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Effect of Fluorides and Other Solutions on Solubility of Powdered Enamel in Acid. (22633)

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Considerable interest has been shown recently in the sarcosinates and in dehydroacetate as possible inhibitory agents of human dental caries. It has been suggested that mechanism of action in this regard is the inhibition of acid formation in the mouth through interference with enzyme activity(1). However, a recent publication(2) suggests that the sarcosinates are as effective as fluorides in decreasing the solubility of powdered enamel in acid and, thus, may be of importance in prevention of dental caries by this mechanism also. Since stannous fluoride has been shown to be considerably more effective than sodium fluoride in reducing enamel solubility(3), experimental dental caries in rats(4) and hamsters(5), and human dental caries when applied topically(6) or in a dentifrice(7), it was of interest to compare sodium N-palmitoyl sarcosinate with stannous fluoride. Similarly, sodium oxalate(8) has been suggested as possessing "fluoride-like" protection action on enamel, and it was of interest to compare this compound with stannous fluoride and sodium N-palmitoyl sarcosinate.

Methods. The procedure used for measuring the effectiveness of the 5 compounds has been described(3,9). In this study, a 5.0-ml portion of an aqueous solution of the compound to be studied was added to a 100-mg portion of powdered enamel. In all instances the solutions were used as prepared without adjustment of the pH. After the mixture was shaken for 20 minutes at 25°C it was promptly centrifuged. The clear supernatant was decanted and 1.0 ml of redistilled fluoride-free water was used to wash the enamel. The supernatant and the wash solution were combined and suitable aliquots were analyzed for phosphorus(10). This served as a measure of the amount of decalcification occurring during the treatment period with any of the proposed protecting solutions. Following this, 10.0 ml of 0.2 N acetic acid (pH 4.0) was added to the powdered enamel, and the mixture was shaken for 20 minutes as before. Following prompt centrifugation the supernatant solution was decanted, the enamel was washed, and the combined solutions were analyzed for phosphorus. Controls were run in the same manner except that distilled water was used in place of the treatment solutions.

The amounts of phosphate dissolved by the treatment solution (fluoride, sarcosinate, dehydroacetate, or oxalate) and by the decalcification solution (acetic acid) were combined to give a figure representing the total amount of tooth substance lost. The effectiveness of each treatment solution was then calculated by comparing this value with the corresponding control value (for untreated enamel), and expressing the result as percentage reduction in solubility.

Results. The data obtained are presented in Table I. The stannous fluoride was by far the most effective compound tested; a 1% solution reduced enamel solubility by 86%, and a 0.1% solution was 85% effective. Under similar conditions, sodium fluoride reduced enamel solubility by 44 and 36%, respectively. The sodium N-palmitoyl sarcosinate was only moderately active, a 1.0% solution reducing the solubility of the powdered enamel by only 20% and a 0.1% solution by only 4%. Volker *et al.*(2) also evalu-

TABLE I. Effects of Stannous Fluoride, Sodium Fluoride, Sodium N-Palmitoyl Sarcosinate, Sodium Dehydroacetate, and Sodium Oxalate on Solubility of Powdered Tooth Enamel in Acid.

Compound	Concentration (%)	pH	No. of samples used	P lost during protection	P lost during acid treatment	Reduction in enamel solubility (%)
				(mg P/100 mg enamel)		
Stannous fluoride	1.0	3.5	10	.09	.38	86.6 ± 1.9*
	.1	3.7	12	.01	.50	85.4 ± 1.6
Sodium "	1.0	7.2	10	.14	1.80	44.3 ± 4.1
	.1	6.7	14	.40	1.84	36.5 ± 4.0
" N-palmitoyl sarcosinate†	1.0	8.5	12	.55	2.25	20.0 ± 3.5
	.1	8.2	14	.16	3.20	4.0 ± .9
" dehydroacetate	1.0	3.8	8	.36	2.96	5.0 ± 1.1
	.1	4.1	8	.30	3.13	2.0 ± .2
" oxalate	1.0	6.3	10	.10	3.36	1.0 ± .02
	.1	6.9	10	.37	3.20	—
Control (distilled water)		5.5	24	.40	3.10	—

* Stand. dev. † The purity of this compound was 95.3%.

ated a 0.01% solution, but, since a 0.1% solution was so ineffective in these studies, the lower concentration was not investigated. Sodium dehydroacetate and sodium oxalate were not effective to any appreciable degree in reducing the solubility of powdered dental enamel.

