Liposomes as carriers of anticancer drugs in drug delivery systems

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Abstract

Introduction: Nowadays, cancer is one of the most important issues in global health and for the time being, it is one of the reasons for 12%of all deaths worldwide. some scientific research has been done in the cause of cancer ،its recognition, and medical treatment up to now. But unfortunately due to the increasing of resistance of the cancer cells against the chemotherapy drugs, the attempts ended in failure. For this reason, scientists are looking for the methods to increase the response to the cancer cells to anticancer drugs and also find the best methods with less side effects. Currently, the usage of liposomes are notable as one of the most famous and the most stable nanocarriers in drug delivery system. Liposomes are colloidal substances with two or more phospholipid membrane which are created by the mixture of lipids and other amphipathic molecules such as cholesterol. Common medicinal compounds that use of liposome for defeating in cancer disease, including Doxil and Evacet that both of them consist of chemotherapic drug "doxorubicin". To design an efficient nanocarrier for drug delivery system, we should consider the actions to maximize performance and prolong liposome circulation time in the blood stream such as the ability to protect it from immune system ,the way that exhibits greater stability and diminished toxicity of liposomes and target the area of the purpose tissue in the body and release drugs in a controlled manner.

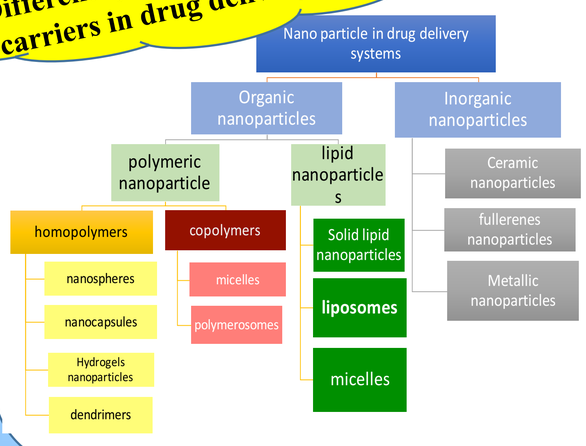
Methods: All the methods of preparing the liposomes involve four basic stages:1-Drying down lipids from organic solvent. 2- Dispersing the lipid in aqueous media. 3- Purifying the resultant liposome. 4- Analyzing the final product. The following methods are used for the preparation of liposome based on drug loading:1-Passive loading techniques 2-Active loading technique. Passive loading techniques include three different methods: 1-Mechanical dispersion method. 2-Solvent dispersion method. 3-Detergent removal method

Results and discussion: Despite the many disadvantages of liposomes as drug carrier like high production cost, low efficiency in trapping the drugs and slow drug release, they have lots of benefits. Liposomes are non-toxic, flexible, biocompatible, completely biodegradable, and they help reduce the exposure of sensitive tissues to toxic drugs

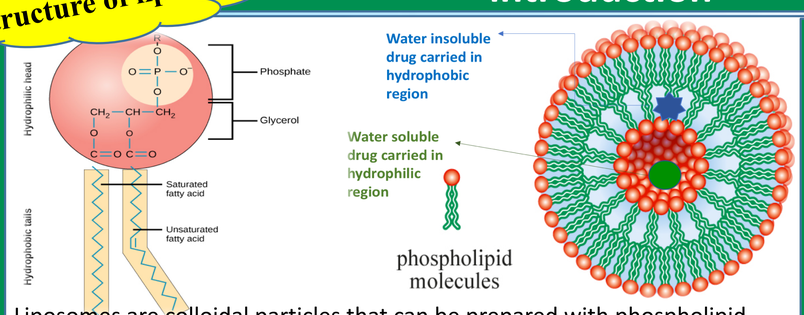
Conclusion: Despite the limitations and drawbacks that exist today, science and research go towards the use of nanocarriers and drug delivery system for the treatment of cancer and it is hoped that in the near future drug delivery systems, will be problem solver of treatment of many patients with incurable diseases.

introduction

Different types of pharmaceutical carriers in drug delivery system



Structure of liposome



Liposomes are colloidal particles that can be prepared with phospholipid molecules. Phospholipids are amphipathic molecule i.e. having affinity for both aqueous & polar moieties, as they have a hydrophobic tail & hydrophilic head.

