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A Review on Liposomal Drug Delivery in Cancer Therapy

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ABSTRACT

A promising approach to cancer treatment, liposomal drug delivery systems provide better pharmacokinetics, more precise tumor targeting, and less systemic toxicity—the lipid bilayer spherical vesicles known as liposomes are both hydrophilic and hydrophobic. Due to the increased permeability and retention (EPR) effect, liposomes raise the concentration of anti-cancer medications in tumor tissues. Clinical approval has been granted to certain liposomal formulations, such as Doxorubicin, which are superior to non-liposomal forms. PEGylation and ligand attachment, two modifications to liposomal surfaces, have enhanced targeting and circulatory sustenance. Additionally, the tumor microenvironment can control drug release thanks to the combination of sensitive stimulation systems. Nevertheless, biological barriers, liposome stability, overcoming further biological obstacles, and bulk manufacturing optimization are still problems. Research and clinical work are needed to take full advantage of liposomal systems in cancer therapy.

Keywords: Liposomes, drug delivery, liposomal drugs, carcinoma.

1. INTRODUCTION

Liposomes are small, self-assembling phospholipid-based vesicles that form a bilayer shape, encasing a central water-filled region in either a single layer (uniflagellar) or many layers (multilamellar) [1]. The α-helix consists of nearly every amino acid within a protein lying forming a helical spiral around the helical axis at a radius between 0.7 to 1.0 nanometers and helps stabilize the polypeptide in a spiral form or six to seven residues along the axis [1–5]. Also, the length of the helix is determined by two main factors: first, the number of hydrogen bonds formed, the overall bond length, and helix portion energy, leading to or damaging the coil formation [1,2]. Thus, the turn of each region of the coil must at least equal the distance of the bond within the helical section, or the coil cannot be modified; otherwise, defaults will occur due to tension built during stabilization. One last crucial point is that the α-helix, like any higher order structure, is not obtainable in its default state, which means that an energetic state must be reached to mark that it has captured sufficient energy, or in the context of being applied energy for said purpose [1,6,8]. In liposomes, the phospholipid bilayer is around 4-5 nanometers thick, with a diameter anywhere from 30 nanometers to several micrometers[1,4]. In the mid-1960s, Alec Bangham, alongside his co-workers at Babraham Cambridge, began researching liposomes, and in 1964, Bangham et al published the first structural liposome model. Since then, liposomes, imaging agents, proteins, nucleic acids, as well as

small medicative, have all been thoroughly researched as potential deliverable carriers to a broad range of materials by other scientists [2,3]. Many methods to enhance patient compliance and therapeutic efficiency, such as parenteral, pulmonary, oral, trans-ocular, and nasal, have been developed, as Liposomes have been incorporated within the cosmetic and food industry [10,11]. Because of their composure, liposomes can provide large benefits when deliveredasadrugorcanevendeliveredthroughcosmeticlipsomisedcreams[15]. They allow better control over the release period of the drug, sustain the time the drug survives inactive state, and avoid destruction of the body's encapsulated compounds [16]. In addition, they possess the capability to release their contents solely at designated affected areas, hence minimizing unwarranted side effects and magnifying their therapeutic importance [17,19].

(Properties of) Solid tumors or inflammatory areas have tissues that form blood vessels, which are more porous, giving them the ability to take in blood as compared to normal tissues, which have closely bound cells [20-22]. This differential fosters the enhanced permeability and retention (EPR) effects, which permit nipple-like structures in sick areas to get through liposomes. Additionally, liposomes can be designed for Targeting Systems where certain interactions occur between ligands.

andreceptorsontumorouscells[23–27].Manyreceptorsthatareoverexposesdintumorcellsare known to greatly preferentially express [28-30]. These receptors include vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), folic acid (FA), Integrins, CD44, inadequately utilized glycoprotein, CD13, and prostate-specific membrane antigen.

