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LIPOSOME AS CARRIER FOR CANCER TREATMENT: A REVIEW

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ABSTRACT

Liposome are risen up out of self-shaping lipid bi-layer upon hydration; liposomal medicate have job in strong medication detailing to improve therapeutics. Liposome definitions assists with diminishing poisonousness and increment aggregation at the objective site. New techniques for liposome readiness dependent on lipid medicate communication or liposome aura component. Likewise incorporate the restraint of quick freedom of liposome by diminishing molecule size, charge or surface hydration. The liposomes are portrayed by physical, substance and natural parameters. This method of medication have more security and viability to organization of a few classes of medications like antimicrobial, antiviral, antibodies, against tubercular, antifungal, medications and quality therapeutics. Utilizations of the liposomes are in the tumor treatment immunology, antibody adjuvant, eye issue, cerebrum focusing on, infective malady, dermatology. New improvements in this field is explicit restricting properties of a medication transporter of liposome to target cell as a tumor cell and explicit atoms in the body. Secrecy liposomes are particularly utilized as transporters for hydrophilic (water solvent) consumption of macrophages.

KEYWORDS: Preparations Method, Characterization, Liposome Classification, Liposomal Drugs in Cancer.

INTRODUCTION

Late improvements on the field of liposome, with malignancy treatment are principle region of intrigue. Liposomes are utilized to improve malignant growth treatment because of their ability to expand the dissolvability of inadequately hydrophilic antitumor medications. Liposomes were found around 40 years prior by A.D. Bingham. Significant enemy of tumor sedate doxorubicin figured as liposome in 1980 to improving the remedial record. Liposome definition are utilized to lessen harmfulness and increment collection at the objective site. Secrecy liposomes utilized as bearers for hydrophilic anticancer medications like doxorubicin. The liposomes are described on premise of physical, synthetic and natural parameters. These methodologies decrease tranquilize debasement and inert when its organization, they likewise increment the medication's bioavailability and the part of medication conveyed in the obsessive territory, they improving adequacy and additionally limiting medication poisonousness. Liposomes as drug carrier with great variety of molecules such as nucleotide, small drug molecules, proteins, plasmids.(Anwekar, Patel, and Singhai 2015)

DEFINATION AND STRUCTURE OF LIPOSOME

(Shashi K., 2012)

When phospholipids spread in water, they form close structure with internal aqueous environment bounded with phospholipid bilayer membranes, and create vesicular system is called as liposome. Liposome is spherical sac of phospholipid molecule enclosing water droplet as formed to carry drug or other substance into the tissue. Liposomes are spherical vesicles composed one or more lipid bilayers, involve an aqueous compartment.

Basic structure & composition of liposome

Biodegradable and biocompatible phospholipids and sphingolipids are the lipids that are most commonly used to prepare liposomes. These structural lipids can be natural or synthetic origin, natural origin consist mixture of various lipids. Cylindrical molecular-shape lipids, such as phosphatidylcholine, phosphatidylserine, phosphatidylglycerol, and sphingomyelin, are choose for liposome formulations. These lipids, are used due to their appropriate stability and their ability to act again changes in pH or salt concentrations in the product or biological environment.

Conventional liposomes possess different lipid compositions, the most commonly used lipids are cholesterol and phosphatidylcholines. Drawback of conventional liposomes is their rapid uptake by MPS after systemic administration. In 1980, development of long-circulating liposomes increases interest in the

clinical application of liposomes as a drug delivery system for various types' cancer treatment.

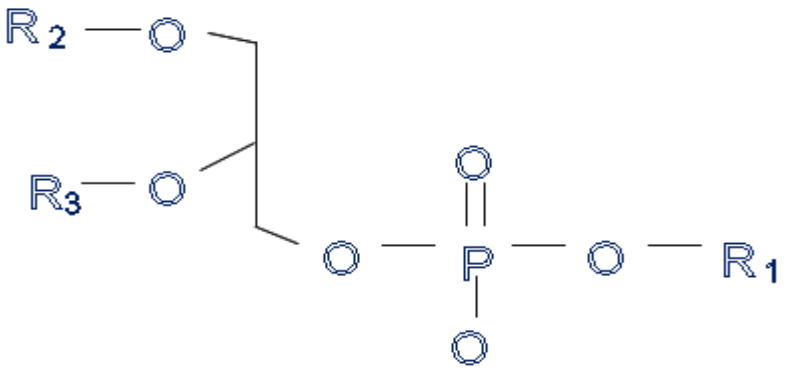

Fig. 1: Chemical Structure of Liposome.

