Role of Liposomes in Dermatology

Essay

Submitted for Partial Fulfillment of Master Degree in Dermatology, Venereology and Andrology

Presented by

Naglaa Fathy El-Sayed Abd El-Fatah
(M.B., B.Ch.)

Under Supervision of

Prof. Dr. Mostafa Mokhtar Kamel

Professor of Dermatology, Venereology and Andrology
Faculty of Medicine - Ain Shams University

Dr. Heba Mahmoud Diab

Associate Professor Dermatology, Venereology and Andrology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2012

دور الجسيمات الشحمية فى الأمراض الجلدية

رسالة

توطئة للحصول على درجة الماجستير الأمراض الجلدية والتناسلية
وأمراض الذكورة

مقدمة من

الطبيبة/ نجلاء فتحى السعيد عبد الفتاح

تحت اشراف

الأستاذ الدكتور/ مصطفى مختار كامل
أستاذ الأمراض الجلدية والتناسلية وأمراض الذكورة
كلية الطب- جامعة عين شمس

الدكتورة/ هبة محمود دياب
استاذ مساعد الأمراض الجلدية والتناسلية وأمراض الذكورة
كلية الطب- جامعة عين شمس

جامعة عين شمس
كلية الطب
٢٠١٢

Summary

Skin is the largest organ in the human body and functions as a protective barrier. The large surface area and easy accessibility of skin make it one of the attractive routes for drug delivery in the treatment of skin diseases and systemic diseases. These include various types of formulations delivery systems such as powders, solutions, sprays, suspensions, emulsions, ointments, creams, pastes, gels, and patches ***(Torchilin, 2006)***. The rate and extent of drug penetration into different layers of skin and into systemic circulation are governed by drug properties and formulation characteristics. The recent emergence of nanotechnology has opened up new opportunities to develop nanosystems for topical and transdermal applications .One of the lipid-based nanosystem is liposomes ***(Fang et al., 2006)***.

Liposomes are microscopic vesicles formed from phospholipids as biological membranes. A fundamental feature of cell membranes is the organization of lipids into bi-bilayer, providing permeability barriers between exterior and interior compartments ***(Dreher et al., 2003)***.

The ability of phospholipids to form a bi-layer structure is because of the presence of a polar or hydrophilic (water-attracting) head-group region and a non-polar, lipophilic (water-repellent) tail. Therefore, liposomes contain a lipophilic

List of Contents

List of Abbreviations

Abbrev.	
AA	Alopecia areata
AIDS	Acquired immunodeficiency disease
ALA	Aminolevulenic acid
BBB	Blood brain barryer
BPO	Benzylperoxide
BV	Bleomycin + vincristine
CCL	Coated cationic liposome
CER	Ceramide
CHOL	Cholesterol
CL	Cutaneous leishmaniasis
CPD	Cyclobutane pyrimidine dimers
cptT	Critical phase transite temperature
Cs A	Cyclosporin
CTCL	Cutaneous T cell lymphoma
DNX	Daunorubicin citrate liposome (Dauno Xome)
EMC	Ethylhexyle methyl cinnamate
GD2	Disialoganglioside
HAART	Highly active anti retroviral therapy
HIV	Human immunodeficiency virus
HSV	Herpes simplex virus
Hu IFN	Human interferone
I v	Intravenous
IL	Inter leukin

List of Abbreviations (Cont.)

Abbrev.