1.1StructuresandMainComponentsofLiposomes

Circular soft matter vesicles called liposomes are created when one or more bilayer membranes split apart to isolate aqueous [36]. The component of liposomes.50–1000nmindiameter,whichservesasfocuseddeliveryvehiclesforbiological compounds that are active[37].

- **The two main components of a liposome are cholesterol and phospholipids.**

Phospholipids:

Phospholipids, which are mostly found in liposomes, are made from phosphatidic acid. The parent component that gives these molecules their structure is glycerol. Using a hydroxyl esterification process, the OH group is attached to phosphoric acid at the C3 position. These molecules like due to the bonding of hydroxyl ions with long chain fatty acids on the C1 and C2 sites [38].

One of the remaining OH groups in phosphoric acid can be esterified to create other organic alcohols. Among them are inositol, ethanolamine, serine, glycerol, and choline. Consequently, this group is referred to as the glycerol ester compound.

Phospholipids include the following examples:

Among these are phosphatidylcholine (lecithin), phosphatidylethanolamine(cephalin), phosphatidylserine (PS), phosphatidylinositol (PI), and phosphatidylglycerol (PG).

For stable liposomes, saturated fatty acids work best. Unsaturated fatty acids are typically not used [39].

1.1.1MethoofPreparation

GeneralMethodofPreparation:

Step 1: Dissolve 10- 20 mg/L of lipids in chloroform.

Step 2: Use a rotary evaporator to remove the solvent, leaving a thin film of lipids. Step 3: Allow the thin film to desiccate for the necessary amount of time.

Step4:Hydratethedesiccatedproductfortherequiredduration.Once fully hydrated, the liposomes will form

as multilamellar vesicles (MLVs) within a size range of 200-1000 nm.
Step5:ReducethesizeoftheMLVsusingextrusion. Step 6: Purify the resulting liposomes.
Step7:Analysethefinalproduct.

Other Methods:

The different methods involved in the preparation of liposomes include:

1. **Passive Loading Techniques**

a. Mechanical dispersion method

- Sonication
- French pressure cell
- Membrane extrusion
- Microencapsulation
- Lipid hydration method
- Membrane extrusion

b. Solvent dispersion method

- Ethanol injection
- Ether injection
- Double emulsion
- Reverse phase evaporation

c. Detergent removal method

2. **Active Loading Techniques**

a. Pro liposomes

b. Lyophilization

Passive loading techniques: This technique is used to encapsulate the drug during the formation of liposomes.Thehydrophilicmedicationsareloadedintotheliposomes'internal core by mixing with the hydrating buffer, which is used to hydrate the thin lipid layer during liposome production. Gel filtration chromatography and dialysis are used to remove the released drug molecules from the liposome suspension.

a. Mechanical Dispersion Method:

Sonication: Sonication is the method most commonly used to prepare SUVs. Here, either a bath-style or a probe-style sonicator is used to sonicate MLVs in a passive atmosphere. The main disadvantages of this approach are its incredibly small interior capacity, ineffective encapsulation, phospholipid degradation and removal of large molecules, metal contamination from the probe tip, and the presence of MLV in addition to SUV. There are two sonication techniques:

Probe sonication: This sonicator instantly immerses the liposome dispersion. The energy input into the lipid dispersion during this phase is extremely substantial. Because of the localized heat caused by the energy coupling at the tip, the vessels must be immersed in ice or a water bath. The sonication process, which can go on for up to an hour, can break down more than 5% of the lipids. It's crucial to remember that employing a probe sonicator could contaminate the solution by causing titanium to flake off.

Bath sonication: The liposome-containing cylinder is kept at a regulated temperature in a bath sonicator. In general, this approach is simpler than employing a direct dispersion technique. The material can be shielded during sonication by a probe unit, sterile container, or inert environment.

French Pressure Cell: French Pressure Cell uses the technique of ejecting MLV through a tiny opening.

