacher *et al.* 2006; Islam *et al.* 2008b).

**Table 2** - Performance of broilers fed diets containing salinomycin at 66ppm combined or not with tiamulin from 1 to 42 days of age\*.

| Body Weight Gain, g   |       |        |          |          |         |          |          |
|-----------------------|-------|--------|----------|----------|---------|----------|----------|
| Treatments, ppm       | 1 - 7 | 7 - 14 | 14 - 21  | 21 - 28  | 28 - 35 | 35 - 42  | 1 - 42   |
| T1 - Negative Control | 98    | 226    | 442 a    | 553      | 652     | 666      | 2.637    |
| T2 - Tiamulin (20/15) | 88    | 221    | 435 ab   | 572      | 692     | 674      | 2.682    |
| T3 - Tiamulin (30/20) | 90    | 215    | 422 b    | 560      | 658     | 675      | 2.620    |
| Mean                  | 92    | 221    | 432      | 562      | 677     | 672      | 2.647    |
| P values              | 0.18  | 0.12   | 0.01     | 0.30     | 0.22    | 0.32     | 0.41     |
| CV %                  | 9.17  | 5.07   | 3.53     | 4.41     | 6.32    | 8.85     | 4.06     |
| Feed Intake, g        |       |        |          |          |         |          |          |
| Treatments, ppm       | 1 - 7 | 7 - 14 | 14 - 21  | 21 - 28  | 28 - 35 | 35 - 42  | 1 - 42   |
| T1 - Negative Control | 114   | 313    | 559 a    | 855      | 1.108   | 1.357    | 4.306 a  |
| T2 - Tiamulin (20/15) | 103   | 302    | 532 ab   | 838      | 1.099   | 1.316    | 4.190 ab |
| T3 - Tiamulin (30/20) | 106   | 303    | 523 b    | 827      | 1.061   | 1.356    | 4.176 b  |
| Mean                  | 107   | 306    | 538      | 840      | 1.089   | 1.343    | 4.190    |
| P values              | 0.37  | 0.35   | 0.03     | 0.10     | 0.25    | 0.67     | 0.03     |
| CV %                  | 10.04 | 4.89   | 4.47     | 3.45     | 4.75    | 7.40     | 2.85     |
| Feed Conversion       |       |        |          |          |         |          |          |
| Treatments, ppm       | 1 - 7 | 7 - 14 | 14 - 21  | 21 - 28  | 28 - 35 | 35 - 42  | 1 - 42   |
| T1 - Negative Control | 1.166 | 1.384  | 1.265 b  | 1.548 b  | 1.699   | 2.037 b  | 1.632 b  |
| T2 - Tiamulin (20/15) | 1.172 | 1.363  | 1.223 a  | 1.466 ab | 1.588   | 1.956 a  | 1.560 a  |
| T3 - Tiamulin (30/20) | 1.178 | 1.415  | 1.239 ab | 1.458 a  | 1.612   | 2.008 ab | 1.594 ab |
| Mean                  | 1.172 | 1.385  | 1.243    | 1.491    | 1.633   | 2.000    | 1.595    |
| P values              | 0.99  | 0.28   | 0.01     | 0.01     | 0.17    | 0.01     | 0.01     |
| CV %                  | 5.66  | 3.88   | 2.11     | 2.97     | 5.73    | 7.31     | 2.95     |

a,b Means within columns with no common superscript are significantly different ( $P < 0.05$ ). \* Values within parentheses adjacent to tiamulin stand for the doses in the starter and grower feeds, ppm.



**Table 3** - Processing yields and abdominal fat (%) at 42 days of broilers fed diets containing salinomycin at 66 ppm combined or not with tiamulin\*.

| Treatments, ppm       | Carcass | Fat    | Thighs | Drum   | Breast | Tender | Wings  |
|-----------------------|---------|--------|--------|--------|--------|--------|--------|
| T1 - Negative Control | 77.14   | 1.71   | 14.06  | 18.72  | 23.94  | 4.96   | 11.24  |
| T2 - Tiamulin (20/15) | 77.83   | 1.43   | 13.71  | 18.70  | 24.98  | 4.89   | 11.30  |
| T3 - Tiamulin (30/20) | 77.77   | 1.42   | 13.72  | 18.64  | 24.85  | 5.02   | 11.31  |
| Mean                  | 77.58   | 1.52   | 13.83  | 18.69  | 24.59  | 4.96   | 11.28  |
| P values              | 0.7241  | 0.0735 | 0.5659 | 0.6486 | 0.1443 | 0.1188 | 0.7916 |
| CV %                  | 4.31    | 17.44  | 5.21   | 6.83   | 5.86   | 5.21   | 5.55   |

(P ≤ 0.05). \* Values within parentheses adjacent to tiamulin stand for the doses in the starter and grower feeds, ppm.

