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AN OVERVIEW OF MAGNETIC LIPOSOMES - TRENDS AND APPLICATIONS

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ABSTRACT

Magnetic liposomes excels limitations that are associated with liposomes therefore they have procured enhanced attention as novel drug delivery system. Magnetic nanoparticles provide increase in the drug release and helps in monitoring therapy. The main objective of this article includes the study of novel advances to enhance the sequential release of different therapeutic agents. Magnetic liposome are spherical vesicles in which the drug can be encapsulated either in the bilayer of lipids or in the vesicle's core. This review summarizes about the methods used in preparation of magnetic liposomes and various bio medical applications of the same. This article also includes the recent advances used in magnetic liposomes like thermo therapeutic strategies. Protein and gene delivery is another approach where proteins are used to prevent hydrolysis and enzymatic degradation and increases stability of the drug. Magnetic liposomes resulted in successful delivery of drugs to the heart with severe myocardial infraction.

KEYWORDS

Magnetic liposomes, Magnetic nanoparticles, Protein, Gene delivery and Thermo therapeutic strategies.

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INTRODUCTION

Liposomes

Liposomes were first discovered by English hematologist Alec Bangham in 1961 and used extensively as delivery of vehicles for pharmaceuticals into the cell or even inside individual compartment. Liposomes are the nanocarriers for targeted drug delivery. Basically liposomes are small spherical shape vesicles made up of cholesterol and natural non- toxic phospholipids. Liposomes can transport both hydrophilic and hydrophobic molecules in their aqueous compartment and their lipid bilayer. Liposomes are the most extensively studied

delivery vehicles due to their functional flexibility. Liposomes, the simplest bionic membrane, have recently seen increased application in screening bio membrane-permeable substances and signalling permeability via cell membranes[1]. Liposomes were added with the ligands to increase efficiency and to target the damaged cells[2]. Novel liposomes have been developed by researchers which can release the encapsulated contents in response to the environmental stimuli like temperature, pH, light, ultrasound, magnetic field and so on[3].

MAGNETIC NANOPARTICLES

Magnetic nanoparticles (MNPs) composed of metal nanoparticles (NPs), metal oxide NPs and metal alloy NPs. Gold, silver, iron, cobalt and nickel are commonly used (NPs). They posses the characteristic of nonvirulence and nonimmunogenicity and excellent biocompatibility. These magnetic nanoparticles produces thermal effect by alternating magnetic field for tumor thermotherapy[4].

Magnetic nanoparticles referred to as potential particles in drug delivery system and plays a significant role in magnetic resonance imaging device (MRI). The methods used in preparation of MNPs include Bottom up and top down method. The most preferred method is the bottom up method because of limited particle size. These bottom up method includes hydrothermal, co-precipitation, reverse micelle and thermal decomposition.

Super paramagnetism can be defined as the ability of magnetic nanoparticles to show robust paramagnetic nature with high susceptibility and saturation magnetization under the influence of a magnetic field and the tendency of losing the same nature completely once the magnetic field is removed, resulting in zero magnetic remanence and zero coercivity. Among several nanoparticles Super paramagnetic iron oxide nanoparticles (SPIONs) are used. These are clinically approved metal oxide nanoparticles (NPs). Magnetite and meghamite are particularly used in cancer theranostics. They are applied in the field of magnetic resonance imaging (MRI) and magnetic hyperthermia[5].

MAGNETIC LIPOSOMES

Magnetic liposomes have a bilayered compositional structure with lipid and aqueous layers arranged in different configurations. These are nanometric-sized biocompatible vesicular-shaped structures that are used to encapsulate water- and oil-soluble medicinal medicines. Active compounds that are water soluble are incorporated in the aqueous layer of magnetic liposomes, while active medications that are lipid soluble are incorporated in the lipid layer. Ingeneral, there are two types of magnetoliposomes: one that contains metal oxides in the aqueous layer and another that has metal oxides enclosed in a lipid layer after being stabilised with laureth[6] Figure No.1.

Magnetic liposomes are nanoparticles containing a magnetic core with liposomes. Magnetic liposomes are spherical lipid vesicles in which (magnetic nanoparticles) MNPs are encapsulated either in lipid bilayers or in the core of the vesicles. The hydrophilic and hydrophobic agents are enclosed within the liposomes. By altering the type or molar ratio of lipids present in the bilayer of the liposomes the magnetic liposomes can be made thermo sensitive (ml4). Magnetic nanoparticles entrapped liposomes are significant in drug delivery as well as in cancer treatment[7].

