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## Haematological and serum changes in goats experimentally intoxicated with sodium selenite

AHMED (K. E.), ADAM (S. E. I.), IDRIS (O. F.), TAG EL DIN (M. H.). Changements sériques et hématologiques chez des chèvres expérimentalement intoxiquées avec du sélénite de sodium. *Revue Elev. Méd. vét. Pays trop.*, 1988, 41 (4) : 319-325.

On a enregistré les changements chimiques, biochimiques et hématologiques chez des chèvres de Nubie qui avaient reçu, quotidiennement, par voie orale, des doses uniques ou fractionnées, selon le cas, de 160, 90, 40, 20, 5, 1, 0,5 et 0,25 mg/kg de sélénite de sodium. Aux doses les plus élevées, il a provoqué insomnie, écume au museau, dyspnée, diarrhée, parésie des membres postérieurs, décubitus puis mort. L'augmentation des valeurs de l'hémoglobine, de l'hématocrite et du nombre des globules rouges indique une hémococoncentration. Chez les chèvres qui ont reçu 5 mg/kg/jour de sélénite de sodium, on a observé une anémie macrocytaire hypochromique et une leucopénie avant la mort. Une augmentation dans l'activité des SGOT et de la  $\gamma$ -GT, et dans la concentration de l'urée et du phosphore minéral et une diminution dans celle des protéines totales et du calcium ont été détectées dans le sérum. Le sélénite de sodium, aux doses quotidiennes de 1, 0,5 et 0,25 mg/kg n'était pas toxique pour les chèvres. *Mots clés* : Chèvre - Sélénite de sodium - Intoxication - Sérologie - Hématologie - Sudan.

### INTRODUCTION

Changes in the activity of a number of enzymes in serum have been investigated in many diseases of man and animals and have been found to be useful diagnostic and prognostic aids. It is generally accepted that an increase in the activity of an enzyme in the serum can be attributed to leakage from injured tissues. Many enzymes are widely distributed in the tissues and are detected in the serum in increased amounts in diseases of various organs. Other enzymes are found in higher concentrations in one organ than in the other one and leakage into plasma is likely to arise from damage to the tissue with high enzyme activity.

Increases in the activity of serum sorbitol and glutamic dehydrogenases and arginase have been described in experimental poisoning by carbon tetrachloride and halothane (13) and *Senecio jacoboea* in calves (14), sporidesmin in sheep (11) and sodium selenite in chickens (9).

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Changes in other serum parameters and haematology in domestic animals are also considered useful in the diagnosis of disease. Accordingly, a study of changes in haematology and serum constituents would be especially valuable in diagnosis. In the Sudan, changes in haematology and serum constituents have been studied in experimental poisoning by *Heliotropium ovalifolium* (1), *Crotalaria saltiana* (6) and copper sulphate (3, 21) in sheep and goats, diminazene aceturate in camels (15), chloroform in donkeys (16) and *Jatropha curcas* in calves (5).

The pathology of sodium selenite poisoning in goats was described by AHMED, ADAM, IDRIS and WAHBI (4). In this paper, the biochemical and haematological aspects of selenite toxicity in Nubian goats are presented.

### MATERIALS AND METHODS

#### Animals and dosing

Thirty-one 6-8 month-old Nubian goats of either sex were used. The animals were clinically healthy, kept in pens at the Central Veterinary Research Laboratory, Soba, and fed a concentrate ration plus forage sorghum and water *ad libitum*. The goats were allotted to ten groups. Sodium selenite was dissolved in water and given at 160 mg/kg to goats 1, 2, 3 and 4 (group 1), 80 mg/kg to male goats 5, 6 and 7 (group 2), 80 mg/kg to female goats 8, 9 and 10 (group 3), 40 mg/kg to goats 11, 12, 13, 14 (group 4) and 18 (group 5) as a drench. A daily drench of 20 mg/kg of sodium selenite was given to goats 15, 16 and 17 (group 5), 5 mg/kg to goats 19, 20 and 21 (group 6), 1 mg/kg to goats 22, 23 and 24 (group 7), 0.5 mg/kg to goats 25 and 26 (group 8) and 0.25 mg/kg to goats 27 and 28 (group 9). Goats 29, 30 and 31 (group 10) were undosed controls. Daily drenching was continued until the goats died or were killed.

