Proceedings
of the
Society
for
Experimental Biology and Medicine

VOL. 37. NOVEMBER, 1937. No. 2.

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Inhibition of Tissue Respiration by Sodium Benzoate and Sodium Hippurate.

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The consumption of oxygen by minced tissue and by tissue slices in the presence of sodium benzoate was studied in order to determine whether this experimental procedure might be used in the investiga-

* These experiments were performed in the Department of Biochemistry, Oxford, with the generous cooperation and aid of Professor R. A. Peters.

tion of the *in vitro* synthesis of hippuric acid. The oxygen uptake of the tissue was measured at 38° C. in an atmosphere of oxygen using the Barcroft differential manometer. The tissue was suspended in the isotonic salt solution of Krebs and Henseleit[1] with and without the addition of extra phosphate. Sodium benzoate or hippurate, equal to 5 mg. of benzoic acid per cc., replaced an equivalent amount of sodium chloride in the experimental solutions. In most cases glucose was added as a substrate.

Sodium benzoate decreased the oxygen uptake of the following tissues of the rat: liver and kidney slices, diaphragm, and minced brain, liver and kidney. A similar effect was obtained with minced pigeon brain. The inhibition of respiration varied with the concentration of benzoate. It was always more marked if glucose was used as a substrate in a poorly buffered medium due to the production of acid and the resulting decrease in pH. By using tissues, such as minced brain or washed minced liver, which possessed low respiratory activity in the absence of added substrate, it was possible to demonstrate that the inhibitory effect was on the glucose or lactate respiratory mechanism rather than on the succinate mechanism. With minced brain the inhibition was only slightly evident in the presence of succinate and marked in the presence of glucose, lactate or pyruvate. Benzoate toxicity in the presence of pyruvate was unaffected by the addition of vitamin B. Jowett and Quastel[2] have reported that concentrations of benzoate smaller than those used in these experiments affected that respiratory process in liver concerned with the oxidation of fatty acids to aceto acetic acid.

Sodium hippurate resembled sodium benzoate in its inhibition of respiration. It was somewhat less toxic for kidney tissue but was equally toxic for the other tissues listed above, including liver slices with which it has recently been possible to demonstrate the *in vitro* synthesis of hippurate.[3] The similarity in the effects of benzoate and hippurate indicated that the synthesis of the latter was not a detoxication as far as the oxygen uptake was concerned.

[1] Krebs, H. A., and Henseleit, K., *Z. physiol. Chem.*, 1932, **210**, 33.

[2] Jowett, M., and Quastel, J. H., *Biochem. J.*, 1935, **29**, 2143.

[3] Griffith, W. H., *Chem. and Ind.*, 1937, **56**, 552.