The liposomes which entrapped in a magnetic nanoparticle is known as aqueous magneto liposomes (AMLs) whereas the MLs which is covered within the lipid bilayer is known as solid magneto liposomes (SMLs). They exhibit a size around 150 nm. The magnetic properties, shape and size distribution depend on the preparation method of magnetic nanoparticles[8].

Magnetic liposomes could be directed into a specific location of tumour cells, then encourage another specialised function, such as drug release and destroying cancerous cells, using the guidance of an external magnetic field. The high-frequency magnetic field (HFMF) has been developed as a method to help magnetic nanoparticles develop certain functions based on the interaction between magnetic nanoparticles and HFMF exposure[3].

Many researchers have examined magnetic liposomes as a type of drug delivery system; RGD-anchored magnetic liposomes were devised and synthesised for brain targeting, while Zhao et al. developed Amphotericin B-loaded magnetic liposomes for brain targeting. We chose the ethanol injection approach to manufacture liposomes based on the preceding studies since it is straightforward, convenient, and easy to control. Meanwhile, PEG-coated Fe3O4 NPs were changed on the surface of liposomes but not contained in liposomes, suggesting that this method may be more suitable to demonstrating its superior magnetic effect[9].

A high permanent gradient magnetic field is used to concentrate magnetic nanoparticles and magnetic liposomes in a target tissue such as a tumour, a concept known as magnetic drug targeting, MDT. Magnetic nanoparticles and magnetic liposomes can be utilised as a T2 (spin-spin relaxation) contrast agent for magnetic resonance imaging (MRI), allowing non-invasive monitoring of their bio-distribution *in vivo*[10].

Types

Magneto liposomes are classified into two types

Aqueous Magneto liposomes (AMLs)

Solid Magneto liposomes (SMLs)

The liposomes which entrapped in a magnetic nanoparticle is known as aqueous magneto liposomes (AMLs) whereas the MLs which is covered within the lipid bilayer is known as solid magneto liposomes (SMLs). They exhibit a size around 150nm. The magnetic properties, shape and size distribution depend on the preparation method of magnetic nanoparticles[8].

ADVANTAGES OF MAGNETIC LIPOSOMES

Using the theory of magnetic drug targeting (MDT), magnetic liposomes encapsulating anticancer medications can be physically targeted to any region of interest by external magnetic fields. The fact that it can be used for both active and passive targeting is a plus. Modification of the nanoparticle surfaces is not required for passive targeting, and they can be guided to the place of interest just as active targeting. As a result, it serves as a versatile drug delivery mechanism for all forms of treatment-resistant cancers. By solving the major shortcoming of chemotherapy treatment, specific medication targeting prevents normal cell death.

Magnetic liposomes lower the concentration of free medicines in the blood, reducing the negative effects that these drugs can cause. The use of an external liposomal coating improves medication absorption, resulting in higher drug deposition in solid tumours, which aids in the fight against drug resistance. Magnetic liposomes carrying doxorubicin, for example, were given intravenously to osteosarcoma-bearing hamsters in one investigation. The introduction of a 0.4 Tesla magnetic field for 60 minutes resulted in a fourfold increase in medication concentration in the tumour when the tumor-implanted limb was positioned between two poles of the magnet.

Magnetic liposomes can be used to overcome drug resistance caused by enzymatic degradation of active anticancer medicines. Liposomal carriers protect integrated pharmaceuticals against enzymatic degradation and the inactivating effects of external circumstances, but they do not have any unwanted side effects.

Most nanocarriers have poor drug unloading at the target location, whereas magnetic liposomes make it easy to unload the drug at the target site. For example, at 42°C, thermosensitive liposome formulations including dipalmitoylphos-phatidylcholine / dipalmitoylphosphatidyletha-nolaminess (DPPC/DSPE–PEG2000; 95/5 mole ratio; gel-to-liquid phase transition temperature: 41°C) released 85 percent of the medication in 10 minutes.

Magnetic liposomes can be utilised for magnetic hyperthermia (exposing target tissue to alternating current magnetic fields), which has been discovered to be particularly successful for cancer treatment. MDR phenotypic cells harbouring a high amount of MRP1 protein respond well to hyperthermia. When anticancer medications are combined with hyperthermia, their cytotoxic effects are amplified. Hyperthermia acts synergistically with quercetin to improve cytotoxic death of doxorubicin-resistant

human myelogenous leukaemia cells, according to Shen *et al*, (2008). According to studies on the mechanism of action, hyperthermia works by increasing cell membrane permeability to anticancer medicines, allowing for increased drug accumulation for the cytotoxic impact.

