

The Toxicity of some Dipping Fluids containing Arsenic and Sulphur.

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I. ARSENICAL DIPPING FLUIDS.

ARSENICAL dipping fluids are very extensively used in the Union of South Africa in the eradication of ticks, lice and scab mites. The occurrence of so many cases of accidental arsenical poisoning in stock is therefore not surprising. In view of all the cases of accidental poisoning with dipping fluids the information supplied in this paper will be of interest.

A. SODIUM ARSENITE.

The following solutions of sodium arsenite are employed on a very large scale as dipping fluids for cattle and sheep:—

- (a) Three-day dipping fluid containing 0.08 gm. of As_2O_3 per 100 c.c. Of this fluid approximately 1,200 to 2,500 c.c. ($= \pm 2$ to ± 4 pints) would be fatal for a full-grown beast and 300-600 c.c. ($= \pm \frac{1}{2}$ to ± 1 pint) for a sheep.
- (b) Seven-day dipping fluid containing 0.16 gm. of As_2O_3 per 100 c.c. Of this fluid a fatal quantity for a full-grown beast would be approximately 600 to 1,250 c.c. ($= \pm 1$ to 2 pints) and for a sheep 150 to 300 c.c. ($= \pm \frac{1}{4}$ to $\frac{1}{2}$ pint).
- (c) Fourteen-day dipping fluid containing 0.24 gm. of As_2O_3 per 100 c.c. Of this fluid approximately 400 to 800 c.c. ($= \frac{2}{3}$ to $1\frac{1}{3}$ pint) would be fatal for a full-grown beast and 100 to 200 c.c. ($= \pm \frac{1}{8}$ to $\frac{1}{4}$ pint) for a sheep.

B. COOPER'S POWDER.

Cooper and Nephews (South Africa), Limited, are the manufacturers of (a) Cooper's Double Dipping Powder and (b) Cooper's Powder.

(a) Cooper's Double Dipping Powder.

The following is the registered composition of Cooper's Double Dipping Powder:—

Total arsenic equivalent to	9.4 per cent. As_2O_3 .
Free sulphur	57.5 per cent.
Combined sulphur	6.1 per cent.
Total sulphur	63.6 per cent.

TABLE I.

Experiments with Cooper's Double Dipping Powder.

Rabbit No.	Weight in Kg.	Quantity of Cooper's Double Dipping Powder given.	Result.
A.	3.0	0.2 gm. of dry powder per os.	Transient apathy and loss of appetite which lasted for about 2 days.
B.	1.9	0.5 gm. of dry powder per os.	Listlessness and loss of appetite set in within four hours after dosing; on the following day there were pronounced apathy, profuse diarrhoea, marked paresis, especially of hindquarters, laboured respiration, and weak and accelerated pulse. Death occurred within 36 hours after dosing. <i>P.M. appearances:</i> General cyanosis; hyperaemia of lungs; pronounced acute catarrhal gastroenteritis; fatty degeneration of the liver and kidneys.
C.	2.8	0.5 gm. of dry powder per os.	Symptoms and post mortem appearances similar to those described in B. Death occurred seven days after dosing.
D.	2.25	1.0 gm. of dry powder per os.	Symptoms of poisoning as described above set in within three hours after dosing. Death occurred 8 hours after dosing.
E.	2.1	1.5 gm. of dry powder per os.	Profuse diarrhoea within 5 hrs. after dosing; the animal died 6 hours after dosing. <i>P.M. appearances:</i> pronounced acute haemorrhagic gastroenteritis, pronounced hyperaemia of lungs and liver; further as in B.
F.	2.22	2.5 gm. of dry powder per os.	Profuse diarrhoea within 4 hrs., death occurring within 6 hrs. <i>P.M. appearances:</i> as in E.
G.	2.22	15 c.c. (= 0.2 gm.) of dipping strength solution per stomach tube.	Result as in A.

TABLE I (continued).

Rabbit No.	Weight in Kg.	Quantity of Cooper's Dipping Powder given.	Result.
H.	2.15	37.5 c.c. (= 0.5 gm.) of dipping-strength solution per stomach tube.	Result as in B.
I.	2.05	37.5 c.c. (= 0.5 gm.) of dipping-strength solution per stomach tube.	Symptoms and post mortem appearances as in B. Death occurred within 70 hours after dosing.
J.	2.05	75.0 c.c. (= 1.0 gm.) of dipping-strength solution per stomach tube.	Died $4\frac{1}{2}$ hours after dosing. Symptoms and post mortem appearances as in E.
K.	2.36	75.0 c.c. (= 1.0 gm.) of dipping-strength solution per stomach tube.	Died 6 hours after dosing. Symptoms and post mortem appearances as in F.
L.	2.82	112.0 c.c. (= 1.5 gm.) of dipping-strength solution per stomach tube.	Profuse diarrhoea within 3 hours after dosing and death within 4 hours. Symptoms and post mortem appearances as in E with the gastroenteritis of a less acute nature.