#### Chemical methods

All goats were bled from the jugular vein on several occasions before dosing and at appropriate intervals thereafter for the determination of the activity of

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serum glutamic oxalo-acetic transaminase (GOT), glutamic pyruvic transaminase (GPT) and  $\gamma$ -glutamyl transferase ( $\gamma$ -GT) and the concentration of total cholesterol and uric acid by use of a kit (Boehringer Mannheim GmbH, Diagnostica, West Germany). The concentrations of serum potassium, sodium and inorganic phosphate were determined by the methods described by VARLEY (20). Serum samples were also examined for the concentrations of urea (10), magnesium (18), calcium (19) and total protein (22).

### Haematological methods

Blood samples were collected into clean bottles containing EDTA as anticoagulant. Haemoglobin concentration (Hb) was measured by the cyanmethaemoglobin technique using a Corning colorimeter 252/6946 (Corning Limited, Halstead, Essex, England). The packed cell volume (PCV) was measured in a microhaematocrit centrifuge (Hawksley and Sons Ltd., England). Red and white blood cells (RBC and WBC) were counted with an improved Neubauer haemocytometers (Hawksley and Sons Ltd., England). A differential leucocyte count was made by the battlement method (17). Mean corpuscular haemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH) and mean corpuscular volume (MCV) were calculated from PCV, RBC and Hb values.

## RESULTS

### The course of toxicity

The course of toxicity to goats of sodium selenite is given in table I. In animals receiving different oral doses of sodium selenite, there were varying mortality rates.

All the goats in groups 1, 2, 3 and 4 died within 2-96 hours after the administration of a single dose of selenite. Three goats in group 5 receiving daily doses of 20 mg/kg of selenite died within 27-53 hours and one goat in the same group was slaughtered 15 days after the administration of a single dose of selenite. All goats of group 6 receiving daily doses of 5 mg/kg of selenite died within 7-31 days. The remaining goats in groups 7, 8 and 9 survived throughout the experimental period and were subsequently slaughtered between days 220 and 225.

The symptoms observed in animals of the different groups were very much alike but they were severe in goats receiving larger doses of selenite. The main signs were hyperexcitability, frothing at the mouth, dyspnoea, diarrhoea and paresis of the hind limbs. The latter sign culminated in recumbency which was followed by death.

### Haematological findings

Haematological examination were not conducted on goats in groups 1, 2 and 3 because none survived more than 20 hours after dosing. The changes in haematology are given for selected goats. In goats 13 (group 4), 16 and 17 (group 5), there were increases in the values of Hb, PCV, RBC and WBC (Fig. 1). Leucocytosis was followed by a terminal leucopenia due to a decrease in the number of lymphocytes. In goats 20 and 21 (group 6) which lived for 17 and 31 days respectively, there were small decreases in the values of Hb, PCV, RBC and WBC. MCV increased and MCHC decreased during terminal stages of the disease (Fig. 2, 3).

### Changes in serum constituents

Assays of serum GOT, GPT,  $\gamma$ -GT, total protein, total

TABLE I The course of toxicity to goats of sodium selenite.

Group	Goat No.	Age (months)	Oral dose of selenite mg/kg	Duration of disease	Remarks
1	1-4	6	160	2 hrs	Died
2	5-7	6	80	2 hrs	Died
3	8-10	6	80	2-20 hrs	Died
4	11-14	6	40	2-96 hrs	Died
5	15-18	6	20	27 hrs-15 days	Died*
6	19-21	6	5	7-31 days	Died
7	22-24	8	1	225 days	Slaughtered
8	25-26	8	0.5	222 days	Slaughtered
9	27-28	8	0.25	220 days	Slaughtered

\* One goat No. 18 was slaughtered 15 days after the administration of a single dose of selenite.

