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Near-infrared spectroscopy of newly developed PEGylated lipids

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Abstract

Near-infrared (NIR) spectroscopy has been used to analyze a suite of synthesized PEGylated lipids (1–3) trademarked as QuSomes™. The three amphiphiles used in this study, differ in their hydrophobic chain length and contain various units of polyethylene glycol (PEG) head groups. Whilst the spectra of QuSomes™ show a common pattern, differences in the spectra are observed which enable the lipids to be distinguished. NIR absorption spectra of these new artificial lipids have been recorded in the spectral range of 4800–9000 cm^{-1} (∼2100–1100 nm) by using a new miniaturized spectrometer based on micro-optical-electro-mechanical systems (MOEMS) technology. Three NIR spectral regions are identified, (a) the high wavenumber region between 6500 and 9000 cm^{-1} attributed to the first overtone of the hydroxyl stretching and second overtone of the C–H stretching mode; (b) the 5350–5900 cm^{-1} region attributed to first overtone of the C–H stretching mode; and (c) the 4800–5300 cm^{-1} region attributed to the combination O–H stretching and second overtone of the C=O stretching mode. For each of these regions, the lipids show distinctive spectra which allow their identification and characterization. NIR spectroscopy is a less used technique which does have great potential for the study of lipids, particularly to examine the behaviour of nanovesicles (liposomes) formed from lipids in aqueous suspensions. The study of such lipids is important since they are used as membrane models and prominent candidate for substance and drug delivery systems.

Keywords: PEGylated lipids; QuSomes™; NIR spectroscopy; Vibrational bands

1. Introduction

Lipid nanovesicles or liposomes are an active research topic due to their prospective application as membrane models and substance and drug delivery vehicles [1–5]. Such liposomes are spherical self-closed nanostructures, composed of curved lipid bilayers, which enclose a part of the surrounding solvent into their interior. Furthermore, they are made predominately from amphiphiles, a special class of surface-active molecules, which are characterized by having a hydrophilic (water-soluble) and hydrophobic (water-insoluble) group [6]. These complex systems have numerous interesting physical properties, such as unique osmotic activity, membrane permeability, solubilising power, chemical composition and surface characteristics, etc. In addition, they are dynamic entities and occur naturally for example in human milk and in synaptic tissue for trafficking and neurotransmission [7]. Their scientific and commercial benefits are primarily related to substance delivery, ranging from vitamins to cancer drugs and from antineoplastic agents to dermal anesthesia. The detailed potential application of such liposomes in the health and medical sector has been addressed by Lasic and Papahadjopoulos [8].

Near-infrared (NIR) spectroscopy provides a suitable method for the characterization of chemical structures and conformation of the materials. Although this technique has been widely applied in the identification of minerals [9–12], it has been rarely used for the analysis of lipids and liposomes. It should be noted that NIR spectroscopy is also known as proton spectroscopy because this type of spectroscopy is most useful for measuring bonds involving hydrogen such as O–H, C–H, N–H, etc. Thus, the technique appears most suitable for the identification of compounds having hydrated and hydroxyl groups. NIR spectroscopy can also be used to monitor the behaviour of lipids nanovesicles (liposomes) in aqueous suspensions with different temperatures and concentrations of lipids [13]. This technique has proven to be tremendously useful to study the interactions and stability of nanoparticles in an aqueous environment.

In this work, we focus on new synthetic lipids that spontaneously form liposomes (nanovesicles) upon hydration

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having multilayer structures which are thermodynamically stable. Recently, BioZone Laboratories Inc. (http://www.biozonelabs.com) has introduced a new patented revolutionary delivery technology trademarked as QuSomes^{TM}, i.e. a lipid-based delivery system that is more stable and cost effective, when compared to conventional natural compounds and technologies [14]. These species are also substantially more versatile for topical and oral delivery. Such lipid compositions include diacylglycerol (DAG) polyethylene glycol (PEG) compounds and spontaneously form liposomes upon mixing them with polar solvents like water (H_2O) and heavy water (D_2O). These lipids do not contain the typical phosphate ester head group (and are hence nonphospholipid) and are non-ionic. Instead of an ester group, such lipids are comprised of a PEG head group, namely $(CH_2–CH_2–O)_n–OH$ ($n = 12$ for lipid 1 and 2 and 23 for lipid 3) and long hydrocarbon chains. Since PEG is an inert biocompatible polymer, soluble as well as highly hydrated, it is used to build hydrophilic coating. This coating enables to serve as an efficient steric protector for nanovesicles delivery systems. When administered for the purpose of substance and drug delivery system, those PEG head groups in the nanovesicles act as a shield thus interactions with numerous components inside the human or animal body are reduced.

