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Review Article

Applications of Liposome in Cancer Drug Delivery and Treatment: A Review

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ABSTRACT

In the world the biggest challenges to cure the cancer because of the abnormal cancer cells growth in the human body which is near to uncontrollable. These cells known as the malignant cell because it produced the cancer. There are several treatments for cancer such as surgery, chemotherapy, radiation treatment etc. however such treatments have major side effects like normal cell got killed, loss of hair, the surgery person skill also in consideration and high chances of reoccurrences. Due to such side effects these treatment drugs are less popular. To reduces such side effects the liposomal based treatments are the most preferable solution. The liposomes are the phospholipid bilayer vesicles and it has high encapsulation capacity. Therefore, liposomal based treatment plays significant role in the cancer treatment with less toxicity and other many advantages. The liposomal based drug pegylated liposomal doxorubicin and daunorubicin have advanced effect in the body. Furthermore, the development of the liposomes as immunoliposomes, ligand targeted and molecular targeting. This review explores the liposomal based drug delivery system, its advance effect on the cancer cells and clinically approve liposomes formulations.

Keywords: Nanocarriers, Liposomes, cancer therapy, Drug delivery

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INTRODUCTION

The cancer is the most health concern issue worldwide because as per the research data high number of deaths were noticed due to cancer[1-2]. The cancer is killing the millions of people and it is the crucial situation for the medical industry. The clinically treatment for the cancer[3] is not effective because of the phenotypic levelsand genetic complexity in cancer cell. According to the research estimate the cancer treatment drug has very poor pharmacokinetics and bioavailability [4]. Thus, the development of the such targeted or site location delivery system which can improve the pharmacokinetics, bioavailability, improve the healthy cells and reduced the side effects. To overcome such side effects and improve the treatment effects[5] the Nanocarriersbased drug delivery system is vital option instead of the other conventional cancer treatment[6]. Nanocarriers surface area is larger in comparison to the bigger particles therefore encapsulated[7] large amount of drug can be easily modified. In addition to this such drugs can increase the blood circulation time and accumulated in the tumor cell[7-8] through enhanced permeability and retention[9].

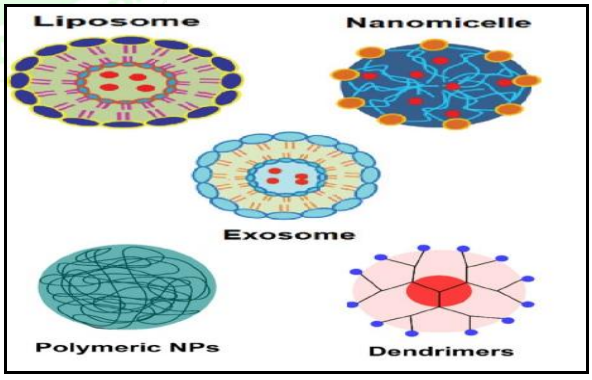

Figure 1. Different types of nanocarriers

The other advantages of this nanocarriers are pharmacokinetics properties, bioavailability and improve the solubility[10]. Currently the various nanocarriers are available such as liposomes, micelles, polymeric nanoparticles[5]. The figure 1 is showing the most popular nanocarriers. This review Summarized liposome preparation, current development in the liposomes and clinically available liposomal drugs.

The liposomes

In 1965 it was first time observed that phospholipids have aqueous medium form which is closely related to binary structure[11]. Later on, this closely realated binary structure were known as liposomes in 1968[12]. The one or more lipid bilayers surrounded by the liposomes[10]. The liposomes were used for physical behavior of the biological members such as lipids orientation, ion transport and lipids physiochemical characterization[13]. Investigation and the current research trend say that the liposomes are used and drug delivery systems for cancer treatment as they meet the good vehicle drug delivery requirement. The liposomes have good characteristics such as stable in colloidal solution, biocompatible and biodegradable[14]. In addition to this the liposomes are reducing the surg toxicity, degradation of drug and can be used as targeted drug delivery system[9,15]. The liposomes contain the surface ligands for unhealthy tissue attachments. The Multilamellar vesicle, Small unilamellar, Large unilamellar vesicle are the major types of liposomes. However, in the cancer treatment the drug delivery system plays a Significant role because only Drug delivery systems can enhance the therapeutic index of anticancer agents. This therapeutic index can be improved by increasing the amount of drug in the cancer tumor.

As discussed in the above sections the liposomes have ability to released the drug at the targeted location in the tumor. In healthy human endothelial walls tightly bounded by the endothelial cells. These tightly bounded endothelial walls are helping to stop the large particles leaking from the vessels. In the tumor vessel such arrangements were not established therefore it is diagnostically leaky and such ability is known enhanced permeability and retention effect. The liposomes size is about lesser than the 400nm thus it can easily enter in to the tumor site from the blood.

Design and Development of the Liposomes

Basically, liposomes contain the aqueous solution region. This region is encapsulated inside hydrophobic membrane henceforth water-soluble solute cannot pass through the lipids. Therefore, the hydrophobic drugs can dissolve into membrane, according to this the liposome carries the hydrophobic and hydrophilic molecules. Liposomes mostly used for artificial model because liposomes do not have lipophobic contents. The liposomes are the design based on their application and its particular size is made by using the macrophage phagocytosis and made them viable for the target delivery, so liposome can be digested and released the drug. Also, liposome can be combination of ligands and opsonin to activate endocytosis. Designed liposomes can be used for transformation of DNA[16] which is known as lipofection. Liposomes can be used in many other delivery systems such as Pesticides to plants, Cosmetics to the skin, Dyes to textiles etc. There are many other parameters to be considered to prepare the liposomal formulation the figure 2 showing all the parameters.

