oldithiocarbamate was estimated with a Beckman model B spectrophotometer at 432 mμ. A detailed account of the microdiffusion analysis for CS_2 is in preparation for publication elsewhere.

The results are presented in Table I.

Neither tetrabutyl- nor tetraisobutylthiuram disulfide is readily reduced by GSH, probably owing to their relatively lower solubility in comparison with the other compounds. Neither of the butyl compounds is reduced by sodium hydrosulfite in aqueous medium, but they are easily decomposed in a 50% alcohol solution by this reagent.

From these data it seems possible that the action of TETD on glyceraldehydephosphate dehydrogenase, at least, may be explained on the basis of its oxidizing action on the glutathione prosthetic group of the enzyme rather than as a competition with the substrate, since Racker and Krimsky (5) have shown that phosphoglyceraldehyde first forms a thiol ester with the—SH group of the enzyme. Moreover, results reported earlier (6) that TETD is broken down by liver homogenates in the presence of glucose 6-phosphate, zwischenferment, and triphosphopyridine nucleotide to give CS_2, may be explained in terms of the glutathione reductase system which is in liver (7).

The instability of at least some of the thiuram disulfides toward reducing agents suggests that caution should be exercised in interpreting the inhibitory actions of this class of compounds on enzyme systems.

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Division of Pharmacology,
Food and Drug Administration,
Federal Security Agency,
Washington, D. C.
Carter D. Johnston

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The Metabolism of Histamine-β-C^{14}

Evidence has accumulated that imidazoleacetic acid is a major product of oxidation of histamine *in vitro* (1) and *in vivo* (2, 3). It appears also that the imidazole ring of the histamine molecule undergoes very little, if any, degradation. However, as to the stability of the carbon side chain no direct information is yet available. In the course of our studies on histamine metabolism, we have obtained evidence that the carbon side chain of the histamine molecule is not broken down *in vivo* to any significant extent.

We have prepared, by the method of Pyman (4) and Koessler and Hanke (5), histamine labeled in the beta position with radiocarbon. Chloromethylimidazole

was made to react with $KC^{14}N$ [1 millicurie (mc.)] and the cyano group of imidazoleacetonitrile thus formed was reduced by the action of alcohol and metallic sodium. Radioactive histamine was isolated as the bis(*o*-dichlorobenzenesulfonate) derivative, and treatment of this product with HCl gave the dihydrochloride. The prepared histamine dihydrochloride melted at 229–231° (uncorr.); analysis calculated for $C_5H_9N_3 \cdot 2HCl$: C, 32.62; H, 6.02; N, 22.83; found: C, 32.75; H, 6.27; N, 22.94. One-dimensional ascending paper chromatography in *n*-butanol–95% ethanol–concentrated ammonium hydroxide (8:1:3 by volume) (6) of the synthetic radioactive compound and of an Eastman Kodak histamine sample gave single spots with similar R_f values. The radioactivity of the prepared product was measured with an internal gas counter and evaluated at 3.17×10^5 counts/min./mg. of histamine base. Aqueous solutions of 9.5 and 19.0 mg. of radiohistamine, adjusted at pH 7.4, were administered by intraperitoneal injection to two Wistar strain rats weighing 53 and 109 g., respectively. Each animal was placed in a glass metabolism cage and the respiratory carbon dioxide was collected for various time intervals up to 24 hr. In each case, the total C^{14} excretion in the expired CO_2 represented about 1% of the dose injected, a value considered negligible. On the other hand, nearly 82% of the injected radioactivity was present in the 24-hr. urine, and not more than 3% was present in the trichloroacetic acid extracts of the whole tissues of each animal. The presence of an insignificant amount of isotope in the respiratory CO_2 indicates that in histamine metabolism, the carbon side chain of the molecule undergoes little if any scission.

In each urine sample, imidazoleacetic acid with R_f approx. 0.19 and also histamine [acetylhistamine cannot be excluded (6)] with R_f approx. 0.79 were identified by one-dimensional paper chromatography followed by radioactivity measurement of 1-cm. segments of each paper strip. This method also revealed the presence of another radioactive peak (R_f approx. 0.08) representing, as yet, an unidentified metabolite; a similar observation was reported by Schayer (6). Furthermore, by the use of the carrier technique, samples of histamine [purified as the bis(*o*-dichlorobenzenesulfonate)] and imidazoleacetic acid (recrystallized several times to constant radioactivity in a mixture of water and acetone) were examined for their radioactivity. We have found that histamine and imidazoleacetic acid account respectively for 34 and 37% (average values for the two rats) of the total activity contained in the urine. It remains therefore to account for the residual urinary radioactivity. Our investigation is being carried out further and the details of this work will be submitted for publication at a later date.

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Department of Biochemistry,
Université de Montréal,
Montreal, Canada
L. P. Bouthillier
Moe Goldner

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