Colloids and Surfaces B: Biointerfaces 136 (2015) 744–751

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

Interactions of liposomes with dental restorative materials

Sanko Nguyen[a,*], Malgorzata Adamczak[b], Marianne Hiorth[b], Gro Smistad[b], Hilde Molvig Kopperud[a]

[a] Nordic Institute of Dental Materials (NIOM), Sognsveien 70A, NO-0855 Oslo, Norway
[b] Department of Pharmacy, School of Pharmacy, University of Oslo, Sem Sælands vei 3, NO-0371 Oslo, Norway

ARTICLE INFO

Article history:
Received 27 July 2015
Received in revised form
30 September 2015
Accepted 18 October 2015
Available online 21 October 2015

Keywords:
Liposomes
Adsorption
Retention
Dental restorative materials
Resin composites
Glass ionomer cements

ABSTRACT

The *in vitro* adsorption and retention of liposomes onto four common types of dental restorative materials (conventional and silorane-based resin composites as well as conventional and resin-modified glass ionomer cements (GIC)) have been investigated due to their potential use in the oral cavity. Uncoated liposomes (positively and negatively charged) and pectin (low- and high-methoxylated) coated liposomes were prepared and characterized in terms of particle size and zeta potential. The adsorption of liposomes was performed by immersion, quantified by fluorescence detection, and visualized by fluorescence imaging and atomic force microscopy. Positive liposomes demonstrated the highest adsorption on all four types of materials likely due to their attractive surface charge. They also retained well (minimum 40% after 60 min) on both conventional resin composite and GIC even when exposed to simulated salivary flow. Although an intermediate initial level of adsorption was found for the pectin coated liposomes, at least 70% high methoxylated-pectin coated liposomes still remained on the conventional resin composite after 60 min flow exposure. This indicates significant contribution of hydrophobic interactions in the prolonged binding of liposomes to resin composites. Based on these results, the present paper suggests two new possible applications of liposomes in the preservation of dental restorations.

1. Introduction

Liposomes are nanosized, vesicular structures that are now well-recognized for their function as drug delivery systems [1,2]. In the simplest form, liposomes are composed of amphiphilic lipids forming a bilayer structure with the ability to encapsulate hydrophilic drug substances inside the core and/or entrap lipophilic compounds in the lipid membrane. Due to easy tuning and the versatile properties that can be obtained, the potential use of liposomes has also been introduced to the area of dentistry. Liposomes have recently been proposed as dental drug delivery systems in the treatment of caries and periodontitis [3,4], local delivery vehicles for dental anesthesia [5,6], carriers of photosensitizers in antibacterial photodynamic therapy of the oral cavity [7,8], and explored as loading compartments of inorganic minerals for the biomimetic remineralization of the tooth enamel [9,10].

We have previously investigated the adsorption of liposomes to the dental enamel for protective functions based on the concept of biomimicking [4,11]. The dental enamel *in vivo* is continuously covered by a thin, proteinaceous layer called the acquired enamel pellicle. The formation of this organic film on the enamel surface is based on the selective adsorption of saliva-derived phosphoproteins followed by protein aggregates of approximately 100–500 nm, so-called micelle-like globules, by means of protein–protein interactions [12]. The acquired enamel pellicle serves as the interface between the dental surfaces and the oral environment and, as such, plays an important role in the lubrication and protection of the dental surfaces [13,14]. Given this background, a constructed layer of bioadhesive phospholipid-based vesicles could provide similar physical protection on the tooth surfaces. Moreover, these structures may entrap and release drug compounds for a simultaneous chemical action. It has been demonstrated that liposomes, in particular those with a positive surface charge, adsorbed *in vitro* onto hydroxyapatite, a model substance for the dental enamel [15]. Further, liposomal adsorption to extracted human teeth in a salivary environment has also been

* Corresponding author. Present address: Department of Pharmacy, School of Pharmacy, University of Oslo, Sem Sælands vei 3, NO-0371 Oslo, Norway.
E-mail addresses: s.h.nguyen@farmasi.uio.no (S. Nguyen), m.i.adamczak@farmasi.uio.no (M. Adamczak), marianne.hiorth@farmasi.uio.no (M. Hiorth), gro.smistad@farmasi.uio.no (G. Smistad), h.b.m.kopperud@niom.no (H.M. Kopperud).

