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A REVIEW ON: SOLID LIPID NANOPARTICALS USED IN CANCER TREATMENT

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ABSTRACT

Solid lipid nanoparticles are going to be used much more in medicine, particularly for drug delivery. Many chemicals are currently being studied for their potential to transport drugs, particularly for cancer therapy. In cancer therapy, technology is the newest trend. It aids the pharmacist in creating a product with the greatest possible therapeutic benefit and the fewest possible negative effects. Cancer is a group of diseases defined by aberrant cell proliferation that multiplies uncontrollably. One of the main drawbacks of anticancer medications is that they are not selective for tumor tissue, which leads to serious side effects and low cure rates. As a result, using the traditional drug delivery technique to target the abnormal cells is quite difficult. In keeping with these methods, the fundamental strategy is based on the idea that solid lipid nanoparticles' revolutionary potential for patient care is one of their key characteristics. This paper outlines the potential application of solid lipid nanoparticle technology to cancer targeted medication therapy. We investigated solid lipid nanoparticles' potential as a cancer treatment strategy.

KEYWORD: Cancer Therapy, Solid Lipid Nanoparticles, Quantum Dots.

INTRODUCTION

An abnormal cell's ability to spread to other cells or parts of the body is what causes a tumor, a type of sickness. Among more than 100 different types of cancer, it is one of the leading causes of death. Fifteen percent of cancers in developing countries are caused by pathogens such as HIV, hepatitis B, hepatitis C, hepatitis V, and H. pylori. A cell's genes are changed by such circumstances, at least partially. Pre-cancerous changes may require several genetic

modifications. In five to ten percent of instances, cancer is caused by inherited genetic defects. Cancer can be identified with the use of medical tests and a variety of symptoms and markers. Once confirmed by a biopsy, it would typically be further investigated via diagnostic imaging. In 2015, there were approximately 90.5 million cancer diagnoses. 2019 will see the recording of close to 18 million new cases annually. Nearly 8.8 million deaths were attributed to it annually. The four types of cancer that affect men most frequently are stomach, colorectal, lung, and prostate. The four types of cancer that affect women the most frequently are cervical, lung, colorectal, and breast. If the total number of new cancer cases had been taken into consideration, skin cancers other than melanoma would have accounted for about 40% of new cancer cases annually. Apart from Africa, where non-Hodgkin cancer is more common, acute lymphoblastic and brain cancer appear to be the most common in young people.[1]

"Lipid" appears to be another word for "fat." The lipids appear to be a substance that dissolves well in alcoholic solutions, (C2H5)2O, and chcl3, but not in water. An integral part of human cells were lipids. The main constituents of plant and animal cells were lipids, proteins, and Cx (H2O)y. Lipids include both triglycerides and cholesterol. Lipids are obtained quickly and held in the system. It is a crucial part of the makeup of cells and acts as a reference for energy. Steroids (such as cortisone), neutral fats, fatty acids, and waxes are examples of lipids. Lipoproteins, glycolipids, and phospholipids—lipids complexed with another kind of chemical molecule—are examples of compound lipids. Lipids can be classified as either amphiphilic or aquaphobic small molecules. Their amphiphilic nature allows us to develop a variety of formations in aqueous environments, such as membranes, huge uniflagellar liposomes, and vesicles. The two kinds of biochemical subunits, or "building blocks," that make up biological lipid are isoprene and ketoacyl groups. Lipid emulsion, liposomes, and SLN structures are displayed in Figure 1.

