CXCII. METABOLISM OF SULPHUR

IX. THE NON-PRODUCTION OF GLYCOGEN FROM CYSTINE, CYSTEINE AND METHIONINE AND THEIR PARTIALLY OXIDIZED DERIVATIVES¹

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THE recent work of Butts *et al.* [1938], showing that the feeding of cystine to normal fasting rats does not lead to glycogen deposition in the liver, has made it desirable that the fate of methionine and cysteine in this respect be investigated also. A separate study of these amino-acids is especially important since there is evidence that methionine and cysteine do not always follow the same metabolic pathway as cystine. In this investigation possible glycogen production from some of the partially oxidized derivatives of cysteine and methionine has been included, since it has been shown that their fate in metabolism also differs from that of the parent amino-acids in that their administration leads to inorganic sulphate excretion to a less degree than does consumption of the disulphide or thiol amino-acids.

In general, the technique employed by Butts *et al.* was followed. The rats were starved for 36 hr., during which time they had free access to filter paper. The solutions were then administered in four equal portions at hourly intervals. A small catheter attached to a syringe was used as a stomach tube. One hour after the fourth feeding the rat was killed by a blow on the head, the liver was removed immediately, dropped into previously weighed alkali and the tubes re-weighed. Liver glycogen was determined by the method of Good *et al.* [1933].

The following is a list of the compounds employed, together with their modes of preparation:

Cystine was administered in gum tragacanth as described by Butts *et al.*

Sodium cystinate and *methionine sulphoxide* were administered in aqueous solution.

Methionine was dissolved in 10–12 drops of conc. HCl and the solution neutralized to Congo red with NaOH.

Cysteinesulphinic acid and *cysteic acid* were dissolved in water and neutralized to Congo red.

The amount fed, following the procedure of Butts *et al.*, was 0.0178 m.-equiv. of *S* per cm.² body surface. The surface area was estimated from the formula $S = kW^{2/3}$, where $k = 9.1$ [Wilson & Lewis, 1929]. The total volume in each case was about 15 ml. The results are expressed in g. glycogen per 100 g. liver and are given in the last column of Table I. Each glycogen figure is the average of two or usually three duplicate samples.

The results with cystine agree with those of Butts *et al.* in that the percentages of glycogen in the livers do not differ significantly from those of the controls which were starved without subsequent feeding of amino-acid, and the figures for alanine are of about the same order as those obtained by them. Another rat

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Table I. *Glycogen in the liver of albino rats following feeding of sulphur-containing amino-acids and their partially oxidized derivatives*

Exp. no.	Wt. of rat g.	Period starved hr.	No. of doses	Interval before killing hr.	Substance fed	Amount fed g.	Glycogen in liver %
1	—	—	—	—	—	—	7.278
2	—	24	—	—	—	—	0.114
3	455	36	4	1	Glucose	5.0	3.953
4	399	36	4	1	Alanine	0.781	1.908
5	357	36	4	1	Alanine	0.726	2.436
6	335	36	4	1	<i>l</i> -Cystine	0.945	0.065
7	332	36	4	1	<i>l</i> -Cystine	0.940	0.072
8	353	36	4	1	Na- <i>l</i> -cystinate	1.164	0.086
9	347	36	4	1	<i>dl</i> -Methionine	1.192	0.070
10	336	36	4	1	<i>dl</i> -Methionine	1.166	0.099
11	248	36	4	1	<i>dl</i> -Methionine	0.953	0.079
12	372	36	4	1	<i>l</i> -Cysteine	1.014	0.077
13	287	36	4	1	<i>l</i> -Methionine sulfoxide	1.163	0.068
14	283	36	4	1	<i>l</i> -Methionine sulfoxide	1.152	0.069
15	368	36	4	1	<i>l</i> -Cysteinesulphinic acid	1.273	0.070
16	360	36	4	1	<i>l</i> -Cysteic acid	1.385	0.053
17	305	36	4	1	<i>l</i> -Cysteic acid	1.240	0.078
18	332	24	1	6	<i>dl</i> -Methionine	1.157	0.115
19	242	24	1	6	<i>dl</i> -Methionine	0.937	0.105
20	335	36	1	6	<i>l</i> -Cysteine	0.945	0.114

(animal 3) was employed, feeding glucose as a further test of the method. The results show that none of the sulphur-containing amino-acids fed under these conditions gave rise to glycogen in the liver. In this respect, then, cystine, methionine and cysteine agree metabolically.

Although cysteinesulphinic acid and cysteic acid give rise to taurine in the bile [Virtue & Doster-Virtue, 1939] and produce less inorganic sulphate in the urine than the corresponding naturally occurring amino-acids, nevertheless there is a slight rise of inorganic sulphate in the urine following their ingestion, and it was thought that at least these molecules might contribute to glycogen formation. But the results indicate otherwise.

Stöhr [1938] recently published a table in which the results of feeding cystine and cysteine differed radically from these. His method also differed somewhat in that the substance to be fed was given at one dose, followed by an interval of 6 hr. before the rat was killed. He used this procedure since he had evidence that repeated feedings accelerated the resorption of glycogen from the liver, so that lower results were obtained. In the case of cysteine he obtained a liver glycogen of 0.584 ± 0.111 %, as contrasted with 0.071 ± 0.009 % in the controls. When he used *d*-alanine, 0.524 ± 0.075 % was found. We therefore repeated three experiments using his procedure, one with cysteine and two with methionine. They are recorded in Table I as exps. 18 and 19 (methionine) and 20 (cysteine). As may be seen, while the glycogen percentages in the liver obtained by his procedure are slightly higher than those given by the method used above, they are not more elevated than our controls and are considerably lower than the corresponding figures given by him.

SUMMARY

Cystine, methionine and cysteine, fed to rats starved for 24 or 36 hr. before receiving 0.0178 m.-equiv. of the compound per cm.² body surface, fed in four hourly portions, do not give rise to glycogen in the liver, as shown by analysis

1 hr. after the final feeding. Methionine sulphoxide, cysteinesulphinic acid and cysteic acid also do not lead to glycogen deposition in the liver under these conditions.

REFERENCES

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