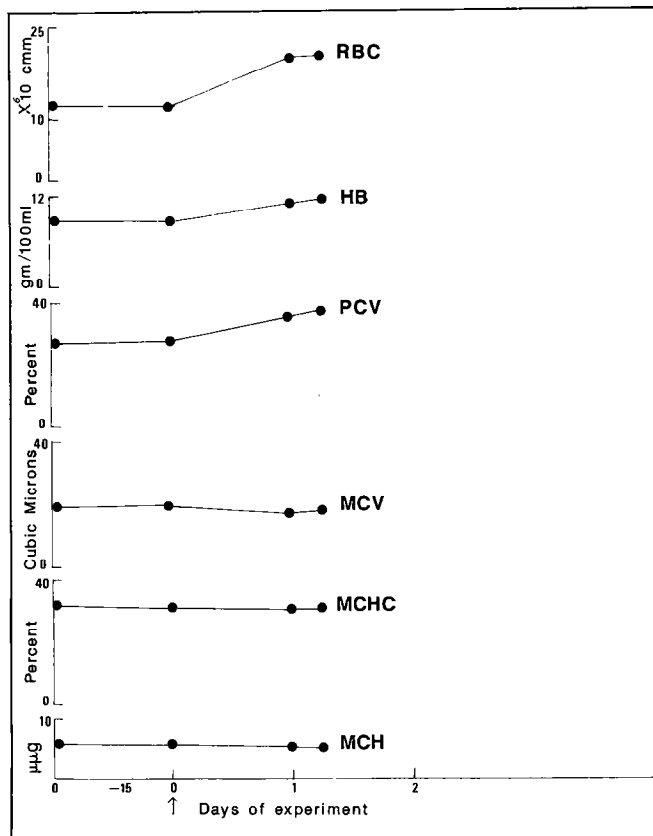


Fig. 1 : Changes in the red cell parameters in group 4, orally dosed with 40 mg/kg of sodium selenite on day 0.

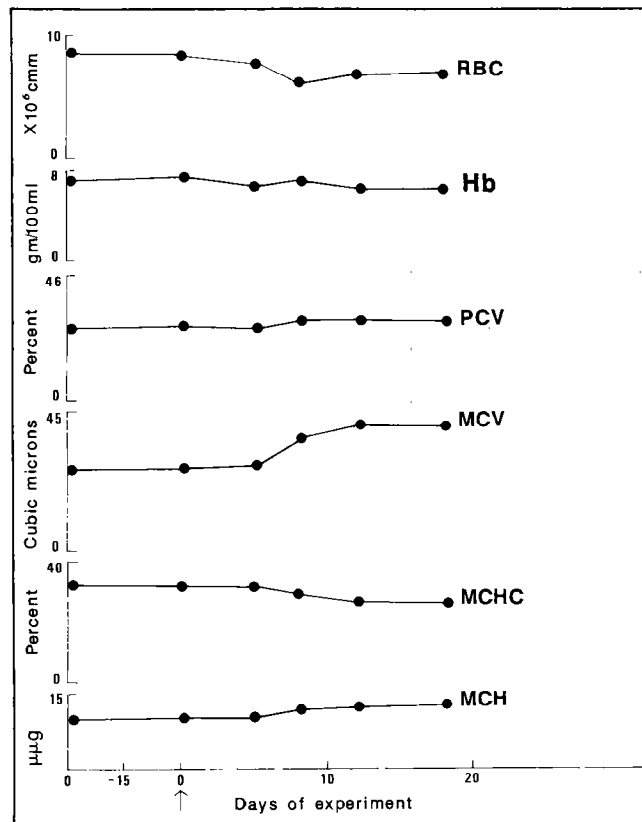


Fig. 2 : Changes in the red cell parameters in goat 20 in group 6, orally dosed with 5 mg/kg/day of sodium selenite for 17 days.

cholesterol, urea, sodium, potassium, calcium, magnesium, inorganic phosphate and uric acid were not done in goats in groups 1, 2 and 3 because none survived more than 20 hours after dosing. Changes in the concentration of serum constituents are given for selected individual animals since they tended to follow a similar pattern in all goats. There were no significant changes in the activity of GPT or in the concentrations of sodium, potassium, cholesterol, magnesium and uric acid in the serum of any of the goats. In goat 14 (group 4) which died on day 4, there were terminal increases in the activity of GOT and  $\gamma$ -GT and decreases in the concentration of calcium and total protein (Fig. 4). In goat 15 (group 5) which died 27 hours after dosing, there were increases in the activity of GOT and  $\gamma$ -GT and in the concentration of urea and decreases in the concentrations of calcium and protein (Fig. 5). In goat 20 (group 6) which died on day 17, the activity of GOT and concentration of urea commenced to rise on day 7 and reached peaks on days 14 and 17, respectively. The concentration of total protein and calcium were reduced terminally (Fig. 6). The activity of  $\gamma$ -GT and concentration of inorganic phosphate fluctuated during the course of the disease. In goat 21 (group 6) which died on day 31, there were significant decreases in the concentrations of calcium and total protein between days 14 and 31. The increase in the concentration of urea occurring on the 7th day were followed