Depending on whether the molecule(drug) is hydrophilic or hydrophobic, it could be incorporated in the entrapped aqueous interior or in the lipid bilayer of the liposome

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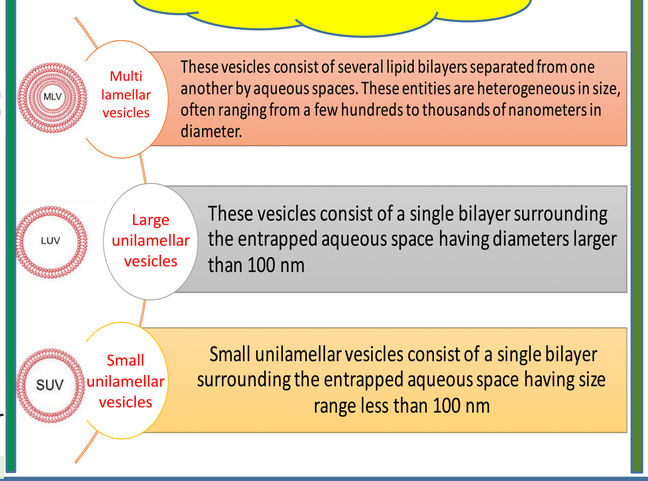
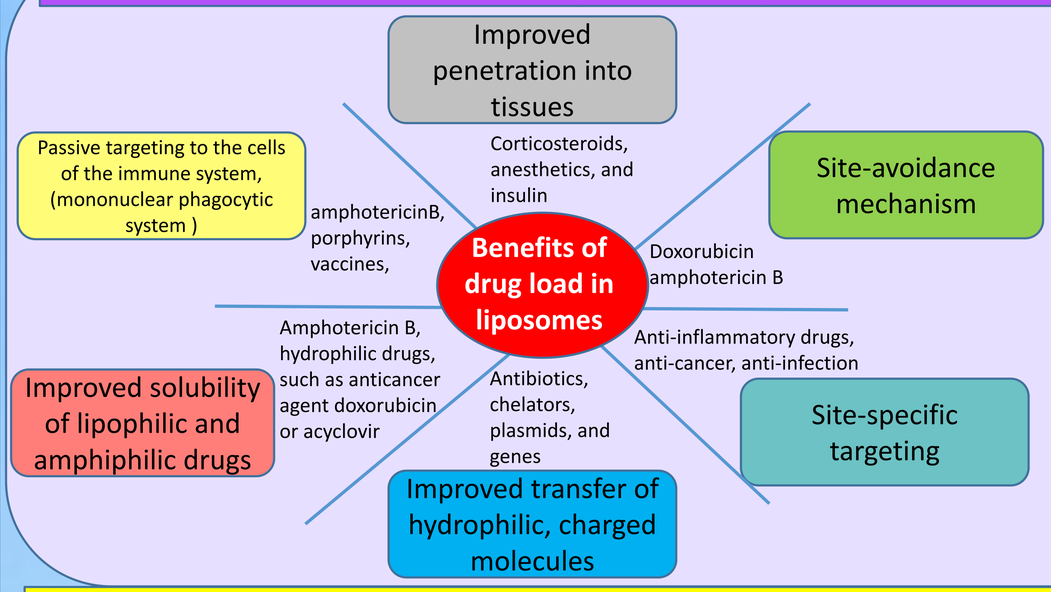
Classification of Liposome Based on size and number of bilayers



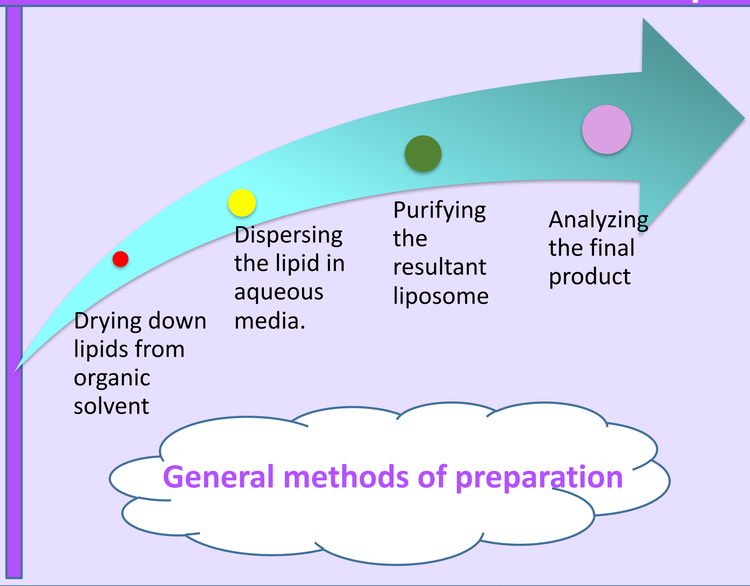
Different types of anticancer drugs with liposome carrier

