

Histidine Administration and Glutamine Content of Rat Tissues¹

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Little is known concerning the catabolism of histidine. It is recognized as one of the amino acids essential for growth of the rat, but the disposition of that in excess of the growth requirement is uncertain. Edlbacher and Neber (3) suggest that L-histidine is converted to glutamic acid during the process of metabolism. Crookshank and Berg (1) concluded that L-histidine was probably not converted to other derivatives of imidazole but that the ring was ruptured with the formation of an alpha-amino compound. Featherstone and Berg (4) in studies of the metabolism of histidine by kidney and liver slices suggested that L-histidine might be converted to alpha-amino products other than glutamic acid. Crookshank and Clowdus (2) studied the blood levels of glutamic acid, histidine, total imidazole, and amino nitrogen before and after feeding single doses of D- and L-histidine to rats. They concluded that either no conversion to glutamic acid occurred, the conversion proceeded too slowly to be detected by their methods, or that any glutamic acid formed was rapidly converted to some other metabolite retaining the alpha-amino group. In line with this latter postulation, it seemed possible that if glutamic acid were formed it might be converted to glutamine by combination with ammonia. Tigerman and MacVicar (5) had demonstrated a rise in tissue glutamine levels in rats resulting from the simultaneous administration of ammonium ion and glutamic acid. This could account for the fact that no increase in blood glutamic acid was observed by Crookshank and Clowdus following histidine ingestion. The effect of histidine administration upon the glutamine level in certain rat tissues was therefore investigated.

TABLE I
Effect of Histidine Injection on Glutamine Level in Rat Tissue

TREATMENT NUMBER*	1	2	3
TISSUES	GLUTAMINE (MG. % \pm STD. DEV.)		
LIVER	156 \pm 39	114 \pm 32	96 \pm 36
KIDNEY	50 \pm 18	68 \pm 20	67 \pm 15
HEART	172 \pm 22	166 \pm 28	187 \pm 33
NUMBER OF ANIMALS	5	5	5

*1—0.9% NaCl injected

2—NaCl + NaHCO₃ injected

3—NaCl + NaHCO₃ + histidine injected

EXPERIMENTAL

Tissue glutamine was estimated by nesslerization of a protein-free filtrate of a tissue homogenate before and after hydrolysis of the amide group by digestion in NH₄SO₄ in a boiling water bath for 10 minutes. Mature rats were injected intraperitoneally with L-histidine at the level 0.16 gm. of amino nitrogen per kg. body weight. The solution of histidine for injection was prepared by dissolving histidine monohydrochloride in normal saline and adjusting the pH to 7.4 by addition of sodium bicarbonate. To determine the effect of the NaCl or NaHCO₃ control groups were simultaneously in-

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jected with NaCl and with NaCl + NaHCO₃ at the same level which was used with the histidine injection. The rats were killed 15 minutes after injection and tissues removed for analysis. In previous work, this period has been shown to be adequate for mobilization of the injected material from site of injection. The results are shown in Table I.

Comparison of the values found for the animals receiving treatments one and two shows that the administration of histidine did not induce an increase in the level of glutamine in the tissues examined. Thus, glutamic acid, if formed from histidine, is apparently not converted to glutamine to any appreciable extent. No support for the hypothesis that glutamine is the alpha-amino compound reported as a result of histidine metabolism is afforded by these results.

It will be noted that the liver glutamine level of the animals receiving bicarbonate is reduced with respect to the animals receiving only saline. It is not believed that any significance should be attached to this observation, since the usual value for liver glutamine is near 100 mg.%. Both previous and subsequent tests have failed to reveal any influence of the injection of normal saline, and the observed differences are therefore attributed to the rather wide variation between animals observed and the small number of animals involved.

SUMMARY

Parenteral administration of L-histidine to normal adult rats was not found to affect the glutamine levels of liver, kidney and heart tissues.

LITERATURE CITED

1. CROOKSHANK, H. R. AND CLARENCE P. BERG. 1948. Changes in the composition of the blood of rats fed L-histidine. *Federation Proc.* 7:150.
 2. ———, AND BERNARD F. CLOWDUS. 1950. Ingestion of histidine and the glutamic acid blood level in rats. *J. Biol. Chem.* 184:307-312.
 3. EDILBACHER, S. AND M. NEBER. 1934. Zur Kenntnis des intermediären Stoffwechsel des Histidins. *Z. physiol. Chem.* 224:261-272.
 4. FEATHERSTONE, R. M. AND CLARENCE P. BERG. 1947. The metabolism of L- and D-histidine by slices of liver and kidney. *J. Biol. Chem.* 171:247-253.
 5. TIGERMAN, HENRY AND ROBERT MACVICAR. 1951. Glutamine, glutamic acid, ammonia administration and tissue glutamine. *J. Biol. Chem.* 189:793-799.
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