From the above table it could be concluded that 0.15 gm. of Cooper's Double Dipping Powder per Kg. of body weight constitutes the *m.l.d.* for the rabbit. As the powder is stated to contain 9.4 per cent. of As_2O_3 the *m.l.d.* of the arsenic (expressed as As_2O_3) present in it is approximately 0.014 gm. per Kg. of body-weight for rabbits.

(b) *Cooper's Dip.*

The registered composition of Cooper's Dip is as follows:—
 “ Arsenic present as trioxide = 12.5 per cent. As_2O_3 , arsenic present as pentoxide = 6.0 per cent. As_2O_3 , arsenic present as sulphides and sulphur-arsenic complexes = 4.0 per cent. As_2O_3 . Sodium combined with arsenic = 4.9 per cent. Na_2O . Total sulphur = 68.0 per cent.”

The Cooper's Powder was administered per stomach tube in a small quantity of water.

TABLE II.

Experiment with Cooper's Powder.

Rabbit No.	Weight in Kg.	Quantity of Cooper's Dip administered.	Result.
A.	1.15	0.075 gm.	The animal developed transient loss of appetite and diarrhoea lasting approximately four days.
B.	1.75	0.075 gm.	Same symptoms* as in A but to a less marked degree.
C.	1.7	0.15 gm.	Died within 2½ hours after dosing.
D.	1.65	0.15 gm.	Died within 36 hours after dosing.
E.	2.05	0.3 gm.	Died within 27 hours after dosing.
F.	1.9	0.3 gm.	Died within 28 hours after dosing.
G.	1.6	0.5 gm.	Died within 5 hours after dosing.
H.	1.8	0.5 gm.	Died within 15 hours after dosing.

* The symptoms are similar to those described in Table I.

From the above table it is evident that 0.06 gm. of Cooper's Powder (= ± 0.014 gm. As_2O_3) could be considered the approximate *m.l.d.* per Kg. body-weight of rabbit.

From the results of the above experiments it appears that Cooper's Powder given *per os* is approximately two and a half times as toxic as Cooper's Double Dipping Powder. This naturally does not apply to cases where animals are dipped in solutions prepared with these two powders.

According to experiments conducted by Theiler (1912) the *m.l.d.* of Cooper's Dip for sheep appears to be approximately 2.0 gm.

From the results of a large number of experiments conducted upon rabbits by one of us (D. G. S.) with different arsenical preparations (sodium arsenite, Cooper's Dip, Cooper's Double Dipping Powder, Rademeyer's Locust Poison) it appears that they all possess approximately the same degree of toxicity when the toxic doses are calculated on the bases of their As_2O_3 content, namely 0.014 gm. As_2O_3 per Kg. body-weight for rabbits.

Sheep, cattle and horses are more susceptible than rabbits to the effects of arsenic.

It is obviously impossible to lay down a definite figure as *m.l.d.* of an arsenical preparation for any particular class of animal as its degree of toxicity depends upon:—

- (1) Its degree of solubility in water;
- (2) whether water is drunk soon after having ingested it, or not;
- (3) whether taken on a full stomach, or not; and
- (4) whether vomiting occurs after ingestion, or not.

II. SULPHUR DIPS.

CAPEX.

This is a liquid lime-sulphur dip, consisting of polysulphides of calcium [generally CaS_x ($X=4\cdot6$)], manufactured by Messrs. Cape Explosives, Somerset West, C.P. The specimen of undiluted dipping-fluid employed in our experiments contained 34·47 per cent. of polysulphide sulphur and the diluted dip (dipping-strength) contained 1·5 per cent. of polysulphide sulphur.

Capex is very extensively used in the eradication of scab in sheep and mange in goats.

The following table (III) is a summary of the drenching experiments conducted with Capex upon rabbits and sheep.

TABLE III.