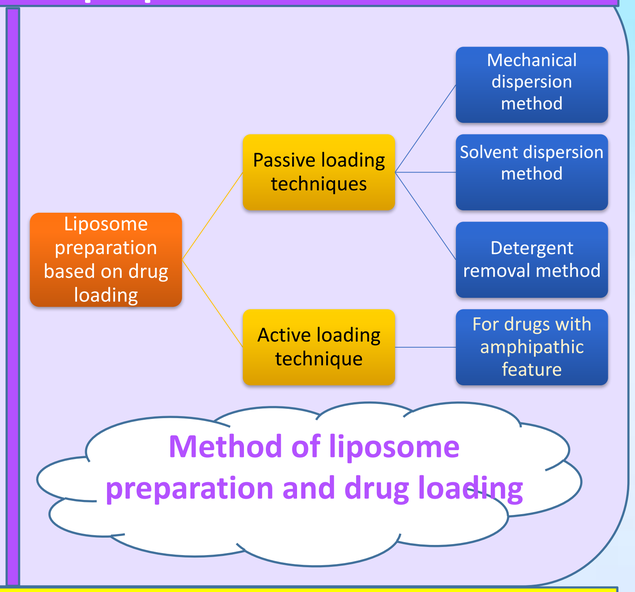
Carrier	Name of the product	Drug
Non PEGylated liposome	Daunoxome	Daunorubicin
Non PEGylated liposome	Myocet	Doxorubicin
PEGylated liposome	Doxil/Caelyx	Doxorubicin

Benefits of drug load in liposomes



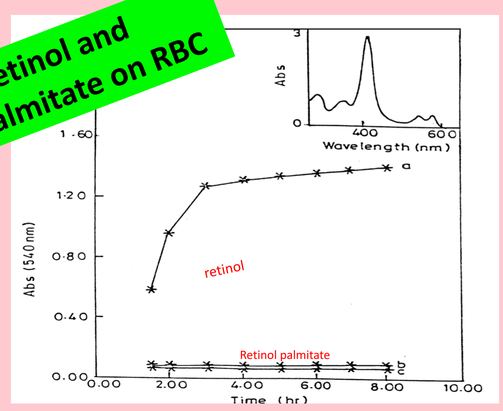
Methods of liposome preparation





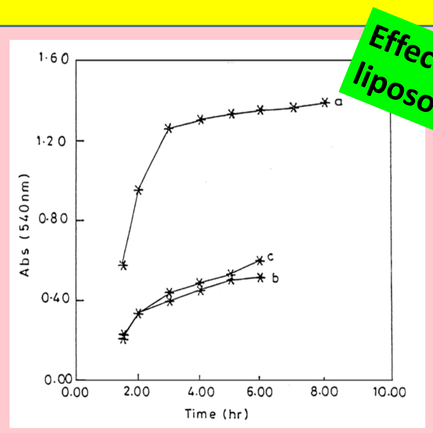
*Effect of **liposomal** and **non-liposomal retinol** and **retinol palmitate** on red blood cells (RBC)*

Effect of retinol and retinol palmitate on RBC



A plot of change in absorbance at 540nm with time for incubation of :
a)retinol b)retinol palmitate c)control with erythrocyte in phosphate buffered saline at 37 C . Inset :absorption spectrum of erythrocyte after lysis by retinoids

Effect of liposomal and non-liposomal retinol on RBC



A plot change in absorbance at 540 nm with time for incubation of
a)retinol in phosphate buffered-saline
b) PC liposome. c) PC liposomes with erythrocyte at 37 C

result

the liposomes can sequester the drug and prevent its interaction with erythrocytes