One notable feature of the French press vesicle method is that the proteins seem to be somewhat unassuming during the sonication process. It's important to note that encapsulated solutes appear to be retained far longer by French press vesicles, which are produced by sonication or detergent removal, than by SUVs.The method requires careful handling of unstable materials. Compared to sonication, the approach has some advantages. As a result, the liposomes formed are identical in size to the sonicated SUVs. There are a few restrictions to take into account, though: it can be challenging to reach the necessary high temperature, and the amounts employed are somewhat limited—50mLat most.

Membrane extrusion: This method uses a pressure of roughly 250 psi to push multilamellar vesicles through a polycarbonate membrane. The layers of multilamellar liposomes peel off until just one little layered vesicle remains.

Micro-emulsification technique: This approach is used in the commercial development of small lipid spheres. Fatty blends could be micro-emulsified under a homogenizer's shearing stress to accomplish this. By raising the rotation rate from 20 to 200, microemulsion can be created for natural applications.

Lipid hydration method: The most popular and widely used method for preparing MLV is the hydration procedure. Before hydrating the thin layer, the procedure comprises vortexing the dispersion, adding fluid buffer, and dehydrating the lipid arrangement. The hydration phase is complete. Depending on their solubility, substances that must be enclosed are either added to a watery buffer or an organic solvent that contains lipids. The reduced application efficacy can be addressed by hydrating the lipids adjacent to immiscible solvents, such as petroleum ether and diethyl ether. Sonication is then used to emulsify it. When nitrogen passes through, a natural layer is released, forming MLVs.

b. Solid Dispersion Method:

Ethanol injection: When a lot of buffer is rapidly added to an ethanol lipid solution, multilamellar vesicles (MLVs) are created. This approach does, however, have several drawbacks. The resultant liposomes are highly diluted, and the MLVs range in size from 30to110nm. Because ethanol forms an azeotrope with water, it is also difficult to remove entirely. Furthermore, ethanol can deactivate a variety of physiologically active macromolecules in even minute concentrations.

Ether injection method: This method dissolves lipids in either diethyl ether or ether/methanol. This lipid mixture is then injected into an aqueous solution that contains the material to be enclosed. Lower pressure and temperatures between 55 and 65 degrees Celsius are used for this. When organic solvents are used in a vacuum, they evaporate. Finally, liposomes are created.

Double-Emulsification Strategy: Three commercial products—DepoCyte, DepoDur, and Eliminate—use the process known as the Depo Foam platform TM to create multi-layer vesicles (MLVs). To concentrate, exchange, and release the free drug, this procedure entails making two emulsions: a "water-in-oil" and a "water-in-oil-in-water" emulsion(Yeetal,2000).Additionally,solubleextractionmethodslikevacuumweightor gasstrippingareusedinconjunctionwithmicrofiltration(Mantripragada,2002).

Since MLVsmade at scale cannot be generated as sterile batches with a 0.22 µm filter, it is crucial to provide aseptic evidence throughout manufacturing. When certain MLVs rupture, the drug may leak from the secondary emulsion's fluid phase, reducing the effectiveness of encapsulation during the extraction procedure. Additionally, higher temperatures can enhance the fluidity and modification of the lipid bilayer, resulting in lipid mixing and the closure of the fluid compartments.

Reverse-phase evaporation technique: We begin by quickly sonicating a two-phase mixture containing phospholipids and soluble substances such as isopropyl ether, diethyl ether, or a combination of isopropyl

ether and chloroform, combined with an aqueous buffer to produce a stable water-in-oil emulsion. These natural materials decompose and create a polymer when exposed to lower temperatures. The fact that this technique produces liposomes that are more than 80% densely packed is one of its main advantages.

c. Detergent removal method(removal of non-encapsulated material):

Lipids can be solubilized through dialysis using detergents at their critical micelle concentrations (CMC). As the detergent separates from the micelles, the phospholipid content increases, eventually leading to the formation of large uniflagellar vesicles (LUVs). During dialysis, the detergents are removed.One effective tool for this process is the Lepper system from Drachmae in Switzerland, which is specifically designed for dialysis.

