Galactose and Bile Flow.* (24860)

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Galactose and lactose have several physiologic properties not characteristic of other carbohydrates(1,2,3). Rats ingesting these sugars in sufficiently high amounts exhibit transient diarrhea, ruffed fur and paw edema and eventually develop cataracts. Galactosuria, polyuria and polydypsia occur. In some studies concerning dietary carbohydrates and gastrointestinal secretions another property peculiar to these sugars appeared. Bile volume flow is depressed following ingestion of these but not other sugars.

Method. Rochester colony albino rats (125 to 150 g) were maintained on diet of dog checkers. After 24-hour fast they were anaesthetized with di-ethyl ether and the bile duct cannulated with polyethylene tubing. In some animals the carotid artery was similarly cannulated. Animals were then placed in restraining cages and allowed to recover from the anesthesia. Bile flow was measured in 30-minute periods by means of graduated pipette attached to polyethylene cannula. After 4 or more determinations of flow during fasting state, the animals were administered a test dose of carbohydrate by stomach tube or *via* intra-arterial cannula. Volume flow determinations were continued for 6 or more periods. Collected bile was not returned to animal. Calcium analyses were done by flame photometer.

Results. During fasting control periods, flow rates in individual rats varied less than 5% but the range was 0.25 ml of 0.80 ml/hour. In each animal average flow rates during 4 or more fasting periods were averaged and this flow rate assigned a value of 100%. Flow rate during each period was computed as percentage of average control rate of flow.

Every sugar tested by intra-arterial injection caused a transient drop in flow lasting 30 minutes. In Table I are summarized data on flow rates as percentage of control during a 2 hour interval, starting 30 minutes after administration of test sugar. Glucose administered by stomach tube or by intra-arterial injection did not modify bile volume flow. Of several pentoses tried a small and barely significant depression in flow followed only administration of L-xylose and D-lyxose. Preliminary observations suggest that fructose and sucrose likewise do not change bile flow. Galactose in dosages of one mg and more/g of body weight causes depression in bile flow lasting 2 or more hours. Fig. 1 shows time course of bile flow following oral administration of several dosages of galactose. In general response is proportional to dosage used. Dosages of 25 mg of this sugar given intra-arterially appear to enhance slightly volume flow. Lactose administered orally depressed bile flow to lesser extent than would be predicted on basis of its galactose content. This may be related to differences in absorptive rates of the monosaccharide administered alone as compared to galactose in the disaccharide which must first be hydrolyzed.

When protein was fed along with galactose or lactose the depression in bile flow was much less marked. In animals administered 500 mg of lactose plus 200 mg of protein (egg albumin) volume flow averaged 103 ± 6% of control flow. Following feeding of 500

TABLE I. Volume Flow of Bile.

Sugar	Dosage	Route	No. animals	Bile flow (% control flow)
Glucose	500	Oral	9	100 ± 7†
	250	I.A.*	9	96 ± 4
Galactose	250	Oral	9	75 ± 4
	500	"	8	59 ± 5
	25	I.A.	9	114 ± 4
	250	"	10	65 ± 5
Galactose + glucose	250 each	Oral	9	73 ± 6
Lactose	500	"	9	82 ± 4
D-ribose	200	I.A.	4	107 ± 4
D-arabinose	"	"	7	100 ±11
L-arabinose	"	"	7	106 ± 6
D-lyxose	"	"	4	88 ± 4
L-xylose	"	"	6	86 ± 4

* Intra-arterial. † Mean ± stand. error.

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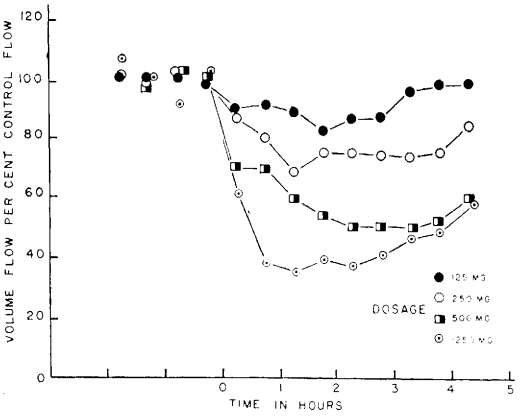

FIG. 1. Bile volume following oral galactose administration.

mg of galactose plus 300 mg of protein, volume flow of bile averaged 81 ± 2% of control rate in comparison to 59% when this quantity of galactose was given alone.

When volume flow remained constant there was no change in total solids content of bile collected during 2 successive periods before and after feeding. In 8 animals, at flow rate of 0.35 ml/hour total solids were 3.4 ± 0.4% in both periods. Inorganic solids were 1.18 ± 0.11% during first period and 1.08 ± 0.08 during second period. In 8 animals in which flow rates decreased from average of 0.50 ± .02 to 0.35 ± .02 ml/hour due to galactose administration, solids content likewise remained unchanged. In fasting period total solids were 3.60 ± .20% with 1.13 ± .07% inorganic solids. In the period following galactose administration with lower flow rates, total solids were 3.50 ± 0.37% and inorganic solids were 1.08 ± .06%. Calcium concentration in bile was likewise unchanged when volume flow was reduced by galactose administration. In 15 animals at flow rates of 0.48 ml/hour calcium concentration was 6.57 ± .42 meq/liter as compared with 5.98 ± .54 meq/liter when flow rate reduced to average of 0.29 m/hr.

The mechanism by which depression of bile flow is produced is unknown. Galactose has a trans arrangement of the hydroxyl groups on carbon atoms 4 and 5. Glucose, fructose and 3 of pentoses used that did not influence bile flow have a cis arrangement of these comparable hydroxyl groups. The 2 pentoses that produced small reductions in bile volume flow have the same arrangement of these hydroxyl groups as does galactose. This raises the possibility of stearic induced inhibition of secretion of bile. Further studies are planned using other carbohydrates with cis and trans arrangements of these hydroxyl groups and the effect of increasing amounts of glucose on inhibition of bile flow by standard dosage of galactose.

Summary. Galactose and lactose depressed volume flow of bile in the rat. This depression is in general proportional to dosage of galactose administered. Addition of protein to test meal of galactose or lactose lessens the effect of these sugars on bile flow. Since composition of bile as to inorganic and organic solids and calcium remained constant at different rates of flow, the excretion of these substances is proportional to volume flow.

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