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Letter to the editors

Biochemical and morphological changes of the rat adrenal medulla induced by peroral xylitol

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Sir,

Boelsterli and Zbinden (1985) reported in this journal on biochemical and morphological changes of the rat adrenal medulla induced by xylitol. This paper was interesting, multifaceted and it elucidated an important biomedical issue related to xylitol which is becoming a leading nutritive sucrose substitute by virtue of its noncariogenicity and anticariogenicity, and its suitability in the diabetic diet. Although the methodology and the presentation of data of the above paper were by and large impeccable, we oppose the authors' view, presented in their Discussion, that peroral administration of xylitol would cause hyperinsulinemia and hypoglycemia. Our perusal of the study of Boelsterli and Zbinden showed that some of the data presented does not justify the conclusions made. Our view is based on the following methodological features and conclusions of their study.

Hyperinsulinemia-hypoglycemia. Peroral administration of xylitol does not induce any significant hyperinsulinemia and hypoglycemia. This has been convincingly demonstrated by several research teams who have studied either humans (Muller-Hess et al. 1975; Huttunen 1976; Förster and Mehnert 1981) or experimental animals (Salminen et al. 1982; Hämäläinen and Mäkinen 1982). The xylitol report of the Federation of American Societies for Experimental Biology (1978) came to the same conclusion. Boelsterli and Zbinden sought support for their conclusions from the studies of Kosaka (1969), Montaque and Taylor (1968) and Asano et al. (1977). However, Kosaka administered xylitol intravenously to rats and Montaque and Taylor obtained their results from in vitro studies using pancreas cells. Asano et al. used an intravenous infusion technique to administer xylitol to fasting dogs. In contrast to these procedures, Boelsterli and Zbinden gave xylitol to the rats enterally, the method which we have used in rat experiments as the only (physiological) route of administration. We have repeatedly emphasized the importance in making a clear distinction between enteral and parenteral administration techniques, or between enteral feeding and any procedure which bypasses the only physiological way of administration (Mäkinen 1978; Hämäläinen and Mäkinen 1981). In a peroral feeding study, slowly absorbed carbohydrates like xylitol cannot be expected to produce changes equal to those occasionally associated with other type of studies.

The blood glucose assay method (a test strip) used by Boelsterli and Zbinden may not be sufficiently accurate to justify the conclusion that hypoglycemia was present. Their paper did not mention whether or not the rats were in a fed state or not at the termination of the xylitol treatments. Furthermore, Table 4 in their article shows large differences for blood glucose levels in the control animals between the 2- and 8-week stages. Our rat experiments, as well as those of most other authors, have shown that the consumption of xylitol is associated with a slight decrease in blood glucose levels, but all values have been within the normal physiological range. This is evidenced by the normal serum glucagon levels, for example, of xylitol-fed rats; increased glucagon could be regarded as a primary indicator of hypoglycemia.

Decrease of the synthesis of catecholamines. We think that the decrease in the rate of the synthesis of catecholamines reported by Boelsterli and Zbinden (1985) was not convincingly demonstrated. These authors showed only marginal differences in the conversion of radioactively labelled tyrosine into catecholamines. The determination of the activities of tyrosine hydroxylase, dopamine-β-hydroxylase and phenylethanolamine-N-methyltransferase also revealed only slight differences between the control animals and those fed xylitol. In the case of catecholamines, the small differences between the control diet and the xylitol diet can be examined in the light of the extremely low CPM values (which we regard as falling in the borderline of reliable measurements), and the small number (four to five) of animals tested. In fact, the conversion of labelled tyrosine into catecholamines in the xylitolfed rats was lower in one case only: A decrease in the synthesis of [^{14}C]-dopamine was reported in rats given 20% xylitol in food. However, in this comparison $p<0.02$ and the number of animals was four to five. In this case Boelsterli and Zbinden gave the animals 25 μCi [^{14}C]-tyrosine (5.5×10^7 DPM) and found only about 130–200 DPM in the form of dopamine. Consequently, we would like to question the capacity of the analytical high-performance liquid chromatographic technique used in the fractionation of all the catecholamines from both glands. The procedures presented in the papers involved (Boelsterli et al. 1984; Boelsterli and Zbinden 1985) did not provide enough details for us to judge the validity of these methods. Taking into account the contam-

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ination risks and the relatively complex purification procedure of catecholamines, these data seems to be random. It is necessary to point out that the authors themselves showed that the *chemically* determined catecholamine values were almost identical in all experimental groups.

Volume of the chromaffin cells. The volumes (V) of the chromaffin cells of the adrenal medulla reported by Boelsterli and Zbinden (1985) do not follow the logical age order of the animals, because V was smaller (0.472 mm^3) in the 14-week-old rats than in the 8-week-old rats (0.517 mm^3). In contrast to their present findings, Boelsterli and Zbinden (Boelsterli et al. 1984) have previously demonstrated an increase in V as a function of age (7 weeks, 0.420 mm^3; 12 weeks, 0.643 mm^3). In both cases the values presented were from untreated control rats. Consequently, the reported increase in the total volume of the adrenal medulla of rats fed xylitol in the later study of these authors (Boelsterli and Zbinden 1985) may be an artefact resulting from labile experimental arrangements.

Based on the above considerations, our view is that the paper of Boelsterli and Zbinden (1985) does not reveal any significant changes taking place in the metabolism of the rat adrenal medulla of rats fed xylitol. We have reached a similar conclusion on the basis of our rat studies (Hämäläinen and Mäkinen 1986).

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