KS ..... Kaposi sarcoma

LA..... Linoleic acid

LEA ..... Liposome entrapped antigen

LMWH ..... Low molecular weight hapten

LuVs ..... Large unilamellar vesicles

MAL..... Methylaminolevulinate

MRSA ..... Methecillin resistant staph aureus

NPLD ..... Non pegylated liposomal doxorubicin

OA ..... Oleic acids

PC..... Phospholipidcholine

PDT ..... Photo dynamic therapy

PEG ..... Polyethylene glycerol

PLD ..... PEGYLATED liposomal doxorubicin

PLE..... Polymorphic light eruption

PpIX ..... Protoporphyrin IX

RES ..... Reticuloendothelial system

RES ..... Reticuloendothelial system

SC..... Stratum corneum

SPF..... Sun protection factor

SUVs..... Small unilamellar vesicles

TNF ..... Tumour necrosis factor

TPP..... Tetrakis phenyl prophyrin

UV ..... Ultraviolet

List of Table

List of Figures

Introduction

Skin is the largest organ in the human body and functions as a protective barrier. The large surface area and easy accessibility of skin make it one of the attractive routes for drug delivery. Drugs are delivered to and through the skin for the treatment of skin diseases and systemic diseases, respectively. These include various types of formulations delivery systems such as powders, solutions, sprays, suspensions, emulsions, ointments, creams, pastes, gels, and patches ***(Torchilin, 2006)***.

For dermatological applications, formulations are targeted to different layers of the skin to protect, enhance the appearance and deliver medicaments to the skin. The rate and extent of drug penetration into different layers of skin and into systemic circulation are governed by drug properties and formulation characteristics. The recent emergence of nanotechnology has opened up new opportunities to develop nanosystems for topical and transdermal applications. One of the lipid-based nanosystem is liposomes ***(Fang et al., 2006)***.

A liposome is a microscopic vesicle, made out of the same material as a cell membrane. Liposomes can be filled with drugs, and used to deliver drugs for various diseases including cancer. They are also used in diagnostic imaging including gamma-scintigraphy, magnetic resonance, computed tomography and ultrasonography ***(El-Maghraby et al., 2008)***.

In spite of promising prospects, the systemic application of liposomal drugs has been limited to just a few indications, but the topical application of liposomal preparations has attracted increasing attention in dermatology ***(De Leeuw et al., 2009)***.

Aim of the Work

The aim of this essay is to emphasize the development of new era of drug delivery systems especially liposomes, outlining their characteristics, types , their different application and forward insight on nanomedicine not only the use of nanometer-sized materials for the treatment but also for the diagnosis of diseases especially in the therapy of various neoplasms.

Definition and Structure of Liposomes

Liposomes are microscopic vesicles formed from phospholipids as biological membranes. A fundamental feature of cell membranes is the organization of lipids into bi-bilayer, providing permeability barriers between exterior and interior compartments. A large group of biological membrane lipids that spontaneously form bi-layers in water are the phospholipids ***(Dreher et al., 2003)***. The ability of phospholipids to form a bi-layer structure is because of their amphipathic character resulting from the presence of a polar or hydrophilic (water-attracting) head-group region and a non-polar, lipophilic (water-repellent) tail. The hydrophilic head groups orientate toward the aqueous phase and the lipophilic tails orientate to each other in the presence of water (Fig.1). Therefore, liposomes contain a lipophilic compartment within the bi-layer membranes and hydrophilic compartments between the membranes (Fig.1) ***(De Leeuw et al., 2009).*** So the liposomes are used as models for biological membranes and represent one of the safest and potentially most versatile transfer vectors so that they have recently been exploited as delivery vehicles for systemic administration of drugs and topical use in dermatology ***(Yarosh, 2001).***

