LXVI. A NOTE ON THE POSSIBLE LIPOTROPIC ACTION OF ALKYLAMMONIUM COMPOUNDS.

BY ELINOR HUNTSMAN MAWSON AND
ARNOLD DEMERRITT WELCH.

*From the Departments of Physiology and Pharmacology,
University of Toronto.*

(Received February 1st, 1936.)

THE fact that choline, the nitrogenous constituent of lecithin, prevents the deposition of fat which occurs when rats are fed on a high fat diet, and also accelerates the removal of fat from fatty livers has been established by Best and his collaborators [1932; 1934; 1935]. This has been termed the "lipotropic action" of choline. It was found also that betaine, the acid corresponding to choline, is active in this respect but aminoethanol, the nitrogenous constituent of kephalin, is inactive. Both choline and betaine were administered as chlorides.

An attempt has been made to determine whether compounds related to choline chloride but without the hydroxyl group possess any lipotropic action. Trimethylammonium chloride (trimethylamine hydrochloride), trimethylethylammonium chloride, tetramethylammonium chloride and trimethylphenylammonium chloride have been used.

The following experiment was carried out to test the possibility that trimethylammonium chloride might influence liver fat. The rats were fed on a diet of mixed grain with added beef fat for 3 weeks, after which 15 were sacrificed to ensure that the livers had become fatty. The remainder were placed on a diet consisting entirely of sucrose. This procedure was shown by Best and Huntsman [1935] to cause a further accumulation of fat in the liver. One group of 15 animals received on the average 20 mg. of trimethylammonium chloride daily per rat (equivalent to about 100 mg. per kg.) and another, 20 mg. of choline chloride for comparison. A third group (controls) received sucrose only. The average liver fatty acid contents at the end of 12 days were as follows: trimethylammonium chloride 24.3 %, choline chloride 5.2 %, controls 16.7 %. Similar results were obtained when larger amounts of the amine, up to 100 mg. per rat per day, were given in other experiments.

The other substances tested, namely trimethylethyl-, tetramethyl- and trimethylphenyl-ammonium chlorides were prepared by the usual methods and analysed to determine purity. Such tetraalkylammonium compounds almost invariably exert a powerful pharmacological action of the curare type. As was expected, it was found that each of these compounds is extremely toxic even when administered orally in small doses in dilute solution. It was impossible to give a sufficient quantity to correspond with a known effective amount of choline chloride or to obtain evidence of lipotropic activity. In all cases where appreciable quantities were given the animals sickened, refused food and eventually died.

It is interesting to note that the triethyl homologue of choline (triethyl- β -hydroxyethylammonium hydroxide) has been shown by Channon and Smith [1936] to be effective in preventing deposition of liver fat although its action is not so intense as that of choline.

REFERENCES.

- Best and Huntsman (1932). *J. Physiol.* **75**, 405.
Best (1934). *Lancet*, i, 1155, 1216, 1274.
—— and Huntsman (1935). *J. Physiol.* **83**, 255.
Channon and Smith (1936.) *Biochem. J.* **30**, 115.