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Liposomes: Applications

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ABSTRACT: -
Liposomes are made of phospholipids and lipids. Liposomes are spherical or multilayered spherical vesicles with a lipid bilayer structure that form in aqueous solutions when diacyl chain phospholipids self-assemble. The number of bilayers and vesicle size both have an impact on the quantity of drug encapsulation in the liposomes, which is a key factor in determining the circulation half-life of liposomes.
This method involved coating a medication and a lipid onto a soluble carrier to create a pro-liposome that was free-flowing and granular and that, when hydrated, formed an isotonic liposomal solution. The pro-liposome strategic strategy will provide motivation for mass production of liposomes containing medications that are lipophilic at low cost. Due to some special properties like increased drug solubility (amphotericin B), molecule protection (DNA, RNA), enhanced intracellular uptake (anti-cancer drugs), serving as a drug depot, and increasing the stability of the drug, these systems were successfully used for delivery of different categories of drugs such as anti-viral, anti-cancer, anti-inflammatory, antibiotics, and anti-fungal etc. Preparation and evaluation of liposomes of brimonidine tartrate as an ODDS(Occular). Development and characterization of liposomal drug delivery system for Liposomes: from a clinically Established drug delivery system to a nanoparticle platform for Theragnostic nanomedicine**.**

Keyword: - Liposomes, Drug, lipid, lymph, phospholipid

I. INTRODUCTION:-

Historical Background:-

Liposomes, which have spherical lipid bilayers with diameters ranging from 50 nm to 1000 nm, are useful delivery systems for substances with biological activity [1]. They are osmotically sensitive model membrane systems that are 105 times more permeable to anions than cations and are created by the interaction of amphiphilic lipids suspended in an aqueous phase [2].

The ability of phospholipid molecules to spontaneously form closed bilayer vesicles in water was originally found by Bangham A [82] in 1965Soon after, liposomes with a size range of 5 to 200 nm [83] were reported to be able to encapsulate hydrophilic or lipophilic drugs in the aqueous phase or bilayer membrane phase by utilising the affinity of various parts of vesicles. Liposomes were then introduced into the field of drug delivery systems. Low molecular weight medicines (often less than 1000 Da) are the foundation of traditional chemotherapy for cancer[84,85].

A (phospho)lipid bilayer sequesters some of the solvent, in which they freely float, into the core of liposomes, which are spherical, self-closed vesicles of colloidal dimensions [3]. Small or big unilamellar vesicles are used when one bilayer surrounds the aqueous core, whereas huge multilamellar vesicles are used when there are numerous concentric bilayers [4].Liposomes (phospholipid bilayer vesicles) were used as models for biological membranes for a long time before 1971. One part of these investigations involved trapping tiny solute molecules inside liposomes in order to gauge how permeable the model membranes were to these molecules [5].

There are many papers that contain electron micrographs of these liposomes, including those by Hauser et al. [6]. Up to one cholesterol molecule can be incorporated into a liposome under standard circumstances [80], while some researchers have observed up to a 2:1 cholesterol:phospholipid ratio in highly sonicated liposome preparations [81].

The Physiochemistry of Liposomes:-

Liposomes' suitability as a drug delivery system is solely dependent on the physicochemical characteristics of their membranes, the make-up of

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their constituent parts, as well as their size, surface charge, and lipid structure. (7).

Phospholipids, amphiphilic molecules with a hydrophilic head and two apolar hydrophobic chains, make up the majority of liposomes. Phospholipids have a great propensity to form membranes when dispersed in aqueous solutions because of their amphipathic character.[8]Their lengthy a polar aliphatic chains encourage interaction with one another, while their polar heads prefer to interact with the watery environment. These two characteristics encourage the creation of two lipid layers in aqueous solutions. Each layer's hydrophobic chains are oriented toward one another, forming a lipophilic inner compartment that serves as a permeability barrier both internally and externally. Last but not least, this arrangement is stabilised by hydrogen bonds and polar contacts between the water molecules of the aqueous environment and the polar heads of lipids. Lipids are eventually arranged according to their nature, concentration, temperature, and geometric form. (9). In actuality, cholesterol is a hydrophobic molecule that interacts primarily with the membrane's centre, stabilising it. For use in biosensing or as "stealth" medication carriers, cholesterol can also be utilised to bind other molecules, such as polyethylene glycol (PEG) or deoxyribonucleic acid (DNA), to liposomes(10) (reviewed in Hosta-Rigau et al). 11 Additionally, materials that push the transition temperature past 37°C and the utilisation of phosphatidylcholine with saturated fatty acyl chains provided even more stabilization.