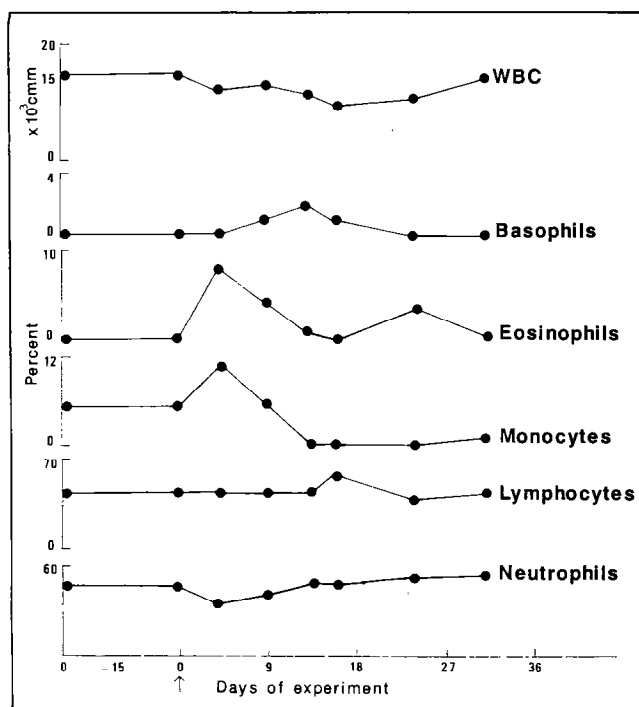


Fig. 3 : Changes in the number of white blood cells in goat 21 in group 6, orally dosed with 5 mg/kg/day of sodium selenite for 31 days.

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TABLE II The concentration of serum constituents in goats dosed daily with small amounts of sodium selenite for 220-225 days.

Group	GPT	GOT	-GT	Cholesterol	Total protein	Urea	Uric acid	K	Na	Mg	Ca	P
7 (1 mg/kg)	(2.5-4) 3.1±0.57	(11.5-26) 18.7±3.4	(30-54) 39.3±13.2	(51-183) 91±36.26	(5.2-6.8) 5.7±0.26	(22.8-59) 40.6±15.58	(0.4-3.5) 1.6±1.27	(12.6-18.5) 14.3±1.89	(246-292) 265.8±13	(1.8-2.5) 2.2±0.24	(7-10) 8.5±0.56	(5-10) 6.3±0.82
8 (0.5 mg/kg)	(2.2-4.5) 3.2±0.54	(13-27.5) 21.4±4.5	(32-62) 44.9±8.3	(52-168) 96.9±34.3	(5-6.8) 5.8±0.69	(17-55) 37.9±11.65	(0.5-3.9) 3.5±1.5	(11.9-22) 16.4±2.4	(260-298) 282±10.3	(1.7-2.8) 2.1±0.23	(3-10.6) 8.6±0.59	(4.25-8) 6±1.19
9 (0.25 mg/kg)	(2.5-4.5) 3.3±0.5	(10-26.5) 19.3±7	(20-51) 34±9.2	(52-124) 75.8±20	(4.8-6.8) 5.2±0.8	(10-94) 42±25.26	(0.9-4) 2.8±1.2	(12.6-22.7) 16.8±2.6	(240-298) 266±15	(1.8-2.7) 2.2±0.25	(8-9.5) 8.7±0.45	(2.8-8.25) 5±1.3
10 (undosed controls)	(2.25-9) 3.25±0.82	(16.5-30.5) 22.8±5.3	(25-56.9) 37.5±9.8	(62-85) 63.8±12.97	(5.2-6.4) 5.7±0.47	(21-54) 35±13.67	(0.8-3.4) 1.4±1.1	(14-17.5) 14.7±1.58	(264-312) 290±11	(2-2.6) 2.3±0.2	(8-12) 10±0.45	(4-7.6) 5.6±1.24
Units	I.U.	I.U.	I.U.	mg/100 ml	g/100 ml	mg/100 ml	mg/100 ml	mg/100 ml	mg/100 ml	mg/100 ml	mg/100 ml	mg/100 ml

Values represent the means ± S.D. ; ranges in parentheses, of 4 groups.

