Construction and Evaluation of an Inexpensive Device that Simulates Oral Clearance

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The clearance pattern of a specific substance is very important to estimate its oral availability. Devices or models that simulate clearance in the mouth are important to study the effects and retention time of foods and drugs. This report describes an efficient device which was assembled with low-cost materials in our laboratory and that can be used to study the clearance of cariogenic substrates, mouthwashes, programmed-release drugs as well as adsorption of drugs to enamel. The device can have up to three chambers with varying minimum and maximum volumes that can be eluted simultaneously at different flows. The simulated swallowed volumes are adjustable and the ratio between the maximum and minimum volumes can be programmed. We also present the results of an evaluation study using the device to determine the clearance of fluoride from a fluoride-containing mouthwash, the clearance of a 1% glucose solution and the programmed release of fluoride from a methacylate bioadhesive using artificial saliva as eluent.

Key Words: device, artificial mouth, clearance, saliva, drugs.

INTRODUCTION

The role of saliva is of crucial importance for the maintenance of oral health because several events that take place in the oral cavity, such as the enamel demineralization and remineralization processes, the clearance and adsorption of foods and therapeutic agents or the control of microorganisms, depend on the composition and flow rate of this organic fluid (1). The clearance pattern of a specific substance is very important to estimate its oral availability and can be determined in vivo (2,3) or in vitro (4,5) using models or devices that can simulate the oral cavity. The design of experiments using caries models must take into account the static and dynamic effects of saliva (6). Several models have been proposed in the literature to study in vitro clearance such as the one suggested by Dawes (4) and Dawes and Weatherell (5) and the computer models that simulate fluoride clearance or the events that occur in dental plaque during a cariogenic challenge (7). In this paper we describe the construction of a simple, inexpensive and efficient device which can be used to study: 1) oral clearance of conventional or programmed-release drugs and fermentable carbohydrates; 2) adsorption of therapeutic agents to enamel or hydroxyapatite; 3) influence of acid substances (such as soft drinks) on the mentioned adsorption processes.

We also present the results of an evaluation study using the device to determine the clearance of fluoride from a fluoride-containing mouthwash and an intra-buccal bioadhesive as well as the clearance of a 1% glucose solution, using artificial saliva as eluent.

MATERIALS AND METHODS

All solutions were prepared with commercially available reagents of pure grade and MilliQ® purified water. The 230 ppm fluoride-containing mouthwash
and 1% glucose solution were prepared in our laboratory. The polymethyl methacrylate intra-oral bioadhesive for the programmed release of fluoride was prepared by Dr. Vinicius Pedrazzi (Faculty of Dentistry of Ribeirão Preto, University of São Paulo). The artificial saliva (without fluoride) was prepared as described by Nakamoto (8).

The device that simulates oral clearance was constructed on the basis of the model described by Dawes (4) and Dawes and Weatherell (5) and consists of an external vessel which contains three different chambers, each of specific capacity. Figure 1 shows a schematic representation of one chamber in the external vessel and construction details of the device. The temperature control is provided by a set of electric resistance thermostat and a micro-fan installed inside the external vessel to obtain a regular current of warm air for the maintenance of the desired temperature (from room temperature to 40ºC).

The clearance studies were carried out by filling the chamber with a solution of either 230 ppm fluoride-containing mouthwash or 1% glucose solution up to the minimum volume level of the chamber and submitting it to a specific flow of artificial saliva.

The programmed release of fluoride was performed by placing a tooth-bioadhesive system inside the chamber and submitting it to regular changes of artificial saliva flow every 12 h, for 5 days, in order to simulate the physiological decrease of saliva flow which occurs during the night. The mean artificial saliva flow during the day was 1.2 ± 0.34 ml/min (mean simulated swallowed volume = 8.03 ± 2.3 ml and mean time of fraction collection = 6.69 ± 1.91 min) while the mean artificial saliva flow during the night was 0.4 ± 0.08 ml/
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min (mean simulated swallowed volume = 8.20 ± 3.47 ml and mean time of fraction collection = 20.2 ± 8.32 min).

The chamber effluents were collected periodically into test tubes and the volume of each fraction (simulated swallowed volume) was measured, followed by quantitative analysis of fluoride or glucose. Fluoride analysis was performed using an Orion combined fluoride ion-specific electrode model 96-09 (9) and glucose was determined by the phenol-sulfuric acid method (10). The data were analyzed for descriptive statistics by the Prism GraphPad Software version 1.03 (San Diego, CA, USA).

