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# Liposome Based Nanocarriers for Anti-tumour Medicines

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**ABSTRACT:** This review focuses on the use of liposomes for effective treatment in tumour. Liposomes are spherical vesicles containing one or more bilayers of phospholipids discovered by Dr. Alec D. Bangham in 1961. In the field of medicine, the drug delivery technology has produced vigorous progress. Liposomes have various properties such as biocompatibility, efficacy, capability targeting and increased effectiveness in vivo due to this, liposomes have become famous versatile drug carrier systems. Use of liposomes causes reduced systemic toxicity, monitored and maintained drug release and increased features of pharmacokinetic and pharmacodynamic drugs. The present study will explain the basic structure of liposomes, mechanism of liposomes in skin penetration, a study of pharmacokinetic of encapsulated liposomes with anti-tumour drugs, clearance and deposition study of liposomes.

**KEYWORDS:** Liposome, skin, mechanism of liposome in skin penetration, anti-tumour medicines, clearance study.

## I. INTRODUCTION

The liposomes were first described in 1965. By changing the lipid compositions, it can be customized to have different rigidities, biological property and sizes. For the treatment of fungal infections, Amphotericin B loaded liposomes were approved and commercialized with the brand name Amphotec and Ambisome.

Liposomes are well-known nano-sized lipid vesicles that may be useful as topical drug delivery. In this type of drug delivery system one or more lipid bilayers surround a separate aqueous phase. It has several advantages as a drug delivery vehicle, including the ability to encapsulate both water-soluble and lipophilic compounds, as well as being non-toxic and biodegradable. Liposomes can easily penetrate the epidermal barrier more effectively than any other dosage forms because it has similar lipid content to that of the epidermis. In comparison to free drug, conventional liposomes offer the potential to provide extended drug release, as well as a higher efficacy for local dermal drug delivery through intact skin. By applying liposomes to the skin, wounds can be healed. It should be noted that open wounds impair the skin barrier, allowing for greater penetration and absorption across the skin. [2]

The formulation of liposome is consisted of natural or synthetic lipids, surfactants and copolymers, which can be used to generate effective drug delivery therapy in a variety of biological applications. It entraps lipophilic and hydrophilic molecules which allows these vesicles to encapsulate a wide range of medications. Characterization of liposome nanocarriers could be done by easily controlled features (such as ligand, particle dimensions, shape, lipid content, and surface functionalization with polymers and charge) that can influence their colloidal stability in vitro and in vivo. Depending upon the phospholipid composition liposomes can have positive, negative or neutral surfaces. phospholipids spontaneously assemble into bilayers that are like the structures found in biological membranes, when they are disseminated in water. physiochemical properties and morphology of lipid-based liposomes are influenced by geometry, nature and size of lipid components, as well as surface charge, concentration and temperature.[3]

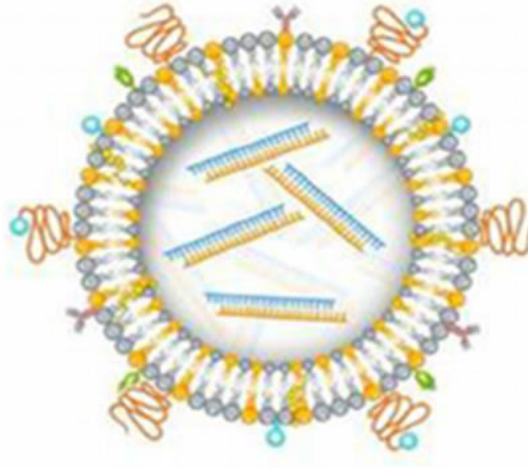


Fig. 1 : Structure of liposome

#### Interaction involved in liposome nanocarriers

- 1) hydrogen bonding and hydrophobic forces
- 2) Vander Waal forces
- 3) Electrostatic interaction: Electrical double layer
- 4) Steric stabilization forces.