Dialysis can also be performed using bags that are submerged in large, detergent-free buffers, a method known as equilibrium dialysis. Additionally, mixed micelles containing detergents like cholate, alkyl glycoside, and Triton X-100 can be removed through a process called absorption. This involves shaking a mixed micelle solution with beaded organic polystyrene adsorbers, such as Bio-beads SM2 from Bio-Rad Laboratories and XAD-2 beads from SERVA Electrophoresis. The use of detergent adsorbers is particularly beneficial, as they can effectively eliminate detergents with very low CMCs, even when they are partially depleted.

2) **Active loading techniques:**

A transmembrane gradient, or distinct aqueous phases inside and outside the liposomes, is produced during the active loading process. The phospholipid bilayer is then broken down by dissolving an amphipathic drug in the external aqueous phase. Following this penetration, the drug may interact with the trapping agent and the Core, securing the drug within the liposome. Catecholamines can be loaded into liposomes with a pH gradient to provide persistent drug retention in vitro, according to a 1976 work by Deamer and Nicols [31–33].

1.2.Cancer

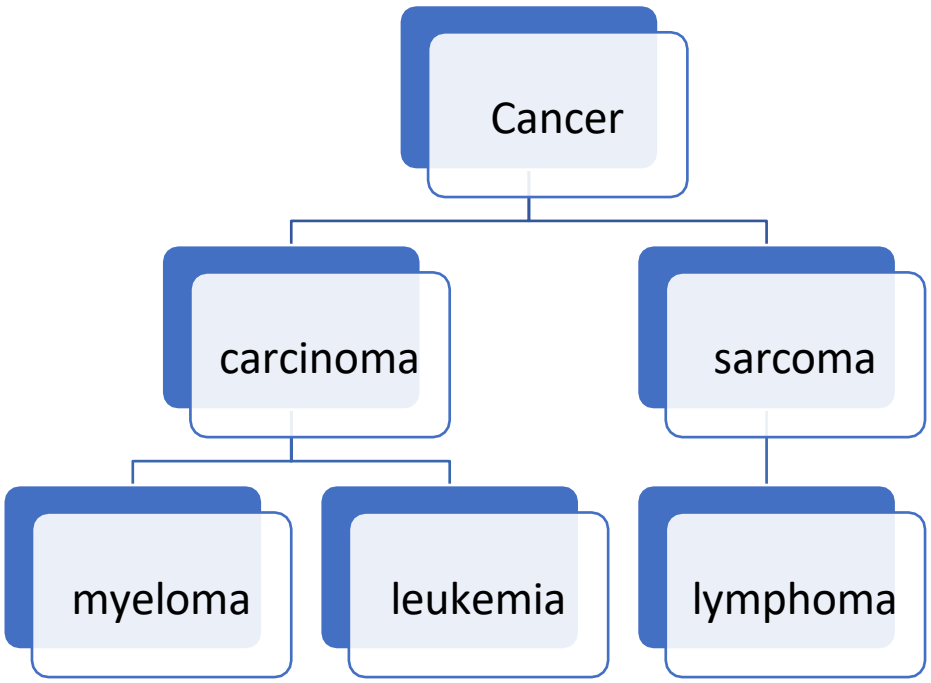
Novel approaches must be developed to overcome the limitations of traditional treatments like chemotherapy and radiation therapy, which frequently cause severe side effects and produce suboptimal results, because cancer is such a complex disease that has long presented difficult treatment challenges [34]. In this era of medical necessity, nanotechnology has become an intriguing new paradigm for cancer detection and therapy. Nanotechnology makes use of the capacity to engineer and modify materials at the nanoscale, typically between 1 and 100 nm. Such small materials' unique physicochemical characteristics allow for selective interactions with cells and tissues, opening the door to novel nanoscale targeting strategies that could fundamentally alter cancer treatment and diagnosis [35].