Pulse medication of broilers from 1 to 10 and 21 to 27 d with TIA at 0, 20, 30, or 50 ppm did not affect the live performance of broilers fed SAL at 60 ppm (Islam *et al.*, 2008b). Actually, some studies showed that TIA at 20 and 30 ppm improved body weight gain and feed conversion (Islam *et al.* 2008a; Islam *et al.* 2008b). Considering production cost, Islam *et al.* (2008a) found that 30 ppm of TIA produced the best economic return per unit of body weight gain.

## CONCLUSIONS

Tiamulin included in broiler diets and fed from 1 to 21 and 22 to 42 days at 20 and 15 ppm, respectively, led to improvements in feed conversion.

The administration of 30/20 or 20/15 ppm of TIA in diets from 1 to 21 and 22 to 42 days of age, which also contained 66 ppm SAL, did not impair broiler performance when evaluated using industry standard measurements of live performance and processing yields.

## REFERENCES AND NOTES

Augustine PC, Walkins KL, and Danforth HD. Effects of monensin on ultrastructure and cellular invasion by turkey coccidian *Eimeria adenoides* and *Eimeria meleagridis*. *Poultry Science* 1992; 71:970-978.

Chapman HD. Use of anticoccidial drugs in broiler chickens in the United States: Analysis for the years 1995 to 1999. *Poultry Science*, 2001; 80:572-580.

Chapman HD, Johnson ZB. Use of antibiotics and roxarsone in broiler chickens in the USA: Analysis for the years 1995 to 2000. *Poultry Science*, 2002; 81:356-364.

Hanrahan L, Corrier D, Nagi S. Monensin toxicosis in broiler chickens. *Veterinary Pathology* 1981; 18:665-671.

Horrox NE. Monensin-tiamulin interaction risk to poultry. *Veterinary Record* 1980; 106:278.

Islam KMS, Afrin S, Khan MJ, Das PM, Hassan MM, Valks M, Burch DGS, Pesti GM. Compatibility of a combination of tiamulin plus

chlortetracycline with salinomycin in feed during a long-term co-administration in broilers. *Poultry Science* 2008a; 87:1565-1568.

Islam KMS, Afrin S, Das PM, Hassan MM, Valks M, Klein U, Burch DGS, Kempainen BW. Compatibility of a combination of tiamulin and chlortetracycline with salinomycin in feed during a pulsed medication program co-administration in broilers. *Poultry Science* 2008b; 87:2528-2534.

Kart A, Bilgili A. Ionophore antibiotics: Toxicity, mode of action and neurotoxic aspect of carboxylic ionophores. *Journal of Animal and Veterinary Advances* 2008; 6:748-751.

Lodge NJ, Comben N, Roberts NL, Fairley C. Safety of lasalocid in turkeys and its compatibility with tiamulin. *Veterinary Record* 1988; 122:576-578.

Meingassner J, Schmook F, Czok R, Mieth H. Enhancement of the anticoccidial activity of polyether antibiotics in chickens by tiamulin. *Poultry Science* 1979; 58:308-313.

Nebbia C, Ceppa L, Dacasto M, Carletti M, Nachtmann C. Oxidative metabolism of monensin in rat liver microsomes and interactions with tiamulin and other chemotherapeutic agents: Evidence of the involvement of cytochrome P-450 3<sup>a</sup> subfamily. *Drug Metabolism and Disposition* 1999; 27:1039-1044.

SAS Institute. SAS User's Guide. Version 8 ed. SAS Inst. Inc., Cary, NC 2001.

Schuhmacher A, Bafundo KW, Islam KMS, Aupperle H, Glaser R, Schoon HA, Gropp JM. Tiamulin and semduramicin: effects of simultaneous administration on performance and health of growing broiler chickens. *Poultry Science* 2006; 85:441-445.

Stipkovits L, Salyi G, Glavits R, Burch DGS. Testing the compatibility of a combination of tiamulin/chlortetracycline 1:3 premix (Tetramutin-Novartis) given in feed at different levels with salinomycin in chickens. *Avian Pathology* 1999; 28:579-586.

Uchimura M, Iwasaki H, Asaoka M, Tsuchiya H, Udatsu S, Hamaguchi S, Oshikawa N. Leg weakness of chickens due to combined administration of monensin and Terra-egg. *Journal of the Japanese Society of Poultry Diseases* 1978; 14:121-128.

Umemura T, Nakamura H, Goryo M, Itakura C. Histopathology of monensin-tiamulin myopathy in broiler chicks. *Avian Pathology* 1984; 13:459-467.

Van Vleet J, Runnels L, Cook J, Scheidt A. Monensin toxicosis in swine: Potentiation by tiamulin administration and ameliorative



effect of treatment with selenium and/ or vitamin E. American Journal of Veterinary Research 1987; 48:1530-1534.

Witkamp R, Nijmeijer S, Monshouwer M, Van Miert A. The antibiotic tiamulin is a potential and inhibitor of cytochrome P-450 /3A via the formation of a stable metabolic intermediate complex. Drug Metabolism and Disposition 1995; 23:542-547.