Due to the T2 shortening effect of magnetic nanoparticles encapsulated within liposomes, magnetic resonance imaging (MRI) can be used to track the bio-distribution of magnetic liposomes.

MAGNETIC LIPOSOMES are biodegradable and are absorbed by the body before being excreted after treatment[11].

METHODS OF PREPARATION OF MAGNETIC LIPOSOMES

Ethanol injection method (EI)

Thin film hydration method (TFH)

Preparation of magnetic liposomes

Preparation of magnetic liposomes by thin film hydration method

Preparation of magnetic liposomes.

Incorporation of magnetic nanoparticles into liposomes by encapsulation technique.

Preparation of MAGNETIC LIPOSOMES

The TFH approach involves drying an organic lipid solution, hydrating with an aqueous solution containing nanoparticles, and shrinking the lipid film using sonication and extrusion to produce evenly sized magnetoliposomes.

Magnetic liposomes were prepared by using thin film hydration method. In this method thin layer of lipid film was obtained by dissolving phosphotidylcholine (PC) in 200ml of chloroform and dried under vacuum by using rotary evaporator. It is further hydrated with water. The dispersion of liposomes were passed through the polycarbonate membrane with an extruder. The liposomes are then centrifuged (1hat 6000 rpm Centrikon T-124 high speed centrifuge, Kontron, France) and re-dispersed in water until the conductivity of supernatant was ≤ 10μS/ cm. The magnetic liposomes were composed Fe_3O_4: PC (3:4 mass ratio) which is equal to the preparation of pure liposomes in which the thin lipid film layer was dispersed by using aqueous suspension of Fe_3O_4. The magnetic cleaning procedure were used for the separation of particles from the liquid medium by using permanent magnet. The particles were redispersed in water until the conductivity of supernatant was ≤ 10μS/cm[12].

Incorporation of magnetic nanoparticles into liposomes by encapsulation technique

Incorporation of pharmaceutical agents and water soluble SPIONs into liposomes were first revealed by Amstad *et al*, Sabate *et al* and Bulte *et al*. it involves two approach.

The large volume was taken up by well stabilized SPIONs and the unstabilized SPIONs react with the membrane of liposome causing a leakage.

SPIONs were heated to cause a thermal transition to the entire environment.

Hydrophobic SPIONs were inserted into the bilayer of lipid bilayer which acts on the capsule wall directly without the necessity to heat the surrounding for the release. The ability of encapsulation depends on the size of the particles.

Smaller SPIONs were incorporated in the membrane, the SPIONs which are >5nm may leads to the formation of micelle. Smaller SPIONs which has weak magnetic moment (□d3) and it reacts less with magnetic field. The stability and the membrane permeability of liposomes were affected by the density and stability of nanoparticles. The leakage of the encapsulated compounds is due to the excess of physical absorption ligands. Fabrication of magnetic liposomes resulted in monodisperse SPIONs with high loading capacity, stable and heavy hydrophobic coating is required to maximize its efficiency. The magnetic liposomes were prepared by the thin film hydration method and it includes the diffusion of magnetic nanoparticles in aqueous medium which is observed by extrusion and hydration of the liposomes is concluded to reduce its size[8].

Preparation of magnetic liposomes by ethanol injection method

The injection of a lipid solution in ethanol into an aqueous solution of nanoparticles, above the melting temperature of the lipids and under strong

agitation. The process is simple, low-cost, and repeatable approach for the manufacture of homogenous AMLs.

The lipids l-phosphatidylcholine from egg yolk (Egg-PC) and 1, 2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) were utilised at a final concentration of 1mM for the synthesis of magneto liposomes. To obtain aqueous magnetic liposomes, the ethanol injection method was used (AMLs). A 20mM lipid solution in ethanol was injected into an aqueous dispersion of magnetic nanoparticles (with a concentration of 4mg/mL) under rapid vortexing. The ferrofluid is rinsed with water after encapsulation and purified using magnetic decantation to eliminate any non-encapsulated nanoparticles. Because of the diamagnetic contribution of water, aqueous magnetoliposomes are not attracted to the magnet, despite the large difference in maximum magnetization of magnetic nanoparticles and aqueous magnetoliposomes (as previously described). As a result, this approach exclusively separates non-encapsulated magnetic nanoparticles, leaving magnetoliposomes in the supernatant phase. After decantation, the lipid phase (in the supernatant) stays unaltered, with the same initial and final lipid concentrations.

