Chapter 2

Liposomes: Properties and Therapeutic Applications

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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). Currently 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).

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

<table>
<thead>
<tr>
<th>Name of the Medicinal Product</th>
<th>Pharmaceutical Form</th>
<th>Qualitative and Quantitative Composition</th>
<th>Carrier</th>
<th>List of Excipients</th>
<th>Manufacturer</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caelyx®/ Doxil®</td>
<td>Concentrate for solution for infusion</td>
<td>Doxorubicin hydrochloride 20 mg/10 ml 50 mg/25 ml</td>
<td>PEGylated liposomes (80 – 100 nm)</td>
<td>or- (2-[1,2-di(stearyl-sn-glycerol (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</td>
<td>Janssen-Cilag, UK / Ortho Biotech, Johnson &amp; Johnson, USA</td>
<td>Metastatic breast cancer, ovarian cancer, multiple myeloma, Kaposi’s sarcoma in patients with AIDS</td>
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</table>
| 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: Distearoylphosphatidylcholin (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 | Nexstar 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 unilamellar liposomes (<100 nm) | Hydrogenated soy phosphatidylcholine (213 mg), cholesterol (52 mg), distearoylphosphatidylglycerol (84 mg), alpha-tocopherol (0.64 mg), sucrose (900 mg), sodium 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) |

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