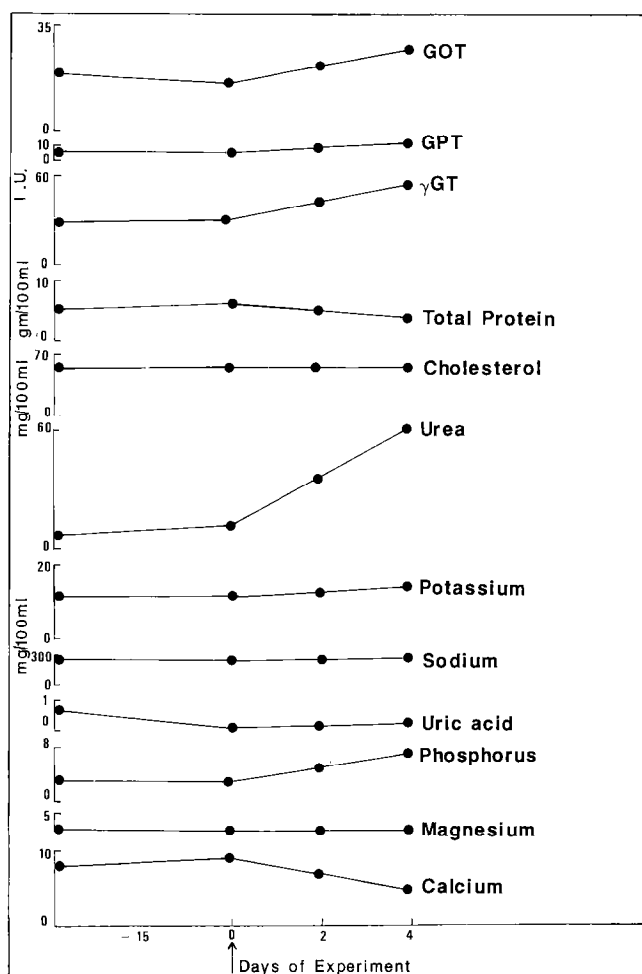


Fig. 4 : Changes in the activities of GOT, GPT and  $\gamma$ -GT and in the concentration of urea, inorganic phosphate, calcium, total protein, cholesterol, sodium, potassium, magnesium and uric acid in the serum of goat 14 in group 4, orally dosed with 40 mg/kg of sodium selenite on day 0.

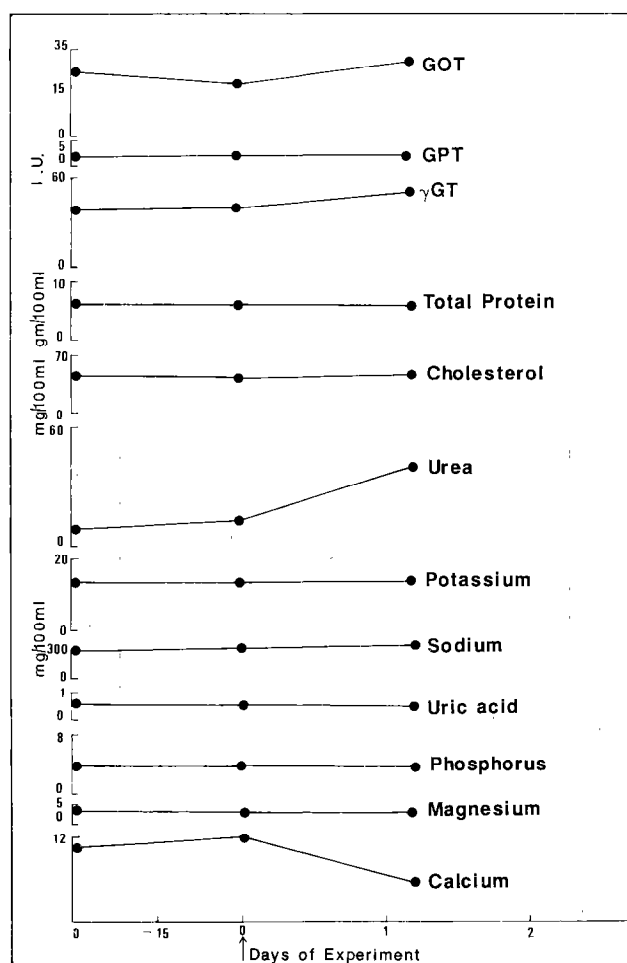


Fig. 5 : Changes in the activities of GOT, GPT and  $\gamma$ -GT and in the concentration of urea, calcium, total protein, inorganic phosphate, magnesium, cholesterol, sodium, potassium and uric acid in the serum of goat 15 in group 5, orally dosed with 20 mg/kg of sodium selenite on day 0.

