

## FURTHER STUDIES ON THE EFFECTIVENESS OF ARSENIC IN PREVENTING SELENIUM POISONING<sup>1</sup>

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ONE FIGURE

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Recent work at this laboratory (Moxon, '38; Moxon and DuBois, '39) has shown that arsenic will counteract selenium poisoning. It is the purpose of this paper to report further research along this line. This work was carried out on rats as an extension of that already reported.

It has been concerned mainly with the effectiveness of different forms of arsenic in preventing the toxic action of selenium in the form of seleniferous wheat and the effectiveness of arsenic as sodium arsenite in preventing the toxicity of different forms of selenium.

### *Different forms of arsenic*

The effectiveness of different arsenic compounds was compared in controlled experiments with albino rats. The diet used and the management of the animals has been described in a previous publication (Moxon and DuBois, '39). Arsenic compounds were fed according to table 1.

Sodium arsenite ( $\text{Na}_2\text{HAsO}_3$ ) and sodium arsenate ( $\text{Na}_2\text{HAsO}_4$ ), when used as sources of arsenic, were equally effective in preventing the toxic action of the selenium in the diet (groups 3 and 4 of table 1) as indicated by growth, mortality rate and pathological condition of the livers.

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Arsenic at this level (5 p.p.m. in the drinking water) did not give full protection against the 14 p.p.m. of selenium in the diet. It has been shown, however, that arsenic at this level will protect rats against 11 p.p.m. of selenium in the diet (Moxon and DuBois, '39), and 10 p.p.m. of arsenic as sodium arsenite protected the rats in group 9 against 18 p.p.m. of selenium in the diet as is shown in figure 1.

In group 5 (table 1) the 10 p.p.m. of arsenic as sodium arsenite, mixed in the diet, prevented the development of symptoms of selenium poisoning slightly better than 5 p.p.m.

TABLE 1  
*Effectiveness of different forms of arsenic against selenium found in wheat*

GROUP OF RATS	SELENIUM USED (IN DIET)	ARSENIC USED
1	14 p.p.m. (seleniferous wheat)	None
2	14 p.p.m. (seleniferous wheat)	None
3	14 p.p.m. (seleniferous wheat)	5 p.p.m. as $\text{Na}_2\text{HAsO}_3$ in drinking water.
4	14 p.p.m. (seleniferous wheat)	5 p.p.m. as $\text{Na}_2\text{HAsO}_4$ in drinking water.
5	14 p.p.m. (seleniferous wheat)	10 p.p.m. as $\text{Na}_2\text{HAsO}_3$ in diet.
6	14 p.p.m. (seleniferous wheat)	10 p.p.m. as $\text{AsS}_2$ in diet.
7	14 p.p.m. (seleniferous wheat)	10 p.p.m. as $\text{AsS}_3$ in diet.
8	18 p.p.m. (seleniferous wheat)	None
9	18 p.p.m. (seleniferous wheat)	10 p.p.m. as $\text{Na}_2\text{HAsO}_3$ in drinking water.

of arsenic, as the same compound, when fed in the drinking water (group 3). The level of arsenic intake with a diet containing 10 p.p.m. of arsenic is slightly higher than the level of intake when rats are given 5 p.p.m. of arsenic in the drinking water which will account for the greater protection offered by the arsenic in group 5 than in group 3.

The arsenic sulfides ( $\text{AsS}_2$  and  $\text{AsS}_3$ ) used in groups 6 and 7 failed to give any indication of protection against the selenium in the diet. The mortality rate in these two groups was equal to that in group 2 where no arsenic was fed with the selenium.

As a continuation of the study, "the influence of arsenic and certain other elements on the toxicity of seleniferous grains" (Moxon and DuBois, '39), lead as lead acetate and bismuth as bismuth subnitrate were fed at levels of 5 p.p.m.

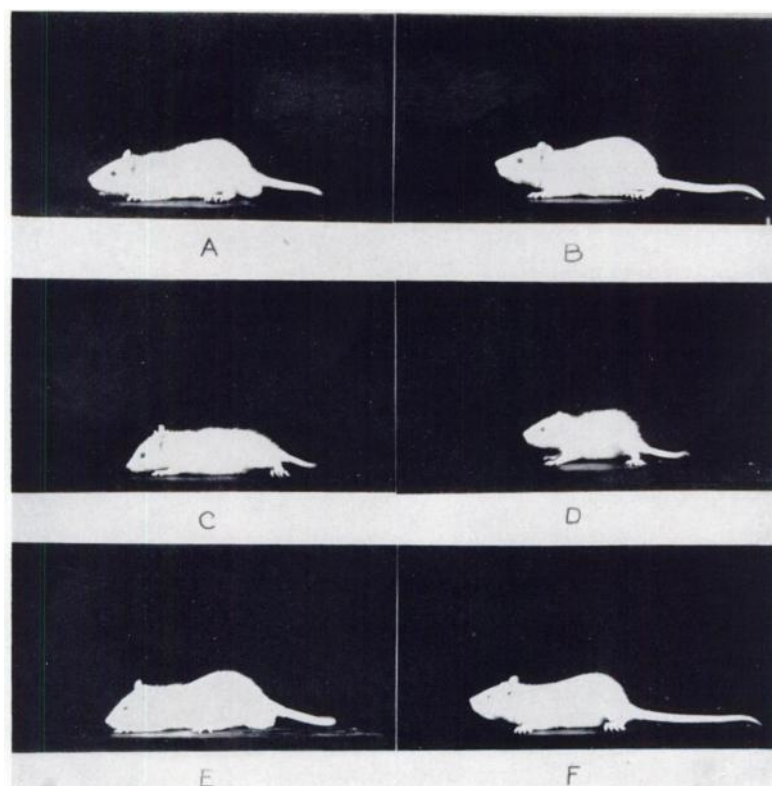


Fig. 1 A, C and E, males; B, D and F, females. A and B, control diet; C and D, seleniferous diet (18 p.p.m. Se); E and F, seleniferous diet (18 p.p.m. Se) + 10 p.p.m. arsenic in drinking water.

