The action of the various homologs listed here in attracting several species of insects which occupy rather widely different habitats suggests that naturally occurring aldehydes may comprise a class of compounds of some considerable importance in influencing the chemosensory behavior of insects.

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The Effect of Choleretic and of Hydrocholeretic Agents on Bile Flow and Bile Solids in the Isolated Perfused Liver[1]

Ralph W. Brauer[2] and Rita L. Pessotti[2]

Department of Pharmacology and Experimental Therapeutics, School of Medicine, Louisiana State University, New Orleans

The mechanisms of bile formation and the factors controlling bile flow rates have hitherto been studied *in vivo* only; innervation, complex blood supply, variable oxygen tensions in the organ, and other factors that may influence bile secretion cannot be separated under those conditions. The development of an isolated liver preparation secreting bile for 12 hr or more (*1*) promises to greatly facilitate analysis of the physiology of bile secretion. The present communication is an example of the application of this preparation to the solution of a problem formulated but not resolved on the basis of studies in the intact animal.

Bile flow can be stimulated by various agents; prototypes of these are the conjugated bile acids on the one hand and oxidized unconjugated bile acids like dehydrocholanic acid on the other. The former (*2*) produces a marked increase of bile flow as well as bile concentration; the latter (*3*) produces an enhanced flow of bile with constant or diminished solid content. Drugs acting like dehydrocholates-hydrocholeretics, in dogs, cause marked increases in hepatic arterial, but not in total hepatic, blood flow (*4*). By contrast, choleretics like taurocholate cause no significant changes in hepatic circulation.

Is, then, the difference between choleresis and hydrocholeresis based on this circulatory effect, or is the circulatory effect secondary to a difference in response of the hepatic parenchyma to agents of these two groups? If hydrocholeresis as well as choleresis could be observed in the isolated organ, this preparation with its simple and controllable circulation should permit a resolution of the question raised.

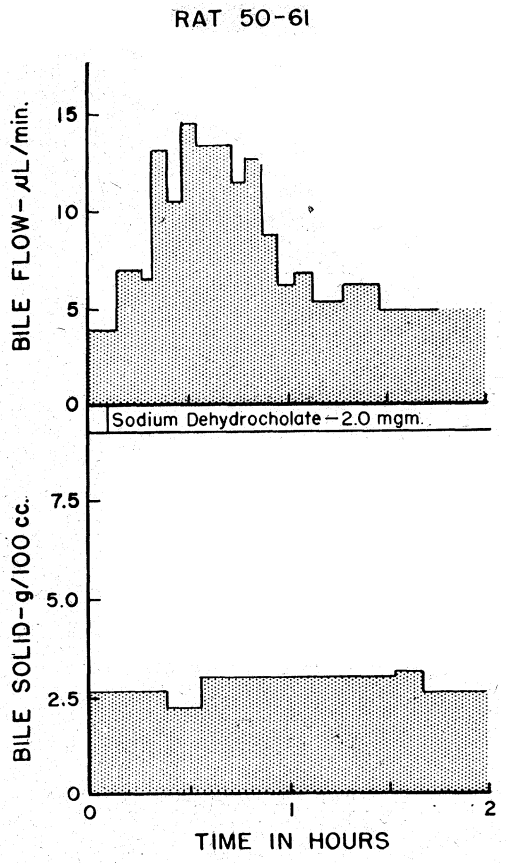

FIG. 1. Bile flow and bile solids after Na dehydrocholate. Rat liver perfusion 50-61, ♀, 280 *g*; 0 time—470 min perfusion. Perfusate flow = 73 ± 3 ml/min.

Livers of mature Sprague-Dawley rats were perfused as described in (*1*). Blood flow, bile flow, and bile total solids were determined (*1*). All studies were made during the steady bile flow phase of each preparation.

Conjugated bile salts were prepared from dog hepatic bile according to (*5*), recrystallized twice from alcohol-ether, and dried over silica gel. Sodium dehydrocholate (Procholon sodium, Squibb) was obtained in 20% solution; 2% solutions of both agents were used for injection.

Bile production by the isolated liver is readily affected by choleretic agents. In a series of 11 preparations the maximal increases in flow rates produced by injecting 2.0 mg sodium dehydrocholate averaged 250 ± 45%. For comparison, administration of the same dose to intact rats with bile fistulas resulted in a mean maximal increase of only 79 ± 17%. The administration of conjugated bile salts similarly caused increased bile flow rates (mean maximal increase after

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[2] Present address: U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.

2.0 mg—120 ± 15% above preinjection values—5 preparations). Time courses of bile flow after these two agents in typical experiments are shown in Figs. 1 and 2.