A technology that had previously been established was employed to make solid magnetoliposomes. First, 10mL of a solution of produced magnetic nanoparticles (0.02mg/mL) was ultrasonicated for one minute at 189W, followed by 3mL of chloroform. The initial lipid layer of the SMLs was formed by injecting 150L of a 20mM methanolic solution of the lipid DPPC (1, 2-dipalmitoyl-sn-glycero-3-phosphocholine) under vortexing immediately after strong agitation. The particles were cleaned twice with ultrapure water by magnetic decantation to eliminate the lipid that was not bound to the nanoparticles surface. A further infusion of 150mL of 20mM lipid methanolic solution, vortexing, in 3mL of aqueous dispersion of the particles with the first lipid layer finished the lipid bilayer. By magnetic decantation, the solid magnetoliposomes were washed and filtered with ultrapure water[13].

RECENT ADVANCES OF MAGNETIC LIPOSOMES IN CONTROL DRUG DELIVERY SYSTEM

Advances in the optimization of membrane-embedded magnetoliposomes have recently been made, surpassing earlier limits of nanoparticle size that could be embedded. Furthermore, this system's improved membrane stability and speedier responsiveness make it a strong contender for future improvements in on-demand drug delivery. This design could be especially useful in drug delivery to sensitive tissues like the brain, because a low-frequency magnetic field can be used instead of hyperthermia to efficiently trigger drug release, despite the fact that the nanoparticles' post-therapy fate needs to be determined in future studies. Alternatively, combining photothermia and magnetic hyperthermia by producing AMLs and/or SMLs containing core/shell magnetic/plasmonic nanoparticles should provide a viable option for less damaging techniques with higher therapeutic efficacy. In this regard, and in light of the growing number of imaging modalities that can be used to track therapy in real time, such as MRI, computed tomography, and magnetic particle imaging, as well as the potential use of novel imaging techniques, plasmonic magnetoliposomes are seen as promising systems in the future.

The combination of photosensitizers with magnetic nanocarriers for photodynamic therapy resulted in a significant improvement, allowing better targeted delivery and increased tumour cell accumulation. The combination of these nanoparticles with photosensitizers to form nanocomplexes could be addressed in future magnetic nanocarriers, with the potential for negative physiological effects taken into account.

Magnetic liposomes have potential as nonviral carriers for cancer gene therapy because they can guide genetic material to the tumour site and facilitate regulated release using magnetic hyperthermia. The majority of research that use magnetic liposomes for this purpose use magnetite as the magnetic component, which limits the variety of magnetic nanocarriers that can be made. Other

ferrites, such as manganese ferrite, calcium ferrite, or anisotropic-shape iron-based magnetic nanoparticles, can produce a more efficient magnetic response, resulting in a better therapeutic effect. Overall, numerous advancements have been made in optimising magnetoliposomes, which offer unique and promising multimodal properties to safe and effective cancer therapies that can be coupled in a single nanocarrier.

THERMOTHERAPEUTIC STRATEGIES

Magnetic liposomes were used in the thermo therapeutic techniques. The presence of magnetic nanoparticles allows for the application of magnetic hyperthermia, in which tissues are exposed to high temperatures (42–45°C) in order to trigger cancer cell death by apoptosis or increase susceptibility to radiation and anticancer medicines. As a result of the magnetic nanoparticles relaxation period being slower than the oscillating AMF, the heating effect is related with the Neel (spin reversal) and Brownian (particle rotation) relaxation of the nanoparticles magnetic moments upon application of an AMF. Furthermore, the former is significantly size-dependent, occurring at sizes where only a small amount of energy is required to induce magnetic moment rotation, whereas the latter is influenced by medium viscosity because it involves physical rotation of the nanoparticle.

When dealing with biological applications, however, the maximum field amplitude and frequency are limited in order to avoid eddy currents. Different extrinsic and intrinsic features must be addressed in order to improve the heating efficiency of the nanoparticles, hence lowering the required dose and avoiding undesired cytotoxic effects. In fact, when compared to neat magnetic nanoparticles, maximising the magnetic characteristics of nanoparticles is critical for magnetoliposomes application, as both diamagnetic mass contribution and clustering of nanoparticles in the core contribute to reduced saturation magnetization.

Magnetic hyperthermia can promote medication release in materials that exhibit a phase shift, in addition to its potential utility to induce cancer cell death. In the case of magnetoliposomes, the use of magnetic hyperthermia in conjunction with temperature-sensitive liposomes (thermosensitive liposomes, TSLs) allows for controlled drug release by raising the temperature above the lipid phase transition temperature (Tm).