Classification

1. Classification Based on Structure

Types of vesicle with their Dimeter Size and Number of Lipid Bilayers

Vesicle Type	Abbreviation	Diameter Size	No of Lipid Bilayer
Unilamellar vesicle	UV	All size range	One
Small Unilamellar vesicle	SUV	20-100 nm	One
Medium Unilamellar vesicle	MUV	More than 100nm	One
Large Unilamellar vesicle	LUV	More than 100nm	One

2. Based on Method of Preparation

Liposome Preparation Methods and Formed Vesicles types

Preparation Method	Vesicle Type
Single lamellar vesicle made by reverse phase evaporation	REV
Multi lamellar vesicle made by reverse phase evaporation	MLV-REV
Stable lamellar vesicle	SPLV
Frozen lamellar vesicle	FATMLV
extrusion technique	VET
Dehydration- Rehydration method	DR V

3. On basis of Composition and Application

Liposome and their Compositions

Type of Liposome	Abbreviation	Composition
Conventional liposome	CL	Negatively or neutral charge cholesterol and phospholipids
Fusogenic liposome	RSVE	Reconstituted sendai virus envelops
Cationic liposome	-	Cationic lipid with DOPE
Long circulatory liposome	LCL	Neutral high temp, cholesterol, and 5-10% PEG, DSP
Immune liposome	IL	recognition sequences or LCL with attached monoclonal antibody

4. on basis of Conventional Liposome

A. Mixtures of Stabilize natural lecithin
B. Chain phospholipids, Synthetic identical
C. Glycolipids.

5. on basis of Specialty Liposome

A. Bipolar fatty acids
B. Liposome directed by Antibody.
C. Methyl/ Methylene x- linked liposome.

D. Lipoprotein coated liposome.
E. Carbohydrate coated liposome.
F. Multiple encapsulated liposome.(Delivery and View 2007)

Biological Properties of Liposome

1. Liposomes are biocompatible.
2. Liposomes can entrap water-soluble (hydrophilic) pharmaceutical agents in their internal water compartment and water-insoluble (hydrophobic) pharmaceuticals into the membrane.
3. Liposome-incorporated pharmaceuticals are protected from the inactivating effect of external conditions, yet do not cause undesirable side reactions.
4. Liposomes provide a unique opportunity to deliver pharmaceuticals into cells or even inside individual cellular compartments.
5. Size, charge and surface properties of liposomes can be easily changed by adding new substance to the lipid mixture before liposome preparation.

Mechanism of Liposome in Body

Liposome attaches to cell membrane and releasing their content into the cell. They are taken by the cell and their phospholipids are incorporated into the cell membrane. In the case of phagocyte cell, the liposome are taken up the phospholipid walls are act on organelles called lysosomes and the active pharmaceutical substance are released.

METHODS OF LIPOSOME PREPRATION (Lasic 1995)

At the point when phospholipids are hydrate liposome are shaped. Liposome arranged by three stages: vesicle development, vesicle size decrease, and decontamination. Arrangement techniques dependent on the creation and different contemplations, for example, tranquilize exemplification proficiency, the medication's physicochemical attributes, and the organization course. The most usually utilized strategies for liposome readiness are lipid hydration and the substitution of natural solvents by a fluid media. The lipid hydration by vortex or manual mixing, known as Bang ham's strategy.

