Chapter 4
Non-Ionic Surfactant Vesicles (Niosomes) as New Drug Delivery Systems

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ABSTRACT

Lipid vesicular systems composed of hydrated amphihiles with or without bilayer inducing agents such as cholesterol. On the basis of used amphiphilic molecule different nomenclature are used as liposomes, ufasomes and niosomes. Nonionic surfactants with mono-, di- or trialkyl chains form niosomes which are lipid vesicles with more chemical stability in comparison with phospholipids of liposomes. Both hydrophobic and hydrophilic chemicals can be encapsulated in niosomes as a new drug delivery system. This drug carrier system could have administered via injection, oral, pulmonary, vaginal, rectal, ophthalmic, nasal or transdermal routes with penetration enhancing potential. This chapter presents a detailed explain about niosome forming components, methods of preparation and routes of administration. Many examples for drug delivery potential of niosomes are also available in this review. Vaccine adjuvant and genetic substances vector capabilities are not given here.

INTRODUCTION

There are versatile lists of amphiphilic compounds for production of lipid vesicles which on the basis of used amphiphiles or structural compounds, different nomenclature has been used such as liposomes (Kaminskas et al. 2012), niosomes (Moazeni et al. 2010; Akbari et al. 2013), ufasomes (Patel et al. 2011), ethosomes (Liu et al. 2012), eliposomes (Lattin et al. 2012) and so on. In lipid vesicular systems, polar headgroups of amphiphilic molecules are oriented into aqueous compartments and their lipophilic parts form bilayer membranes. Niosomes are bilayer vesicles composed mainly of hydrated non-ionic surfactants in addition to, in many cases, cholesterol (CHOL) or its derivatives (Pardakhty and Moazeni 2013). Cosmetic industry was the place for the first account of niosome production (Handjani-Vila et Al. 1979) after which a large number of niosome applications in drug, vaccine and gene delivery have been

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explored. While most niosomes are in the nano or sub-micron (colloidal) size range, not many authors used the "nanoniosome" or "nanovesicle" titles in their published articles due to introduction the new nanotechnology related phrases during the few recent years. Niosomes are capable to encapsulate both hydrophilic and lipophilic substances which the first ones usually are entrapped in vesicular aqueous core or adsorbed on the bilayer surfaces, and lyophobic molecules are encapsulated by their partitioning into the lipophilic domain of the bilayers. Incorporation of charged molecules into non-ionic surfactant vesicles forms charged or hybrid niosomes (Sennato et al. 2008). Vesicles can be also prepared from the mixed cationic and anionic surfactant systems such as cetyltrimethylammonium bromide and sodium lauryl sulfate (CTAB-SLS) (Aiello et al. 2010). These types of vesicles are presented as "cat-anionic" or "catanionic" vesicles. Catanionic vesicles can also be formed from electrostatic interaction between an ionized drug, such as diclofenac (Zhao et al. 2013) or alprenolol (Dew et al. 2012) and a positively/negatively charged surfactant.

Non-ionic surfactants have more chemical stability against oxidation and are less thermo-labile in comparison to phospholipids, the main constituent of liposomes (Fang et al. 2001; Tarekegn et al. 2010) thus less significant care in handling and storage are needed. Furthermore, greater versatility and lower cost make this type of vesicles more attractive in drug, gene and vaccine delivery (Florence 1993). From the pharmaceutical manufacturing stand of view the superiority of niosomes is simple methods required for industrialized and large–scale production of them without the use of pharmaceutically unacceptable solvents (Sahin 2007). In this chapter the most important aspects of niosomes and drug delivery potentials will be reviewed. Application of niosomes as gene or vaccine delivery tools will not discussed in this chapter.

Amphiphiles (Surfactants)

Following the application of some forms of energy such as mechanical or heating, the formation of niosomes is a self-assembly process due to high interfacial tension between aqueous medium and the lipophilic alkyl chain(s) resulted in the association of non-ionic surfactant monomers into vesicles (Uchegbu and Vyas 1998). Concurrently, the hydrophilic headgroups of amphiphilic molecules make water mediated interactions counter the previous formed force, finally result in bilayer formation. The energy required to form vesicles with amphiphile molecules has three contributors related to the surface energy, the mechanical energy due to overpressure and the chemical potential excess (Manconi et al. 2005).

Formation of niosomes needs at the first step to an amphiphilic molecule, but in many cases the presence a wedge shaped molecule such as CHOL is essential to turn the micellar structure of surfactant aggregates to bilayer arrangement (Pozzi et al. 2009). The lipophilic moiety of amphiphile molecule may be contain one (Varshosaz et al. 2003), two (Okahata et al. 1981)or three (Yoshioka et al. 1994; Jain and Vyas 1995; Jain et al. 2005)alkyl or perfluoroalkyl(Zarif et al. 1994)groups or in some cases a single steroidal group(Echegoyen et al. 1988).

Amino acid-based surfactants (Guedj et al. 1994; Polidori et al. 1994), glycolipids (Polidori et al. 1997) and crown ether compounds (Echegoyen, Hernandez et al. 1988; Darwish and Uchegbu 1997; Muzzalupo et al. 2007; Paolino et al. 2007)were used to form niosomes in aqueous hydration media. More recently gemini surfactants, composed of two amphiphilic molecules connected to each other by a spacer, were also used to form niosomes (Muzzalupo et al. 2008; Paolino et al. 2008) (Figure 1).

The flexibility of compounds capable for vesicle forming is due to different and various polar head groups attached to saturated or unsaturated alkyl chain(s) composed of 12 to 18 carbon atoms (C_{12}-C_{18}).

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