Some pharmacodynamic interactions between salinomycin and vitamin E or selenium in chickens

S.E. El-Sadek¹, M. A. Tohamy¹, Abeer A. El-Badry², Noha A. M. Fouad², A. A. M. El-Gendy¹*

¹Department of Pharmacology, Faculty of Veterinary Medicine, Beni-Suef University, Beni-Suef 62511, Egypt and ²Animal Health Research Institute, Qena, Egypt.

The present study was conducted to determine the effect of salinomycin at a concentration 60 and 120 ppm alone and with vitamin E or selenium on haematological and biochemical parameters and histopathological changes of the treated chicken. Salinomycin (120 ppm) induced decrease in body weight, feed consumption and feed conversion efficiency. In addition, when salinomycin (120 ppm) given with vitamin E, the body performance improved significantly, but when sodium selenite used, body performance significantly decreased. Salinomycin at concentration 120 ppm induced decrease in blood parameters (RBCs count, TLC count, Hb content and PCV %). Concurrent use of vitamin E with salinomycin leads to improvement of these parameters. Salinomycin at 120 ppm induced significant increase in enzymes activities (ALT and AST). The uses of vitamin E with salinomycin (120 ppm) caused significant decrease in these activities. In contrast to selenium, which reduce the activity of AST enzyme only. Salinomycin at 120 ppm decreased the total protein concentration and increased the level of creatinine and uric acid. Concurrent administrations of vitamin E or selenium with salinomycin have no effect on these parameters. At 120 ppm salinomycin, selenium increased the creatinine concentration in blood serum. The drug at 60 or 120 ppm induced various pathological changes in certain tissues (liver, heart, kidney and skeletal muscle) ranged from degeneration to necrosis of these tissues. Concurrent administration of salinomycin with vitamin E or selenium revealed that vitamin E decreased the pathological changes of studied tissues.

Coccidiosis is among the most important diseases of poultry worldwide caused by a protozoan parasite, *Eimeria*. The parasite invades the cells of the intestine producing enteritis, diarrhoea and mortality. The bird develops a disability to absorb sugars, amino acids, vitamins, fats and minerals through the disruption of the integrity of the intestinal mucosa (Greif, 2000; Persia et al., 2006; Zhao et al., 2006 and Mansoori et al., 2008). In order to prevent, control and/or treat poultry coccidiosis, several coccidiostats and coccidiocidal drugs have been developed and used commercially. The ionophore antibiotics such as lasalocid, maduramicin, monensin, narasin and salinomycin are widely used in poultry for the prevention and treatment of coccidiosis caused by *Eimeria* species (Lindsay and Blagburn, 2001). Salinomycin, a polyether antibiotic drug belonging to the group of ionophores, is produced by fermentation by the Streptomyces albus strain (Blazsek and Kubis, 2005). Salinomycin is extensively used as a coccidiostat in poultry and other livestock and is also commonly fed to ruminant animals to improve feeding efficiency of animals (Sparidan et al., 2007). Ionophores toxicity could be probably due to oxidative damage (Khan et al., 1995 and Kamashi et al., 2004). Such damage can be prevented by the supplementation of antioxidants in feed (Main, 2000).

Vitamin E plays important roles in various biochemical and physiological processes, including antioxidation (Brigelius-Flohe et al., 2002, Fang et al., 2002). In nutritional and physiological research, vitamin E supplementation has been proven to improve growth performance (Kocaba and Gatlin, 1999), enhance immunity (Gatlin, 2002; Sealey and Gatlin, 2002; Puangkaew et al., 2004; Trushenski and Kohler, 2007) and restore impaired immunity (Montero et al., 1998; Sahoo and Mukherjee, 2002), as well as influence neuroendocrine function (Khan and Thomas, 2004).
Selenium is an important part of the glutathione (GSH) peroxidase family of seleno-enzymes (Gladyshev and Hatfield, 1999) that are involved in the antioxidant protection of cells against oxidative stress (Tapiero et al., 2003; Elango et al., 2006 and Ortac et al., 2006). Selenium exerts its protective effect against oxidative damage by decreasing the amount of free radicals and increasing the synthesis of glutathione peroxidase, which catalyses the breakdown of toxic hydrogen peroxide and lipid hydroperoxides (Schrauzer, 2005).

The present study aimed to demonstrate the effects of administration of salinomycin (at a concentrations 60 and 120 ppm) alone and in combination with vitamin E or selenium on performance of broilers. Also, haematological and biochemical parameters as well as histopathological changes were studied.

