

Several investigators^{1,2,3,4} have furnished evidence that alcohol can be oxidized by higher plants. However, the previously expressed opinion,⁵ based on analogy with animal tissues, that alcohol is less quickly oxidized than sugar and the finding by Kostytschew³ that it is not always oxidized seem to have dominated much of the later thought on the subject.^{6,7,8,9} Partly as a result of this impression, the idea that alcohol is an intermediate in normal plant respiration has been largely abandoned. While the results discussed here clearly do not prove the hypothesis, they do seem to remove one weighty objection to it.

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THE EFFECTS OF A BEEF LIVER FRACTION UPON FAT SYNTHESIS IN RATS

WE have previously shown^{1,2} that thiamin causes a synthesis of fat in rats and in pigeons. If a diet low in choline is used to study this effect of thiamin the amount of fat in the liver is increased markedly. Choline, subsequently supplied, exercises its well-known lipotropic action. In the course of an investigation of the effects of other members of the vitamin B complex upon fat metabolism we have employed a fraction of beef liver which contains several B vitamins, including pantothenic acid and factor W. Rats fed a fat-free diet devoid of the B vitamins for a period of three weeks lose considerable weight, and the amount of the fat in the body is greatly reduced. If the animals are then given small amounts of the liver fraction the body fat is increased, for example, from 3 to 7 per cent. and the liver fat from 3 to 17 per cent. The administration of choline, even in large dosage, will not cause the liver fat to be normal in

amount, but this effect is secured in a few days by feeding a pancreatic extract, "lipocaic" (kindly supplied by Eli Lilly and Company). A reduction in liver fat may also be produced by feeding a concentrate from rice polish or by giving yeast; neither of these supplements is as effective as "lipocaic" when equal weights are used.

The liver fraction is prepared in the course of the manufacture of an anti-anemic extract from beef liver. The fraction effective in causing fat synthesis is secured by removing the alcohol from the 92 per cent. alcohol solution from which the anti-anemic fraction had been precipitated previously. Information is not available to indicate which constituent of the liver fraction is responsible for the increase in fat synthesis.

The effect of this liver fraction is not a toxic one, as might be produced by chloroform or carbon tetrachloride, since there is a coincident increase in body fat and a rapid gain in weight of the rats. Young animals double their weight in seven days and are active and healthy. We regard these observations as confirmation of the conclusions of Blatherwick and associates³ that liver contains a water-soluble, alcohol-soluble substance which causes fatty livers when fed to rats. However, in their experiments there was no demonstration of fat synthesis such as we have secured.

Preliminary results show that the liver fraction causes a definite increase in cholesterol. The basal diet and the liver fraction are both free of cholesterol, and it seems likely that the increase in cholesterol may have been due to synthesis. "Lipocaic" not only reduces the total amount of fat in the liver but also diminishes the cholesterol. It is suggested that choline may be concerned with the reduction of neutral fat in the liver, while "lipocaic" possibly exerts its effect upon cholesterol esters. If this assumption is correct, "lipocaic" would not be expected to affect the fatty liver produced by thiamin other than would be anticipated from its choline content, as has been found by Best and Ridout.⁴

These results demonstrate that beef liver contains a substance which will markedly stimulate fat synthesis when fed to rats. The total amount of cholesterol in the liver is also increased in amount. The fatty liver thus produced is highly resistant to the lipotropic action of choline but readily responds to "lipocaic." A rapid means of assaying the potency of preparations of "lipocaic" is thus available.

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⁴ C. H. Best and Jessie H. Ridout, *Am. Jour. Physiol.*, 122: 67, 1938.

¹ M. F. Bugajewski, *Biochem. Ztschr.*, 238: 60, 1931.

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³ S. Kostytschew, *Jour. Soc. Bot. Russie*, 1: 182, 1915.

⁴ W. Zaleski, *Chem. Ztschr.*, 69: 289, 1915.

⁵ T. Takahashi, *Bull. Coll. Agr. Tokyo Imp. Univ.*, 5: 241, 1903.

⁶ E. C. Barton Wright, "General Plant Physiology," p. 383. London: Williams and Norgate, Ltd., 1937.

⁷ S. Kostytschew, "Plant Respiration" (American edition, translated and edited by C. J. Lyon), p. 92. Philadelphia: P. Blakiston's Son and Co., Inc., 1927.

⁸ Walter Stiles and William Leach, "Respiration in Plants," p. 75. London: Methuen and Co., Ltd., 1932.

⁹ Meirion Thomas, "Plant Physiology," p. 281. Philadelphia: P. Blakiston's Son and Co., 1935.

¹ E. W. McHenry and Gertrude Gavin, *Jour. Biol. Chem.*, 125: 653, 1938.

² E. W. McHenry and Gertrude Gavin, *ibid.*, 128: 45, 1939.