#### Skin

The largest organ of the Human body is the skin it covers almost 10% of the body mass and 2 m<sup>2</sup> of body surface area. Skin is multi layered organ with 3 layers which are epidermis(outermost), dermis(middle) and the third one is hypo-dermis(inner). All three layers of the skin significantly vary upon the virtue of their structure and function. [5] It protects the body from UV light, pathogens and chemical or physical injury. Regulation of water and temperature is also dependent on skin.[4]

The epidermis further has five layers: stratum corneum, granulosum, spinosum, Basale and lucid.[5]

1. **Stratum Basale:** is the inner most layer, having cells cuboidal to columnar and keratinocytes are being produced by active stem cells. Melanocytes are present here.
2. **Stratum spinosum:** This is 8-10 cell layers; prickly shaped cells present, which are polyhedral, possessing extended cytoplasmic processes that maintain the contact to nearby cells by desmosomes.
3. **Stratum granulosum:** Diamond-shaped cells of 3-5 layers contain keratohyalin granules and lamellar granules. This layer helps to keep cells together.
4. **Stratum lucidum:** This layer is found in thicker skin as palms and soles. It is a 2-3 cell layer of skin.
5. **Stratum corneum:** It is an uppermost layer having 20-30 cells also. In this layer keratin, and horny scales are present.

These layers of epidermis help in the penetration of drug.[5]



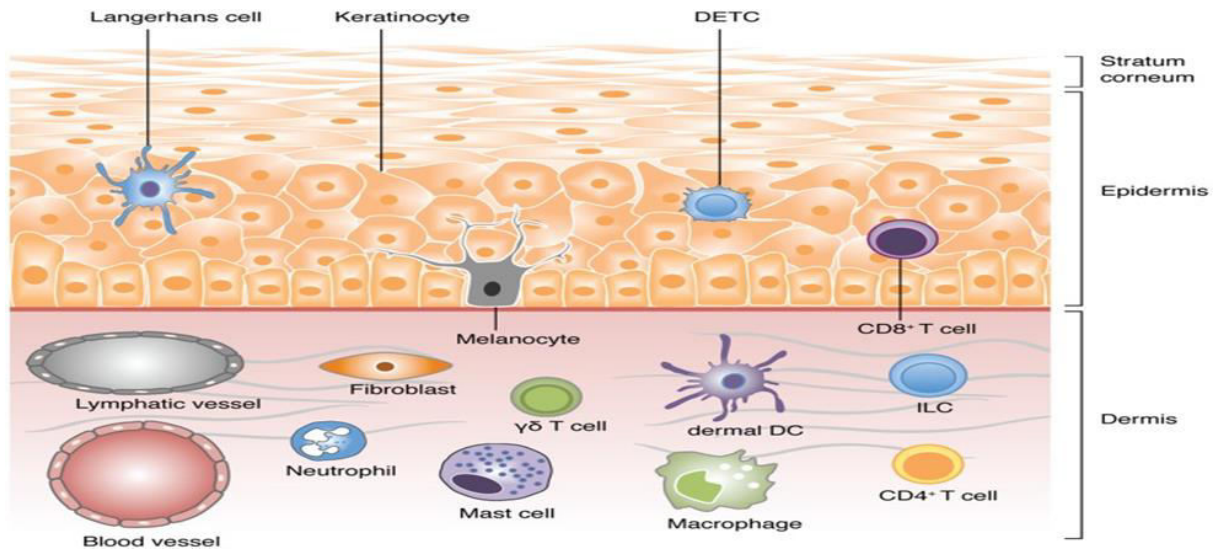


Fig 2 Layers of epidermis

The best route of drug administration is through skin. In the case of hydrophilic drugs and big protein molecules, drug administration is difficult so, there is a need for chemicals that would help to enhance the permeability of the skin. There we use special carriers like **nanoparticles** (NPs) to deliver drug molecules deeper into the skin[4]