Low-field AMF has been recommended as a safer technique for medication delivery applications due to the potential adverse effects of hyperthermia and eddy currents on nearby tissues. This method has also been tested in nanosystems containing large unilamellar liposomes or hydrophobic iron oxide nanoparticles embedded in a lipid bilayer. The inclusion of nanoparticles increases stiffness and morphological in homogeneity dis the latter, facilitating rupture owing to mechanical vibration of the nanoparticles when an LF-AMF is applied. Using different liposome compositions and nanoparticle sizes, Vlasova *et al*. investigated the mechanism of drug release of liposomes embedded with nanoparticles (N-palmitoyl-6-nitro-dopamine-coated iron oxide). The scientists discovered that adding cholesterol to saturated lipid-based liposomes or replacing saturated lipids with unsaturated lipids reduced dye release when AMF was applied, and that this was dependent on field strength but not frequency. This has been linked to the rupture of saturated lipid gel-phase membranes, whereas flaws and deformations in unsaturated lipids are likely to repair. Other methods, such as the use of short magnetic pulses or pulsed electromagnetic fields, have been investigated to trigger the quick release of the liposomes payload.

Despite recent developments in the use of plasmonic nanoparticles and liposomes, there is currently no literature that combines both magnetic and plasmonic modalities. Both AMLs and SMLs were shown to benefit from the use of plasmonic magnetoliposomes (liposomes encasing nanoparticles with both plasmonic and magnetic components) for phototherapy. Photothermal (heat generating) and magnetic features (magnetic hyperthermia, magnetic drug delivery) are combined in these magnetoliposomes, resulting in a

synergistic effect. Theranostics (the combination of diagnostics and therapy) is particularly interested in the magnetic-plasmonic combination because it overcomes limitations associated with imaging modalities and hyperthermia. The created plasmonic magnetoliposomes with core/shell magnetic/plasmonic nanoparticles and tenofovir disoproxil fumarate (TDF) provided not only a high negative and positive contrast in MRI and magnetic particle imaging (MPI), but also a dazzling positive contrast in X-ray computed tomography (CT). Because of the features of magnetic-plasmonic nanoparticles, plasmonic magnetoliposomes are projected to be more beneficial than neat magnetoliposomes.

PROTEIN AND GENE DELIVERY

Protein administration is highly susceptible to hydrolysis and enzymatic degradation, whereas nucleic acids such as plasmid DNA, mRNA, and siRNA have a highly negative and polar nature that prevents them from passing through the cell membrane, as well as having low stability and being easily degraded by endonucleases in the bloodstream. The inclusion of these biological elements into nanodelivery devices enables a safer and more effective delivery with low cytotoxicity and immunogenic response, reduced off-target effects, and cell-specific distribution via surface functionalization. Polymeric nanoparticles, liposomes and other lipid-based nanoformulations, inorganic nanoparticles, micelles, and dendrimers have already been employed to transport proteins and genes. Magnetoliposomes share some of the same advantages as the previously stated nanocarriers. Magnetic targeting allows for guided delivery of therapeutic proteins and genes due to the presence of magnetic nanoparticles. Magnetic hyperthermia and thermosensitive liposomes are also used to achieve a regulated and triggered release, with the loading content of magnetoliposomes only being released in the target tissues. Magnetic immunoliposomes have been produced by Thomsen and colleagues with the goal of crossing the blood-brain barrier (BBB). PEGylated liposomes containing L—phosphatidylcholine and the cationic surfactant dimethyldioctadecylammonium bromide were used to coat magnetite nanoparticles (18:0 DDAB). Antibodies targeting the rat transferrin receptor (OX26) were attached to the magnetic liposomes, allowing for selective delivery to brain capillary endothelial cells (BCECs). The researchers used in situ brain perfusion with external magnetic force to show that magnetic immunoliposomes accumulated preferentially in BCECs and that magnetic nanoparticles treated to a magnetic force were transported across the BBB. The whole magnetic immunoliposomes were not detected in the brain parenchyma, implying that OX26-liposomes are kept in the BCECs while magnetic nanoparticles are drawn out of the liposomes. Although the cytotoxic action of 18:0 DDAB in mammalian cells is unknown, cell viability experiments in this study revealed that treatment of rat brain endothelial cells with magnetic liposomes or magnetic OX26-liposomes had no effect on viability.