Due to their ability to encapsulate medications or therapeutic genes, these tiny carriers offer several benefits over the drawbacks of conventional therapy [36]. These benefits include reduced damage to healthy cells, improved therapeutic payload efficacy, and targeted precision in identifying cancer cells [37]. By altering the surface of nanocarriers with particular targeting ligands, on the other hand, active targeting enables more accurate and effective cellular contact by binding to receptors on the surface of cancer cells [38]. Few nanocarriers have reached clinical usage, mainly those carrying molecular moieties intended to bind preferentially with cancer cells, even though several varieties have passed preclinical testing and been authorized for use in human clinical trials. Here, the complexity of converting laboratory findings into successful clinical treatments is highlighted, highlighting the need for more studies to maximize the therapeutic efficacy of nanocarriers for cancer treatment [39].

The confluence of nanotechnology and the treatment of cancer is capable of enhancing patient outcomes,

minimizing collateral harm to normal cells, and optimizing the potency of therapeutic drugs. Exploring this rich ground is not without its challenges, however, such as the creation of effective and cost-benefit nanocarriers, the demonstration of the safety profile of these carriers in environments in humans, and the elimination of barriers preventing findings in the laboratory from being translated to actual clinical outcomes. [39]

1.3Majortypesofcancer:-



a. Carcinomas:

Definition: Cancer originating in the epithelial cells, which are cells that cover the surfaces of the body and line the inside of organs and glands. Examples: Breast cancer, lung cancer, skin cancer, colon cancer, prostate cancer. Types: Basal cell carcinoma, adenocarcinoma, squamous cell carcinoma.

b. Sarcomas:

Definition: Cancer that begins in the supportive or connective tissues, including bones, cartilage, fat, muscle, and blood vessels

Examples: Bone cancer, or osteosarcoma, Cartilage cancer, or chondrosarcoma, Fat cancer, or liposarcoma Connective tissue cancer, or fibrosarcoma.

c. Leukemias:

Definition: Cancer that begins in the blood-making tissues, such as bone marrow.

Examples: Acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML).

d. **Lymphomas:**

Definition: Cancer that begins in cells of the immune system, most often lymphocytes. Examples: Hodgkin lymphoma, non-Hodgkin lymphoma.[40]

2. Nanobody-Liposomes as novel cancer vaccine

Starting an immune response against malignant cells is the main goal of cancer vaccination techniques. The development of vaccination techniques that can elicit strong immune responses capable of eliminating

cancer cells while also having little damage was aided by the identification of tumor-specific antigens (TSAs) and tumor-associated antigens (TAAs). TAAs aregermline-encodedself-antigensthatarereexpressedinmalignancies.For example, cancer testis antigens are often only expressed in the testis or placenta. Although TAAs are produced in a variety of malignancies and may be used in inexpensive off-the-shelf vaccination strategies, their tolerance induction mechanisms that are unique to self-antigens make them generally less immunogenic. TSAs or neoantigens are more promising since they are highly specific, originate from genomic abnormalities linked to tumors, or are encoded by viral genes implicated in the genesis of cancer. Neoantigen-based vaccinations have been used in encouraging phase I trials, which have demonstrated reduced metastases in a subgroup of patients, no tumor recurrence following resection, and sustained progression-free survival.

Typically, various combinations of tumor antigen, adjuvant, and delivery platform make up cancer vaccines. In women with HPV-16-positive vulvar intraepithelial neoplasia, a vaccination based on synthetic long peptide (SLP) has demonstrated encouraging outcomes.

- **Vaccines**

Vaccine	Trade Name	Abbreviation	Manufacturer	Route	Doses in routine series	Approved Ages
DTaP, Polio	Kinrix	DTaP-IPV	GlaxoSmithKline	IM	1	4-6years
	Quadracel	DTaP-IPV	Sanofi	IM	1	4-6years
DTaP, Hepatitis B, Polio	Pediarix	DTaP-HepB-IPV	GlaxoSmithKline	IM	3	6weeks-6 years