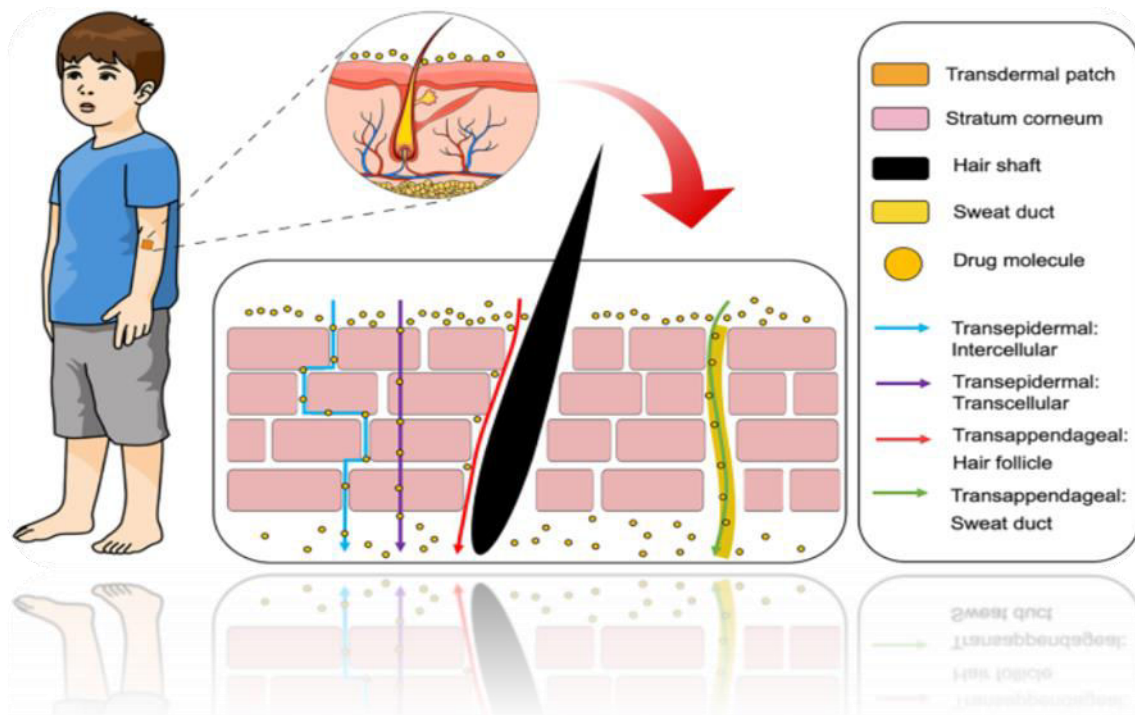


Fig 3 Skin Structure &amp; Penetration Pathways

## II. MECHANISM OF LIPOSOMES SKIN PENETRATION

Penetration of the liposome is more effective through epidermal barrier of skin than other conventional dosage forms because liposome have a lipid composition which is same as of epidermis layer of skin. The following are four probable mechanisms for liposomes skin penetration.