Magnetic cationic liposomes can also be used in gene therapy as non-viral nanocarriers. Small interfering RNA (siRNA) was encapsulated in thermosensitive magnetoliposomes with cell-penetrating peptides (CPPs) to provide efficient delivery of siRNA to tumour cells using an AC magnetic field. *In vitro* and *in vivo* investigations revealed efficient siRNA delivery, gene silencing activity, increased tumour accumulation, anticancer efficiency, and decreased nonspecific accumulation of siRNA-CPPs-loaded magnetoliposomes in healthy organs.

Aside from heating and targeting, image-guided delivery can be accomplished using magnetoliposomes by utilising magnetic nanoparticles as contrast agents for T2-weighted MRI, giving magnetic liposomes theranostic capabilities. Do *et al*. recently published an optimised synthesis of cationic magnetoliposomes for magnetic transfection of a pFAR4-luciferase plasmid into CT26 cells, focusing on this. The cosolvent sonication method produced magnetoliposomes with better r2 relaxivity and *in*

vitro transfection effectiveness than the reverse-phase evaporation method. At 30 minutes or 3 hours of magnetic induction time, the maximum magnetic transfection enhancement was attained. These findings show that magnetoliposomes have a promising future in magnetically guided gene delivery[14].

HEART DRUG DELIVERY

Zhang et al. created a dependable magnetic NP-adenoviral vector multi-molecule for the treatment of severe MI by successfully delivering the therapeutic medicine into the infarcted heart in a trial. MNPs have the ability to deliver the medicine to the damaged cardiac tissue following systematic delivery in vivo, according to Kohane's group, which combined liposomes with a ligand complex targeted to angiotensin II type 1 (AT1). MLs were the first effective hybrid liposome/NP created and assembled for drug administration, and various researchers have proved their efficacy. Because of their magnetic features, MLs are a powerful multifunctional drug delivery carrier with magnetic targeting capabilities.

However, the effectiveness of these tactics may be hampered by the micro-particles' inability to remain in the afflicted area, necessitating the development of a more potent approach (biomaterials) capable of successfully delivering biomolecules to the affected site. Targeted MNPs are supplied intravenously and circulate throughout the body via the bloodstream, delivering solely to the damaged region or organ. MNPs have also been utilised to successfully target macrophages and blood arteries in a heart that has been infarcted. Previous research has demonstrated that following a heart attack, the left ventricular blood arteries become permeable and leaky, which could lead to the penetration of nano-sized magnet particles, similar to how improved permeation and retention occurs (EPR).

Successful heart-targeted MLs drug delivery systems, on the other hand, are based on researchers' understanding of the fundamentals of various heart diseases, the activeness and stability of the carriers' targeting properties, and the appropriate targeting ligands of the carrier, ensuring interaction between the carrier and the surface molecules of the targeted cells. When compared to its applications in oncology, the use of MLs-based technologies to diagnose and treat cardiac-vascular disease has received less attention; yet, MLs heart-targeted delivery system is a potential medication delivery method to unhealthy cardiac tissue like MI. Toxicity, immunogenicity, and undesired pharmacokinetic behaviour are among of the drawbacks of employing MLs for drug administration, which can be overcome by thorough and in-depth research[8].

APPLICATIONS

Cancer imaging, targeted drug administration, and combination hyperthermia and chemotherapy applications are all possible with magnetic liposome.

The primary focus of magnetic liposome research has been on drug delivery and membrane characteristics. The use of magnetoliposomes can be expanded to bioelectronics, a field that combines biological systems (biomolecules, organelles, and cells) with electronics to allow biological to electrical signal transduction at the bioelectronic interface. In opto-bioelectronics and magneto-bioelectronics, respectively, a bioelectronic device can be controlled via light and magnetism. Nanotechnologies scope extends beyond a multiplicity of nanoparticles and their static assembly[15].

Magnetic liposomes have been used in a variety of applications. When compared to magnetic DOX liposomes without an external magnet, Nobuto *et al*. found that administering magnetic DOX liposomes with a subsequent application of a magnetic field (0.4 T) caused a 3 to 4 fold greater doxorubicin concentration in tumours of osteosarcoma-bearing hamsters. With the delivery of lyophilized paclitaxel magneto liposomes under the influence of an external magnet, Zhang et al. increased the circulation half life of paclitaxel and lowered absorption by reticuloendothelial system (RES)[16].