Materials and Methods

Drugs. Salinomycin (Coxistac®) was obtained from Animal Health Division Pfizer Company, Cairo, Egypt. Vitamin E obtained as a pure powder from F. Hoffmann-La Roche, Basle, Switzerland. Selenium (sodium selenite) obtained as a pure powder from Animal Health Research Institute, Giza, Egypt.

Experimental protocol. Two hundred and ten, one-day old Ross broiler chicks were used in this study. The birds were obtained from the Hatchery of Cairo Poultry Company. The birds were fed on a ration prepared in Faculty of Agriculture (South Valley University) according to National Research Council (NRC 2004). The chicks were reared in a well cleaned shed under standard hygienic conditions. Feeds and water were provided ad libitum to birds. Each pen was equipped with ventilation fans which used to control recommended temperature and 24 hours of light. The birds were vaccinated at the 7th day of age with the Hitchner B1 strain against Newcastle disease in drinking water then vaccinated at the 18th day of age by LaSota vaccine (against Newcastle disease) in drinking water. Moreover, birds were vaccinated against infectious bursal disease at days 14, 21 and 35. The broiler chicks were divided into 7 groups (each group 30 chick) as follow: The first group was fed only on basal diet as negative control. While the 2nd and 3rd groups were fed on the basal ration mixed with salinomycin only at concentrations 60 and 120 ppm (Kamashi et al., 2004), respectively. The 4th and 5th groups were fed on the basal diet containing salinomycin 60 and 120 ppm with vitamin E 300 mg kg⁻¹ (Jayasree et al., 2003), respectively. At the same time, the 6th and 7th groups were fed on the basal ration mixed with salinomycin at the same two concentrations with selenium 0.1 ppm (Yarsan, 1998), respectively.

Birds of each group were weighed every week individually using a sensitive balance and the mean body weight was calculated and recorded. A known weighed amount of feed was given to birds of each group daily in the morning, then the remaining amount was weighed and subtracted from the original amount of offered feed. The average amount of feed consumed per bird was calculated and recorded after respective time of weighing of bird. Mean weight gain of each group was calculated weekly by subtracted the previous body weight and the next one then recorded. Feed conversion ratio (FCR) was calculated according to Brady (1968) using following formula:

\[
\text{FCR} = \frac{\text{Feed consumption in a given period}}{\text{Body weight gain at the same period}}
\]

Two blood samples were collected from the wing vein of five birds in each group weekly after the first week. The first blood portion added to an anticoagulant EDTA (1 mg ml⁻¹) and used in haematological studies, while the second portion was taken without anticoagulant, left to clot then centrifuged at 3000 rpm for 15 minutes to obtain serum that kept at -20 °C until assayed for biochemical analysis.

Total erythrocyte and leukocyte counts, Hb content, PCV %, erythrocyte indices, differential leukocyte count, Total protein, albumin and globulin concentrations, ALT and AST activities, creatinine and uric acid concentrations were determined according to methods described by Natt and Herrick (1952), Varley (1980), Schalm et al., (1975), Wintrode (1932), Schalm (1961), Gornall et al., (1949), Doumas et al., (1971), Reitamand and Frankel (1957), Doolan et al., (1962), Richterich and Colombo (1978), respectively.

At the end of the experimental period, five birds from each group were slaughtered and tissue samples from liver, kidney, heart and skeletal muscle were taken in buffer formalin 10 % solution then sectioned and stained with Haematoxylin and Eosin (H&E) (Claydan, 1971) for histopathological examination.

Results were expressed as mean and standard error (S.E) and statistically analyzed using student "t" test and analysis of variance...
Results

The effects of salinomycin and vitamin E or selenium on the different body performances are presented in table (1). Salinomycin (120 ppm) induced a decrease in the body weight, feed consumption and feed conversion efficiency. In addition, when salinomycin (120 ppm) was given with vitamin E, the body performance improved significantly, but when sodium selenite was used, the body performance significantly decreased.

The effect of salinomycin and vitamin E or selenium on blood picture is recorded in table (2). Salinomycin at concentration 120 ppm induced a decrease in blood picture (RBCs count, TLC count, Hb content and PCV %). Concurrent use of vitamin E with salinomycin caused an improvement of these parameters.