In a series of 16 preparations involving 35 injections, the total solid contents of bile before and after choleretics were determined on samples collected at 10-min intervals. Ten of these experiments involved the administration of dehydrocholate only (20 injections), 3 of bile salts only (5 injections), and 3 of bile salts and dehydrocholate administered in succession to the same preparation (5 injections of bile salts, 5 of decholin). Typical results of the experiments are represented in Figs. 1 and 2: choleresis induced by

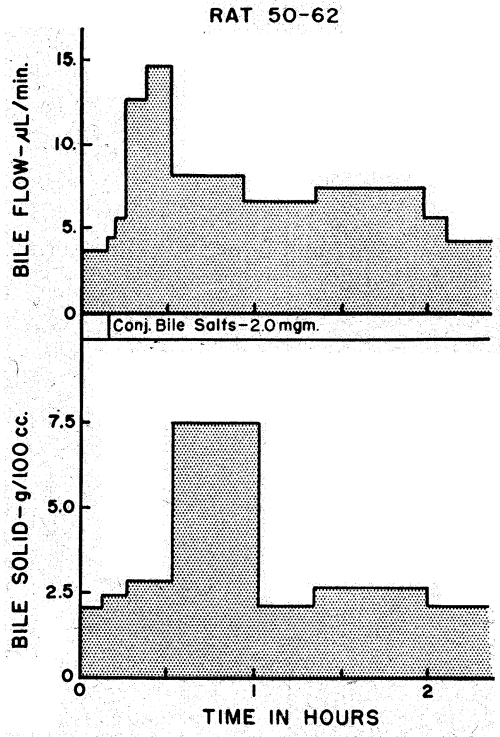

FIG. 2. Bile flow and bile solids after conjugated bile salts. Rat liver perfusion 50-62, ♀, 291 g, 0 time—240 min perfusion. Perfusate flow = 66 ± 3 ml/min.

dehydrocholate was accompanied by unchanged total solid concentration in 17 injections, and by decreased total solids in 8 injections; choleresis induced by conjugated bile salts was accompanied by pronounced increases in the total solid content of the bile in 9 out of 10 injections.

Perfusate flow through the liver, determined at 2-min intervals, showed no consistent changes following injections of either drug. The method employed was such that 10% changes in flow would have been detected.[3]

In the isolated liver preparation choleretic as well as hydrocholeretic effects can be elicited. In fact, the preparation responds more markedly than the intact animal, possibly as a result of bile salt depletion in the isolated circulation.

The parallel responses of isolated, perfused livers and of livers in intact animals justify application of the present results to the question raised originally. The isolated liver is perfused through the portal vein only; thus, changes in hepatic arterial blood flow cannot possibly occur. Since hydrocholeresis and choleresis are nonetheless clearly distinguishable in this preparation, a specific vascular response cannot be the basis of the difference in action between conjugated bile salts and dehydrocholic acid.

Again, total blood flow also remained unchanged in these experiments. Recalling that the blood supplied to the liver *in vitro* is saturated with oxygen—differing from that supplied in the intact animal—these facts lead to the following conclusion: If sufficient oxygen is supplied to the liver, choleresis as well as hydrocholeresis can be observed without accompanying changes in blood flow. Hence, differences between the two types of drug action depend upon some direct effect on the hepatic parenchyma, most likely on the hepatic cells.

[3] This has since been confirmed by using a continuously recording flowmeter, sensitive to fluctuations in flow of ± 1%.

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The Purity of Crystalline Lactic Dehydrogenase

J. B. Neilands[1]

Nobel Medical Institute, Stockholm, Sweden

In view of the results obtained by Theorell (*1, 2*) on the kinetics and mechanism of action of alcohol dehydrogenase, it seemed of interest to investigate lactic dehydrogenase in the same manner.

The lactic dehydrogenase investigated in the present study was Straub's (*3*) crystalline enzyme from heart muscle. Several preparations were made, and all gave the electrophoretic pattern shown in Fig. 1. This observation is the subject of the present communication.

In Fig. 1 two components are shown migrating to the anode, the major component having the greater velocity. Experiments in the pH range of 5–7 showed the two components to have a mobility difference of -0.8×10^{-5} cm^2 v^{-1} sec^{-1}. Electrophoresis was therefore used to obtain pure samples of each component. In 0.5 saturated ammonium sulfate solution the pure major component yielded crystals that appeared

[1] National Research Council fellow in the medical sciences. Present address: Department of Biochemistry, University of Wisconsin, Madison. The author is indebted to Hugo Theorell for interest and advice.