MRI- BASED TUMOR IMAGING

Due to its superiority over other imaging modalities, MRI has been widely employed to image the soft tissue structure of the musculoskeletal system. Contrast agents, are used in this imaging technology which modify the response of protons in close proximity to heighten the contrast. Gadolinium (Gd) chelates are being employed in clinical MRI scans as a contrast agent. As a result, imaging is only possible for a limited time. It's been known for a long time that putting magnetic particles into tissue can boost the MRI signal by a factor of ten. SPIOs can be utilised as a very effective contrast agent because colloidal superparamagnetic iron oxide nanoparticles (SPIOs) are biocompatible. The size of biocompatible polymer-coated SPIOs is divided into two groups. The first category is known as SPIOs (superparamagnetic iron oxides), which includes nanoparticles larger than 50nm, while the second group is known as USPIOs (ultrasmall superparamagnetic iron oxides), which includes nanoparticles smaller than 50 nm. Both kinds of iron oxide particles are currently accessible on the market. On the market, there are two types of SPIO: Lumiren, which are silicon-coated particles with a diameter of 300 nm, and Endorem, that is now utilised for tumour detection on the market. For use in MRI imaging, maghemite (Fe2O3) nanocrystals loaded with very stable, biocompatible large unilamellar vesicles of egg phosphatidylcholine (EPC) and distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(poly (ethylene glycol))-2000] (DSPE–PEG2000) were reported. The presence of these magnetic liposomes considerably improved the contrast of the pictures in an *in vivo* MR angiography in a mouse model, and these magnetic liposomes were available in the blood even 24 hours after injection due to PEGylation.

CANCER HYPERTHERMIA

Due to the drug exposure to normal healthy tissues, current cancer therapies have a number of acute and chronic adverse effects. Photothermal therapy with gold nanoparticles (Gobin *et al*, Gannon *et al*), hyperthermia with magnetic nanoparticles (Jordan et al., Johannsen *et al*) and hyperthermia and chemotherapy combinations (Ito *et al*, Pradhan *et al*, Yoshida *et al*, Kulshrestha *et al*) are some of the novel treatment methods. It also prevents heat from escaping the tumor and prevents the tumor from expanding in reaction to heat like normal tissues do, making tumour tissues vulnerable to heat. Hyperthermia combined with drug-loaded magnetic liposomes can be an effective cancer treatment since it has two effects: the drug is released and the tumor cells are killed. AH60C tumor-bearing mice were treated with Dextran magnetite integrated into thermosensitive magnetic liposomes consisting of DPPC (dipalmitoyl phosphatidylcholine). RH was discovered to promote antitumor immunity, which aided in tumour regression. A prostate tumour in a rat's bone was treated using MCL-mediated heat therapy. Hyperthermia therapy decreased tumor proliferation and the rate of bone degradation in the bone microenvironment, according to the findings. To improve treatment efficacy and prevent therapy-related toxicity, a homogeneous distribution of magnetic liposomes within the tumor mass is necessary. Antibody-tagged magnetic liposomes were created to promote the deposition of magnetic liposomes in malignancies. Due to their greater binding affinity for tumour markers, these liposomes were observed to aggregate more in tumours than conventional liposomes. Magnetic liposomes tagged with human glioma-specific antibody fragments tagged magnetic liposomes (G22-FMLs) (Le *et al*), Fab9 fragment of G250 antibody (Shinkai *et al*) and anti-HER-2 antibody (HMLs) were used in hyperthermia tests. These magnetic liposomes were found to have a larger cellular absorption in their respective cell lines than normal cells, implying that hyperthermia was more effective in normal cancer cells than regular magnetic liposomes.

MAGNETIC DRUG/ GENE TARGETING FOR CANCER THERAPY

Chemotherapy is one of the most widely used cancer treatments. Chemotherapeutic medicines, on the other hand, are neither specific nor selective in their killing of cancer cells. They kill both normal and cancerous cells, and their severe side effects necessitate drug doses that could not be given to a patient, jeopardising therapeutic processes. The therapeutic chemicals are liberated from their magnetic carriers once they reach the sick. Magnetic targeting was used to promote the accumulation of magnetic liposomes in the murine melanoma cell line B16-F10 and endothelial cells HMEC-1.An in vivo investigation found that applying external magnetic targeting for 2 hours dramatically boosts the formation of magnetic liposomes. In a human prostatic adenocarcinoma (PC3) cell line, Martina *et al*, investigated the effect of a magnetic field gradient on the cellular uptake of magnetic liposomes composed of l-phosphatidylcholine (EPC)/1.2-diacyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)–2000] (DSPE–PEG2000)/N. With the use of an external magnet, dextran-coated iron oxide nanoparticles loaded with magnetic liposomes were reported to concentrate in the livers of male ddY mice. The combination action of a magnetic field and folate targeting was reported to promote cellular absorption of folic acid-tagged doxorubicin loaded with magnetic liposomes in KB and Hela cells. The therapeutic efficacy of magnetic liposomes containing doxorubicin (magnetic DOX liposomes) was tested in the treatment of primary tumours and lung metastases employing magnetic targeting. In the treatment of primary tumours, all doxorubicin formulations were found to be efficacious. In a metastasis model, a magnetic-targeted DOX liposome formulation was demonstrated to be beneficial in diminishing tumour colonies.