This technique comprises of dissolving the lipids in an appropriate natural dissolvable, for example, methanol or chloroform. This procedure is trailed by expelling the dissolvable under diminished tension, revolving vanishing, until a meager film has been shaped. After, slim film is hydrated in a fluid medium, over the stage change temperature, bringing about the development of MLV liposomes. This is the least complex technique for vesicle arrangement; be that as it may, it is restricted being used on account of its low exemplification capacity. There are several groups of phospholipids that can be used for the liposome preparation which are as follows:

I. Natural source Phospholipids
II. Modified Phospholipids from natural source
III. Semi synthetic phospholipids
IV. Fully synthetic phospholipids
V. Phospholipids with natural head groups

Cholesterol can be added to the bilayers mixture for the following purposes:

1. Act as a fluidity buffer.
2. Cholesterol intercalated with phospholipids molecules they Alters the freedom of carbon molecule formation of in the acyl chain.
3. Transformation of Trans to gauche conformation is restrict.

Cholesterol decreased the permeability coefficients of positive, negative, neutral as well as negatively charged membranes to K+, Na+, Cl- and glucose. Cholesterol is necessary for lowering the membrane permeability, and imparting better stability. Cholesterol also modulates membrane-protein interactions.

Strategies for the preparation of liposomes:

1. Mechanical methods

A. Film Method

The original method is simplest procedure for the liposome formation, in this technique liposome are prepared by hydrating thin lipid film in an organic solvent then organic solvent is removed by film deposition under vacuum. When all the solvent get removed, the solid lipid mixture is hydrated by using aqueous buffer. The lipids spontaneously hydrate and swell to form liposome.

B. Ultrasonic Method

Ultrasonic method is used for the preparation of SUVs with diameter in the range of 15-25 m. Ultra-sonication of an aqueous dispersion of phospholipids is done by either probe sonicators or bath sonicators. The probe sonicators used for the small volume which requires high energy and bath sonicators are employed for the large volume.

METHODS BASED ON REPLACEMENT OF ORGANIC SOLVENTS

In that method lipids is co-solvated in organic solution, then dispersed into aqueous phase which containing material to be entrapped within the liposome. Replacement of organic solvents has two types:

A. Reverse Phase Evaporation: The lipid mixture is added in to round bottom flask and solvent is removed under reduced pressure by using rotary evaporator. This system is purged with nitrogen and lipids they re-dissolved in the organic phase. Diethyl ether and isopropyl ether is used as solvents. After re-dissolution of lipid the emulsion is obtained then the solvent is removed from emulsion by evaporation into semisolid gel under reduced pressure. Then Non encapsulated material is removed. The resulting liposomes are called reverse phase evaporation vesicles (REV). Reverse Phase Evaporation used for the preparation of large uni-lamellar and oligo-lamellar vesicles formulation and also

it has the ability to encapsulate large macromolecules with high efficiency.

B. Ether Vaporization Method: There are two method according to the solvent used: a) Ethanol injection method. b) Ether injection method. In ethanol injection method, the lipid is inserted rapidly through a needle into an excess of saline or other aqueous medium. In ether injection method the lipid is inserted slowly through a needle into an excess of saline or other aqueous medium.

METHODS BASED ON FUSION OF PREFORMED VESICLE OR SIZE TRANSFORMATION

A. Freeze Thaw Extrusion Method: This method is an extension of the classical DRV method. Liposomes is prepared by the film method is vortexed with the solute is entrapped until the entire film is suspended and the resulted MLVs is frozen into Luke warm water and then again vortexed. After 2 cycles of freeze thaw and overtaxing the sample is thrust three times. This is followed by 6 freeze thaw cycle and addition eight thrust. This process break and defuses SUVs during which the solute equilibrates between inside or outside and liposome themselves fuse and boost in size to form large Uni lamellar vesicle by extrusion technique (LUVET). This method is widely used for the encapsulation of protein.

B. The Dehydration- Rehydration Method: In this method the empty buffer which containing SUVs and rehydrating it with the aqueous fluid containing the material is entrapped after they are dried. This leads to a dispersion of solid lipids in finely subdivided form. The vesicles are rehydrated. Oligo lamellar vesicle liposomes obtained by this method.

LIPOSOME CHARACTERIZATION (Koudelka S, Masek J, 2010)

After preparation and before use in immunoassay the liposome must be characterized. Evaluation could be classified on basis of physical, chemical and biological methods. The physical methods include parameters such as shape, surface features, size, Lamellarity, drug release profile, phase behaviors.

