Brief Notes and Comments

Xylitol Absorption in Healthy Men

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SUMMARY

Xylitol absorption from the human intestinal tract was studied directly, by aspiration and analysis of ileal contents after ingestion of xylitol (5 to 30 gm.) mixed with glucose and a nonabsorbable marker, polyethylene glycol. Studies in five healthy subjects showed that xylitol absorption ranged from 49 to 95 per cent. Chronic xylitol administration (30 gm. daily for two to three weeks) did not alter significantly the rate of xylitol absorption. Neither symptoms nor laboratory abnormalities were observed following chronic xylitol ingestion.

Nearly complete intestinal absorption must be taken into account in considering the usefulness of xylitol in the diet, since untoward responses to intravenous xylitol infusions have been reported. DIABETES 22:279-81, April, 1973.

It has been suggested that xylitol, a five-carbon sugar alcohol, may be useful as a sweetener in the diabetic diet.[1-7] On the other hand, reports of possible harm from *intravenous* administration of xylitol have appeared.[8-10]

To understand the fate of xylitol in the diet, it is necessary to know whether a great deal or very little is absorbed from the human small intestine. The only available study, by Dehmel, Förster, and Mehnert,[11] showed at most 30 per cent absorption of xylitol from human duodenum, leaving the impression that absorption of xylitol as a food additive can be neglected. We decided to study xylitol absorption over the entire length of human small bowel.

EXPERIMENTAL PROCEDURES AND METHODS

The subjects were five healthy men aged from twenty-one to thirty-two years who were fully informed of the possible risks of the study. They showed no evidence of diabetes mellitus.

The technic used to study absorption was essentially that described by Dahlquist,[12] which gives a direct, although approximate, estimate of the percentage of a substance absorbed over the entire length of small bowel. Each subject was intubated with a mercury-weighted polyvinyl tube, passed until the distal orifice was 250 to 300 cm. from the teeth. This distance is adequate to reach the terminal ileum.[13] The test meals consisted of either 5 or 10 gm. of xylitol* plus an equal amount of glucose in 200 ml. of water, or 15 or 30 gm. of xylitol plus an equal amount of glucose in 600 ml. of water. Glucose was added to simulate the conditions of mixed diet, in which we were interested, and also as a check on our technic (glucose would be expected to be completely absorbed). The test meal also contained 0.2 to 0.4 μc of C-14 polyethylene glycol (PEG) as a nonabsorbable reference marker. Following ingestion of the test meal, ileal fluid was continuously aspirated for three to four hours in a series of samples until the C-14-PEG count became negligible. Blood samples for xylitol and glucose were collected at 60 and 120 minutes, and urine for xylitol measurement from zero to twelve hours and from twelve to twenty-four hours after swallowing of the test meal.

A second series of tests was carried out in three subjects who took 15 gm. of xylitol powder twice a day with meals for two to three weeks immediately after the first set of tests ("chronic xylitol ingestion"). Blood chemical tests reported to show abnormalities after intravenous xylitol[8,9] (serum bilirubin, GOT, alkaline phosphatase, uric acid) were carried out before and after chronic ingestion.

Analyses. Intestinal fluid samples were counted for C-14 PEG in a Packard liquid scintillation counter, after appropriate preparation and with correction for quenching. The concentration of sugars was determined only in those samples containing appreciable quantities of

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PEG, in protein-free filtrates. Glucose was analyzed by a modification of Lowry's method[14] using hexokinase and G-6-P dehydrogenase. Xylitol was also measured enzymatically, using L-xylulose dehydrogenase (Boehringer) and conversion of NADP to NADPH at 340 mμ over five minutes.* Twelve samples were also analyzed independently for xylitol by gas-liquid chromatography;* the results were somewhat lower than by the enzymatic method (mean, 89 ± 7 per cent S.E.M.). Hence, estimates of absorption based on the enzymatic method would be somewhat below those based on the chromatographic method.

Calculation. The percentage of sugar absorbed was calculated from the following formula:[12]

$$\text{Absorption } (\%) = 100 \left(1 - \frac{[\text{carbohydrate}]\ \text{aspirated} \cdot [\text{C-14 PEG}]\ \text{ingested}}{[\text{carbohydrate}]\ \text{ingested} \cdot [\text{C-14 PEG}]\ \text{aspirated}}\right)$$

RESULTS

The table shows that in most of the ten tests, xylitol was nearly completely absorbed (72 to 92 per cent), over a dose range from 5 to 30 gm. One subject, K.C., showed lower values—49 and 66 per cent—but the other four subjects showed very similar results. Glucose, as expected, was completely absorbed in all tests.