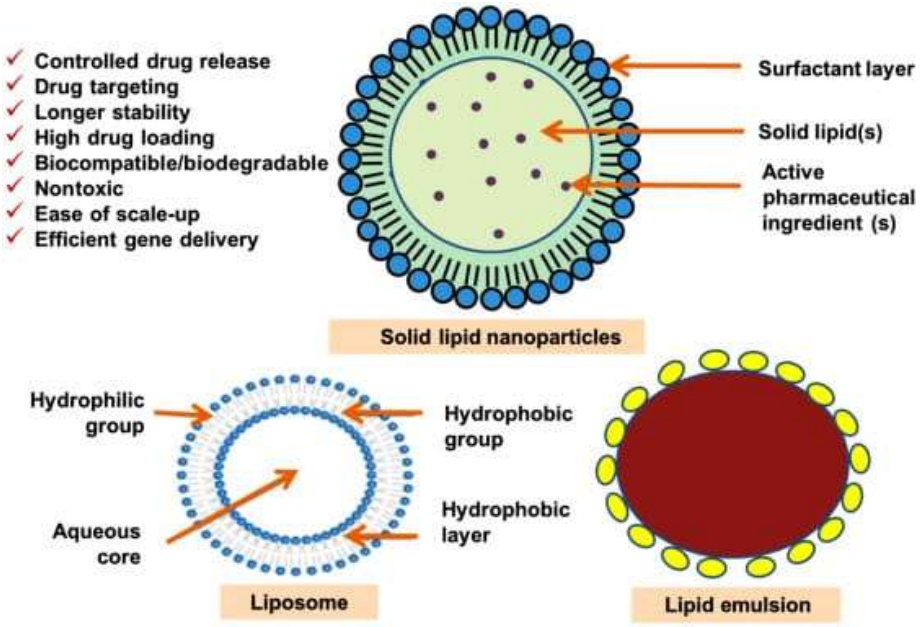

Figure 1: The overall arrangement of solid lipid nanoparticles, which have benefits over liposomes and lipid emulsions, is represented schematically. Adopted from.[4]

Lipids have drawn a lot of attention since the dawn of pharmacology due to their biocompatibility as transporters. Because of their strong hydrophobicity, they have minimal oral absorption.[2] Consequently, there was an unfulfilled desire to expand the spectrum of uses for these carriers, and they were only used in colloidal delivery systems until 1900, when they were finally deployed in propulsion systems. In the development of nanoparticle-based delivery systems, lipid nanoparticles (LNPs) were shown to be more advantageous than polymeric nanoparticles, and this has led to their widespread use in drug delivery. These lipid-based carrier systems are also called "Nano safe" carriers because LNPs are composed of physiologic and/or biodegradable lipids. Solid lipid nanoparticles (SLNs) were developed in the early 1990s and are a highly effective LNP production. This delivery approach was created because to the advantages of earlier carriers such as liposomes, emulsifiers, and polymeric nanoparticles. What sets SLNs apart from liposomes are the absence of polar chemicals, the GRAS (generally regarded as safe) quality of all formulations, and the viability of the production processes and levelling-up process.[3]

Nowadays, antitumor medication delivery by tumor nanotechnology has emerged as a promising cancer therapy approach. The therapeutic bioavailability and anticancer drug selectivity are enhanced by nanoparticles, which can have sizes ranging from 1 to 1000 nm. Recent presentations of a wide range of nanoparticles (NPs) and nanotech approaches to cancer treatment are depicted in Figure 2.

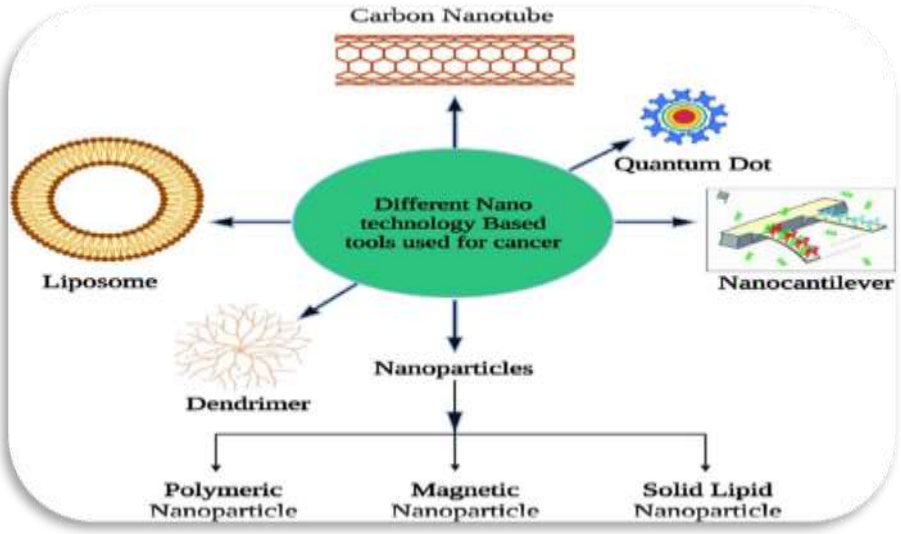

Figure 2: Various Nanotechnology based tools utilized in treatment of cancer. Adopted from.[6]