Methods of liposome characterization

CHARACTERISTICS	METHODOLOGY
Phospholipids quantification	Bartlett method (Lipid phosphorus content)
Lysophospholipids quantification	Bartlett method combined with Liquid chromatography
Lipid oxidation	Spectroscopy, high-performance liquid chromatography (HPLC), gas-liquid chromatography (GC), TLC,
Determination of the encapsulation percentage	Spectrophotometry, fluorescence spectroscopy, enzyme-based methods, electrochemical techniques and HPLC
Size	field-flow fractionation and analytical centrifugation, microscopy techniques (light, electronic and atomic force), Static and dynamic light scattering, size-exclusion chromatography,
Surface charge	electrophoretic mobility associated with the Photon correlation spectroscopy
Lamellarity	Nuclear magnetic resonance (^{31}P-NMR), electron microscopy, small angle X-ray scattering
Lipid phase	X-ray diffraction, differential scanning calorimetry
Phase-transition temperature	Differential scanning calorimetry and nuclear magnetic resonance (^{31}P-NMR or ^{1}H-NMR)

Biological characterization is used in establishing the suitability and safety of formulation for the in vivo application for therapeutic use. The characteristics of the carrier with appropriate choice of size, membrane components, charge determines the final behavior of liposomes in-vitro and in-vivo.

Characterization of Liposomes with their Quality Control Assays.

A. Biological Characterization

Characterization parameter	Instruments for analysis
Sterility	Aerobic/anaerobic
Pyrogenicity	Rabbit fever response
Animal toxicity	Monitoring survival rats

B. Chemical Characterization

Characterization parameter	Instruments for analysis
Phospholipid Concentration	HPLC / Barrelet assay
Cholesterol Concentration	HPLC / Cholesterol oxide assay
Drug Concentration	Assay method
Phospholipid peroxidation	UV observance
Phospholipid hydrolysis	HPLC / TLC
Cholesterol auto oxidation	HPLC / TLC
Antioxidant degradation	HPLC / TLC
PH	PH meter
Osmolarity	Osmometer

C. Physical Characterization

Characterization parameter	Instruments for analysis
Vesicle shape and surface morphology	TEM and SEM
Vesicle Size and size distribution	Dynamic light scattering, TEM
Surface Charge	Free flow Electrophoresis
Electrical surface potential and surface PH	Zeta potential measurement
Lamellarity	P^{31} NMR
Phase behavior	DSC, Freeze facture electron microscopy
Percent capture	Gel exclusion
Drug release	Diffuse

Stratergies to Optimize Liposome Stability (Abdelwahed W, 2006)

Business item including in liposome plan contain security attributes and timeframe of realistic usability over one year. It is presently conceivable to acquire a reproducible readiness of enormous volumes of stable liposomes and long haul security issues have additionally been effectively explained.

Security of liposomes is significant part in their improvement for pharmaceutical applications. Potential utilization of liposomes as helpful instruments is tested by their inborn synthetic and physical shakiness in water mediums, they can bring about expanded bilayer porousness and vesicle combination, resulting drug spillage and precipitation. Dangers of liposome is invigorated by bilayer surrenders instigated by synthetic debasement and by physical factors(heating or freezing) because of stage advances happen when these fluid scatterings is put away for expanded periods. The significant method to support liposome dependability is to get ready suitable plan, which help for the choice of the proper lipid fixation and organization, also the expansion of different substances for improve its timeframe of realistic usability. Item that can assists with expanding liposomal soundness include lyophillization and proficient detailing. Definition includes the choice of the appropriate lipid sythesis, centralization of bilayers, cancer prevention agent, and watery stage fixings as supports, cryo protectants and metal chelators. Charge including lipid as phosphotidyl glycerol consolidate into liposome bilayers to lessen combination while cholesterol and sphingomyelin can be remembered for the detailing to diminish penetrability and spillage of epitomized substance. Supports at impartial pH help to diminish hydrolysis; expansion of cancer prevention agent, for example, sodium ascorbate can decrease oxidation. In general, formulation of stable liposomal drug product requires the following precautions:

1. Processing with purified, fresh lipids and solvents.
2. Avoidance of high temperature and excessive shear forces.
3. Maintenance of low oxygen potential.
4. Use of metal chelators and antioxidant.
5. Formulating at neutral pH.
6. Lyo protectant used for freeze drying.