II. APPLICATIONS:-

Applications of liposomes in basic sciences:-

Two-dimensional surfaces called lipid membranes are suspended in three-dimensional space. In the most basic forms, their main distinguishing feature is their flexibility, which is connected to their bending elasticity. To comprehend their structural behaviour, some fresh theoretical ideas were developed [15].

Despite being used widely, liposome formation's mechanism is still poorly understood. The observations (Fig. 1) and equilibrium calculations of the morphologies of large unilamellar vesicles [16,17] and [18,19]

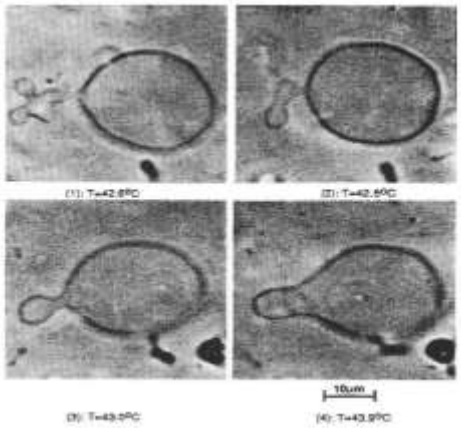

Fig. 1. Phase contrast optical micrographs of various liposomes. : Several shapes of giant unilamellar vesicles (from ref. (18), with permission).

Studies on the physical-chemical makeup of membranes containing sterols, such as cholesterol, may also provide some insights into the history of life. The development of multi-organelle prokaryotic cells from eucaryotic ones, which lack cholesterol and internal organelles, appears to have been made possible by the presence of cholesterol, which could only have been synthesised at specific geological times when the atmosphere became rich in oxygen and makes membranes more cohesive at increased bilayer fluidity [19].

The replication of photosynthesis and the extraction of the plentiful light energy by artificial photosynthesis or the dissociation of water into its reactive components are two of the main research objectives. These systems, which include finely controlled photosensitizers, electron relay mechanisms, and catalysts enmeshed in lipid bilayers, are highly complex. Liposomes are used in artificial systems to mimic the arrangement, orientation, activity, and reactivity of the contained chemicals. Several artificial systems have already photolyzed water, despite the fact that the yields are still relatively low [20], despite the fact that these are extremely hard challenges.

Applications of Liposomes in bioengineering:-

Modern genetic engineering and gene recombinant technologies are based on introducing genetic material, such as DNA fragments, into different cells and microorganisms in order to change their genetic makeup and force them to manufacture specific proteins or polypeptides [21].

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To avoid interacting with DNA molecules, which may contain up to several thousand negative charges, the traditional method mostly used huge unilamellar vesicles generated from phosphatidylserine that are negatively charged [22]. In certain instances, transfection efficiencies were multiplied hundreds of times, and it was possible to successfully genetically modify plant protoplast, which is notoriously difficult to transfect [23].

Recently, however, tiny unilamellar vesicles consisting of positively charged lipids were used to successfully carry out transfection. The cationic lipid dioleoyl-propyl-trimethylammonium (DOTMA) was first employed in investigations [24]. Using some of the commercially available catioiiic lipids, later experiments demonstrated improved transfection efficiency [25]. Using liposomes containing positively charged cholesterol has been reported to improve transfection efficiency while reducing toxicity [26].

Gene therapy can also utilise these techniques. Delivering the healthy gene to the right cells in the hopes that they will respond is the idea. For instance, individuals with cystic fibrosis have a faulty gene that produces a protein necessary for the transfer of salts through the lung's cell membrane

In recent studies, mice's lungs' lining cells integrated 70% of human gene copies after inhaling them together with liposomes, and they started utilising them to produce significant amounts of protein [27].