Discussion. These data demonstrate that, under the conditions of this study, the 2 fluoride salts are markedly superior to sodium N-palmitoyl sarcosinate and dehydroacetate in their ability to decrease the solubility of powdered enamel, and that stannous fluoride is considerably more effective than sodium fluoride. Sodium oxalate is without effect. The results with the sarcosinate are in contrast to those of Volker *et al.*(2), who found the effect of this compound to be equal to that of sodium fluoride. In the present study, the sarcosinate was essentially ineffective even at 10 times the concentration tested by Volker *et al.* This discrepancy is particularly difficult to understand since results obtained for sodium fluoride were quite similar in the two investigations. Since most studies of this nature serve only to screen potential anticariogenic substances, one should accept all such results as presenting only suggestive evidence as to how they might act in reducing human dental caries. The final criterion for such an evaluation must be the demonstration of effectiveness by dental caries studies. However, laboratory studies are of considerable value in predicting potentially useful compounds. It is interesting, however, to note that studies have already indicated the superiority of stannous fluoride over sodium fluoride when applied topically(6) or when incorporated in a dentifrice(7). The suggestion of usefulness for the sarcosinate on the basis of enamel solubility reduction is not in keeping with the proposed mechanism for reduction of caries by an antienzyme action. Indeed, the present data cannot be interpreted as suggesting a fluoride-like action for the sarcosinate, dehydroacetate, or sodium oxalate.

Summary. The solubility of powdered human tooth enamel was measured after treatment with stannous fluoride, sodium fluoride, sodium N-palmitoyl sarcosinate, sodium dehydroacetate, or sodium oxalate by a method which measures the amount of phosphorus dissolved from the treated enamel by acetic acid. The data indicate that stannous fluoride is markedly superior to sodium fluoride and that the sarcosinate is of only questionable value in its ability to reduce powdered enamel solubility. Sodium dehydroacetate and sodium oxalate were without effect in decreasing the solubility of powdered enamel.

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Chlorpromazine Counteraction of Trauma Induced Death.* (22634)

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Chlorpromazine(1) has been reported to have a pronounced protective action against death induced in dogs by severe hemorrhage (2,3) and in rats by tumbling trauma(3). This paper deals with the counteraction by chlorpromazine of hemoconcentration and death induced in mice by tourniquet trauma, and by heat trauma. An abstract of part of this work has already appeared(4). Findings similar to certain of those reported here have been published recently by Millican and Stohlman(5).

Methods. Mice used were Carworth Farms males, 2-5 months of age and 20-30 g weight. In any one experiment mice were sorted into such groups that the average body weights for all the groups were nearly the same. Traumatization procedures were those of Rosenthal(6,7). In the tourniquet trauma experiments the hind leg tourniquets were left in place 2 or 3 hours; in the heat trauma experiments etherized mice were submerged to the neck in water at 60°C for 12 seconds. All injections were made intraperitoneally. Chlorpromazine was dissolved in distilled water at such a concentration that the desired dose was secured by injection of .01 ml per g, or in .9% NaCl at such a concentration that the desired dose was secured by injection of .05 ml per g. Since initiation of shock presumably begins at the time of removal of hind leg tourniquets, or at the time of immersion in very hot water, this time has been designated *zero hour* (Tables). Prior times have been assigned minus (—) values, later times plus (+) values. For the present purposes shock in mice is defined as the condition after severe traumatization wherein mice are prostrated, relatively indifferent to stimuli, cold to the touch, and likely to die within 48 hours after traumatization if untreated. *Hematocrit studies*: Hematocrit values were obtained using heparinized fine capillary tubes and an International "Hemacrit" centrifuge. A control tail blood sample was secured for each mouse. In all except the earliest experiments those mice exhibiting tail blood hematocrit values below 40 were replaced. The second (test) blood sample was taken from the heart, since insufficient blood could be obtained from the tail after traumatization. Hemodilution was indicated by a heart blood hematocrit value appreciably smaller than the previously obtained tail blood hematocrit value, hemoconcentration by the reverse. For any one group, the standard error of the average difference between tail and heart blood hematocrit values was calculated using this difference for each mouse as the unit. The probability value, p, was secured from a (t,

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