COMPOSITIONS AND METHODS FOR TOPICALLY FLUORIDATING AND/OR MINERALIZING DENTAL TISSUE

This is a continuation of copending Application Ser. No. 478,888, filed Mar. 25, 1983, now abandoned.

BACKGROND OF THE INVENTION

1. Field of the Invention

This invention was made during research supported in part by a grant from the National Institute of Dental Research. The present invention relates to compositions and methods for topically fluoridating and/or mineralizing dental tissue, such as enamel, dentin, and exposed root surfaces.

2. Background of the Invention

Topical fluoridation of teeth has been extensively used in the past three decades in attempts to reduce the incidence and severity of dental caries. See Newbrun, E. (ed.): *Fluorides and Dental Caries*, 2d ed., Springfield, IL: C. C. Thomas (1975); Keyes, P. H. et al, "Fluoride Therapy in the Treatment of Dentomicrobial Plaque Diseases." J. Am. Soc. Preventive Dentistry 5:17–26 (1975); Brudevold, F. et al, "A Study of Acidulated Fluoride Solutions-I In vitro Effects on Enamel." Archs. oral Biol. 8:167–177 (1963). The typical procedure introduces simple fluoride containing compounds onto the surface of the dental enamel. This produces a relatively large and immediate fluoride uptake in the enamel. Most of this fluoride, however, is present in the form of CaF_2 and quickly leaches out of the enamel. Thus, typical topical fluoridation treatments result in little or no long-term increase in enamel-bond fluoride content, and can actually cause a net loss of tooth mineral and fluoride content. See, McCann, H. G., "The Solubility of Fluorapatite and Its Relationship to That of Calcium Fluoride." Archs. oral Biol. 13:987–1001 (1968); Heiftz, S. B. et al, "In vivo Fluoride Uptake by Enamel of Teeth of Human Adults from Various Topical Fluoride Procedures." Archs. oral Biol. 15:1171–1181 (1970); Wei, S. H. Y. et al, "In Vivo Microsampling of Enamel Fluoride Concentration After Topical Treatments." Caries Res. 9:50–58 (1975) Chow, L. C. et al, "Apatitic Fluoride Increase in Enamel from a Topical Treatment Involving Intermediate $CaHPO_4.2H_2O$ Formation, an In vivo Study." Carries Res. 15:369–379 (1981). Since both ambient and enamel-bound fluoride appear necessary to combat caries (see Brown, W. E. et al (eds.), "Cariostatic Mechanisms of Fluorides," Caries Res. 11 (suppl. 1)1–327 (1977)), it appears that the short-lived, beneficial effects of most known topical fluoride treatments are due to a temporary elevation in the ambient fluoride level in the mouth. The inability to incorporate fluoride into the enamel crystals appears to be the major reason behind the limited effectiveness of these topical fluoride treatments.

A significant step in topical fluoridation was made by the present inventors in discovering that $CaHPO_4.2H_2O$, dicalcium phosphate dihydrate (DCPD), reacts rapidly with fluoride to form fluorapatite, $Ca_5(PO_4)_3F$, under appropriate conditions. Thus, conventional fluoride treatments can incorporate significant amounts of fluorapatite into dental enamel if DCPD is first formed in the enamel as an intermediate product. In general, DCPD will form in dental enamel from solutions at ambient temperatures that contain calcium and phosphate ions in concentrations approaching saturations with respect to DCPD and having a pH less than or equal to approximately 4.3, which is the pH of a solution saturated with respect to both DCPD and $Ca_5(PO_4)_3OH$, hydroxyapatite, in which both compounds are in equilibrium with the saturated solution at an ambient temperature. Such a pH is referred to as a singular point pH. In solutions at ambient temperatures with a pH above approximately 4.3, hydroxyapatite will precipitate rather than DCPD. See, Chow, L. C. and Brown, W. E., "The Reaction of Dicalcium Phosphate Dihydrate With Fluorides." J. Dent. Res. 52:1220–1227 (1973); Chow, L. C. and Brown, W. E., "Formation of $CaHPO_4.2H_2O$ in Tooth Enamel as an Intermediate Product in Topical Treatments." J. Dent. Res. 54: 65–76 (1975); see also, Brown, W. E., "Solubilities of Phosphates and Other Sparingly Soluble Compounds," in Griffith, E. J. et al (eds.), *Environmental Phosphorus Handbook*, New York: John Wiley and Sons (1973). A solution that can react with hydroxyapatite or tooth mineral to form DCPD may be called a "DCPD-forming solution". The present inventors have also shown that highly acidic, saturated solutions of $Ca(H_2PO_4)_2.H_2O$, monocalcium phosphate monohydrate (MCPM), will form DCPD in solution under appropriate conditions. See Chow, L. C. and Brown, W. E., "Phosphoric Acid Conditioning of Teeth for Pit and Fissure Sealants." J. Dent. Res. 52:1158 (1973); Chow, L. C. and Brown, W. E., "Topical Fluoridation of Teeth Before Sealant Application," J. Dent. Res. 54:1089 (1975).

The fluoride compound incorporated into the enamel by DCPD-forming solutions is identified as fluorapatite because previous in vitro studies show that fluorapatite forms when DCPD reacts with a relatively dilute fluoride solution. See, Chow, L. C. and Brown, W. E., "The Reaction of Dicalcium Phosphate Dihydrate with Fluorides." J. Dent. Res. 52:1220–1227 (1973); Chow, L. C. and Brown, W. E., "Formation of $CaHPO_4.2H_2O$ in Tooth Enamel as an Intermediate Product in Topical Treatments." J. Dent. Res. 54:65–76 (1975); and Wei, S. H. Y. et al, "Reactions of Dicalcium Phosphate Dihydrate with Fluoride Solutions." J. Dent. Res. 53:1145–1154 (1974). Because the primary components of tooth mineral are fluorapatite and hydroxyapatite, $Ca_5(PO_4)_3OH$, the incorporation of additional fluorapatite into dental enamel can, in effect, remineralize demineralized tooth material. This is especially helpful in combating the demineralization of the enamel's subsurface that precedes the onset of dental caries or cavities. Since the presence of fluoride ions prevents or retards tooth decay, the use of DCPD-forming solutions in conjunction with fluoridation agents both prevents dental caries and repairs incipient damage that might already have occurred. This combination of prevention and restoration is far more desirable than the conventional filling of cavities.

Studies with animals (Shern, R. J. et al, "Effects of Sequential Calcium Phosphate Fluoride Rinses on Fluoride Uptake in Rats." J. Dent. Res. 58(supp. B):1023 (1979); Brown, W. E. et al, "Animal Studies of Fluoride Penetration Procedure." IADR Program and Abstracts of Papers, No.827 (1978)), as well as a recent clinical study (Chow, L. C. et al, "Apatitic Fluoride Increase in Enamel from a Topical Treatment Involving Intermediate $CaHPO_4.2H_2O$ Formation, an In vivo Study." Caries Res.: 15:369–376 (1981)) show that treatment of dental enamel with solutions that form DCPD followed by treatment with a conventional fluoride source in-