in the drinking water to rats on a diet containing 14 p.p.m. of selenium. In these experiments the lead did not influence the toxicity of the selenium during the duration of the feeding trials (100 days) but bismuth had a slightly beneficial effect.

*Different forms of selenium*

In a later experiment the efficacy of arsenic as  $\text{Na}_2\text{HAsO}_3$  in preventing the toxic action of different forms of selenium was determined. The diet used was the same as in the above experiments. Selenium and arsenic were fed as shown in table 2.

TABLE 2  
*Effectiveness of arsenic as sodium arsenite against selenium in wheat and in sodium selenite*

GROUP OF RATS	SELENIUM USED (IN DIET)	ARSENIC USED (IN DRINKING WATER)
1	None	None
2	11 p.p.m. Se (seleniferous wheat)	None
3	11 p.p.m. Se (seleniferous wheat)	5 p.p.m. As
4	11 p.p.m. Se ( $\text{Na}_2\text{SeO}_3$ )	None
5	11 p.p.m. Se ( $\text{Na}_2\text{SeO}_3$ )	5 p.p.m. As

The rats in group 2 were all dead within 35 days while those in group 4 were all dead at the end of 60 days. All rats in groups 3 and 5 were still alive at the end of 100 days when the experiment was terminated. The growth curves and condition of the livers on autopsy indicated that the arsenic as arsenite ( $\text{Na}_2\text{HAsO}_3$ ) gave full protection against the toxic action of selenium as seleniferous wheat and as sodium selenite.

In studies involving the comparative toxicities of selenium as selenium-cystine, sodium selenite and seleniferous wheat<sup>2</sup> we have found that 10 p.p.m. of arsenic as arsenite ( $\text{Na}_2\text{HAsO}_3$ ) will give adequate protection against 18 p.p.m. of selenium as selenium-cystine.

*The response to arsenic after selenium had been fed for various periods of time*

Soon after it was found that arsenic would protect against selenium poisoning (Moxon, '38) we became interested in determining what effect arsenic would have on animals in

<sup>2</sup> Unpublished data, this laboratory. 1938.

various stages of selenium poisoning. Six groups of rats were used as indicated in table 3.

The results indicate that arsenic is quite effective if selenium has been fed less than 30 days or not more than 20 days before the arsenic treatment is initiated. When selenium had been fed for 30 days before arsenic feeding began there was little growth response (compare groups 2 and 6 in the last column of table 3).

Liver glycogen levels have been determined (Potter, DuBois and Moxon, '39) on rats which had been fed selenium and selenium plus arsenic. Rats which had been fed a selenium diet had a lower glycogen level than the controls or the selenium plus arsenic groups.

TABLE 3  
*The response to arsenic after selenium has been fed  
for varying periods of time*

GROUP OF RATS	DIET	ARSENIC (IN DRINKING WATER)	AVERAGE WEIGHTS AT	
			30 DAYS	90 DAYS
1	Control (no selenium)	None	115	190
2	18 p.p.m. selenium (wheat)	None	91	128
3	18 p.p.m. selenium (wheat)	10 p.p.m. As from beginning	109	187
4	18 p.p.m. selenium (wheat)	10 p.p.m. As after first 10 days	105	183
5	18 p.p.m. selenium (wheat)	10 p.p.m. As after first 20 days	102	174
6	18 p.p.m. selenium (wheat)	10 p.p.m. As after first 30 days	88	131

The protein content of diets used in selenium studies is of extreme importance. It has been shown (Moxon, '37; Smith, '39) that high protein diets offer more protection against selenium poisoning than low protein rations. The same basal diet has been used for all of our selenium-arsenic studies on rats. It contains approximately 22% protein ( $N \times 6.25$ ).

Although some interesting clues are being followed, no explanation for the antagonistic action of selenium and arsenic can be offered at present. A similar antagonistic effect between elements has been reported for thallium and iodine.<sup>3</sup>

<sup>3</sup> Research item, Iodides as antidotes in thallium poisoning, *Nature*, vol. 142, p. 440. 1938.

## SUMMARY

Sodium arsenite and sodium arsenate were equally effective as sources of arsenic for preventing the toxic action of the selenium present in seleniferous wheat in the diet of albino rats; the arsenic sulfides ( $\text{AsS}_2$  and  $\text{AsS}_3$ ) were ineffective.

Arsenic as sodium arsenite was equally effective against selenium when the latter was given as seleniferous wheat, sodium selenite and selenium-cystine.

Arsenic was effective in treating rats which had been fed selenium for 20 days but was of little value after selenium had been fed for 30 days.

## LITERATURE CITED

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