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Antibacterial Drug Releasing Zinc Phosphate and Glass Ionomer Dental Cements for Secondary Caries Prevention: *in vitro* Study

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Zinc phosphate and glass ionomer dental cements have long been used in dentistry for filling carious teeth. However secondary or recurrent caries occur due to limitations in cleaning carious teeth. This work checks the suitability of dental cements in releasing drug locally. In addition the compatibility of drug and dental cements, weight variation tests and drug content uniformity tests of the drug releasing units, bioactivity of the drug released and the effect of cement types, drug release medium and size of units on drug release were also studied. The results of the work suggest the use of zinc phosphate cement units for delivery of antibacterial drug locally and in a controlled fashion for the prevention of secondary caries.

Key Words: Secondary caries, Antibacterial, Dental cement, Drug delivery.

INTRODUCTION

Secondary caries is the etiology of failure in 50 to 60 per cent of restorations after dental caries treatment[1]. Dental caries is a disease of the calcified tissues of the teeth. The Department of Health of Washington State reports that in US 20 % of children ages 2-4 years and 80 % of all children age 17 years experience dental decay. In addition, more than two-thirds of adults aged 35 to 44 years have lost at least one permanent tooth due to dental caries. The outer surface of the crown of the teeth is made up of enamel, mainly composed of hydroxyapatite. Beneath the enamel lies another layer called dentine. About 70 % of dentine is made up of hydroxyapatite and the rest with collagen and water. Many canals, called dentine tubules

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radiate from the pulp cavity, which is well supplied with nerve fibers to dentine matrix. In the treatment of carious teeth, infected dentine should always be completely removed. However, infected dentine is sometimes left in the cavity for many practical clinical difficulties and considerations. Bacteria left in the cavity are one major reason leading to secondary caries or pulpal injury after restoration. Oral antibacterial treatment is thus recommended before restoration is completed. Advantages of local controlled delivery of drugs in dentistry are well known. Application of dental cements for the reduction of secondary caries is not new[2]. However, the interest was based on the effect of fluoride released from the cement[3,4] which has also resulted negatively sometimes with bacteria adhering to the cement and surviving[5]. Boeckh *et al.*[6] reported that the strongest antibacterial activity was observed with a zinc oxide eugenol cement when commercially available restorative dental biomaterials as a fine-hybrid resin composite, an ion-releasing resin composite, a self-curing glass ionomer cement and a resin-modified glass ionomer cement were compared which could obviously be speculated to the presence of eugenol, an oily liquid obtained from some essential oils with antibacterial property being more effective than the fluoride released from the cements. Natural products, especially oils are known to differ in their extent of exhibiting properties due to seasonal variations. Therefore using a standard drug would be a more logical idea and the main objective of the present study was to determine the suitability of dental cements for the delivery of drugs in effective concentrations and in controlled fashion for prolonged periods of time. The present study also investigated the compatibility of drug with chosen dental cements, weight variation test and drug content uniformity test for the drug releasing units, bioactivity of the drug released and the effect of type of dental cement, size of units applied and drug release medium on the drug release process with moxifloxacin hydrochloride as model drug.

Moxifloxacin hydrochloride was a gift sample from Cross Medineeds Pvt. Ltd., Chennai, India. Zinc phosphate cement (Harvard Cement, manufactured by Harvard Dental International GmBH, Germany) and glass-ionomer cement (Ketac™-Fil Plus, manufactured by 3M, USA) are widely used dental cements purchased from commercial suppliers. Other solvents and ingredients used were of analytical grade. FT-IR studies were conducted to check the compatibility of drug in both the cements. Two sizes of drug releasing units were formed by mixing drug and cements in the ratio of 1:5 and forcing the semisolid mass into Teflon rings with internal diameters so as to yield units with 6 mm (large) and 3 mm (small) width. The entire procedure was carried out in a laminar flow hood. After air-drying in the hood over night, the units were dried under vacuum (0.8 mm Hg) at 45-50 ºC for 16 h followed by 37 °C for 24 h. After which the