As a versatile material system with great potential for biological applications, semiconductor quantum dots (QDs) have gained attention due to their unique optical properties, wide excitation range, and excessively restricted symmetric intensity distribution. QDs on semiconductors are a fascinating new family of fluorescent materials. Applications for biosensing, biolabeling, and bioimaging use them. Compared to regular fluorophores, QDs have a bigger effect. They exhibit greater brightness, greater controllability over fluorescence intensity, and reduced photobleaching. One light source can excite different colored QDs, which have narrow emission and broad absorption spectra. The best substitute for screening cell receptors seems to be the previously described QDs. QDs' surface needs to be modified using a variety of biological materials in order to produce efficient fluorescence probes.[5]

We highlight the lipid-based nano formulations (Figure 2) among the many others used in cancer treatment since significant advancements in preparation and alternative compositions have been made in recent years. Lipid nanosystems can be chemically modified to avoid immune system detection or to improve drug availability. These can also be produced with pH-sensitive compositions to enhance drug release in acidic environments. Moreover, they can be combined with antibodies that identify tumor cells and their receptors, such as folic acid (FoA). It may be possible to use nanoparticle medications in addition to conventional therapy modalities to improve patient response. Many antitumour medications, such as vincristine, cisplatin, irinotecan (IRI), paclitaxel (PTX), doxorubicin (DOX), oxaliplatin, daunorubicin, cytarabine, and doxorubicin, have previously been examined in

nanoformulations; some of these medications were studied in clinical trials and/or are available commercially for use in medicine. Actually, Doxil®, a liposome formulation containing DOX, was the first anticancer medication NanoSystems used in a commercial setting. gives a summary of the several LBNP varieties that have been developed recently (Figure 3), along with their uses and contributions to various cancer kinds.[7]

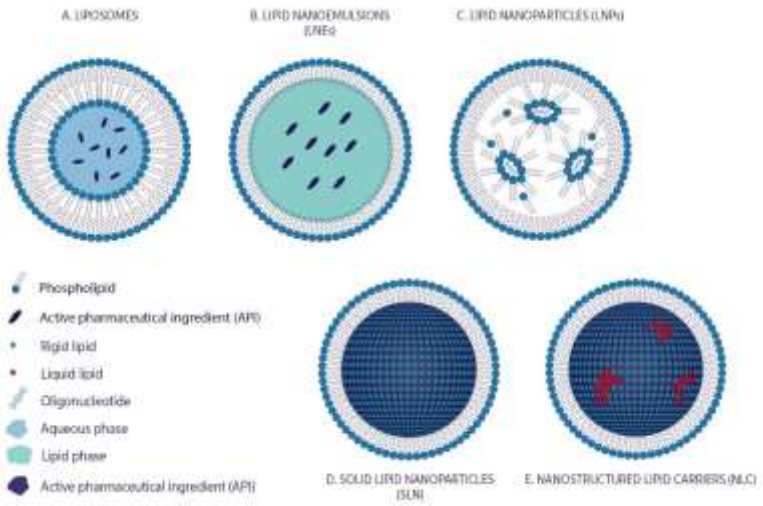

Figure 3: Lipid based nanoparticles showing A) LIPOSOMES, B) LIPID NANOEMULSIONS C) LIPID NANOPARTICLES, D) SOLID LIPID NANOPARTICLES, E) NANOSTRUCTURED LIPID CARRIERS. Adopted from.[10]

2. Solid Lipid Nanoparticles

The hard size range for them is 1–1000 nanometers. Particle sizes typically range from 150 to 300 nanometers. Solid submicronic colloidal nanocarriers (SLNs) range in size from 1 to 1000 nm. The majority of the particles range in size from 150 to 300 nm. Such drug delivery techniques, such as those involving polymeric nanoparticles, offer a framework for controlled releases. The solid SLN matrix enables them to combine the advantages of polymeric nanoparticles, liposomes, and micronized emulsifiers by limiting medicine movement and providing improved stabilization.[8]