LIPOSOME IN CANCER THERAPY (Hofheinz RD, 2005)

The drawn out treatment of anticancer medication prompts a few harmful reaction. The liposomal treatment for the focusing to the tumor cell have been altered the universe of malignancy treatment with least reaction. It has been said that the little and stable liposome are inactively focused to various tumor since they can circle for longer time and they can extra vasate in tissue with improved vascular penetrability. Liposome macrophage take-up by liver and spleen hampered the improvement of liposome as medication conveyance for more than 20 years.

Liposomes have been utilized as bearers of platinum mixes (cisplatin and oxaplatin), anthracyclines (doxorubicin and daunorubicin), paclitaxel, camptothecin subordinates, antimetabolites (methotrexate, cytarabine), and Vinca alkaloids (vincristine, vinblastine and vinorelbine), planned for decreasing the poisonous reactions of cytostatic drugs without hampering their viability. Their applications depend on the capacity of liposomes to change the tissue dispersion of the ensnared tranquilize, which gets reliant on the physicochemical highlights of the liposomes and not the embodied

substance. In malignant growth chemotherapy, the uninvolved focusing of liposomes exploits the inborn size of nanoparticles and the exceptional properties of tumor vasculature. As tumors develop and exceed the accessible flexibly of oxygen and supplements, they discharge particles that enroll fresh blood vessels to the tumor in a procedure called angiogenesis. Not at all like the tight veins in typical tissues, angiogenic veins in tumor tissues contain holes as extensive as 600 to 800 nm between contiguous endothelial cells.

This nature of tumor angiogenesis, combined with poor lymphatic waste, prompts an upgraded penetrability and a maintenance impact (EPR). Thusly, long-circling liposomes will specially extravasate from these anomalous vessels and can specifically gather inside the tumor interstitiumty or common capacity to target malignant growth. The endothelial dividers of all sound human vein are embodied by endothelial cells limited together by close intersections. These tight intersections help to stop the enormous molecule in blood from spilling out of the vessel. Such sort of plan isn't there in the event of tumor vessel and subsequently is demonstratively "cracked". This capacity is knownas upgraded penetrability and maintenance impact. Liposomes of size under 400 nm, can quickly enter tumor locales from blood, however these are then kept in circulatory system by endothelial divider in solid tissue.

Platinum compound: (Mishra 2004)
Cisplatin (CDDP) is one of the most effective chemotherapeutic agents used by intravenous route in the treatment of ovary, lung, testicle, head, and neck carcinomas. Furthermore, CDDP has been widely used in the treatment of peritoneal carcinomatosis by intraperitoneal route. However, the administration of CDDP by both routes is still hindered by toxicity, mainly nephrotoxicity. Conventional liposomes composed of phosphatidylcholine/ phosphatidylserine/ CHOL containing CDDP were evaluated in IgM immunocyto bearing LOU/M rats.

An increased tumor platinum uptake and a significantly improved antitumor effect could be observed with the use of SPI-077, as compared to free CDDP. Another long-circulating liposomal formulation containing CDDP made up of soy phosphatidylcholine (SPC)/ DPPG /CHOL/DSPE-PEG2000 is called Lipoplatin®. This formulation was developed to reduce the systemic toxicity of CDDP while simultaneously improving the targeting of the drug to the primary tumor and metastasis by enhancing the circulation time in body fluids and tissues. Cytotoxicity studies of this formulation were performed in cell lines derived from non-small cell lung cancer, renal cell carcinoma, and in normal hematopoietic cell precursors.

