East and Central African Journal of Pharmaceutical Sciences
Vol. 10 (2007) 14-16

Drug Releasing Dental Cements: An *In Vitro* Study.

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Dental cements are used in dentistry for filling carious teeth. However recurrent caries occur due to limitations in cleaning carious teeth. The suitability of dental cements in releasing drug locally was studied. In addition, weight variation tests, drug content uniformity tests of the drug releasing units, the bioactivity of released drug as well as the effect of cement types, drug release media and size of drug release units on drug release were studied. The findings of the study support the use of dental cements for the delivery of antibacterial drug locally and in a controlled fashion for the prevention of recurrent caries.

Keywords: Recurrent caries, antibacterial, dental cement, drug delivery.

INTRODUCTION

Recurrent caries is the cause of failure in 50 to 60 % of restorations after dental caries treatment [1]. This has a very serious consequence when the traditional caries restorative dentistry is beyond the financial capabilities of the people as is the case in the majority of the low-income nations of the world. Dental caries is a disease of the calcified tissues of teeth. The outer surface of the crown of the tooth is made up of enamel which is mainly composed of hydroxyapatite. Beneath the enamel lies the dentine. About 70 % of dentine is made of hydroxyapatite with the rest being collagen and water. Many canals called dentine tubules radiate from the pulp cavity, which is very well supplied with nerve fibers to the dentine matrix. In the treatment of carious teeth, infected dentine should always be completely removed. However, infected dentine is sometimes left in the cavity due to many practical as well as clinical difficulties and considerations. Bacteria left in the cavity are one major cause of recurrent 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 very well known. Application of dental cements for the reduction of recurrent caries is not new [2]. However, interest in these cements was based on the effect of fluoride released from the cement [3-4]. Unfortunately, their use has sometimes had the unwanted effect of bacteria adhering to the cement and continuing to survive [5]. Boeckh *et al.* [6] reported that the strongest antibacterial activity was observed with a zinc oxide eugenol cement when compared to commercially available restorative dental biomaterials such as a fine-hybrid resin composite, an ion-releasing resin composite, a self-curing glass ionomer cement and a resin-modified glass ionomer cement. This could be attributed to the fact that eugenol, an oily liquid obtained from some essential oils, has greater antibacterial activity compared to the fluoride released from the cements. Natural products, especially oils, are known to exhibit seasonal variations in content and activity of active principles. Therefore, using a standard drug would be a more logical idea. 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 a controlled fashion for prolonged periods. The present study also investigated the weight variation and drug content uniformity of the drug releasing units, the bioactivity of the drug released as well as the effect of type of dental cement, size of drug

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release units applied and drug release medium on the drug release process using ciprofloxacin hydrochloride as the standard drug.

EXPERIMENTAL

Ciprofloxacin hydrochloride was a gift sample from Cross Medineeds Pvt. Ltd., Chennai, India. Zinc phosphate cement (Harvard Cement, Harvard Dental International, GmBH, Germany) and glass-ionomer cement (Ketac^{TM}-Fil Plus Aplicap) (3M, Pittsburgh, PA, USA) were purchased from commercial suppliers. Other solvents and ingredients used were of analytical grade.

Two sizes of drug releasing units were formed by mixing drug and cements in the ratio of 1:7 and forcing the semisolid mass into Teflon rings with two different internal diameters so as to yield units 6 mm (large) and 3 mm (small) in diameter. The entire procedure was carried out in a laminar flow hood. After air-drying in the hood overnight, the units were dried under vacuum (0.8 mm Hg) at 45-50 °C for 16 h and subsequently at 37 °C for 24 h. Subsequently, the units were moved out of the Teflon rings and stored in airtight glass containers pending use.

The weight variation test of the resultant units was performed on 10 samples of each size using a digital balance. Drug content uniformity studies were conducted by crushing the units in an agate mortar and sonicating the resultant powder in pH 6.8 phosphate buffer. Filtered buffer was subjected to spectrophotometric analysis. Drug releasing studies were conducted with the units placed in 5 ml of dissolution medium (pH 6.8 phosphate buffer and pH 6.8 simulated saliva fluid) and maintained at 37 °C. Dissolution medium was replaced in its entirety every 24 h and filtered aliquots were subjected to spectro-photometric analysis. The study was conducted with 6 parallel probes.

RESULTS AND DISCUSSION

The weight variation and drug content uniformity of the drug releasing units was within ± 5% of the average weight and drug content and the units were thus considered acceptable. Figure 1 shows the release of drug in various study conditions.

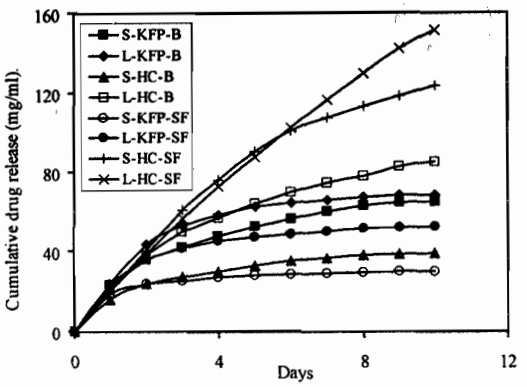

Fig 1: Cumulative Drug Release From Dental Cements. S = Smaller Units, L = Larger Units, KFP = Ketac Fil Plus, HC = Harvard Cement, B = phosphate buffer pH 6.8, SF = Simulated Saliva Fluid.

Irrespective of cement type and medium, larger units released more drug than smaller units. In general, the release of drug from zinc phosphate cement was greater than that from glass ionomer cement. The difference in release between smaller and larger units corresponds with difference in surface area on drug release while the difference in release among cement types may be due to the denser structures of glass ionomer compared to zinc phosphate units. When the effect of drug release medium on drug release was considered, release was highly restricted from units with glass ionomer cement compared to zinc phosphate cement units. This difference could be due to differences in the chemical composition of the cements. The composition and ionic strength of the media vary and the reduction in drug release observed from glass ionomer cement in simulated saliva fluid could be attributed to the calcium deposited on the surface of glass ionomer cement forming chelates with carboxylic groups on drugs [7]. Though in all the cases studied, the drug release curve exhibited a steep slope initially 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 the type of drug release medium.

These results indicate that dental cements could be used as drug releasing materials to

keep the local area sterile during the course of caries treatment and thus prevent recurrent caries. However, further investigation is required to optimize formulation since *in vivo* conditions are likely to drastically differ from *in vitro* conditions.

Surface analysis to study the effect of the pores that would arise on drug release and the mechanical properties of the units to assure the structural integrity of the units throughout the period of use are some areas being studied in our ongoing research.

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