3. Liposomal Drugs:

Doxil: When it became clear in a "first in man" (FIM) clinical trial by Gabizon and Barenholz that a "first generation" liposomal doxorubicin did not warrant further clinical development despite an elevation in drug, Doxil's development was started in Israel and the USA about 14 years ago. MTD (rev. in [1]). Medium-sized, negatively charged oligolamellar liposomes (OLV) made of cholesterol and two low-Tm(fluid) phospholipids—the negatively charged egg-derived phosphatidylglycerol (EPG) and the zwitterionic egg-derived phosphatidylcholine (EPC)—were employed in this FIM experiment. Doxorubicin was membrane-associated and passively loaded during the lipid hydration process in these OLV. [40,41]

Mechanism of action: Doxil is a liposomal formulation of doxorubicin [41],[42] that was FDA-approved in 1995 and has been subsequently approved for other indications, including ovarian cancer and multiple myeloma. Doxilliposomes are about 100nm in diameter and encapsulate 10,000–15,000 doxorubicin molecules [43]. PEGylation of the liposomes results in a long circulation half-time, a small distribution volume, a low clearance rate, and a high area under the curve. Intercalation into DNA and disruption of topoisomerase-II-mediated DNA repair.[44]

Doxorubicin: Clinical performance of phospholipid vesicles (liposomes) containing the chemotherapeutic drug doxorubicin is significantly better than that of free (non-liposomal) doxorubicin, which is the standard of treatment. Liposomal doxorubicin's special pharmacokinetic qualities led to a significant decrease in cumulative-dose-related cardiotoxicity. This increase in patient daily compliance

made it possible to increase the cumulative dose and prolong the doxorubicin treatment period. The ability to selectively target particular cancer cells (such as endocrine cells)or organelles (like mitochondria, lysosomes) was made possible by targeted liposomal doxorubicin, which involved surface functionalization of liposomes with ligands. [45,46].

Mechanism of action: When considering the biological activity of liposomal formulations of doxorubicin, it is important to remember that 47 doxorubicin is released from the liposomes following intravenous administration. Blocking an enzyme called topoisomerase 2 that cancer cells need to grow

3.1 Methods of passive and active targeting

Although there are several obstacles in their way of reaching the intended location, nanocarriers are being studied more and more as a potentially effective cancer treatment strategy [48].The potential of smart nanocarriers in the targeted delivery of therapeutic

Nucleic acids for cancer immunotherapy were investigated in a recent study by Baker et al. The development of immunotherapy, especially the use of antibodies that target immunological checkpoints, has led to significant advancements in the treatment of cancer. Nonetheless, nucleic acid technology, which includes gene regulation, adoptive T-cell treatments, and cancer vaccines, is becoming more and more important in the field of cancer immunotherapy. Although nanocarriers are being studied more and more as a potential cancer therapy method, they encounter many obstacles on the route to the intended location [48].

Researchers Baker et al. recently investigated the possibility of smart nanocarriers for the tailored delivery of therapeutic nucleic acids for cancer immunotherapy. With the development of immunotherapy, especially the use of antibodies that target immunological checkpoints, cancer treatment has advanced significantly. Nonetheless, the area of cancer immunotherapy is changing, with a greater focus on nucleic acid technologies, such as gene regulation, adoptive T-cell therapies, and cancer vaccines.

4. Cancer therapy using nanomaterials

Millions of individuals worldwide suffer from the terrible disease known as cancer. Non-specific targeting and high toxicity to healthy cells are two major drawbacks of conventional cancertreatmentslikechemotherapyandradiationtherapyNewtoolsforcancerdetectionand treatment are made possible by advances in nanotechnology. The field of working with materials at the nanoscale, typically between 1 and 100 nm, is referred to as nanotechnology [49, 50]. Nanomaterials' microscopic size enables them to interact with cells and tissues in novel ways, making them useful for targeted drug delivery and cancer treatment. The study of nanocarriers—microscopic particles that can hold therapeutic drugs—is one of the main focuses of nanotechnology research for cancer treatment. Targeting cancer cells precisely while avoiding normal cells is one of the difficulties in creating nanocarriers for cancer treatment. The EPR effect is one of the passive targeting strategies that capitalizes on the special properties of tumor cells, such as their permeable blood arteries and insufficient lymphatic drainage [51]. Utilizing these materials has increased drug delivery to cancer cells, decreased toxicity to healthy cells, and improved patient performance. For example, liposomes use the pH gradient mechanism to release doxorubicin in a stable and prolonged way in acidic conditions. Polymeric nanoparticles provide stable, regulated paclitaxel diffusion at neutral pH levels. However, despite their instability, dendrimers administer methotrexate through swelling in a pulsatile manner under simple conditions. Gold nanoparticles can release curcumin by a photothermal-triggered mechanism at neutral pH levels, while nano emulsions exhibit pulsatile