Lipoplatin®, when compared to CDDP, produced a stronger cytotoxic effect in both evaluated tumor cells lines and a lower toxicity in normal bone marrow stem cells. Antitumor efficacy of Lipoplatin® was assessed in xenografts of human breast, prostate, and pancreatic cancer, where a reduction in tumor size could be observed. Measurement of platinum levels in the plasma of patients as a function of time showed that a maximum platinum level is attained at 6-8 hrs. The half-life of Lipoplatin® was 60-117 hrs, depending on the dose. The determining of platinum levels in excised tumors and normal tissues showed that Lipoplatin® has the ability to preferentially concentrate on the malignant tissue (10-50 fold) of both primary and metastatic origin.

The pharmacokinetic profile of Lipoplatin® in combination with 5-fluorouracil showed that the liposomal formulation has a greater body clearance and a shorter half-life than does free CDDP, which confirms the clinical observation of decreased toxicity, especially nephrotoxicity. Phase I, II, and III trials have shown that Lipoplatin® presents similar antitumor efficacy to CDDP in pancreatic, head and neck, breast cancers, and non-small cell lung carcinoma, as well as reduced toxicity, nephrotoxicity. Although CDDP is one of the most widely used chemotherapeutic agents, the development of tumor cell resistance against CDDP is a limitation in the clinical application of this drug. The lipid composition of liposomes contained SPC/CHOL/distearoyl phosphatidyl ethanol aminepolyethyl eneglycol (DSPE-PEG). CDDP-containing liposomes were prepared, and the target ability of transferrin receptors (TfR) to correlate CDDP cell uptake with cytotoxicity in sensitive and CDDP resistant ovarian cancer cells.

These liposomes were stable in plasma, circumvented the preclinical resistance to treatment with CDDP. CDDP has also been widely used in the treatment of peritoneal carcinomatosis by the intraperitoneal route. However, CDDP, a low-molecular-weight compound, is rapidly absorbed by the capillaries in the i.p. serosa and transferred to the bloodstream, inducing the appearance of systemic side-effects, such as nephrotoxicity.

Oxaliplatin an analoge of CDDP, has shown a good in vitro and in vivo antitumor effect and a better safety profile than cisplatin. However, the use of oxaliplatin is associated with side-effects which include neurotoxicity, hematologic toxicity and gastrointestinal tract toxicity. Lipoxal® is a liposomal formulation of oxaliplatin made up of hydrogenated soy phospahatidylcholine (HSPC)/DPPG/ CHOL/DSPE-PEG. This liposomal formulation containing oxaliplatin has also proven to induce the complete disappearance of human breast cancers in mice after 6 intravenous injections with 4 days intervals at a dose of 16 mg/Kg. On the other hand, the free oxaliplatin at its MTD could only cause shrinkage, not the disappearance of tumors.

Anthracyclines compound: (Leonard RCF, 2009)
The anthracyclines, represented by doxorubicin, daunorubicin, and their derivatives (Figure 9), are widely

used in the treatment of several hematological and solid tumors and are considered to be a first-line therapy for advanced breast cancer [100]. Although conventional anthracyclines have been extensively used for the treatment of a variety of cancers.

Cardiotoxicity can be increased nearly four-fold when these drugs are administered in association with other chemotherapeutic drugs. Ability of liposomes containing daunorubicin (DNR), made up of DSPC/CHOL.

Another commercial product of conventional liposome (Myocet®), in combination with cyclophosphamide, has been approved in Europe as a first-line treatment of breast cancer. This liposome consists of egg phosphatidilcholine (EPC)/ CHOL and encapsulated doxorubicin (DXR). The ability of Myocet® to locate tumors could be observed in ascitic (L1210 ascitic lymphoma). Doxil®/Caelix® was the first and is still the only long-circulating liposome formulation to be approved in both the USA and Europe to treat Kaposi's sarcoma and recurrent ovarian cancer. Indicating that the pharmacokinetics of liposomal DXR is governed by the liposome carrier and that most of the drug is delivered to the tissues in liposome-associated form [115]. Several studies are currently in progress using Doxil®/Caelix® to treat other malignancies, such as breast cancer and recurrent high-grade glioma.