units were moved out of Teflon rings and stored in airtight glass containers, till further usage. Drug content uniformity studies were conducted by crushing the units in an agate mortar and sonicating the resultant in pH 6.8 phosphate buffer. Filtered buffer was subjected to spectrophotometry. Drug releasing studies were conducted with units placed in 5 mL of dissolution medium and maintained at 37 °C. Dissolution medium was replaced in its entirety for every 24 h and filtered samples were subjected to spectrophotometric analysis. pH 6.8 phosphate buffer and pH 6.8 simulated saliva fluid were used as dissolution medium. The study was conducted with 6 parallel probes. In addition, the bioactivity of moxifloxacin released from the units was determined against *Streptococcus mutans* in a liquid medium, to ascertain the released drug was active.

FT-IR studies exhibited that the moxifloxacin hydrochloride could be applied as a model drug with zinc phosphate and glass ionomer cement. Weight variation test and drug content uniformity test conducted for drug releasing units confirmed their acceptability by lying within ± 5 % of the average weight and drug content. Fig. 1 exhibits the release of drug in various study conditions. Irrespective of cement type and medium, larger units released more amount of drug than smaller units. In general the release of drug from zinc phosphate cement was more than from glass ionomer cement. This difference in release between smaller and larger units agrees with the fact of effect of surface area on drug release and the difference in release among cement types due to denser structures of glass ionomer units than zinc phosphate units. When the effect of drug release medium on drug release is concerned, release was highly restricted from units with glass ionomer cement when compared to zinc phosphate cement units. This difference in release based on drug release medium could be due to the chemical composition of the cement and medium themselves. The composition and the ionic strength of the mediums vary and unlike zinc phosphate cement the reduction in drug release observed from glass ionomer cement in simulated saliva fluid could be speculated due to the calcium and phosphate deposited on the surface of glass ionomer cement, due to chelation with their carboxylic groups[7]. Though in all the cases studied, drug release was exhibited by a steep curve initially and followed by a plateau, the release from larger units of zinc phosphate cement in simulated saliva fluid followed a more controlled fashion with a constant release which makes them preferable. As a whole, drug release was influenced by the type of cement, the size of the units and drug release medium. Bioactivity studies confirmed that the drug released from all cases of study was active.

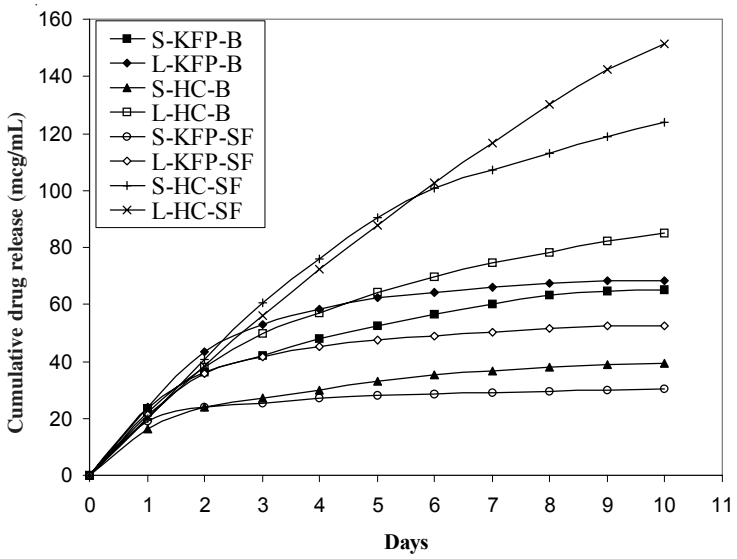

Fig. 1. Cumulative drug release
S = Smaller Units, L = Larger Units, KFP = Ketac Fil Plus, HC = Harvard Cement, B = pH 6.8 phosphate buffer, SF = Simulated Saliva Fluid

These results indicate that dental cements can be used as drug releasing materials to keep the local area sterile during the course of caries treatment and to avoid secondary caries. However much study is required to optimize formulation as *in vivo* conditions would drastically differ from *in vitro* conditions. Surface analysis to study about pores that would arise on drug release and mechanical properties of the units to assure integrity of the structure for the period these units could be relied upon are some areas in our ongoing research.

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