Turku sugar studies
An overview

ARJE SCHEININ & KAUKO K. MÄKINEN

The aim of the present series of studies was to investigate the dental, oral and general effects of chronic consumption of fructose (F), sucrose (S) and xylitol (X) in man. The scope included clinical and radiographic evaluation of the incidence of dental caries, biochemistry of dental plaque and saliva, oral microbiology, observations of periodontal conditions, and lipid and carbohydrate intermediary metabolism. These studies have been presented in the form of separate reports, referred to in the ensuing text by their Roman numerals.

The first reports (I—IV) describe intermediate results obtained during the first study year (I, II, IV), or the initial 8 months (III), of a 2-year trial involving almost complete substitution of dietary S with F or X. Most of the essential observations during the first part of the trial are, however, included in the final reports (V—XVII).

The general planning and administration of the 2-year trial is described (VI). The initial material consisted of 125 subjects, mean age 27.6 years. The material was divided partly on individual preference basis into 3 experimental groups. The S-group comprised 35, the F-group 38, and the X-group 52 subjects; the latter group was made larger due to the possibility of loss of subjects. During the study 10 subjects discontinued or were otherwise excluded. The mean individual monthly intake of S, F and X was 2.2, 2.1 and 1.5 kg, respectively. Osmotic diarrhoea occurring initially in a number of subjects in the X-group gradually disappeared as a phenomenon of adaptation took place. Later the occurrence of diarrhoea in the X-group was of nearly the same frequency as in the S- and F-groups.

The caries incidence during the study (V) showed profound differences in the caries increment rate as affected by peroral F, S and X. F was found somewhat less cariogenic than S. A massive reduction of the caries increment was observed in relation to X-consumption.

The principal biochemical findings on whole saliva and plaque (VII) also included quantification of plaque. Throughout the study, those subjects on the X-diet maintained a significantly lower amount of plaque than those on the F- and S-diets. Decreased lactate concentrations of plaque and whole saliva, diminished activity of whole saliva amylase, and reduced hydrolysis rate of sucrose in plaque and whole saliva were observed in relation to X-consumption. Increased activity in plaque of certain glycosidases and lactoperoxidase in saliva was associated with the intake of X.

The final microbiological observations in conjunction with the 2-year feeding trial involving total substitution of S by F and X are presented in two papers (VIII & X). The dietary regimen did not affect the major microbial categories occurring in plaque or saliva (VIII). On the other hand, the mean values of viable *Streptococcus mutans* in plaque were lower in the X-group than in the other two sugar groups throughout the dietary phase of the study (IV, X). Additionally, the geometric and arithmetic means of the colony forming units on selective Rogosa S.L. and Sabouraud antibiotic agar were significantly lower in the X-group than in the

F- and S-groups. A reduction of the acidogenic and aciduric oral flora was thus observed particularly in the X-group (VIII). During the course of the study, no evidence was obtained of adaptation or mutation enabling acidogenic decomposition of X (X).

A further aim was to determine, using clinical, radiographic and biochemical methods, whether chronic consumption of X could indirectly affect the response reactions of the periodontal tissues. During the diet period, no significant differences among the sugar groups could be established (IX). It should be noted, however, that periodontal registrations were not carried out at the beginning of the trial, and comparisons with the initial level were thus excluded. In all 3 sugar groups the gingival conditions improved toward the end of the study.

During the planning phase of the trial, due consideration was given to the unrealistic nature of the goal of total substitution of S through F or X. Recognition of this fact enhanced the importance of the accompanying surveys on the general health of the subjects. The effects of chronic consumption of F, S and X were thus studied with regard to glucose, lipid and urate metabolism (XI), and further metabolic behaviour, including liver function tests and hematological assays (XIII). These studies were expanded by disc electrophoresis of certain serum proteins (XVI).

No consistent differences were found in serum triglycerides, glucose, insulin, urate, lactate and pyruvate concentrations, or in the urinary excretion of urate among the experimental groups. Serum cholesterol tended to be lower in the F- than in the X-group, but the difference disappeared when subjects with initial high serum cholesterol in the base line examination were excluded (XI).

Individual and pooled serum samples of the subjects were further analyzed for various electrolytes, bilirubin, ascorbate, alkaline and acid phosphatase, amylase, transaminases, lactate dehydrogenase and amino acids. No significant differences among the experimental groups were found for any of the compounds or enzymes studied. A difference approaching statistical significance was observed for amylase which was lower in the F- and X-groups than in the S-group (XIII).

In view of biochemical findings in plaque and saliva during the early phases of the trial, detailed analyses of the effect of the diets was carried out on oral peroxidases, redox potential, and the concentration of ionized fluorine, iodine and thiocyanate (XII). In the X-group a considerable increase in salivary lactoperoxidase activity, was thus demonstrated. The concentration of fluoride was lower in the X-group than in the other sugar groups.

The oral biochemical studies carried out in relation to the 2-year trial included an investigation of the amino acid composition of whole saliva (XIV), and a survey of the activity of glycosidases in oral fluids and plaque (XVII). It was observed that the consumption of F, and particularly of X, increased the amount of most amino acids. The increase was most likely due to an increased protein catabolism of microorganisms deprived of sucrose. On the other hand, no increased destruction of oral collagenous tissues could be demonstrated (XIV).

