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Fluoride varnish containing chitosan demonstrated sustained fluoride release

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Fluoride varnish is a professionally applied product that prevents dental caries. However, fluoride varnishes do not provide sustained fluoride release. The objective of this study was to prepare fluoride varnish formulations containing various amounts of chitosan that would generate sustained fluoride release. We evaluated their chemical structure, viscosity, and *in vitro* fluoride release. Furthermore, the 3-(4, 5-dimethylthiazolyl-2)-2,5diphenyltetrazolium bromide (MTT) assay and direct contact test were used to determine varnish cytotoxicity. We found that all fluoride varnish formulations had the same chemical structure. Their viscosity demonstrated a chitosan concentration-dependent increase. *In vitro* fluoride release showed a sustained fluoride release. The chitosan fluoride varnishes were cytotoxic to human gingival fibroblasts. We propose the new fluoride varnish formulation as a potential material to be used as a sustained release fluoride varnish.

Keywords: Chitosan, Fluoride varnish, Sustained release

INTRODUCTION

Dental caries is a major oral health problem, with the global decayed, missing, and filled teeth scores of 12-year-old children increasing over the past 10 years[1)]. There are several methods for dental caries prevention, including oral hygiene instruction, pit and fissure sealants, and topical fluoride application, *i.e.* fluoride gels and fluoride varnishes. However, the most effective caries-protective results occur when fluoride is consistently maintained at a low level in the oral cavity[2)]. The salivary fluoride levels after using fluoride toothpaste, mouth rinsing, gel and varnish were analyzed and the results indicated that the fluoride level remained above the baseline for 48 h after applying fluoride varnish[3,4)].

The advantage of fluoride varnishes over fluoride gels is that the varnish increases the contact time of fluoride on the tooth surface[5)]. Therefore, fluoride concentration can be maintained in the oral environment and form calcium fluoride that deposits on the tooth surface to prevent dental caries[6-8)]. There are many studies demonstrating that the professional application of fluoride varnish prevents dental caries[9-12)]. The amount of fluoride released from a varnish typically decreases in a few hours and continues to decline for up to 24 h, while the cumulative fluoride ion release increases in the first hour up to 24 h[13)]. However, the release of fluoride ions from dental material can be controlled or sustained by encapsulating or coating sodium fluoride particles with either natural polymers or synthetic polymers, such as gelatin[14,15)], ethylcellulose[15)], and polysiloxane[16)].

Chitosan is a linear copolymer of D-glucosamine and N-acetyl-D-glucosamine[17)]. This polymer is used in biomedical applications because of its biodegradability, biocompatibility, nontoxicity, and antimicrobial-antifungal properties[17)]. Chitosan has been studied in a wide range of dental applications, including drug delivery systems[18-20)], guided tissue regeneration[21,22)], surface modification of dental implants[23-25)], qualitative modification of toothpaste[26,27)], and dental restorative materials[28)]. Furthermore, chitosan was previously investigated for the controlled release of fluoride ions using spray drying[29)] and emulsion dispersion techniques[27)]. These studies demonstrated sustained fluoride ion release. We hypothesized that a controlled release system using chitosan would maintain fluoride release at a low level over time. However, the influence of chitosan on fluoride release from fluoride varnish has not been investigated. The purpose of this study was to prepare new fluoride varnishes containing various amounts of chitosan and characterize the chemical structure, viscosity, in vitro fluoride release, and cytotoxicity of these varnishes.

MATERIALS AND METHODS

Fluoride varnish preparation

The base varnish was prepared by mixing fully hydrogenated rosin (Foral™ AX-E, Eastman Chemical, Kingsport, TN, USA) with absolute ethanol (EMSURE®, Merck, Darmstadt, Germany) at a 3:1 (w/w) ratio in a closed vessel on a stirrer at room temperature for 24 h. Sodium fluoride (NaF), particle size <45 μm, (EMPROVE®, Merck) was added to the varnish base at

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