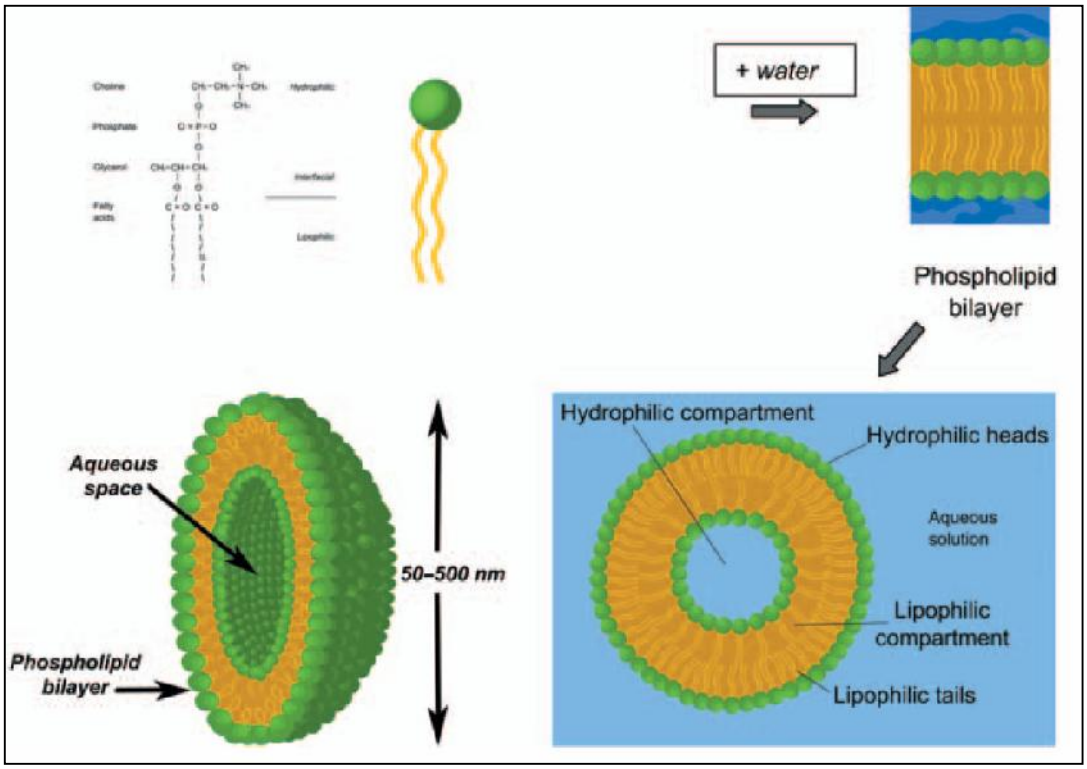

Figure (1): Top left structural formula of the phosphatydylcholine molecule. In the presence of water phospholipids bilayer are formed, which create vesicles, enclosing an aqueous core. Lipid soluble substance can be stored in the outer lipid phase (yellow ring) and water soluble substance in the inner aqueous phase (blue centre) ***(De Leeuw et al., 2009).***

Classification of Liposomes:

The liposomes are classified into natural and artificial liposomes.

I. Natural liposomes:

They are nano-sized vesicles which are water soluble on the outside and carry the fat soluble nutrient on the inside. These are called nano-vesicles micelles and liposomes ***(Kim et al., 2002)***.

Micelles:

A typical micelle is a nanosized vesicular membrane made, soluble in water by having a hydrophillic "head" facing the outside while the hydrophobic "tails" surround the fat soluble nutrient inside Such micelles formation is known as emulsification, a process that allows a compound normally insoluble (in the solvent being used) to dissolve. Technically, this natural formation is referred to as a nano-emulsion ***(Brown, 2004).***

It is essential for the emulsification and subsequent absorption of fat soluble nutrients like Vitamin E, D, K, the carotenoids and omega-3FFAs. It is the bile salts formed in the liver and secreted by the gall bladder that allow micelles of fatty acids to form. These lipid spheres, pictured below (Fig.2), are a true natural nanotechnology, being smaller than 100 nanometers in size ***(Seddon and Templer, 2000)***.

