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THE NATURE AND IMPORTANCE OF SELENIUM METABOLITES IN THE ANIMAL

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Although the toxicity of selenium has been known for several decades (1) and its essentiality has been established for over one decade (2), very little is known concerning the organic forms of selenium occurring within animals and their functions. Dimethyl selenide has been shown to be an exhalation product from rats injected with selenate (3) or selenite (4). Recently trimethylselenonium ion has been shown to be excreted in the urine of rats receiving selenite (5,6). The work reported here concerns the biological activity and metabolism of trimethylselenonium ion.

A. Biological activity of the trimethylselenonium ion in the rat.

Selenium in the form of trimethylselenonium chloride was unavailable to rats for protection against fatal liver necrosis which develops on a Torula yeast diet. Selenite selenium was effective under the same conditions. Injected trimethylselenonium ion was excreted rapidly and unchanged in the urine. Detailed procedures and results are given in Preprint No. 1:

THE INACTIVITY OF TRIMETHYLSELENONIUM CHLORIDE IN THE RAT
Ding-tsair Tsay, A. W. Halverson and I. S. Palmer

B. Toxicity of trimethylselenonium ion to the rat.

Trimethylselenonium chloride was shown to be less toxic than most other forms of selenium. The LD50 was found to be 49.4 mg Se/kg body weight. It was found that arsenic did not decrease the toxicity of selenium in this form and in fact, there appeared to be synergism between the two substances. Procedures and detailed results are given in Preprint No. 2:

TOXICITY OF TRIMETHYLSELENONIUM CHLORIDE IN THE RAT WITH
AND WITHOUT ARSENITE
B. D. Obermeyer, I. S. Palmer, O. E. Olson and A. W. Halverson

C. Biosynthesis of the trimethylselenonium ion (TMSe).

Ganther reported on an extract from mouse liver capable of methylating inorganic selenium (7). We have found a similar system in rat liver and have used it to study the site of TMSe synthesis. Preliminary evidence indicates that TMSe can be chromatographically isolated from the in vitro system. It has been found in only trace amounts and further characterization is needed to say conclusively that the liver is a site of TMSe synthesis.

In the past year work has also been conducted on other phases of the biosynthesis of TMSe. The effect of arsenite on the excretion of TMSe when high levels of selenite-selenium are administered was studied. Although arsenite did not vary the percent of selenium excreted in the urine as TMSe, it did cause a reduction in total selenium excreted. Consequently a loss in total TMSe excreted in the presence of arsenic was observed. The data are presented in Preprint No. 3:

EFFECT OF ARSENITE ON TRIMETHYLSELENONIUM ION PRODUCTION IN THE RAT
B. D. Obermeyer, I. S. Palmer and O. E. Olson

It was considered important to determine whether TMSe was unique for selenite metabolism or if it was a general excretory product of selenium in the rat. Consequently, we studied the urinary excretory products from animals which had been given selenate, selenomethionine, Se-methylselenocysteine, selenocystine and seleniferous wheat. It was found that TMSe was a major excretory product from all the selenium sources which were studied. The procedures and data are given in Preprint No. 4:

TRIMETHYLSELENONIUM ION AS A GENERAL EXCRETORY PRODUCT FROM
SELENIUM METABOLISM IN THE RAT
I. S. Palmer, R. P. Gunsalus, A. W. Halverson and O. E. Olson

When it was found that TMSe was formed from seleniferous wheat as well as several other organic selenium compounds, it became of interest to determine the form of selenium in the wheat. Other workers have shown selenomethionine to be present in wheat seedlings (8) and early work by Smith (9) supplied chromatographic evidence for the presence of selenomethionine and selenocystine in the proteins of wheat seed. More recent work has shown that caution must be used in taking chromatographic evidence as the sole criterion for the identification of selenium compounds (10). Taking advantage of recent improvements in the techniques of separating selenium compounds from their sulfur analogs (11-14), we studied the selenium containing compounds in seleniferous wheat. The wheat was grown in a growth chamber and treated with $K_2^{75}SeO_4$ just after flowering. Gluten from the mature wheat was prepared, enzymatically hydrolyzed and analyzed on a Spinco amino acid analyzer. Selenomethionine accounted for over 50% of the selenium in the protein. No evidence was found for the presence of selenocystine or seleno-half-cystine. Several unidentified materials were found. Some of these appeared to be oxides of seleno-organic compounds. Detailed procedures and results are given in Preprint No. 5:

INVESTIGATIONS ON SELENIUM IN WHEAT

O. E. Olson, E. J. Novacek, E. I. Whitehead and I. S. Palmer

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