Application of liposomes in agro-food industry:-

The encapsulated enzymes can significantly reduce fermentation timeframes and boost the quality of the final product in a variety of fermentation processes using the continuous release system idea. This is brought on by the ingredient(sbetter)'s spatial and temporal release as well as their protection from chemical deterioration throughout specific stages of the process. Making cheese is a traditional illustration. The first significant attempts to use cell-wall-free bacterial extracts to shorten fermentation times were positive enough to spur initiatives to enhance enzyme presentation. The length of time it takes for cheese to ripen can be reduced by 30–50% as a result of preliminary research in which liposome systems were improved [28–30]. Given that some cheeses, like Cheddar, require carefully controlled conditions and take nearly a year to ripen, this translates to a considerable economic profit. Additionally, the texture of cheeses was uniform due to enhanced enzyme dispersion, and the bitterness and uneven flavour caused by the proteolysis of enzymes in the early stage of fermentation was greatly reduced [28, 29].Because liposomes become encapsulated in the water gaps between the casein matrix and the fat globules of curd and cheese, liposome encapsulation can both conserve potency and boost effectiveness. Additionally, this is where the majority of the spoiling organisms are found [30]. Due to the prolonged presence of the fungicides, herbicides, or pesticides and the lessened harm to other life forms, liposomes encapsulated biocides have demonstrated superior activity in various areas of the agro-food industry [31].

Other applications of liposomes:-

Improvements in bioreclamation, as well as numerous monitoring and analytical-diagnostic applications, are provided by liposomes in ecology. For instance, it has been demonstrated that the addition of different bacteria contained within liposomes that may contain nutrients enhances the otherwise very sluggish breakdown rates of carbohydrates in an oil spill. Liposomes also aid in the coagulation and settling of oil that has been sprayed on the water's surface or in its cleanup with floating booms [32] because of the surfactant activity.The capacity of liposomes to give nutrients to oil spills and has been put to the test by the Environmental Protection Agency [33].The Swiss Serum Institute (Bern, Switzerland) has successfully introduced a liposomal vaccination against hepatitis A. (79).

Applications of liposomes in medicine/Clinical Applications:-

Therapeutic Applications

Localised/Regional Use

Liposome topical use in dermatology offers enormous promise. When compared to a non-liposomal commercial pharmaceutical formulation, an in vitro study of the percutaneous absorption of hydrocortisone through human skin showed that the liposomal formulation boosted drug delivery to the living tissues by eight times [40]. As opposed to the initial starting material, the drug to lipid recovery ratio from the epidermis and dermis was greater, indicating that intact liposomes did not diffuse through the stratum corneum.

Masini et al. [41] discovered that retinoic acid percutaneous absorption—the amount of retinoic acid present in the epidermis, dermis, and

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receptor fluid—was higher for a liposome formulation than for an alcoholic gel when used on the skin of hairless rats.T4 endonuclease V, a liposome-encapsulated DNA repair enzyme, has been examined for its delivery in pH-sensitive liposomes made of phosphatidylcholine, phosphatidylethanolamine, oleic acid, and cholesteryl hemisuccinate by Wolf et al (2:2:1:5 molar ratio). The effectiveness of using liposomes with interferon for viral lesions is being researched in clinical studies. For the treatment of warts and herpes simplex infections, the effectiveness of an interferon topical formulation is being investigated [43, 44].Liposomes-encapsulated interferons' antifibrogenic effects on skin wounds were investigated by Takeuchi et al. [45]. Transferosomes, a new class of liposome delivery devices created by Cevc and Blume [46], are easily deformable and can cross the stratum corneum in response to osmotic gradients.Bioactive substances can be passively delivered to hair follicles using liposomes. Possibility of regulated gene expression in focused tissues would increase with topical introduction of plasmid DNA to keratinocytes. The development of vaccinations and the management of cancer may both benefit greatly from this [47]. In order to restore hair growth, physiologically restore or alter hair pigment, and to slow down or speed up hair loss, liposomes have a high potential for selectively targeting large and small molecules, including genes, in the hair follicles [48]. Subconjunctival injections of liposomes containing dichloromethylene diphosphonate could stop corneal allograft rejection in rats [49]

Systemic Applications

Anticancer Therapy:-.

In order to improve the pharmacokinetics of free doxorubicin, Uziely et al. [50] used a formulation of doxorubicin contained in polyethylene glycol coated liposomes (Doxil®, Liposome Technology Inc., Menlo Park, CA). When treating Kaposi's sarcoma, this formulation has been utilised as an alternative to standard care (the most common malignancy in patients infected with human immunodeficiency virus). Doxil® was used by Northfelt et al. [51] to treat 53 patients with advanced Kaposi's sarcoma who had failed standard therapy. According to a research by Ranson et al. [52], liposomal doxorubicin treatment was beneficial for individuals with stage IV breast cancer as well. Complete and incomplete answers were received in 6% and 25% of the cases, respectively. Liposomal doxorubicin had significant effectiveness against refractory ovarian cancer, according to Muggia et al. [53].