Chronic xylitol ingestion (30 gm. a day for two to three weeks) did not alter the xylitol absorption appreciably. Percentage absorption before and after chronic ingestion were as follows: Subject S.P., 91 and 97 per cent (10 gm.); Subject G.R., 92 and 74 per cent before, 76 per cent after (15 gm.); 83 and 70 per cent (30 gm.); Subject K.C., 66 and 70 per cent (15 gm.). There was no alteration in serum levels of bilirubin, uric acid, GOT or alkaline phosphatase.

None of the subjects noted diarrhea or any other untoward symptoms while taking the daily dose of xylitol.

Plasma samples at one and two hours after the test meal showed no xylitol but showed the expected rise and fall in glucose. Quantitative urine analysis for glucose and xylitol showed negligible amounts of either sugar (less than 0.10 gm. per twelve hours) at zero to twelve, or twelve to twenty-four hours, after the sugars were swallowed.

DISCUSSION

The doses of xylitol used in our study were chosen because they have been well tolerated according to previous reports and would be useful as a sweetener (larger doses sometimes cause diarrhea). It is clear that most of xylitol doses up to 30 gm. is absorbed from the gut within three to four hours after swallowing. The results are the same whether xylitol is measured in intestinal fluid by an enzymatic method or by gas-liquid chromatography; in fact, the absorption calculated from chromatographic analyses is even higher than that from the enzymatic assays.

Bässler, Prellwitz et al.[7] also reported low blood levels of xylitol after ingestion of 40 gm. doses and found very little in the urine. They attributed these findings to slow absorption of xylitol, but they did not measure it. It is likely that the absorbed xylitol is readily metabolized by way of the pentose phosphate cycle or some other mechanism. We have carried out intravenous studies in dogs which indicate the same; only when large amounts are rapidly infused does xylitol reach significant levels in plasma and urine.

It is possible that the presence of glucose in our test meals may have enhanced the absorption of xylitol;

*In recovery experiments, 80 to 120 per cent of added xylitol was estimated.

*Thanks to Dr. Howard A. Spalt, Masonite Co. Research Center, St. Charles, Ill.

TABLE 1

Results of xylitol absorption (ten tests, five subjects)

Approx. test solution	Subjects	% Absorption* Xylitol	% Absorption* Glucose
5 gm. xylitol 5 gm. glucose in 200 ml.	L.S.	85 (72-94)	100 (99.9-100)
	G.R.	95 (83-99)	100 (99.9-100)
10 gm. xylitol 10 gm. glucose in 200 ml.	B.C.	83 (81-84)	100 (99.9-100)
	S.P.	91 (87-95)	100 (99.9-100)
15 gm. xylitol 15 gm. glucose in 600 ml.	G.R.	92 (91-94)	100 (99.8-100)
	G.R.	74 (63-82)	100 (99.7-100)
	L.S.	72 (64-82)	100 (99.9-100)
	K.C.	66 (59-71)	100 (99.9-100)
30 gm. xylitol 30 gm. glucose in 660 ml.	G.R.	83 (80-85)	100 (99.9-100)
	K.C.	49 (30-60)	100 (99.7-100)

* Mean and range calculated from eight to twelve samples.

Holdsworth and Dawson[15] found evidence for such an effect of glucose on fructose absorption. However, with the usual diet, glucose would be presented to the gut for absorption along with xylitol, as in our study.

We carried out only limited studies regarding possible xylitol toxicity in our subjects, but found none. Untoward effects after intravenous xylitol (elevated serum bilirubin, GOT and uric acid; metabolic acidosis) were associated with much larger doses—1.2 gm./kg. or more.[8-10] It is still unclear whether xylitol itself, or a possible contaminant, accounted for these effects.

Our results make clear that *if* xylitol itself is toxic at certain dose levels, harmful effects could result from ingestion of xylitol. It also must be regarded as a source of calories. Since it has a palatable, sweet taste, it still may have usefulness as a sweetener, provided a safe dose range can be established and the mechanism of intravenous xylitol toxicity elucidated.

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