To developed the formulation of the liposomes is a time-consuming process it will not a spontaneous process. There are many methods were developed to prepared the liposomes such as detergent removal, ethanol injection, solvent removal and emulsion removal[9,17]. The characteristics like size, shape, efficiency[18] and stability of drug loading are affected to liposomes by the preparation of the methods. Initially, solvent removal or Thin lipid film hydration is the most popular method to prepare the liposomes[19]. The menthol and chloroform mixtures are used to dissolved the lipids. The lipid concentration is about 10-20 $mgmL^{-1}$.

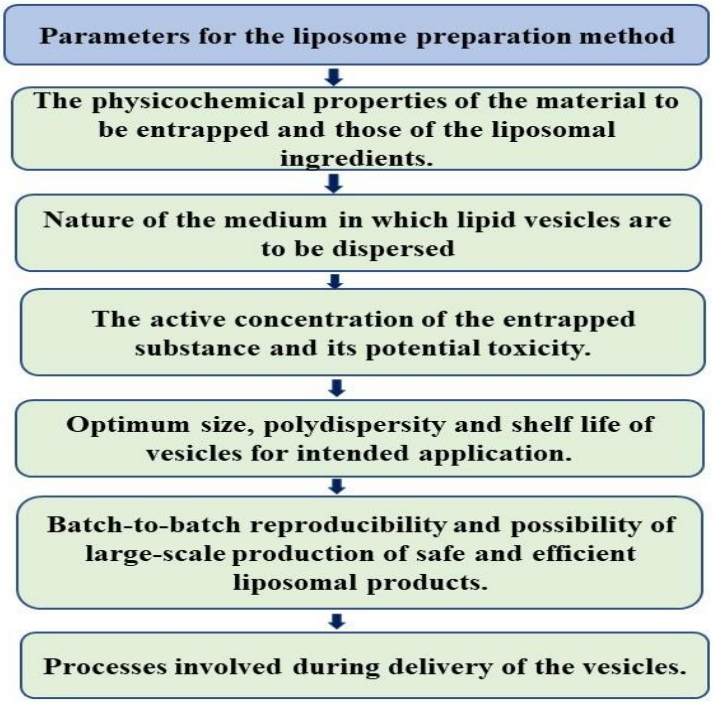

Figure 2. Parameters to be used for the preparation of Liposomal formulations.

The rotary evaporator is used to remove the solvent and prepared the thin film of lipid by reducing the pressure. This thin lipid film needs to be desiccated form through hydration but it is time consuming process. After that the aqueous solution is to be added and liposomes would be multilamellar vesicles type liposomes with the size of 200-1000nm[17,19]. Multilamellar vesicle liposomes can be produced by the extrusion or sonication. Generally, the sonication is performed in the water bath type sonocators. The temperature of water in the sonicator is above the transition temperature of lipids. The sonic waves produced the small unilamellar vesicles by disrupting the outer layers of gaint liposomes and produced the 20-100 nm diameter liposomes[17]. The lecithin phospholipids are place in to the water for its formation therefore one or series of bilayers are separated by the water molecule and finally enough energy is supplied. The sonicating phospholipids in water is mostly used to prepared the material for human use. The continuous research and development in the liposome formulation table 1 is showing the currently clinically approved liposomal based drugs for cancer treatment.

Table 1: Clinically approve liposomal drugs for cancer treatment.

Sr. No.	Name of drug	Trade name	Indication	Route of Administration	Dosage Form
1	Liposomal morphine	DepoDur	Postsurgical analgesia	Parenteral	Injectable liquid
2	Liposomal IRIV vaccine	Epaxal	Hepatitis A		
3	Liposomal cytarabine	Depocyt	Malignant lymphomatous meningitis		
4	Liposomal IRIV vaccine	Inflexal V	Influenza		
5	Liposomal amphotericin B	Ambisome	Fungal and protozoal infections		
6	Liposomal doxorubicin	Myocet	Combination therapy with cyclophosphamide in metastatic breast cancer		
7	Liposomal daunorubicin	DaunoXome	HIV-related Kaposi's sarcoma		
8	Liposomal amphotericin B	Abelcet	Fungal infections		

Current advancement in liposomes-based drug delivery system

In case of advances in liposomal research is to avoid its detection by the body's immune system, especially, the cells of reticuloendothelial system (RES). These liposomes are known as the stealth liposome and they are developed with PEG studding[20]. outside of the membrane. The coating gives the advancement in the drug life during the circulation in the delivery system. Recently the research and investigation are under process for PEG coating and its effect on the cancer treatment. Attachment of the targeting ligands[21] leads the drug delivery at the specific location of the tumor site reduces side effects.

CONCLUSION

The chronic diseases like a cancer the liposome and immunoliposomal formulations plays significant role in the treatment. This formulation leads the liposome technology and antibody engineering together which can analyses and investigate drug delivery systems. In addition to this in vitro and in vivo studies contribution in the targeted drug delivery mechanism[22]. gene silencing and vascular targeting are novel approaches which is under the research. Further studies on the nanocarriers demonstrate the safety and efficiency. Liposomes of Nanocarriers will be a promising method for the cancer treatment. However, many liposomes-based drug delivery systems are already in the market and the many more are in the research.

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