In both sets of chlorpromazine-treated mice there was an increase in liver glycogen, although this was more marked in the set housed at 21°. By contrast the increase in brain sugars in the pentobarbitone-treated group was accompanied by no change in total liver glycogen. This also suggests a generalised disturbance induced by chlorpromazine as opposed to a more selective effect of pentobarbitone on brain glucose utilization.

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Inhibition of biosynthesis of cholesterol by salicylate

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IT IS now known that salicylate inhibits the incorporation of acetate into long-chain fatty acids in rat liver[1] and produces a decrease in serum cholesterol[2] and free fatty acids in man[3] and experimental animals.[4] It has been shown recently that the effect of salicylate on the biosynthesis of long-chain fatty acids is probably connected with inhibition of the activity of acetyl-CoA carboxylase.[5] In view of the fact that mevalonate is derived, at least partly, from malonyl-CoA,[6,7] it is possible to suggest that the reduction in serum cholesterol brought about by salicylate may also be due to the inhibition of acetyl-CoA carboxylase.

In the present work, the effect of salicylate on cholesterol biosynthesis was studied.

METHODS

The incorporation of 1-^{14}C-acetate and 2-^{14}C-mevalonate into cholesterol was studied by using 700 g supernatant fractions of rat liver homogenate. The reaction mixture contained 2 ml of homogenate; NADPH, 3·5 μmoles; NADH, 3·5 μmoles; 1-^{14}C-acetate, 2 μc (3·5 μmoles) or 2-^{14}C-mevalonate, 0·1 μc (2·6 μmoles). In the flasks containing the labelled acetate, $KHCO_3$ (3 mg) was added. Sodium salicylate was used in a concentration of 10^{-3} M. The total volume of mixture was 2·5 ml. It was incubated for 1 hr at 37° in a shaker. Other details of the methods and techniques used for the extraction of labelled sterols and fatty acids have been described earlier.[8]

RESULTS AND DISCUSSION

The data presented in the table show that in all three experiments, salicylate, in a concentration of 10^{-3} M, reduced the incorporation of acetate into the sterol fraction by 26–34 per cent. The decrease

TABLE 1. EFFECT OF SALICYLATE (10^{-3} M) ON THE INCORPORATION OF ^{14}C-ACETATE INTO CHOLESTEROL AND FATTY ACIDS AND ^{14}C-MEVALONATE INTO CHOLESTEROL

Substrate	No.	Condition	Unsaponified fraction (sterols) (cpm/g of liver)	(% inhibition)	Saponified fraction (fatty acids) (cpm/g of liver)	(% inhibition)
1-^{14}C-acetate	1	control	12,757	—	2699	—
		salicylate	9425	26	1634	40
	2	control	18,931	—	4073	—
		salicylate	12,412	34	1678	59
	3	control	33,212	—	6135	—
		salicylate	23,022	30	3080	50
2-^{14}C-mevalonate	1	control	4200	no inhibition		
		salicylate	4408			
	2	control	4299			
		salicylate	4979			
	3	control	4732			
		salicylate	4367			

in the incorporation of acetate into the fatty acids fraction was a little more marked and reached an average of 50 per cent (the same percentage was observed by P. Goldman in his experiments).[5] Meanwhile the salicylate had no effect on the incorporation of mevalonate into cholesterol. It must therefore act on the earlier stages of biosynthesis of cholesterol, connected with conversion of acetate. The data obtained in the present work does not contradict the suggestion that salicylate inhibits the reaction catalysing the carboxylation of acetyl CoA. The lowering of serum cholesterol by salicylate[2] may be connected with the inhibition of its biosynthesis.

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Comparative study of the subcellular distribution of submaxillary kallikrein

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SUBCELLULAR studies indicate that submaxillary kallikrein is held in granules. On differential centrifugation the kallikrein-containing particles sediment at relatively low g^1 and on density-gradient