Antimicrobial Therapy:-

In mice that had previously received sporozoites injections, Alving et al. [54] discovered that intravenous administration of liposomes containing neutral glycolipids with a terminal glucose or galactose suppressed the development of erythrocytic forms of Plasmodium bergei. The aminoglycoside medicines gentamicin and amikacin were liposome-encapsulated, which dramatically increased their activity in treating intracellular mycobacterial infections [55].

Treatment of respiratory disorders includes intravenous injections of liposomal prostaglandin E1 (Lip-PGE1), which reduce lung leak and lung lavage neutrophil buildup in rat models [56]. Intratracheal injection of a liposomal alpha-tochopherol reduced acute lung damage in rats [57].

Antiarthritis Therapy:-

At 37°C, cortisol palmitate-containing liposomes are persistent in rheumatoid synovial fluid, according to Shaw et al. [58]. The degree of chronic inflammation was inversely correlated with the amount of liposomal steroids present in the tissue. Prednisolone was injected into the rat hip muscle, and Shinozawa et al. [59] compared the distribution and absorption of the free steroid with that of liposome-entrapped prednisolone. The injected tissue was observed to retain liposomal prednisolone for a longer amount of time. Aurothiomalate encapsulated in liposomes has been shown to lessen collagen-induced arthritis in mice [60].

As An Oxygen-Carrying Fluid:-

Studies conducted in living organisms have shown that LEH can transport enough oxygen to support life and has a circulation half-life of 16 to 20 hours. Since carbohydrates are expressed on the majority of biological membranes, including the membrane of the red blood cell, improvements to the LEH that boost biocompatibility include the inclusion of carbohydrate moiety. The addition of gangliosides into the liposomal bilayer has been shown to lengthen circulation times [61,62].

Targeted Liposomes :-

By affixing relevant amino acid fragments that target certain receptor sites or antibodies, proteins, or other appropriate pieces, liposomes are utilised to target specific cells. In comparison to

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non-targeted liposomes, targeted sterically stabilised liposomes have a higher therapeutic efficacy against human breast cancer xenographs in naked mice [63]. Liposomes are currently being researched as delivery systems for genes and oligonucleotides due to their improved penetration, protection of associated agents, and capacity to transfer macromolecules across the cell membrane [64].

Scope Of Present Work:-

Future aspects of liposomes:-

The use of liposomes in medical fields has been increasing rapidly in recent years, and their potential applications are immense. The potential of liposomes to improve drug delivery, target specific cells, and provide sustained drug release has made them attractive to researchers and healthcare providers alike. In this review article, we will discuss the current and future applications of liposomes in medicine, focusing on their use as drug delivery systems, their potential for targeted drug delivery, and their role in sustained drug release.

Liposomes are small, spherical vesicles composed of lipid bilayers that can encapsulate hydrophilic or hydrophobic molecules. As such, they can be used to deliver drugs and other therapeutics to specific targets, improving their efficacy and reducing the side effects associated with traditional drug delivery methods. In addition, liposomes can be used to deliver genetic material, such as DNA and RNA, to cells, making them ideal for gene therapy applications. As gene therapy research progresses, the use of liposomes to facilitate gene delivery is likely to increase.

Liposomes can also be used to target specific cells, enabling the delivery of therapeutics to the desired location without affecting other parts of the body.

III. METHODOLOGY:-

Diagnostic :-

Large liposomes are quickly removed from the body by reticuloendothelial system resident phagocytic cells. This characteristic can be used to our advantage in order to deliver diagnostic imaging agents to the liver and spleen by passively targeting big liposomes to the phagocytic cells of the reticuloendothelial system. These organs can be targeted with aqueous contrast-enhancing chemicals contained in liposomal carriers, and computed tomography can be used to distinguish between normal and tumorous tissue [34,35]Iodinating agents in CT imaging require liposomes with bigger collected volumes and higher iodine/lipid ratios for increased resolution. For effective imaging of the liver and spleen, numerous investigations using iodine/lipid ratios ranging from 1 to 9 [36] have been documented. In addition to aqueous contrast-filled liposomes, gas-encapsulated liposomes are crucial for diagnostic use. These gas-filled liposomes are employed in magnetic resonance imaging and ultrasound diagnosis. Such liposomes' efficiency is based on the fact that they reflect sound well and have different magnetic susceptibilities. Such liposomes are typically made using lipids that have surface-active characteristics that aid in stabilising the liposome. Adzamlietal. [38] employed DPPC/DSPC encapsulating gas for echocardiography successfully. Similar air trapped liposomes have been employed for neurosonography by Simon et al. [39].