One of the fundamental properties of the studied samples is the ability to form liposomes by virtue of having the proper packing parameters. These packing parameters are relative measures of a given lipid compositions and depend on factors such as size relationships between the lipid head and hydrocarbon chains, the electric charge, and the presence of stabilizers such as cholesterol [6]. In general, for those liposome compositions the packing parameters have the following values: P_a lies (packing parameter with respect to the surface) in the range of 0.84–0.88, whereas P_v lies (packing parameter with respect to the volume) between 0.88 and 0.93. In this paper, we report the NIR absorption spectra of the PEGylated lipids as part of a comprehensive study by means of NIR, middle infrared (MIR) and Raman spectroscopy. Thus the major goal of this endeavor is to investigate the near-infrared spectral characteristics of this kind of novel lipids.

2. Experimental

2.1. Materials

The lipids used in this work are formed by 1,2-dimyristoyl-*rac*-glycerol-3-dodecaethylene glycol, 1,2-dioleoyl-*rac*-glycerol-3-dodecaethylene glycol and 2,3-distearoyl-*rac*-glycerol-3-dodecaethylene glycol synthesized by BioZone Laboratories (Pittsburg, CA). They have been abbreviated here as GDM-12 (lipid 1), GDO-12 (lipid 2), and GDS-23 (lipid 3), respectively. The number after PEGs in the lipid nomenclature indicates the quantity of molecular C_2H_4O subunits in the PEG hydrophilic head group. The general structures of such lipids are shown in Fig. 1 and the physical properties are summarized in Table 1. As can be seen from Table 1, GDS-23 (lipid 3) has a melting point of 39.8 °C. Therefore, we have recorded all the data at a temperature of 40 °C in order to make a comparison between all three varieties of QuSomes^{TM}.

2.2. Near-infrared (NIR) spectroscopy

The NIR absorption spectra of QuSomes^{TM} in pure form have been recorded using our highly sensitive and compact spectrometer based on modern MOEMS technology. The following section provides more detailed information about the functionality of that system.

Polychromatic radiation generated by a quartz tungsten halogen lamp passes through a quartz cuvette (VWR International

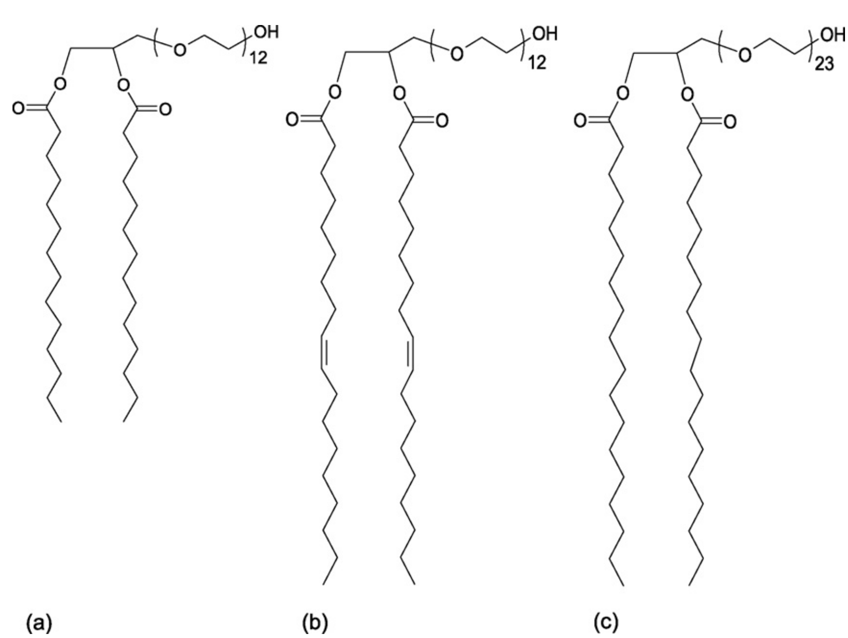

Fig. 1. General structure of PEGylated lipids (QuSomes^{TM}): (a) GDM-12; (b) GDO-12; (c) GDS-23.