Other chemotherapeutic agents

Another important drug in cancer therapy is paclitaxel. This is an alkaloid which stabilizes microtubules and inhibits endothelial cell proliferation, motility, and tube formation. Some studies have presented difficulties in the development of liposomes containing paclitaxel due to its hydrophobic nature. Therapeutic efficacy studies performed in a mouse xenograft model of human ovarian (OVCAR-3), human lung (A-549), breast (MX-1), and prostate (PC-3) cancer, as compared to the administration of free drugs, demonstrated greater tumor growth inhibition after the administration of liposomal paclitaxel. In addition, toxicology studies have shown that liposomal paclitaxel is less toxic than free paclitaxel. An improved pegylated liposomal formulation of paclitaxel was developed, demonstrating that cytotoxicity in human breast cancer cell lines (MDA-MB-231 and SK-BR-3) of the tested paclitaxel formulation was equipotent after 72 hrs of incubation, when compared to Taxol®.

RECENT ADVANCES IN TARGETED LIPOSOME (Sawant RR, 2012)

In an attempt to improve the binding and cellular internalization of liposomes in the tumor area, several ligands were attached to the liposome surface, including monoclonal antibodies, folate, transferrin, vasoactive intestinal peptide (VIP), epidermal growth factor (EGF), hyaluronan, galactosides, and condroitin sulphate.

The majority of research in this area is related to cancer targeting, which uses a variety of monoclonal antibodies. To target HER2-overexpressing tumors, it was suggested that antiHER2 long-circulating liposomes be used. Nucleosome-specific monoclonal antibody (maybe 2C5) capable of recognizing various tumor cells through the tumor cell surface-bound nucleosomes significantly improved Doxil®, by targeting to tumor cells, and increased its cytotoxicity both in vitro and in vivo in different testing systems, including the intracranial human brain U-87 tumor xenograft in nude mice. The same antibody was also used to effectively target long circulating liposomes loaded with an agent for tumor photodynamic therapy (PDT) for both multiple cancer cells in vitro and experimental tumors in vivo, and provided a significantly enhanced elimination of tumor cells under PDT conditions.

Saccharide molecules represent good models for tumor targeting molecules, as many malignant cells express the lectin, sugar-binding protein. They concluded that disaccharide-modified liposomes may be promising cancer targeting carriers which can enhance intracellular uptake and cytotoxicity of the drug-loaded liposomes by means of lectin-mediated endocytosis.

One approach that has received considerable attention has been the use of folic acid to deliver drugs selectively to folate receptor-expressing cancer cells. Studies of folate-conjugated liposomes containing DNR or DXR showed an increased cytotoxicity of the encapsulated anticancer drugs in various tumor cells. The i.v. administration of anti-tumorassociated glycoprotein (TAG)-72 Polyethyleneglycol (PEG)-immunoliposomes showed that they were more effectively located in LS174 T human colon cancer cells than conventional liposomes.

FUTURE PERSPECTIVE AND CHALLENGE (Cukierman and Khan 2010)

The more prominent enthusiasm for the advancement of these complex medication conveyance frameworks is to improve the adequacy and decline the symptoms of new and old enemy of malignant growth drugs. In this specific circumstance, the advanced pharmacokinetic properties of liposomes, bringing about an improved harmfulness profile, is as yet the principle contention for the utilization of liposomal transporters. Other new methodologies in the science and pharmacokinetic conduct of liposomes, for example, the counter angiogenic properties of cationic liposomes, just as the advancement of immunoliposomes or antisense oligonucleotides, likewise offer an incredible restorative collection for these medication conveyance frameworks. There are numerous issues with respect to the shakiness of particles through flocculation and total, their mind boggling stream, and bond designs in the slender system, the heterogeneity of the entrance of medications to explicit tumor locales, the dispersion of free medications, and nanoparticles in tumor tissues just as in single cells.

Many research bunches are taking a shot at progressively "dynamic" treatments that adventure focusing on ligands to convey joined cytotoxic medications specifically to threatening cells. These ligands explicitly perceive and specially tie receptors found on the cells of intrigue, subsequently taking into consideration an increasingly exact conveyance technique. Albeit current investigations have indicated that the utilization of these focused on nanoparticles as a medication conveyance framework is a promising methodology to treat human malignant growths, it is still in its beginning time of advancement. Clinical information utilizing focused on nanoparticles are constrained, since most focused on nanoparticles have not yet arrived at the clinical level.