As indicated from the effect of the drug on the different biochemical parameters recorded in table (3), salinomycin at 120 ppm induced a significant increase in enzymes activities (ALT and AST). The use of vitamin E with salinomycin (120 ppm) caused a significant decrease in these activities. In contrast to selenium, which reduced the activity of AST enzyme only. Salinomycin at 120 ppm decreased the total protein concentration and increased the level of creatinine and uric acid. Concurrent administrations of vitamin E or selenium with salinomycin have no effect on these parameters. At 120 ppm salinomycin, selenium increased the creatinine concentration in blood serum.

The histopathological studies revealed that salinomycin at 60 or 120 ppm in chicken's ration induced various pathological changes in certain tissues (liver, heart, kidney and skeletal muscle) ranged from degeneration to necrosis of these tissues. The histopathological changes resulted in chicken's liver from administration of salinomycin 60 ppm were shown in figures (1) and (2), while figures (3) and (4) show the changes in liver after concurrent administration of salinomycin at 60 ppm with vitamin E or selenium. Concurrent administration of salinomycin with vitamin E or selenium revealed that vitamin E decreased the pathological changes of studied tissues.

Table (1): Effect of salinomycin and vitamin E or selenium on body performance (Mean ± S.E) (N=5)

<table>
<thead>
<tr>
<th>Item</th>
<th>Body weight (gm)</th>
<th>Feed consumption (gm)</th>
<th>Weight gain (gm)</th>
<th>Feed conversion ratio (FCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st week</td>
<td>6th week</td>
<td>1st week</td>
<td>6th week</td>
</tr>
<tr>
<td>Control</td>
<td>131.56±4.16</td>
<td>1519.2±37.3</td>
<td>1010.4</td>
<td>71.48±2.61</td>
</tr>
<tr>
<td>Salinomycin 60</td>
<td>121.4±5.36</td>
<td>1464.7±31.2</td>
<td>980</td>
<td>61.05±2.91</td>
</tr>
<tr>
<td>Salinomycin 120</td>
<td>120.6±3.47</td>
<td>1117.9±36.5</td>
<td>103</td>
<td>78.7</td>
</tr>
<tr>
<td>Salinomycin 60 + vitamin E</td>
<td>132.4±4.44</td>
<td>1499.2±42.2</td>
<td>130.1±4.14</td>
<td>301.3±13.52</td>
</tr>
<tr>
<td>Salinomycin 120 + vitamin E</td>
<td>128.1±5.58</td>
<td>1264.5±35.1</td>
<td>113.3</td>
<td>103</td>
</tr>
<tr>
<td>Salinomycin 60 + Selenium</td>
<td>116.5±4.14</td>
<td>1190.2±38.6</td>
<td>100</td>
<td>78.3</td>
</tr>
<tr>
<td>Salinomycin 120 + Selenium</td>
<td>114.9±2.27</td>
<td>1098.6±20.4</td>
<td>103</td>
<td>74.5</td>
</tr>
</tbody>
</table>

The different small letter in the same column in each time mean significant difference at (P < 0.05), while the capital letter mean significant difference at (P < 0.01).
Table (2): Effect of salinomycin and vitamin E or selenium on blood picture at the 6th week (Mean ± S.E) (N=5).