RESULTS AND DISCUSSION

The clearances of glucose and fluoride-containing mouthwash are reported in Figure 2. The shapes of the two curves are similar and the log C/C₀ x time plot shows that these clearances follow a first order kinetic model with constants of 0.071 min⁻¹ for fluoride and 0.209 min⁻¹ for glucose.

Figure 2C presents the profile of fluoride release from the tooth-acrylic bioadhesive system during a period of 5 days, with alteration of artificial saliva flow every 12 hours. The initial part of the fluoride release curve (fractions 1 to 40) is similar to the curves shown in Figures 2A and 2B, and is followed by a rapid decrease of concentration with nearly 10% recovery from the theoretical total fluoride mass. Fluoride release from fraction 50 became slower and it is important to observe that fluoride concentration increased with the decrease in artificial saliva flow, simulating the nightly conditions of reduced salivary flow rate. The total fluoride recovered during this experiment was nearly 50% from fractions 1 to 442, assuming the theoretical total fluoride mass present in the chamber.

The device described here offers several advantages such as three chambers that can be eluted simultaneously at different flow rates, variable minimum and maximum volumes, adjustable swallowed volumes, the possibility of changing the chamber easily and quickly as a function of the objective of the study, easy access to the substances inside the chambers and the possibility to program the ratio between the maximum and minimum volumes. It is also possible to adapt a low rotation micromixer to the chamber lid while studying drugs that can precipitate to the chamber bottom.

Figure 2. A: Clearance of 10.0 ml (minimum volume) of fluoride mouthwash (230 ppm) with a recovery of 99 ± 3%. B: Clearance of 10.0 ml (minimum volume) of 1% glucose with a recovery of 95 ± 5%. These clearances were determined in chamber 1 of the device described Figure 1 at an artificial saliva flow of 2.3 ml/min, (n = 10). C: Fluoride release from a tooth-bioadhesive system with changes in artificial saliva flow every 12 h (1.2 ml/min and 0.4 ml/min). All experiments were performed at 37ºC ± 0.5ºC.

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The literature presents other laboratory model systems to study plaque metabolism as well as root and enamel caries (11-14). However, the construction of these devices is more complex. Theoretical models are also presented for the study of pH changes in dental plaque, mainly as a function of the presence or absence of a cariogenic substrate (7,10). These studies, combined with the in vitro experiments performed in devices that simulate oral clearance, represent tools for the kinetic study of oral therapeutic agents and cariogenic substrates.

The device described in this report is simple and requires low-cost materials for its construction but is efficient and useful for studies related to oral health (clearance, adsorption, drug delivery, plaque metabolism) and could be used to teach dental students several aspects related to dental education (15) that should allow them to understand the general medical status of a patient. It offers advantages such as two or three chambers that can be eluted simultaneously at different flow rates, adjustable ratio between the minimum and maximum volumes, easy access to the substances inside the chambers and the possibility of changing the chambers quickly according to the purpose of the study.

RESUMO


O perfil do clearance de uma determinada substância é muito importante para se estimar a sua disponibilidade oral. Dispositivos ou modelos que simulam o clearance na cavidade oral são importantes para se estudar os efeitos e tempos de retenção de alimentos e fármacos. Este trabalho descreve um eficiente dispositivo, desenvolvido em nosso laboratório com materiais de baixo custo, que pode ser utilizado para o estudo do clearance de substratos cariogênicos, enxaguatórios bucais e fármacos de liberação programada, bem como, avaliar a adsorção de fármanos ao esmalte. O dispositivo apresenta três câmaras com volumes mínimo e máximo variáveis, que podem ser eluídas, simultaneamente, em diferentes fluxos. Os volumes de deglutição simulados são ajustáveis e a razão entre os volumes mínimo e máximo podem ser programadas. Também são apresentados os resultados de um estudo de avaliação do dispositivo onde determinou-se o clearance de fluoreto proveniente de um enxaguatório bucal, o clearance de uma solução de glicose a 1% e a liberação programada de fluoreto a partir de um adesivo de metacrilato, usando saliva artificial como eluente.

Unitermos: dispositivo, boca artificial, clearance, saliva, fármacos.

REFERENCES


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