The pharmacokinetics of negatively charged paclitaxel-loaded magnetic liposome vesicles of hydrogenated soya phosphatidylcholine/ cholesterol/dicetylphosphate/-tocopherol were studied by Zhang *et al*. In brief, lyophilized paclitaxel-loaded magnetic liposomes are more effective in treating breast cancer because they can be conveniently targeted using an external magnetic field. These findings demonstrated that MDT can help increase medication bioavailability at tumour locations and improve chemotherapy therapeutic efficacy. Magnetofection is the delivery of nucleic acids [such as DNA, antisense oligodeoxynucleotides (AODN), and small interfering ribonucleic acids (siRNA)] into cells using magnetic targeting. The presence of a large number of MNPs near the cells due to the application of an external magnetic field was found to boost the transfection effectiveness of MNP-bound nucleic acid considerably. Magnetic liposomes containing MNP-tagged nucleic acids were created for intracellular delivery to avoid exposing MNP-tagged nucleic acids to the external environment. LacZ and eGFP genes were encapsulated in 1, 2-dioleoyl-3-trimethylammonium propane (DOTAP) and 1,2-dioleoyl-3-sn-phosphatidyl ethanolamine (DOPE) magnetic cationic liposomes. In comparison to the controls (i.e., in the absence of a magnetic field and the liposome-free gene), transfection efficiency in osteoblasts or the He99 lung carcinoma cell line increased in the presence of a magnetic field[11].

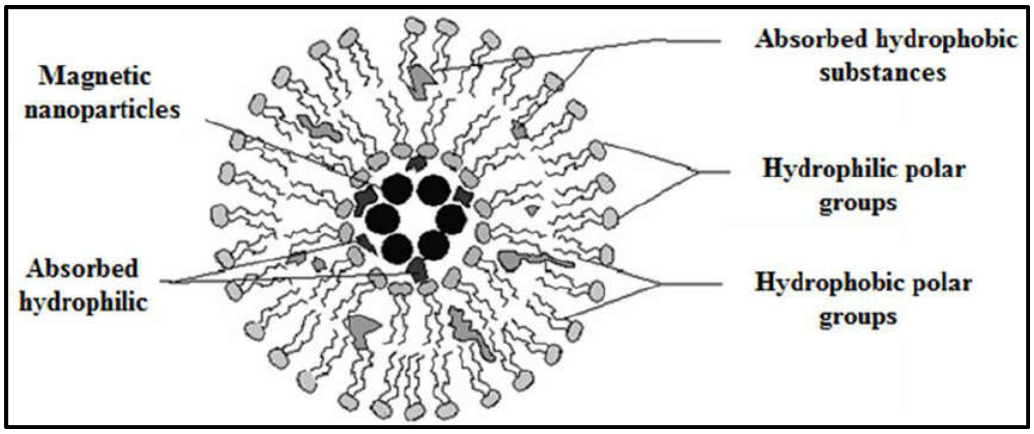

Figure No.1: Structure of MAGNETIC LIPOSOMES

CONCLUSION

Liposomes are the most extensively studied delivery vehicles due to their functional flexibility. Magnetic nanoparticles are incorporated into the liposomes which is known as magnetic liposomes. The liposomes which are entrapped in the magnetic nanoparticle is called as aqueous MLs and MLs that are covered in the lipid bilayer is called as the solid MLs. Recent advances for controlled drug delivery in magnetic liposomes are thermotherapeutic strategies wherein the tissues are exposed to temperatures to around 42-45°C to trigger the death of cancer cells. Another concept used is Protein and gene delivery. Heart drug delivery is another approach which is used in the treatment of MI by delivering the drug into the infracted heart. The magnetic liposomes are used in the treatment of cancer and also in the tumor imaging. Overall this review article is used in better understanding of the magnetic liposomes used in various biomedical and healthcare applications.

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CONFLICT OF INTEREST

All authors' declared no conflict of interests

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