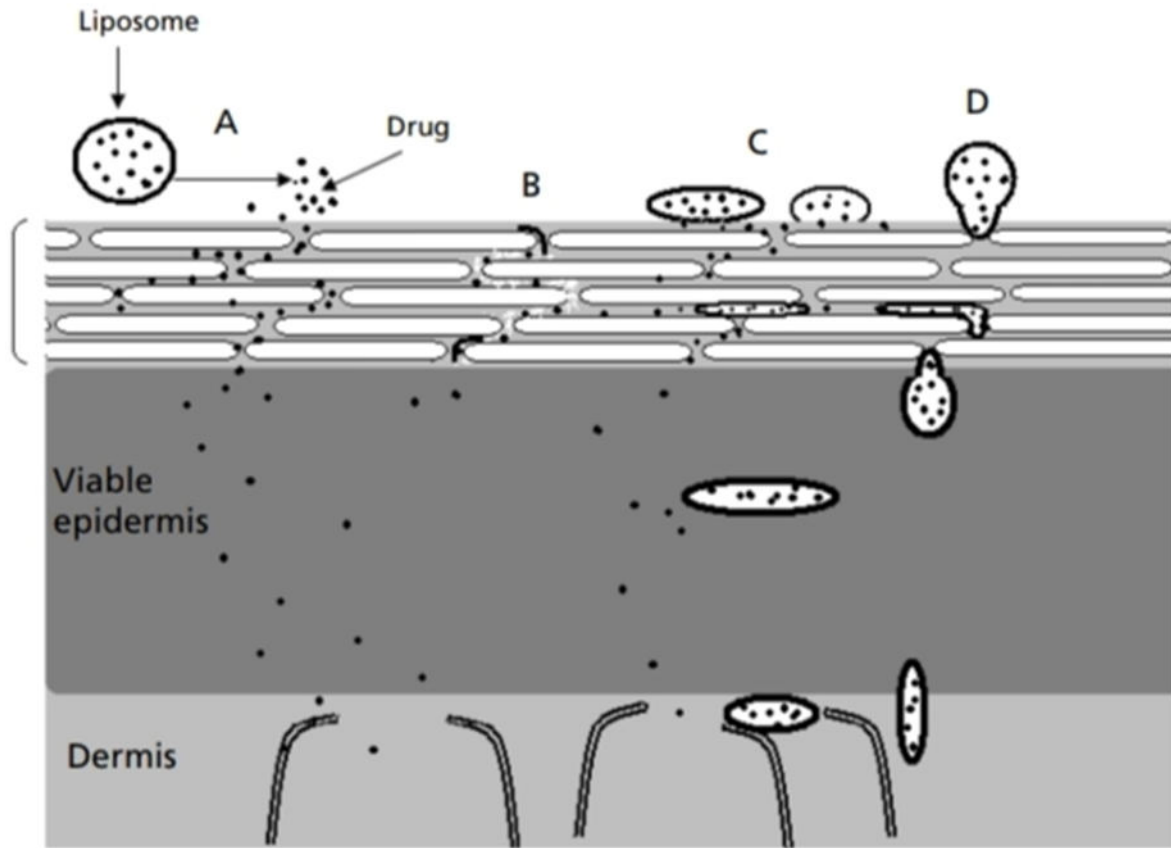


Fig: 4 Mechanisms of Liposome Skin Penetration

#### A) Drug release mechanism

After understanding this mechanism, it came to know that drug molecules penetrate skin on its own as vesicles only enters to the skin surface. Such vesicles can only be considered of as drug carriers with the ability to govern drug release. To test this possibility, each formulation's trans-epidermal flow plot to its in-vitro drug release profile. The greatest flux of oestradiol through skin emerged in all preparations at a time when drug release was minimal. [6]

#### B) Penetration enhancing mechanism

Liposome could penetrate deeply in stratum corneum or mix and fuse with skin lipids which depends on the formulation of the liposomes. The most effective liposomes were those containing diolethylphosphatidylethanolamine (DOPE). It also discovered that DOPE-containing nano-aggregates could fuse and mix with skin lipids as well as loosen their structure. This is proved by the interaction of vesicles with stratum corneum[6]

#### C) Vesicle adsorption to and/or fusion to stratum corneum

Another possibility of the liposome skin penetration is adsorption to the skin surface and fuse with the lipid matrix in stratum corneum. They can be injected into the skin, however they will breakdown and create a unit membrane structure rather than penetrating through an intact healthy stratum corneum. It has also been found that vesicular lecithin penetrates human skin quickly[6]

#### D) Intact vesicular skin penetration mechanism (diffusion)

It was hypothesized that because the liposomes were too big to penetrate the capillary circulation, they acted as drug reservoirs at the site of action. It was impossible to imagine big lipid vesicles penetrating the closely packed stratum corneum in such vast quantities. Liposomes containing colloidal iron (An electron dense marker) applied on guinea pigs for three times (every 12 hour). In the dermis layer, the intact liposomes were detected by electron micrography.



Although the presence of large multilamellar vesicles (LMLVs) in the formulation, majority of liposome found in the dermis layer were unilamellar (300 to 500 nm) with few LMLV's[6]

### III. CASE STUDY OF LIPOSOME

A study of pharmacokinetic of encapsulated liposomes with Vinblastine, actinomycin D, daunomycin, and cytosine anti-tumor medicines.