Experiments with undiluted and diluted (dipping-strength) Capex.*

Animal No.	Weight in Kg.	Quantity of Capex administered per stomach tube.	Result.
Rabbit A.	1·95	2·5 c.c. of undiluted Capex on 16.6.37.	Laboured respiration (costo-abdominal), loss of appetite, and an accelerated and strong pulse persisted for 2 days after drenching.
Rabbit B.	2·6	5·0 c.c. of undiluted Capex on 16.6.37.	The following symptoms of poisoning set in within 7 minutes after drenching:—pronounced laboured respiration (deep, costo-abdominal and accelerated), pronounced restlessness, pronounced general cyanosis, general convulsions, muscular fibrillations. Death occurred 7 minutes after drenching, the heart stopping about 2 mins. after cessation of respiration. After the heart had stopped the animal still showed a few general clonic spasms (asphyxia?). <i>P.M. appearances</i> : Pronounced general cyanosis; pronounced hyperaemia of the lungs and liver, which was almost black in colour, blood dirty-brown in colour, large amount of sulphur precipitated in the stomach and small intestine. No evidence of gastro-intestinal irritation.
Rabbit C.	2·25	10 c.c. of undiluted Capex on 16.6.37.	The animal died within 3 minutes after drenching with symptoms and post mortem appearances as described in rabbit B.
Rabbit D.	2·1	30 c.c. of undiluted Capex on 16.6.37.	Death occurred within 2 minutes with symptoms and post mortem appearances as described in rabbit B.
Rabbit E.	1·95	60 c.c. of undiluted Capex on 16.6.37.	Result identical with that described in rabbit D.

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TABLE III (continued).

Animal No.	Weight in Kg.	Quantity of Capex administered per stomach tube.	Result.
Rabbit F.	2.55	10 c.c. of diluted Capex.	Apart from transient loss of appetite the animal developed no symptoms of ill-health.
Rabbit G.	2.2	30 c.c. of diluted Capex.	Symptoms of pronounced dyspnoea and accelerated heart-beat set in within a few minutes and death occurred within $\frac{1}{2}$ -hour after dosing with symptoms and post mortem appearances as in B.
Rabbit H.	2.35	60 c.c. of diluted Capex.	Death occurred within 4 hours after drenching with symptoms and post mortem appearances as described in rabbit B.
Rabbit I.	2.5	120 c.c. of diluted Capex.	Result similar to that in rabbit H, death occurring within 8 minutes.
Sheep 49206.	6-tooth 50 Kg.	1,000 c.c. of diluted Capex.	Symptoms of pronounced dyspnoea set in within 4 minutes; a few minutes later the animal staggered about as if intoxicated; pronounced acceleration of heart action; about 6 hours after drenching the animal showed considerable improvement, there being only slight laboured respiration and apathy; when chased it soon became exhausted. In spite of this improvement the animal died during the night about 18 hours after drenching. <i>P.M. appearances</i> : Pronounced odour of sulphuretted hydrogen from the nostrils; pronounced general cyanosis; blood of a fairly dirty-brown colour; subepicardial, subendocardial and intramyocardial haemorrhages; pronounced hyperaemia and slight oedema of the lungs; extensive haemorrhage into the subperitoneal, peritracheal and periesophageal tissues and into the intercostal muscles; pronounced fatty degeneration of the liver; gastrointestinal contents dark in colour and contains a large amount of precipitated sulphur; haemorrhages in duodenal mucosa.
Sheep 37511.	Full-mouth. 51 Kg.	3,000 c.c. of diluted Capex.	Very pronounced dyspnoea within 2 minutes; the animal staggered and fell down and was unconscious within twenty minutes after drenching; there were cyanosis and tremors of the superficial muscles of the body; respiration was accelerated and superficial; the heart beat was weak and slow (70 p.m.), eventually it became very irregular and stopped 25 minutes after drenching. The respiration ceased about 2 minutes before the heart-beat. <i>P.M. appearances</i> : Pronounced general cyanosis; blood of an intense dirty-brown colour with delayed coagulation time; numerous subepicardial haemorrhages; hyperaemia of the liver and lungs; dilation of both heart ventricles; large quantity of sulphur precipitated in the rumen, reticulum and small intestine with pronounced odour of H ₂ S; hyperaemia of abomasal mucosa of duodenum, jejunum and anterior portion of the ileum, with petechiae; hyperaemia of caecal mucosa.

* Containing 1.5 per cent. of polysulphide sulphur.

It thus appears that the *m.l.d.* of the undiluted dipping-fluid for the rabbit is approximately 1.5 c.c. per Kg. of body-weight. Of the diluted fluid (dipping-strength) the *m.l.d.* for rabbits is approximately 7.5 c.c. per Kg. of body-weight and approximately 800 to 1,000 c.c. for a full-grown sheep weighing approximately 40 to 50 Kg.

If drawn into the lungs (choking) sulphur dipping-fluids are extremely poisonous.