APPLICATION OF LIPOSOME (Dua J.S, 2012)

1. Enhance drug solublisation (Amphotericin-B, Minoxidil, Paclitaxels, and Cyclosporins)
2. Protection of sensitive drug molecules (Cytosine arabinosa, DNA, RNA, Anti-sensoligo-nucleotides, Ribozymes)
3. Enhance intracellular uptake (Anticancer, anti-viral and antimicrobial drugs)
4. Altered pharmacokinetics and bio-distribution (prolonged or sustained released drugs with short circulatory half-life).

Liposomes can be utilized additionally to convey drugs into the lung. This is frequently done by inward breath of liposome vaporized. This can be utilized either for the treatment of different lung issue, diseases, asthma, or utilizing lungs as a medication stop for the fundamental conveyance. By fitting lipid sythesis an assortment of discharge energy can be acquired. One of the potential uses of these pressurized canned products is in the asthma alleviation wherein the dosing recurrence can be significantly diminished and single inward breath can last expedite. Oral uses of liposomes are at present fairly restricted due to the very liposomicidal condition in stomach and duodenum and regularly the organization of free or liposome epitomized sedate displays ordinarily no distinctions. Intragastrical organization, in any case, shows that liposomes upgrade the foundational bioavailability of certain water insoluble medications and nutrients.

A few structures to balance out liposomes in low pH, degradative catalyst, and bile salts containing situations are being contemplated. Improved solvency of lipophilic and amphiphilic drugs. Models incorporate Porphyrins, Amphotericin B, Minoxidil, a few peptides, and anthracyclines, separately; besides, sometimes hydrophilic medications, for example, anticancer operator Doxorubicin or Acyclovir can be epitomized in the liposome inside at focuses a few crease over their fluid solvency.

This is conceivable because of Precipitation of the medication or gel development inside the liposome with suitable substances typified Passive focusing to the cells of the safe framework, particularly cells of the mononuclear phagocytic framework (in more established writing reticuloendothelial framework). Models are antimonies, Amphotericin B, porphyrins and furthermore immunizations, Immunomodulators or immunosupressors. Supported discharge arrangement of fundamentally or privately controlled liposomes. Models are doxorubicin, cytosine arabinose, cortisones, natural proteins or peptides, for example, vasopressin. Site-evasion instrument: liposomes don't arrange in specific organs, for example, heart, kidneys, mind, and sensory system and this lessens cardio-, nephro-, and neuro-harmfulness. Run of the mill models are decreased nephrotoxicity of Amphotericin B, and diminished cardiotoxicity of Doxorubicin liposomes.

Site specific focusing: in specific cases liposomes with surface connected ligands can tie to target cells ('key and lock' instrument), or can be conveyed into the objective tissue by neighborhood anatomical conditions, for example, flawed and gravely shaped veins, their basal lamina, and vessels. Models incorporate anticancer, hostile to contamination and against inflammatory drugs.

CONCLUSION

This undertaking presumed that liposome as transporter which are the most generally utilized medication nanoparticles in malignancy medicines. Essential ideas were introduced concerning liposomes and a review of the clinically utilized and tried liposomes for the treatment of malignancy. It has been illustrated, in view of earlier examinations, that liposomes offer wellbeing and adequacy when contrasted with other customary medications. Liposome framework is to improve viability and abatement symptom of new and old enemy of malignant growth drugs.

The new advancements in the liposome are the particular restricting properties of a medication conveying liposome to an objective cell (tumor cell and explicit particles), secrecy liposomes for focusing on hydrophilic (water dissolvable) anticancer medications like doxorubicin, mitoxantrone which prompts decline in symptoms on the grounds that the medication is for the most part amassed at the site of activity. Other advancement is bisphosphonate-liposome intervened consumption of macrophages. A few business liposomes have just been found, enrolled and presented with extraordinary achievement in pharmaceutical market. There is much more noteworthy guarantee in future for promoting of progressively complex and profoundly balanced out liposomal details. In future the liposomal tranquilize conveyance framework will reform the vesicular frameworks with wide application particularly in the treatment of malignant growth.

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