first in 0.1 N hydrochloric acid. The reaction of the serum was then adjusted so that the addition of the pepsin solution would bring the reaction to pH 6–7. The process of incubating serum globulin with pepsin was carried out at 37° C., but it was found that the hypertensive substance was produced also at 20° C.

We employed 2 mg pepsin per cubic centimeter of serum globulin. This solution after 30 minutes' incubation was precipitated with three volumes of alcohol, filtered and the filtrate evaporated *in vacuo*. This residue was then taken up in distilled water in such amounts that one cubic centimeter of the solution was equivalent to one cubic centimeter of the original globulin solution. This solution of the filtrate when injected intravenously into dogs under nembutal anesthesia in doses of 0.1 cc per kilo body weight, produced an average elevation in blood pressure of 22 mm Hg. In many of our experiments the pressor activity of this solution equalled that of renin.[5]

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THE EFFECT OF SYNTHETIC VITAMIN K ON THE RATE OF ACID FORMATION IN THE MOUTH[1]

IN 1939 evidence was found that the reactions involved in the production of lactic actid in the mouth, with subsequent dental caries, are analogous to the reactions involved in lactic acid production in muscle tissue.[2] Furthermore, it has been shown that acid formation in the mouth may be very rapid[3,4] and that a difference between the saliva of caries active and caries immune individuals is the rate of acid formation from sugar in the respective salivas.[5]

On the basis of this it was thought that if some nontoxic substance that would inhibit the chain of reactions involved and thus delay acid formation sufficiently so that the saliva could neutralize them could be found, it could be used to prevent caries.

After an extended search for a product which would fulfil these qualifications, it was found that synthetic vitamin K (2 methyl 1-4 naphthoquinone) was such a substance.

In vitro experiments indicate that a synthetic vitamin K concentration of 1 mg per 100 cc of saliva, 10 per cent. in glucose, forms no acid in a 4-hour incubation period, while the same mixture will produce up to 2 mil. eq. of acid under the same conditions in the absence of the vitamin K.

Preliminary clinical experiments wherein the pH of carious lesions was measured indicate that synthetic vitamin K in the same concentration as in the *in vitro* experiments effectually inhibits acid formation. In the absence of vitamin K the acidity of the lesion may increase from pH 6.8 to pH 4 in as little as three minutes.

The synthetic vitamin K has no effect on the bacterial growth in the concentrations used, so the inhibition is not caused by any antiseptic properties. It has no effect on the conversion of phosphoglyceric acid to pyruvic acid or on the reduction of the pyruvic acid to lactic acid. However, it prevents the formation of phosphoglyceric acid from the hexose phosphates. This indicates that the synthetic vitamin K prevents the dismutation of the hexose phosphate or the conversion of the dismutation products to phosphoglyceric acid.

On the basis of the above it is quite probable that if synthetic vitamin K were incorporated in sugar candy or gum it would effectively inhibit dental caries.

It is interesting to note that vitamin K is probably one of the substances removed from the sugar-cane juice during the purification of sugar.

Clinical and laboratory studies are being continued, and the physiological effects of the ingestion of synthetic vitamin K continuously for long periods of time is being investigated.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A MODIFIED WARBURG REACTION VESSEL

WITHIN recent years, the Haldane-Warburg manometric technique has been widely applied,[1,2] and methods based upon the procedure are now commonly used in the routine analytical laboratory.[3,4,5] Despite the many advances in technique, the design of the

[5] Helmer and Page (*Proc. Soc. Exp. Biol.*, 49: 389, 1942) have verified the work of Croxatto and Croxatto. Our findings differ from theirs in the optimum pH for the production of the pressor substance by pepsin. This may be due to the longer incubation time that we employ.

[1] This investigation was made possible by a grant from the Good Teeth Council for Children.

[2] L. S. Fosdick, *Jour. Am. Dental Asn.*, 26: 415, 1939.

[3] L. S. Fosdick, H. L. Hansen and Epple, *Jour. Am. Dental Asn.*, 24: 1275, 1931.

[4] R. M. Stephan, *Jour. Am. Dental Asn.*, 27: 719, 1940.

[5] L. S. Fosdick, E. E. Campaigne and O. E. Fancher, *Ill. Dental Jour.*, 10: 85, 1941.

[1] M. Dixon, "Manometric Methods as Applied to the Measurement of Cell Respiration and Other Processes." Cambridge, 1934.

[2] D. Burke and R. T. Milner, *Ind. Eng. Chem., Anal. Ed.*, 4: 3, 1932.

[3] A. S. Schultz, L. Atkin and C. N. Frey, *Jour. Biol. Chem.*, 129: 471, 1939; *ibid.*, 136: 713, 1940.