docetaxel partitioning in acidic environments.
Thesenanocarriershaveawiderangeofusesasdrugdeliveryvehiclesbecauseoftheir stability, pH sensitivity, and varied release rates. [52]

4.2Diagnosis:

Physicians have access to a wider range of diagnostic techniques that can help identify HCC. Small HCCs that would have gone unnoticed by more traditional diagnostic methods can now be identified because of technological advancements. People who are at risk of developing HCC, such as those with chronic HCV, noncirrhotic and cirrhotic HBV, and other patients with chronic liver disease and cirrhosis, must first undergo screening. The American Association for the Study of Liver Disease (AASLD) has developed screening recommendations for persons at risk for HCC. These were created to identify a group of patients who might profitably use screening techniques. These recommendations apply to patients who have a 1.5% or greater risk of developing HCC if infected with HCV or a 0.2% risk if infected with HBV. Africans, cirrhotic HBV patients, Asian males aged 40 or older, Asian ladies aged 50 or older, and patients with a family history of HCC are among the groups of people infected with HBV. Additionally, screening should be done for patients with hemochromatosis, cirrhosis linked to alpha-1-antitrypsin, stage 4 primary biliary cirrhosis, and cirrhosis associated with HCV [50].
Furthermore, individuals with HIV plus HCV or HBV should be continuously watched because HCC can develop more easily and quickly in this population. This may become moreprevalentsincetheHIVcohorthasmuchimprovedprognosesandislivinglongerwith the disease, even though these are not included in any defined standards [51,52].

4.3Therapy:

TherapeuticalternativesforHCChaveincreasedconsiderableoverthepreviousfewdecades. Resection was the sole option at first; however, transplantation and an increasing variety of locoregionaltherapyhaverecentlybeenshowntobeviableinterventions. Rahman conducted a comprehensive meta-analysis comparing transplantation and resection in similar early cirrhosis patients. Despite similar 5-year overall survival, this study indicated that patients undergoing transplantation had a greater disease-free survival at 5 years (OR=0.39;95%CI: 0.24-0.63; P<0.001). However, this study showed that individuals receiving liver transplants had a clear overall and disease-free survival at 10 years. However, they did show that transplant recipients had a greater short-term death rate [53]. Resection remains the first-line therapy in patients who have preserved liver function and can be completely resected. In patients with no underlying liver disease, roughly 70%-80% of the hepatic parenchyma can be resected safely due to the ability of the liver to regenerate. Ratio of remnant liver volume to body weight should be ≥ 0.8% according to most literature to avoid post-resection major complicationsincludingpost-resectionliverfailure[53].Incirrhoticpatientsitisthoughtthatonly60%oftheparenchymacanberesectedleavin gataminimum 40%offunctioning liver[53].

5. CONCLUSION

Compared to traditional chemotherapy, liposomal drug delivery methods offer focused, effective, and less toxic treatment options, marking a significant leap in cancer therapy. The therapeutic index of various anticancer drugs has been raised by liposomes through improvements in drug solubility, stability, and tumor-specificaccumulation.Theirpotentialisconfirmedbyclinicallyapprovedformulationssuchas liposomal doxorubicin, and continued advancements in surface engineering and stimuli-responsive release

are opening the door for next-generation treatments.

Liposomal delivery is still a promising and developing platform that is continuing to influence the direction of customized and precision oncology, despite certain drawbacks such as scalability and biological complexity.

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