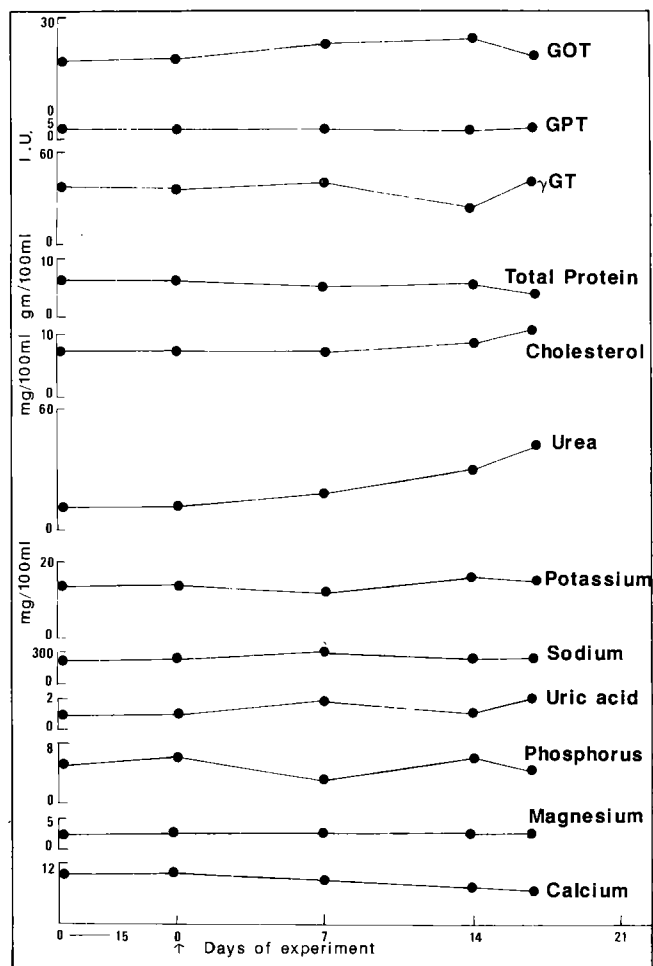


Fig. 6: Changes in the activities of GOT, GPT and  $\gamma$ -GT and in the concentration of urea, inorganic phosphate, calcium, magnesium, cholesterol, total protein, sodium, potassium and uric acid in the serum of goat 20 in group 6, orally dosed with 5 mg/kg/day of sodium selenite for 17 days.

by decreases before death. The activity of GOT was elevated in the period during days 18 and 31. There were no significant changes in concentration of serum constituents in the controls and selenite-dosed goats in groups 7, 8 and 9 (Table II).

## DISCUSSION

The results of this study indicate that goats poisoned by single or repeated daily doses of 160, 80, 40, 20 and 5 mg/kg body weight of sodium selenite developed toxicity within varying periods and succumb to death. In goats, selenite has caused dysfunction of the liver,

kidney, gastrointestinal tract and lungs. The course of selenite toxicity in goats is characterized by significant haematological changes. It is likely that haemoconcentration, indicated by an increase in the values of RBC, PCV and Hb results in urine concentration. However, the fall in the values of RBC, PCV and Hb in goats receiving the small toxic dose of selenite (5 mg/kg/day) may denote development of anaemia (17). The low MCHC values observed shortly before death of the goats may indicate that the anaemia is hypochromic. Since the MCV values are higher than normal in these goats the anaemia thus produced could be described as macrocytic hypochromic. The macrocytic anaemia might have developed as a result of blood loss as evidenced by haemorrhage observed *post-mortem* and the concomitant decrease in the number of RBCs. The observation recorded for WBC in this investigation may denote development of leucopenia. The latter as well as the development of macrocytic hypochromic anaemia were in a way similar to those previously observed in goats and sheep which had been given *J. curcas* (5). It is likely that the presence of aggregates of lymphocytes in the liver, kidneys and lungs (4) and lymphocytopenia point to an immunosuppressive effect. Further investigations will be required in order to examine the effect of selenite on the bone marrow.

