Chapter 2
Liposomes:
Properties and Therapeutic Applications

Ljiljana Djekic
University of Belgrade, Serbia

ABSTRACT

This chapter reviews the current progress in liposome based pharmaceuticals with particular emphasis on the carrier design, size, surface properties, drug delivery performances and therapeutic applications for different routes of administration. There were described selected examples of encapsulation of drug substances by liposomes which allowed improvement of therapeutic index of cytotoxic drugs (such as antineoplastics, antibiotics) or sustained drug release and reduction of the frequency of administration of analgesics and local anesthetics, and potentiate the immunogenicity of vaccines against hepatitis A and influenza. Furthermore, the performances of the marketed pharmaceuticals which represent pulmonary surfactant substituents (in the form of liposome vesicles) in premature infants and topical preparations with high molecular weight actives (e.g., heparin sodium) encapsulated in liposomes, were highlighted. The most important factors that affect the development of new drugs with this type of nanomaterials and their safety were commented.

INTRODUCTION

Liposomes were first investigated in 1976 as colloidal carriers for insulin in order to protect the drug against potential proteolysis in gastrointestinal tract (GIT) (Dapergolas & Gregoriadis, 1976). Until now, this field of investigations is at the preclinical level, primarily due to limited stability of liposomal carriers in the GIT. On the other hand, encapsulation of drug substances in this type of carriers becomes important strategy in development of pharmaceutical preparations for different routes of administration (De Villiers et al., 2009; Farokhzad & Langer, 2009; Park, 2007). Curently available pharmaceutical products based on liposomes are predominantly parenteral preparations for intravenous (*i.v.*), intramuscular (*i.m.*), subcutaneous (*s.c.*), and intrathecal (*i.t.*) administration. Liposomal based products for cutaneous and intratracheal administration are also on the market (Table 1).

DOI: 10.4018/978-1-5225-0751-2.ch002

Table 1. Marketed pharmaceutical products comprising drug substances encapsulated in liposome-type carriers

Name of the Medicinal Product	Pharmaceutical Form	Qualitative and Quantitative Composition	Carrier	List of Excipients	Manufacturer	Indications
Caelyx®/ Doxil®	Concentrate for solution for infusion	Doxorubicin hydrochloride 20 mg/10 ml 50 mg/25 ml	PEGylated liposomes (80 – 100 nm)	α- (2- [1,2-distearoyl-sn-glycero (3) fosfooksi] ethylcarbamoyl) -ω-methoxypoly (oxyethylene) -40 sodium salt (MPEG-DSPE), hydrogenated soy phosphatidylcholine (HSPC), cholesterol, ammonium sulfate, sucrose, histidine, Water for injections hydrochloric acid, sodium hydroxide	Janssen-Cilag, UK / Ortho Biotech, Johnson & Johnson, USA	Metastatic breast cancer, ovarian cancer, multiple myeloma, Kaposi's sarcoma in patients with AIDS
Myocet®	A powder, a dispersion and a solvent for dispersing the concentrate for infusion	Doxorubicin hydrochloride 50 mg	Small unilamellar liposomes	**Powder:** Lactose **Dispersion:** Phosphatidylcholine, Cholesterol, Citric acid, Sodium hydroxide, Water for injections **Solvent:** Sodium carbonate, Water for injections	Cephalon, USA	Metastatic breast cancer
DaunoXome®	Concentrate for solution for infusion	Daunorubicin hydrochloride 50 mg/25 ml	Small unilamellar liposomes (35 – 65 nm)	**Liposomes:** Distearoilfosfatidilholin (28.16 mg/ml), Cholesterol (6.72 mg/ml), citric acid **Vehicle:** Sucrose (2,125 mg), Glycine (94 mg), Calcium chloride, dihydrate (7 mg), Water for Injection (q.s. ad 25 ml) pH 4.9 - 6.0	Nextar Pharmaceuticals/ Gilead Sciences, USA	Kaposi's sarcoma in patients with AIDS
Marqibo®	A solution for injection (vincristine sulfate 5 mg/5 ml). Dispersion of liposomes. Buffer solution.	Vincristine sulfate 5 mg/31 ml	Liposomes (~100 nm)	**A solution for injection of vincristine sulfate of mannitol.** **Dispersion of liposomes:** sphingomyelin, cholesterol, sodium citrate, citric acid. **Buffer:** Sodium phosphate, sodium chloride.	Talon Therapeutics, USA	Acute lymphoblastic leukemia
AmBisome®	Powder for solution for infusion	Amphotericin B 50 mg	Conventional bilamellar liposomes (<100 nm)	Hydrogenated soy phosphatidylcholine (213 mg), cholesterol (52 mg), distearoylphosphatidylglycerol (84 mg), alpha-tocopherol (0.64 mg), sucrose (900 mg), disodium succinate hexahydrate (27 mg), sodium hydroxide, hydrochloric acid. pH 5-6 (after reconstitution of the powder with water for injection)	NeXstar Pharmaceuticals/ Gilead, USA	Severe systemic fungal infections (disseminated candidiasis, aspergillosis, mycetoma, cryptococcal meningitis, visceral leishmaniasis)

continued on following page