According to comparative tests conducted upon rabbits it appeared that the following sulphur dipping-fluids (dipping-strength concentrations) possess the same degree of toxicity as the Capex Lime Sulphur Dip:—

- (1) Tarzan Lime Sulphur Dip;* manufactured by Cape Chemical Company, Limited, Capetown. Thiosulphate (+ tetrathionate) = 0.17 per cent. [$\text{CaSx}(X=4.39)$]. It contains 35.46 per cent. of polysulphide sulphur; and
- (2) Nelson's Sodium Polysulphide Dip* [$\text{Na}_2\text{Sx}(X=4.27)$]. It contains 46.91 per cent. of polysulphide sulphur. In all three these dipping-fluids (dipping-strength concentration) the percentage of polysulphide sulphur is 1.5.

TABLE IV.

*Sulphur Determinations made upon the Blood of Sheep
37511 and 49206.*

Sheep No.	Date of Bleeding.	Total sulphur in mg. per 100 c.c. blood.	
37511	25.6.37	85.15	
	29.6.37—(a) before dosing.....	83.77	
		(b) 10–15 mins. after dosing 3 litres of Capex Lime Sulphur Dip.†	67.30
		(c) Heart-blood collected \pm 1½ hours after death..	75.54
		98.88	
49206	25.6.37.....	95.45	
	29.6.37—(a) before dosing.....	63.87	
		(b) 20 mins. after dosing 1 litre of Capex Lime Sulphur Dip.†.	65.24
		(c) Death occurred during the following night and heart blood was collected the following morning.	93.40

† Analysis of Capex Lime Sulphur Dip used in dosing the sheep:—(1) 1.5 per cent. of polysulphide sulphur; (2) 0.24 per cent. of thiosulphate (including tetrathionate sulphur).

* All the figures quoted here are those obtained with the specimens employed in our experiments.

The two sheep were bled on the 25.6.37 and again a few hours before dosing on 29.6.37 in order to determine the normal value for total sulphur in the blood. From the above table it is evident that the values obtained on the 25.6.37 were much higher than those of the 29.6.37 prior to dosing. The values for both sheep, however, showed an agreement on the same day, namely 85.15 and 95.45 on the 25.6.37 and 67.30 and 63.87 mg. sulphur per 100 c.c. blood on the 29.6.37 respectively. All the determinations were made in the same manner using the method of Stockholm and Koch (*Jour. Amer. Chem. Soc.*, Vol. 45, 1923, p. 1953). Equal quantities of the same reagents were used in every case and in addition duplicate blank determinations, which differed only in the fourth decimal place, were made.

It will be noticed that in the case of both sheep there was a pronounced increase in the sulphur values of the specimens of blood collected a few minutes before dosing and those collected after dosing. There was, however, not such a marked difference in these values of specimens of blood collected a few days before dosing and those collected after death. It is also evident that the blood sulphur values increased at a more rapid rate in the sheep which had received the larger dose of Capex. It is fully realised that the number of sheep in the experiment and the number of determinations made upon the blood sulphur are very limited and that it would be futile to attempt to draw any definite conclusions.

We did expect to find a fairly pronounced sulphaemoglobinemia. Spectroscopic examination of the blood of the sheep however did not reveal it. This does not necessarily mean that no sulphaemoglobin was present as it may have been present in undetectable quantities. Experiments *in vitro* yielded interesting results. Normal blood, which showed the haemoglobin bands spectroscopically, showed the broad band of reduced haemoglobin after addition of a small quantity of Capex Lime Sulphur Dip. Upon shaking this mixture up with air the oxy-haemoglobin bands reappeared and after standing for a while the oxy-haemoglobin was again reduced by the sulphur dip. If a small quantity of Capex dip was added to normal blood and left standing for a while both the sulphaemoglobin band and the broad band of reduced haemoglobin could be clearly seen.

SUMMARY.

1. Experiments to determine the toxic doses of some dipping-fluids containing arsenic and sulphur are described.
2. It appears that in all the more common forms of arsenical preparations, which are soluble in water, the *m.l.d.* for rabbits can be calculated on the basis of approximately 0.014 gm. of As_2O_3 per Kg. of body-weight. Sheep, cattle and horses are more susceptible than rabbits to arsenic.

3. The *m.l.d.* of diluted (dipping-strength concentration) Capex Lime Sulphur Dip for rabbits is approximately 7.5 c.c. per Kg. of body-weight and for sheep approximately 15 to 20 c.c. per Kg. of body-weight.

4. In dipping-strength concentration Tarzan Lime Sulphur Dip and Nelson's Sodium Polysulphide Dip possess approximately the same degree of toxicity as Capex Lime Sulphur Dip.

REFERENCE.

- THEILER, A. (1912). Experiments to determine the safe dose of white arsenic, Cooper's Dip and bluestone for sheep. *South Afr. Agric. Jour.*, Vol. 3, 1912, pp. 321-351.