<table>
<thead>
<tr>
<th>Item</th>
<th>RBCs (10⁶/mm³)</th>
<th>Hb (gm/dl)</th>
<th>PCV (%)</th>
<th>MCV (mm³)</th>
<th>MCH (10¹²)</th>
<th>MCHC (%)</th>
<th>TLC (10³)</th>
<th>Lymphocytes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.67±0.03</td>
<td>8.81±0.12</td>
<td>27.57±0.33</td>
<td>103.14±1.33</td>
<td>32.93±0.12</td>
<td>31.94±0.25</td>
<td>13.26±0.52</td>
<td>64.21±1.9</td>
</tr>
<tr>
<td>Sal-60</td>
<td>2.61±0.01</td>
<td>8.52±0.10</td>
<td>27.49±0.20</td>
<td>105.96±3.86</td>
<td>32.79±0.88</td>
<td>31.01±0.59</td>
<td>11.55±0.61</td>
<td>45.55±2.9</td>
</tr>
<tr>
<td>Sal-120</td>
<td>2.42±0.03 b</td>
<td>8.21±0.09</td>
<td>25.69±0.38</td>
<td>105.75±1.83</td>
<td>33.93±0.31</td>
<td>31.96±0.12</td>
<td>8.60±0.58</td>
<td>39.02±0.7</td>
</tr>
<tr>
<td>Sal-60 + vit. E</td>
<td>2.56±0.06</td>
<td>8.63±0.14</td>
<td>27.54±0.38</td>
<td>107.73±2.55</td>
<td>33.70±0.22</td>
<td>31.32±0.17</td>
<td>13.63±0.57</td>
<td>62.23±3.9</td>
</tr>
<tr>
<td>Sal-120 + vit. E</td>
<td>2.59±0.05</td>
<td>8.28±0.16</td>
<td>26.58±0.36</td>
<td>103.56±2.05</td>
<td>32.05±0.43</td>
<td>31.15±0.26</td>
<td>9.61±0.50</td>
<td>61.07±5.7</td>
</tr>
<tr>
<td>Sal-60 + Se</td>
<td>2.54±0.09 a</td>
<td>8.10±0.12</td>
<td>26.41±0.69</td>
<td>101.01±2.42</td>
<td>32.01±0.72</td>
<td>30.70±0.38</td>
<td>8.10±0.48</td>
<td>35.34±3.3</td>
</tr>
<tr>
<td>Sal-120 + Se</td>
<td>2.45±0.11 a</td>
<td>7.82±0.15</td>
<td>24.71±0.56</td>
<td>99.36±2.98</td>
<td>32.09±1.35</td>
<td>31.66±0.16</td>
<td>7.50±0.76</td>
<td>32.33±3.0</td>
</tr>
</tbody>
</table>

The different small letter in the same column in each time mean significant difference at (P < 0.05), while the capital letter mean significant difference at (P < 0.01).

* RBCs = Red blood cell count  
* Hb = Hemoglobin concentration  
* PCV = Packed cell volume  
* MCV = Mean corpuscular volume  
* MCH = Mean corpuscular hemoglobin  
* MCHC = Mean corpuscular hemoglobin concentration  
* TLC = Total leukocytes count

Table (3): Effect of salinomycin and vitamin E or selenium on content of biochemical parameters at the 6th week (Mean ± S.E) (N=5).

<table>
<thead>
<tr>
<th>Item</th>
<th>Total protein (gm/dl)</th>
<th>Albumin (gm/dl)</th>
<th>Globulin (gm/dl)</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>Creatinine (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.94±2.31</td>
<td>0.85±0.07</td>
<td>2.10±0.07</td>
<td>6.28±0.15</td>
<td>66.89±1.20</td>
<td>0.61±0.04</td>
<td>6.81±0.16</td>
</tr>
<tr>
<td>Sal-60</td>
<td>2.72±2.27</td>
<td>0.85±0.06</td>
<td>1.86±0.09</td>
<td>7.16±0.67</td>
<td>69.71±2.40</td>
<td>0.65±0.06</td>
<td>6.99±0.14</td>
</tr>
<tr>
<td>Sal-120</td>
<td>2.23±2.01 ab</td>
<td>0.80±0.05</td>
<td>1.43±0.07 a</td>
<td>7.77±0.30</td>
<td>74.13±1.67</td>
<td>0.87±0.08 abc</td>
<td>7.62±0.30</td>
</tr>
<tr>
<td>Sal-60 + vit.E</td>
<td>2.63±2.23</td>
<td>0.96±0.09</td>
<td>1.67±0.13</td>
<td>6.18±0.49</td>
<td>66.93±2.35</td>
<td>0.65±0.05</td>
<td>6.76±0.35</td>
</tr>
<tr>
<td>Sal-120 + vit.E</td>
<td>2.41±2.17</td>
<td>0.88±0.05</td>
<td>1.53±0.25 a</td>
<td>7.19±0.28</td>
<td>66.31±2.36</td>
<td>0.70±0.03</td>
<td>7.28±0.40</td>
</tr>
<tr>
<td>Sal-60 + Se</td>
<td>2.56±2.06</td>
<td>0.84±0.04</td>
<td>1.72±0.23</td>
<td>6.59±0.52</td>
<td>67.47±2.47</td>
<td>0.71±0.07</td>
<td>7.37±0.37</td>
</tr>
<tr>
<td>Sal-120 + Se</td>
<td>2.00±2.08 ab</td>
<td>0.81±0.05</td>
<td>1.19±0.25 ab</td>
<td>7.58±0.20</td>
<td>66.82±1.87</td>
<td>1.11±0.08 abc</td>
<td>7.73±0.28</td>
</tr>
</tbody>
</table>

The different small letter in the same column in each time mean significant difference at (P < 0.05), while the capital letter mean significant difference at (P < 0.01).
Fig. (1): Liver of birds treated with Salinomycin (60 ppm) alone revealing diffuse vacuolar degeneration of hepatocytes with individual cell necrosis (H&E x 125).