No significant differences among the sugar groups were observed with regard to most glycosidases in pooled plaque or saliva preparations. However, gingival exudate showed the lowest glycosidase

values in the X-group (XVII). Pooled and individual exudate samples were additionally analyzed biochemically and with regard to reactions occurring in the microvasculature of the hamster cheek pouch. These studies indicated differences in the inflammatory properties between individual exudate samples (XV).

The magnitude of the reduction of the incidence of dental caries (V), and the accompanying biochemical (VII, XII, XIV, XVII) and microbiological effects (VIII, X) necessitated further studies in relation to partial substitution of S by low amounts of X. This was achieved in a second longitudinal study comparing the effects of S- or X-containing chewing gums during a 1-year trial. In this study as well, the clinical and radiographic recordings of caries (XVIII) were supplemented by biochemical (XIX) and microbiological analyses (XX) of plaque and saliva.

Initially the material comprised 102 subjects, mean age 22.2 years, assigned at random to the S- or X-group. During the study 2 subjects were excluded. The consumption of chewing gum, calculated as the number of sticks per day was 4.0 in the S-group, and 4.5 in the X-group. The frequency of sucrose intake was 4.2 times per day in the S-group, and 4.9 in the X-group. This included S consumed in solid form between meals 1.9 times per day in the S-group, the corresponding value being 2.1 in the X-group. The caries incidence (XVIII) assessed independently by clinical and radiographic methods, approximated the corresponding 1-year observations in the diet study.

The accompanying biochemical studies showed, however, that there were no differences in the lactoperoxidase and invertase-like enzyme activities between the S- and X-groups (XIX). On the other hand, a significant decrease in plaque formation was observed in relation to chewing *per se*. There was also a significant difference in this regard between the experimental groups. These findings were accompanied by a decrease of total colony count values during the study in both groups. No bacterial adaptation to utilize xylitol occurred during the trial (XX).

The final study in the present monograph was carried out in order to examine the acute physico-chemical effects in saliva in relation to the presence of various sugars. The effects of F-, S-, X- and sorbitol-containing chewing gums were thus compared to unsweetened gum base and paraffin chewing with regard to electrolyte concentration and pH changes occurring in saliva. Stimulation of salivary secretion, due to the influence of the sugars tested resulted in increased electrolyte concentrations with respect to Na^+, Ca^{2+} and HCO_3^- ions in saliva. This was accompanied by a general increase in salivary pH-values, notably in the case of X (XXI).

It is concluded that the metabolic studies indicate the relative safety of perorally administered xylitol at the present dosage levels. In general, xylitol seems metabolically to behave similarly to fructose, except that it tends to cause a lower degree of metabolic loading. This is interpreted as additional evidence for the organism's tolerance of xylitol, particularly as the utilization of sucrose as a nutritive substrate also involves the metabolic pathways of fructose to a substantial extent.

The results show a massive reduction of the caries increment not only in relation to total, but also in connection with partial substitution of dietary sucrose through xylitol consumption. In the former case fructose is also indicated to be somewhat

less cariogenic than sucrose. It should be noted, however, that the effect in the fructose group was essentially due to a lower increment rate of early carious lesions than observed in the sucrose group.

The results regarding the incidence of dental caries, as affected by sucrose or xylitol chewing gum consumption, show sucrose in chewing gum to be definitely cariogenic. The near zero incidence of dental caries, as observed in the xylitol group of the chewing gum study, indicates the potential value of certain products involving low and repeated dosage of xylitol. Still, consideration should be given to the fact that the present results were obtained in subjects with a moderate sucrose consumption and a satisfactory level of oral hygiene.

The extremely low caries activity level in the xylitol groups of both trials should be considered in relation to the quantity of plaque, accompanying biochemical changes in plaque and saliva, and the corresponding microbiological development. It seems likely that some of the above changes, i.e. the decrease of the acidogenic flora and the reduction of sucrose-splitting enzymes of whole saliva in the xylitol group of the 2-year trial, might have been the result of the absence of sucrose in the experimental condition. On the other hand, it is evident that other essential observations, notably the lactoperoxidase effect and the physico-chemical changes in saliva, must be attributed to the consumption of xylitol. Further studies, involving partial substitution of dietary sucrose, are in progress in order to elucidate these effects.

At present, the information obtained indicates that the process of caries is affected in various, even antagonistic ways by dietary carbohydrates. Any substrate which is subject to microbial degradation would thus exhibit various levels of cariogenic potential. This potential, however, is counteracted by other orally localized effects common to the sugars. These include the stimulation of salivary secretion, elevation of certain electrolyte concentrations and increased buffering of saliva. It should be noted that the latter, protective effects might be rendered valueless due to the marked decrease of pH on tooth surfaces caused by bacterial degradation of the various substrates. On the other hand, the repeated observations that almost all oral acidogenic microorganisms are unable to metabolize xylitol, enhance its merits with regard to remineralizing capacity and other therapeutic effects.

It is thus concluded that the accumulated clinical, radiographic, biochemical and microbiological findings have provided the evidence that xylitol is considered non- and anticariogenic.