Pharmacokinetics Of Liposomes :-

Classical liposome clearance is biphasic, with a rapid initial phase that causes 75% of large unsonicated liposomes to disappear from the blood in the first five minutes and about 50% of smaller sonicated liposomes to be eliminated [65]. This is followed by a noticeably slower rate of clearance after fifteen minutes for both types of liposomes. The delayed second phase of elimination from the blood most likely reflects lecithin uptake by hepatocytes through lipoprotein-mediated transport [66,67]. Classical liposome clearance rises directly as a function of size [68] and surface charge [69] The presence of high-phase transition phospholipids [72] or the addition of cholesterol [71] tighten the phospholipid bilayers and can be employed to reduce the clearance. At all doses, sterically stabilised liposomes have a longer circulation half-life than conventional liposomes. Whether solid-phase phospholipids or additional cholesterol are present, polyethylene glycol-containing liposome circulation times are the same [73,74] with negligible size dependence between diameters of 50-250 nm, clearance of sterically stabilised liposomes is less susceptible to liposome diameter than clearance of classical liposomes [75]. Sterically stabilised liposomes are extensively absorbed into tissues with increased capillary permeability as a result of their prolonged circulation half-lives [76, 77]. The clearance rates of immunoliposomes are comparable to those of antibody-free liposomes at modest surface densities of attached antibody (10–25 antibody molecules per 100 nm liposome) [78].

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Advantages of Liposomal Drug Delivery :-

Drug encapsulation in a liposomal or lipid drug delivery system improves the pharmacokinetic and pharmacodynamic properties to such an extent that the drugs can be brought into regular use [36]. Advantages of liposomes as a drug delivery system for antimicrobials are: • Improvement and control over pharmacokinetics and pharmacodynamics • Decreased toxicity • Enhanced drug activity against intracellular pathogens • Liposomes used as target selective • Enhanced activity against extracellular pathogens [86]

Figure No: 2 Advantages of Liposomes[87]

Benefits of liposome:-

Liposome technology is a rapidly growing field of research that has the potential to revolutionize the way drugs, vaccines and other biological agents are delivered to the human body. Liposomes are tiny bubbles made from natural substances such as phospholipids and cholesterol. They are capable of carrying drugs and other molecules across the cell membrane, delivering them directly to the target site in the body. This technology has the potential to greatly improve the effectiveness of drugs and vaccines, as well as to improve the safety and quality of drug delivery.

The potential of liposomes to enhance drug delivery has been well established over the past few decades. In the last decade, advancements in the field of liposomes have led to increased understanding and application of the technology. Liposomes can be used to improve the bioavailability of drugs and increase their solubility, thus improving their efficacy. Furthermore, liposomes are capable of protecting the drug or vaccine from degradation or inactivation in the body, allowing for a more effective delivery of the therapeutic agent.

In addition to the enhanced effectiveness of drug and vaccine delivery, the use of liposomes offers several other advantages.

IV. RESULT AND CONCLUSION:-

Finally, it appears that liposomes established themselves as a significant model system in a variety of basic sciences and as a workable substitute in a variety of applications. Despite a $1 billion market for cosmetic liposomes, I dare to claim that gene therapy, anticancer treatments, and other medical uses like artificial blood are where liposomes' true potential lies.

The results of liposome drug delivery system studies have demonstrated that liposomes are an effective method of delivering drugs to the body. Liposomes have been shown to improve drug absorption, biodistribution, and bioavailability. Furthermore, liposomes enable the targeted delivery of drugs to specific areas of the body, thus minimizing the systemic side effects of drugs.

In terms of safety, liposomes have been found to be biocompatible and non-toxic, even at high concentrations. In addition, liposomes have been shown to have a low immunogenicity, meaning they do not elicit an immune response. This is beneficial for pharmaceutical applications because it reduces the risk of anaphylaxis or other allergic reactions.

Overall, liposomes have been shown to be an effective and safe drug delivery system for a variety of drugs and compounds. Further research is needed to explore their potential in terms of new drug formulations, as well as their potential for use in combination with other drug delivery technologies.

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