http://dx.doi.org/10.1016/j.colsurfb.2015.10.024
0927-7765/

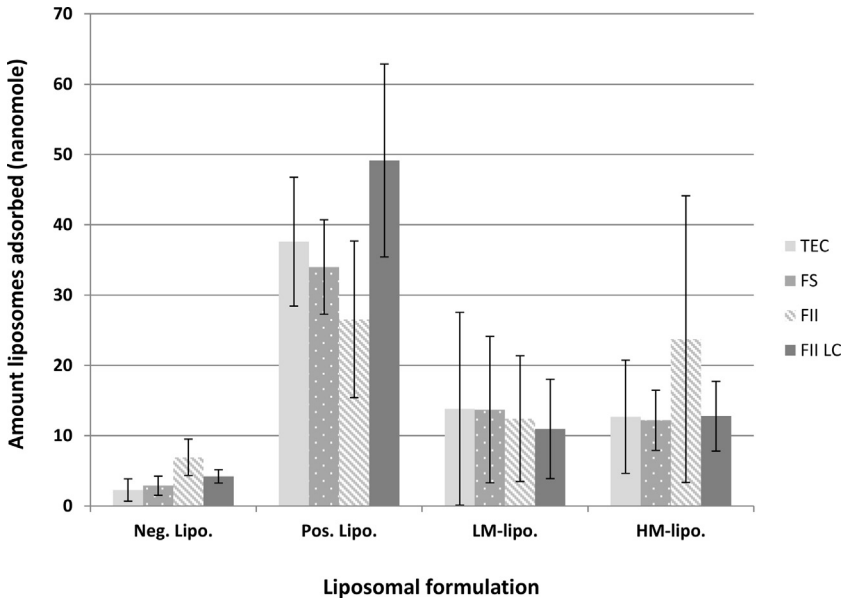

Fig. 1. The adsorption of liposomes to the dental restorative materials Tetric EvoCeram (TEC), Filtek Silorane (FS), Fuji II (FII), and Fuji II LC Improved (FII LC). Neg. Lipo.: negatively charged liposomes DPPC/10% DPPA, Pos. Lipo.: positively charged liposomes DPPC/10% DPTAP, LM-lipo: LM-pectin coated liposomes DPPC/10% DPTAP + 0.05% LM, and HM-lipo: HM-pectin coated liposomes DPPC/10% DPTAP + 0.05% HM. The error bars indicate standard deviations ($n = 9$).

proven [11]. Liposomes coated with the polymer pectin were able to adsorb and retain on the enamel surfaces despite being subjected to a flow similar to that of normal, stimulated salivary flow [11].

The application of pharmaceutical formulations in the oral cavity is highly challenging due to the complexity of the oral environment, including rich bacterial flora, salivary secretions, high masticatory forces, and rapid fluctuations in pH and temperature. Synthetic dental materials are introduced in the oral cavity through restorative therapy and are the foundation for the replacement of tooth structure loss caused by disease or injury. Currently, there is a wide range of restorative materials available in the daily dental practice; ranging from metals, polymers, ceramics, and composites. Based on a particular composition, each material possesses a distinctive, interrelated set of physical, mechanical, and chemical properties that is critical for their clinical performance. Composites, mainly consisting of an organic polymer matrix and inorganic filler particles, are increasingly popular due to esthetic properties and increased concerns over health and environmental effects of mercury in the classical filling material amalgam [16]. In addition to composites, glass ionomer cements (GIC) are other frequently used restorative materials. They consist of fluoroaluminosilicate glass as fillers and (co-)polymer of polyacids as the matrix. Two distinct characteristics have made these filling materials well-accepted; *i.e.,* the ability to bond directly to enamel and dentin (self-adhesive) and the ability to release fluoride from the glass component [17].

Due to the potential use of liposomes to protect enamel surfaces, it was deemed important to study the interaction of liposomes with dental restorative materials as they frequently accompany tooth surfaces. Our hypothesis is that liposomes also interact with dental materials and this may be utilized to preserve the dental restorations. As previously demonstrated, bioadhesive liposomes are able to adsorb to natural materials such as the enamel [11]. However, to the best of our knowledge, liposomal adsorption to synthetic filling materials has not been studied. The aim of the present paper is to examine the *in vitro* adsorption and retention of liposomes onto four common dental restorative materials including resin composites and GIC (Table 1). Four liposomal formulations with different surface properties, including surface charge and surface modification by the polymer pectin, were prepared and characterized for the investigation.

2. Materials and Methods

2.1. Materials

The main lipid, dipalmitoyl phosphatidylcholine (DPPC), and the anionic lipid, dipalmitoyl phosphatidic acid (DPPA), were

Fig. 2. Fluorescence images of (a) positive liposomes alone at 100×, (b) the surface of the resin modified glass ionomer FII LC at 40×, and (c) positive liposomes on FII LC at 100×.