Fig. (2): Liver of birds treated with Salinomycin (60 ppm) alone revealing diffuse vacuolar degeneration of hepatocytes with individual cell necrosis (H&E x 250).

Fig. (3): Liver of birds receiving Salinomycin (60 ppm) with selenium showing few focal areas of necrosis with inflammatory cell aggregation and congestion of some blood vessels (H&E x 125).

Fig. (4): Liver of birds receiving Salinomycin (60 ppm) with vit. E showing dilatation of sinusoidal capillaries and destruction of some hepatic cells (H&E x 125).


**Discussion**

At concentration of 120 ppm salinomycin, the body weight and body weight gain were significantly decreased when compared with those of the control chickens. These findings were in accord with those of Rizvi et al., (1999). Co-administration of salinomycin (120 ppm) with vitamin E revealed significant increase in body weight compared to salinomycin 120-medicated group. The improvement in the body weight of birds fed vitamin E could be attributed to some of its biological function such as its role on enzymatic oxidation-reduction, nucleic acid metabolism and in promoting the activity of easily oxidized substances as carotenoids and vitamin A (Osman, 1999). Moreover, such improvement may be due to the role of vitamin E as an immune stimulant (Franchini et al., 1991) which in turn raises the bird resistance. Another study reported an improved growth rate in chicks supplied with vitamin E due to high bone formation rates (Xu et al., 1995). This possibility was confirmed by Watkins and Chen (1997), who stated that vitamin E supplementation, significantly increased bone calcium and phosphorus and thereby improve growth rate.

Combination of salinomycin (120 ppm) with vitamin E revealed a significant increase in body weight gain compared with the group given salinomycin only at concentration 120 ppm. This improvement in body gain was confirmed by the findings of Swain et al., (2000), Villar-Patino et al., (2002) and Raza et al., (1997). High doses of dietary vitamin E increased nutrient digestibility in Japanese's quails (Sahin and Kucuk, 2001).

At concentration of 120 ppm salinomycin, selenium decreased the body weight gain of chicken compared to those given salinomycin alone. Similar result obtained by Khan et al., (1993). There are significant decreases in total erythrocytic count (TEC), Hb concentration and PCV % in chicken given salinomycin at concentration of 120 ppm and this result was agreed with Salay et al., (2002). Supplementation of vitamin E significantly increased the TEC, Hb content and PCV % and this was confirmed by Abdel-Raheem and Abdel-Ghaffar (2004).

The protective effect of vitamin E against the alterations induced by salinomycin on blood picture (TEC, Hb and PCV) in this study could be attributed to the role of vitamin E as fat soluble antioxidant which protects the biological membranes from oxidative damage and decrease osmotic fragility of erythrocytes. (Abas, 2002).

Chicken administered salinomycin at 120 ppm show significant decrease in WBC's count. This effect could be attributed to the immunosuppressive properties of some anticoccidials ionophores as it inhibit both cellular and humoral immune response (Karlson and Malcolm, 1978).

Concerning differential leucocytic count (DLC), salinomycin at 60 or 120 ppm evoked a significant decrease in the number of lymphocyte with increase in heterophil number and decrease in monocyte count (only at 120 ppm) compared to non-medicated chicken. The same result recorded by Shalaby et al., (1993) who reported that marked immunosuppressive effect caused by using salinomycin characterized by lowered titres of antibodies to Newcastle disease virus vaccine (NDV), decrease in the relative weight of lymphoid organs, reduction in heterophil percentage and lower mitogenic response of peripheral blood lymphocytes.

A significant decrease was recorded in the total protein and globulin but no changes in the level of albumin in serum of chicks given 120 ppm of salinomycin. Arun et al., (2003) recorded a significant decrease in total protein, albumin and globulin in chickens given the drug at 120 ppm. Kamashi et al., (2004) declared salinomycin at level of 120 ppm caused a significant decrease in total protein level in blood but not affect albumin or globulin level. On the other hand Mazurkiewicz et al., (1989) reported that administration of salinomycin sodium in turkeys at toxic level evoked increase in total proteins in blood. This increase may be due to the higher sensitivity of turkey to salinomycin than broiler chicks.