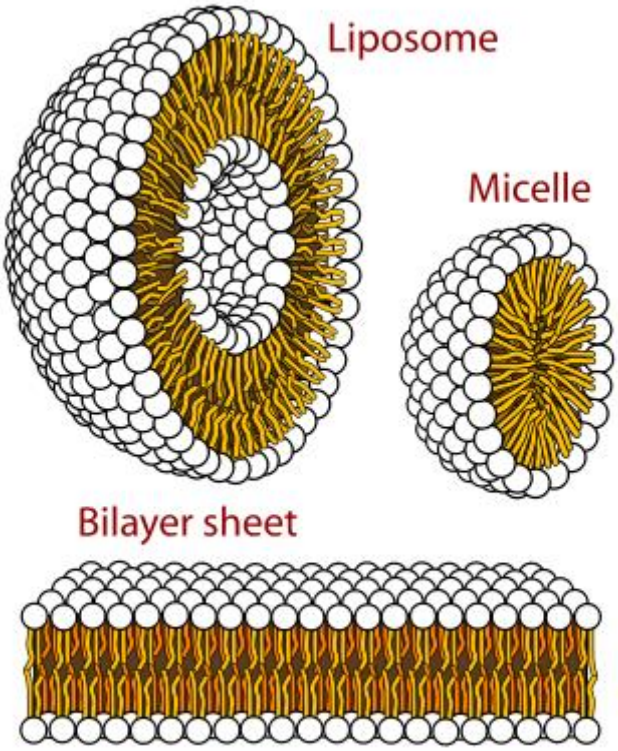

Figure (2): Liposome, micelle and bilayer sheet structure ***(Brown, 2004).***

Liposomes:

Liposomes are lipid spheres that contain an aqueous core meaning literally "fat body". Liposomes are different from micelles structurally in that they have a bilayer membrane, shown above (Fig.2). In the body, natural liposomes are composed of lecithin phospholipids. Though generally larger,

they have the advantage of being able to carry both fat soluble and water soluble nutrients. The fat soluble ingredients are held in the white area between the hydrophobic tails, while water soluble ingredients are held inside the blue area by the hydrophillic heads. The water loving heads on the outside keep the liposome soluble in aqueous solution ***(Xu et al., 2004).***

Liposomes can also be multi-laminar, like a ball within a ball, carrying a much bigger payload of both water soluble and fat soluble ingredients. Multi-laminar liposomes may reach up to perhaps 500 nm (5 micron) in size ***(Torchilin, 2006)***.

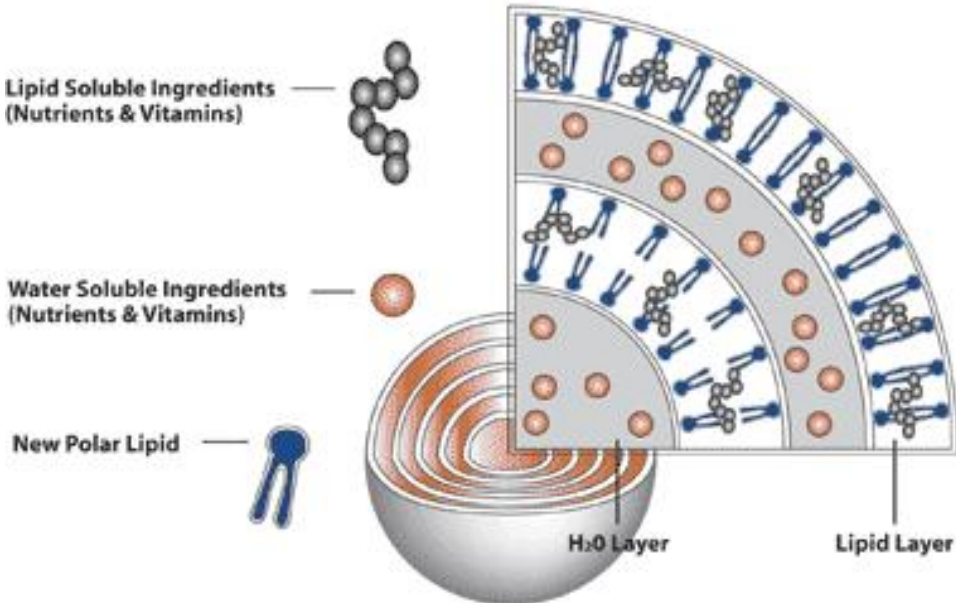

Figure (3): Architecture of absorbed natural liposome in the body ***(Xu et al., 2004).***