Sodium selenite caused a rise in the activity of serum GOT. Since GOT is not a liver specific enzyme, we believe that damage to the liver, kidneys and gastrointestinal tract might have resulted in an increase in the activity of serum GOT. An increase in the activity of serum GOT has been previously observed in *J. curcas* and copper poisonings in goats (3, 5). The lack of change in GPT activity in serum has confirmed previous experiences with this enzyme in ruminants of FORD, ADAM and GOPINATH (13) and ADAM, TARTOUR, OBEID and IDRIS (2). The failure of GPT to leak into plasma is attributed to the small amount of this enzyme in the liver of ruminants. It is likely that the lack of significantly high  $\gamma$ -GT activity in serum was due to the absence of damage to the biliary epithelium. FORD and ADAM (12) mentioned that  $\gamma$ -GT activity in the liver of the horse is similar to that in other species and if this activity is located mainly in the biliary epithelium, leakage into plasma would be expected to accompany biliary lesions in farm animals. The increase in the concentration of urea in the serum indicated renal dysfunction. It is well known that plasma albumin concentration falls in hepato-renal damage. However, intestinal malabsorption of amino acids could be a contributing factor to the low concentration of total serum protein. FORD and ADAM (12) suggested that the activity of  $\gamma$ -GT in the kidney of the horse is higher than in other tissues and that damage to the kidneys could be expected to cause release of the enzyme into urine.

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CORNELIUS and KANEKO (8) suggested that the total serum protein concentration represents the balance between the process of biosynthesis and catabolism or loss by haemorrhage or proteinuria. The same authors mentioned that severe haemorrhage in rats and dogs is accompanied by a decrease in the total concentration of plasma protein. The increase in the concentration of inorganic phosphate and decrease in the level of calcium in the serum of selenite-poisoned goats could have resulted from renal damage. BENTINCK-SMITH (7) suggested that renal damage leads to

the retention of phosphate which in turn results in a reduced absorption of calcium from the intestine and a lowered concentration of calcium in the serum.

There was no change in the concentration of sodium in the serum of selenite-dosed goats. The absence of changes in the concentration of sodium was presumably due to the rapidity with which clinical signs developed in goats giving too little time for changes to be evidenced before the goats died.

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Nubian goats were given single or repeated daily oral doses of 160, 80, 40, 20, 5, 1, 0.5 and 0.25 mg/kg of sodium selenite and the clinical, biochemical and haematological changes were recorded. At higher doses, the selenite produced restlessness, frothing at the mouth, dyspnoea, diarrhoea, paresis of the hind limbs, recumbency and death. Increases in the values of Hb, PCV, and RBC indicated haemoconcentration. In goats given 5 mg/kg/day of sodium selenite, there was macrocytic hypochromic anaemia and leucopenia before death. An increase in the activity of GOT and  $\gamma$ -GT and in the concentration of urea and inorganic phosphate and a decrease in the concentration of total protein and calcium were detected in the serum. Sodium selenite, at daily doses of 1, 0.5 and 0.25 mg/kg was non-toxic to goats. *Key words* : Goat - Sodium selenite - Experimental intoxication - Serology - Haematology - Sudan.

AHMED (K. E.), ADAM (S. E. I.), IDRIS (O. F.), TAG EL DIN (M. H.). Modificaciones serosas y hematológicas en cabras experimentalmente intoxicadas con selenita de sodio. *Revue Elev. Méd. vét. Pays trop.*, 1988, 41 (4) : 319-325.

Se notaron las modificaciones químicas, bioquímicas y hematológicas en cabras de Nubia que habian recibido cada día, por vía oral, dosis únicas o fraccionadas, según el caso, de 160, 80, 40, 20, 5, 1, 0,5 y 0,25 mg/kg de selenita de sodio. Éste provocó, con las dosis más elevadas, insomnio, espumarajos al hocico, disnea, diarrea, paresia de los miembros posteriores, decúbito luego muerte. El aumento de los valores de la hemoglobina, del hematocrito y del número de los eritrocitos indica una hemoconcentración. En las cabras recibiendo 5 mg/kg/día de selenita de sodio, se observó una anemia macrocitaria hipocrómica y una leucopenia antes de la muerte. Se evidenciaron en el suero un aumento en la actividad de SGOT y de  $\gamma$ -GT, y en la concentración de la urea y del fosforo mineral y una disminución en la de las proteínas totales y del calcio. No fue tóxico para las cabras el selenita de sodio a las dosis diarias de 1, 0,5 y 0,25 mg/kg. *Palabras claves* : Cabra - Selenita de sodio - Intoxicación - Serologia - Hematologia - Sudán.

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