Chicks fed salinomycin at a level of 120 ppm evoked a significant increase in ALT and AST activities, compared to non-medicated group. This was agreed with Arun et al., (2003) and Kamashi et al., (2004). Co-administration of vitamin E with salinomycin (120 ppm) induce significant decrease in the activities of ALT and AST., while selenium revealed significant decrease only in AST activity when compared to salinomycin 120-medicated group.

Administration of salinomycin for 6 weeks at concentration 60 or 120 ppm, showed variable concentration-dependent histopathological changes in the liver, kidney, heart and skeletal muscle ranged from degeneration to necrosis (of some hepatic and renal cells), focal areas of degeneration to hyalinization (of heart muscle)
and few focal areas of loss of striation to loss of most of the muscle fiber (of skeletal muscle).

This concentration dependant results were agreed with those reported by Shehata et al., (1990), Gill et al., (1991) and Ahmed et al., (2000). Co-administration of selenium (0.1 ppm) with salinomycin at 60 or 120 ppm not prevents the hazard effect of salinomycin on liver, kidney, heart and skeletal muscle tissues, but administration of vitamin E with salinomycin revealed partial protection against salinomycin hazardous effects especially those in the liver and skeletal muscle. Administration of vitamin E to chicken is more efficient than selenium in the prevention of hazardous effects of monensin on heart and skeletal muscle tissues (Yarsan, 1998).

It is concluded that when salinomycin is given to chicken at concentration of 120 ppm in ration induces undesirable effects on all estimated parameters (physical, haematological, biochemical and histopathological) and on studied tissues. Concurrent use of salinomycin with vitamin E or selenium reveals that, vitamin E is more efficient than selenium in the prevention of the hazardous effects of salinomycin. Therefore, co-administration of vitamin E with salinomycin is recommended in the poultry feed to protect against the hazardous effects of salinomycin.

References
Lindsay, D. S. and Blagburn, B. L. (2001): Antiprotozoan...


بعض التداخلات الفيروموكسيميكية بين عقار ساليتونيسين وفيتامين D3 والسيلينيوم في الدواجن

ضرر هذه الدراسة توضيح تأثير عقار الساليتونيسين متغيرا عند تركيز 60 مجم/كمج أو 120 مجم/كمج ومع فيتامين D3 أو السيلينيوم في الدواجن على الخواص الطبيعية (نوع النمو، معدل التحول الغذائي) ومكونات الدم وكذلك بعض نشاط الإنتاج والعملية. اعتمدت الدراسة على النتائج أساسية نسبية (نسبة الإنتاج النباتية) والناجحة لاحظ أن عقار الساليتونيسين عند تركيز 60 مجم/كمج و120 مجم/كمج على التوالي (نسبة الإنتاج النباتية) والناجحة لاحظ أن عقار الساليتونيسين عند تركيز 60 مجم/كمج و120 مجم/كمج متزامن مع فيتامين D3 عند تركيز 300 مجم/كمج على النمو والناجحة لاحظ أن عقار الساليتونيسين عند تركيز 60 مجم/كمج و120 مجم/كمج متزامن مع السيلينيوم عند تركيز 0.1 مجم/كمج على النمو والناجحة لاحظ أن عقار الساليتونيسين عند تركيز 120 مجم/كمج يحدث نقص واضح في كل من وزن الطائر وكمية الطاقة المستهلكة ونسبة النمو. هذه النتائج قد تحدث تدخلًا يضيف لفترة شهيرة في النمو والناجحة لاحظ أن عقار الساليتونيسين متزامن مع فيتامين D3 عند تركيز 120 مجم/كمج. بعد تدخلات في جودة الدم ونسبة الإنتاج النباتية. إذا ترتبط عقار الساليتونيسين مع فيتامين D3، وقد ينتج عن ذلك نقص واضح في نسبة الإنتاج النباتية. لا يوجد تدخلات في جودة الدم ونسبة الإنتاج النباتية إذا ترتبط عقار الساليتونيسين مع فيتامين D3، وقد ينتج عن ذلك نقص واضح في نسبة الإنتاج النباتية.

الخلايا حسب الجرعة المعتدلة حيث قام عقار الساليتونيسين عند تركيز 120 مجم/كمج. قد أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو. أدى تدخلات غير مرغوب فيها على كل المعايير المقترنة (نوع النمو، معدل التحول الغذائي) ومكونات الدم ونوع النمو.

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