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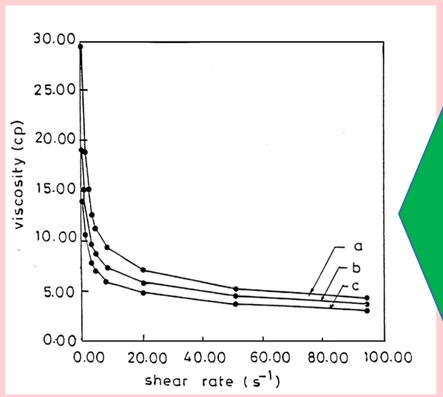
Effects of liposomal and nan liposomal retinol palmitate on erythrocyte's viscosity



result

the presence of an external lipid, the lipids of RBC get exchanged with the former, and as a result, the rigidity of the red cells decreases. Consequently,decrease in the viscosity is observed.

Change of viscosity with shear rate.
a)Erythrocyte
b)Erythrocyte and retinol palmitate
c)Erythrocyte and PC-liposomal.

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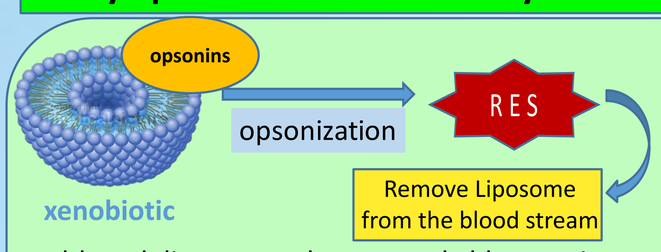
Why liposome should be PEGylated?



although liposomes show remarkable promise as drug carriers, they do have a significant weakness: once injected into the bloodstream, they are vulnerable to attack from the reticuloendothelial system (RES).

circulation time can be increased by decreasing liposome size and modifying the surface/steric effect with PEG derivatives.

Effect of pegylation on liposome

unique properties of PEG

- Nontoxic
- soluble in both polar and nonpolar solvents
- can be eliminated from the body through a combination of renal and hepatic pathways

effect of the PEG corona

- cause significant stabilization of liposome dispersions
- prevent liposome aggregation
- inhibit protein and cellular interactions with liposomes
- considerable increase in the loading efficiency of the liposomes for hydrophobic molecules
- The permeability of PEGylated liposomes was decreased in comparison to DPPC liposomes without PEGylation.
- alter the properties of phospholipid membranes.
- increase in the hydrophobicity of lipid membranes.

discussion

Amphipathic phospholipids property creates spherical particles in water environment which called liposomes. liposome drug delivery systems have played a remarkable role in the formulation of potent drugs to improve therapeutics. Depending on whether the molecule (drug) is hydrophilic or hydrophobic, it could be incorporated in the entrapped aqueous interior or in the lipid bilayer of the liposome. Liposomes are prepared with distinct structure, size, composition, flexibility with a variety of surface modification. Such availability of liposomes with great diverse properties makes them most intelligent carrier system for delivery of bioactive substances

Conclusion

Nowadays the knowledge of using nanoparticles and drug delivery system is progressing and Despite the limitations and drawbacks that exist today, science and research go towards the use of drug delivery system based on liposome carrier in many kinds of field such as cancer therapy, vaccine delivery , pulmonary delivery, gene Therapeutics , ophthalmic drug delivery etc. it is hoped that in the near future we can treat many disease and patient problem with this intelligent drug delivery systems

Reference

1. A new strategy for attachment of antibodies to sterically stabilized liposomes resulting in efficient targeting to cancer cells/Biochimica et Biophysica Acta 1237(1995) 99-108
2. Liposome encapsulated vitamin A compounds exhibit greater stability and diminished toxicity/Biophysical Chemistry 73 Ž1998. 155 162
3. PEGylated Liposomes as Carriers of Hydrophobic Porphyrins /Monika Dzieciuch,† Sami Rissanen,‡ Natalia Szydłowska,
4. Combination Approach: the Future of the War Against Cancer Lan Chen • Anshoo Malhotra /DOI 10.1007/s12013-015-0549-0
5. **The role of surface charge and hydrophilic groups on liposome clearance *in vivo*** - Alberto Gabizon