The effects of encapsulation within liposomes (phospholipid vesicles) on plasma clearance kinetics and tissue deposition of four medicines acting on tumor cells, namely vinblastine, cytosine arabinose, actinomycin D, and daunomycin, were investigated in 1977. In all of these cases, the encapsulated liposome medicines were slowly removed from the plasma after intravenous delivery, compared to when they were free pharmaceuticals. An encapsulated liposome containing daunomycin was shown to have a plasma half-life of 145 minutes or more, while the free form had a plasma half-life of less than 4 minutes. A reasonable approach to cancer chemotherapy necessitates a thorough understanding of the several pharmacodynamics parameters that control the amount of active antineoplastic drug that reaches target sites within the tumors or sensitive normal tissue sites. [7]

#### METHODS:

In these experiments' animals can be used but, in these a rat weighing 270 to 340 grams was used to obtain the experiment. Materials used are phosphatidyl-choline, 2 phosphatide serine, cholesterol, stearyl amine, tritium actinomycin D {ci/mole} and vinblastine sulfate {5-11 ci/mole} and many other materials such as triturated arabinose and non-radioactive agents [8]

#### PREPARATION:

The medicinal liposomes were created following the procedure described in the previous paragraph. 3 In vacuum, triglycerides in an organic solvent were evaporated onto the wall of a glass container [9] Actinides and daunomycin, for example, were dissolved in ethanol and combined with the lipid before evaporation. To make the liposomes, a dry lipids films were immersed in isosmotic phosphorus saline. Vortex and sonication have been used to effectively distribute and mix the material. Water-loving medicines (polar pharmaceuticals) like cytosine arabinose were absorbed into the liposomes by putting them in an aqueous buffer and mixing them. The medication containing lipid membranes was ultrasonic disseminated inside a boiling water instrument (Heat systems 125 Wi under a nitrogen atmosphere, and the temperatures in synthesis of liposomes is generally 35 with a constant control of temperature).

### IV. CLEARANCE AND DEPOSITION STUDIES

Anti-tumor medicines, either free or encapsulate liposomes, were injected into the tail veins of rats. In the case of free medications, each animal received 550 micro grams of the substance. While 15 micrograms of encapsulated drug was often employed, the total amount of drug with lipid injection was kept at a modest level to avoid saturation of the liposome clearance system. According to the findings, the rejected drug's specific activity was usually in the range of 0.1, 0.5, and 1.0 microgram. Plasma samples were obtained at 2-3 minutes after injection and at intervals thereafter to determine the clearance rate from the blood.[10]

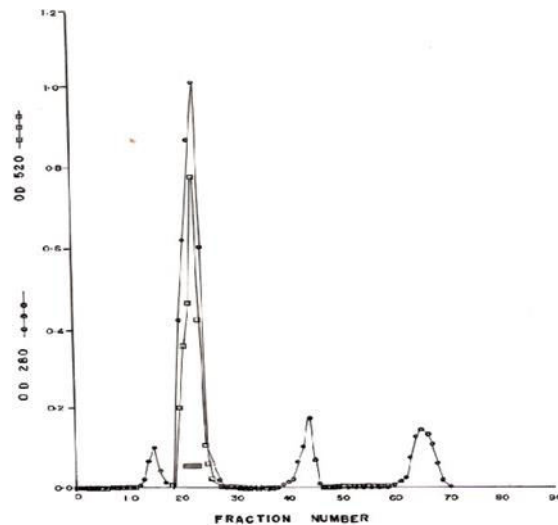


Fig 5 - Liposome-encapsulated daunomycin separation technique with Sephadex. Daunomycin was encapsulated in a liposome containing PC, SA, and cholesterol. separation was performed with sephadex c column

## V. CONCLUSION

In the formation and stability of drug liposome complexes it seems cytosine arabinose is restricted to the internal aqueous compartment of the liposome. while the other drugs insert into the hydrocarbon region of the liposome membrane. The chemical properties of the lipids themselves were expected to influence the formation of drug-liposome complexes.

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