volumes. Volumes and distributions found by this method in 4 goats are within the range of values found in the goat by other methods. Limitations of the method are also discussed.

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Effect of Various Methionine Analogues on Bacteriostatic Action of Methionine Sulfoximine.* (21293).

S. N. GERSHOFF. (Introduced by Frederick J. Stare.)

From the Harvard School of Public Health, Department of Nutrition, Boston, Mass.

In recent years 3 groups(1-3) working with agene (NCl_3) treated proteins have isolated and characterized the causative agent of running fits in dogs. This compound, methionine sulfoximine, is of particular interest not only as a convulsant but because it acts as a methionine antagonist. Reiner *et al.*(4) and Gershoff and Elvehjem(5) have prevented the symptoms of methionine sulfoximine toxicity in animals by the administration of adequate quantities of methionine. Gershoff and Elvehjem(6) have also concluded that the anti-methionine activity of methionine sulfoximine is not specific for the enzyme systems directly involved in running fits but is general in nature. Methionine sulfoximine has also been shown to inhibit the growth of *Leuconostoc mesenteroides*(7), and this inhibition has been reversed by either methionine or glutamine (8,9).

The experiments to be reported here are the first of a series planned to investigate the biochemical and physiological mechanisms involved in the action of methionine sulfoximine. These investigations were made to determine the effect of various methionine analogs on the bacteriostatic action of methionine sulfoximine.

Experimental. These studies were carried out in 18 x 150 mm pyrex culture tubes using *Leuconostoc mesenteroides* P-60 as the test organism. All tubes contained 2 ml of modified Henderson-Snell media(10), containing 3.5 γ of DL-methionine per ml which is a suboptimal amount and allows approximately 50% of the maximum acid production. Acid production on this media with and without supplements of methionine sulfoximine and various methionine analogs was determined after incubation at 37°C for 68 hours. All determinations were made in sextuplicate.

Results. The results of these experiments are shown in Table I. These data, which were selected as being representative of a series of similar experiments, indicate that the ability of analogs of methionine to reverse methionine sulfoximine toxicity may or may not be related to their capacity to substitute for methionine in meeting the growth requirements of *Leuconostoc mesenteroides*.

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TABLE I. Effect of Methionine Analogues on Growth Inhibition of *Leuconostoc mesenteroides* P-60 by Methionine Sulfoximine.

Analogue used*	Methionine sulfoximine†	% of acid produced on unsupplemented media
0	+	49
DL-methionine	—	180
	+	166
3-methylmethionine	—	100
	+	53
S-methylpenicillamine sulfoxide	—	98
	+	48
3-methylmethionine sulfoxide	—	96
	+	48
Glutamine	—	93
	+	96
Methionine sulfoxide	—	178
	+	116
Methionine sulfone	—	93
	+	72
α-hydroxy-γ-methylmercapto butyric acid	—	137
	+	59

* 1.35×10^{-5} moles/tube.
† 6.75×10^{-7} moles/tube.

3-methylmethionine, S-methylpenicillamine sulfoxide, and 3-methylmethionine sulfoxide were without effect under the conditions of this experiment.

Methionine sulfoximine inhibition was completely reversed by glutamine; however, glutamine showed no growth promoting activity in the absence of the antagonist and hence cannot replace methionine for the growth of this organism. Similar studies with asparagine and citrulline were negative.

Methionine sulfoxide can serve as a source of methionine for *E. coli*(11), *L. arabinosus* (12), and *S. faecalis*(13). In these experiments *Leuconostoc mesenteroides* utilized methionine sulfoxide to the same degree as methionine in the absence of methionine sulfoximine, but methionine was more effective than the sulfoxide in reversing the inhibitory effect of the antagonist.

Methionine sulfone does not serve as a source of methionine for *L. arabinosus*(12) or *S. faecalis*(13). Similarly it was inactive for *Leuconostoc mesenteroides* as a source of methionine but appeared to reverse partially the toxicity of the antagonist.

α-hydroxy-γ-methylmercapto butyric acid has been reported to be equivalent to methionine in meeting the nutritional requirements of rats and chicks(14). This hydroxy analog of methionine was found to have considerable but not equivalent methionine activity for *Leuconostoc mesenteroides*. Thus it was unexpected to find that it was perfectly ineffective in reversing methionine sulfoximine toxicity.

Summary. A number of methionine analogs were studied for their ability to replace methionine and reverse methionine sulfoximine induced growth inhibition. Relative activity in replacing methionine and reversing methionine sulfoximine toxicity are not necessarily correlated. Some compounds which counteract methionine sulfoximine toxicity have no methionine-like activity.

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