Additionally, testing reveals that SLNs were very beneficial in several areas (Figure 4), including the avoidance of using organic solvents during manufacture, potential scaling, and the inclusion of both lipophilic and hydrophilic medications in sizable amounts. SLNs are made by substituting a solid lipid (oil) for the liquid lipid (water) in the structure of an oil in water emulsion, or even a mixture of solid lipids. The fact that SLNs are solid at body

temperature as well as room temperature is a crucial characteristic. These drug delivery systems consist of 0.1–30% (w/w) solid lipid distributed in an aqueous solution. Generally speaking, solid-state lipids (SLNs) consist of wax (usually well-known physiological lipids), complex glyceride blends, free fatty acids, free fatty alcohols, and higher purity triglycerides. Moreover, using more intricate structures is possible.[9]

2.1. Limitations Of SLN And Way To Overcome

Even though solid lipid makes up the majority of SLNs, instability and degradation could pose a problem. A number of factors need to be taken into account, such as the kinetics of the delivery process, the minimal drugloading potential, the coexistence of various lipid modifications and colloidal species, and high pressure-induced drug degradation.

2.2. High Pressure–Induced Drug Degradation

Drug degradation is primarily caused by molecular size and structure; high pressure uniformity has also been demonstrated to lower polymeric molecular weight. Even though multiple studies indicate that the vast majority of bioactive metabolites are not concerned about drug degradation caused by high-pressure homogenization, high molecular weight composites or chain length elements are far more susceptible than low molecular compounds with a spherical form. However, because big molecular weight substances like DNA, albumin, and dextrose are more prone to breaking, integrating them into SLNs requires a different strategy.

2.3. Lipid Crystallization And Drug Incorporation

Lipid crystallization is an additional crucial issue to consider. The connection between medicine administration and lipid modification has been the subject of research for the last ten years. Lipid alterations are a well-studied topic. Most of the techniques rely on differential scanning calorimetric measurements and X-rays. However, the vast majority of the data comes from research on large amounts of lipids. The efficiency of SLNs can vary greatly because of the carrier's obvious nanosize and the large number of interface active participants required to maintain the colloidal lipid dispersal. Lipid crystallization and drug incorporation thereby affect the characteristics of lipid particles. When talking about drug capture within SLNs, it's vital to take into account the following significant factors: (1) the development of supercooled melts; (2) the occurrence of numerous lipid modifications; (3) the shape of lipid nanodispersions; and (4) gelation processes.

2.4. Several Colloidal Species Coexist

As important as it is to address, the cohabitation of several nanoparticles within SLNs has not gotten much attention from researchers. The lipid surface and the inside both contain surfactants. Heterogeneous micelles must be recognized in systems that are stabilized by glycocholate/lecithin and related systems. They might be utilized as alternative therapeutic inclusion targets because liposomes, mixed micelles, and micelles are known to breakdown medications. Just having different heterogeneous entities present is not enough to describe the structure of colloidal lipid phase separation since dynamic mechanisms are necessary for the stability and release of the medication. Therefore, consideration must be given to the kinetics of distribution processes. In contrast to lipid molecules, hydrolytic drugs, for example, will break down more quickly in water dissolved and interface localized substances. Drug concentration in the aqueous phase or at the lipid/water interface, as well as the chemical makeup of the medication, will control the rates of breakdown. Drug dispersion equilibrium between different habitats is upset by volatile drugs because they hydrolyze quickly when they come into contact with fluids. Carriers are useful only if they make it impossible for the medication to be transferred. Enhancing the matrix thickness naturally lowers the drug's diffusion coefficient inside the transporter, which is why SLNs are expected to work better than lipid nanoemulsions. In order to establish a successful delivery system, complete clarity regarding the in vitro and in vivo fate of the bits must be given.

3. Nanostructured Carriers Of Lipid (SLN & NLC)

SLNs have numerous significant drawbacks despite their efficiency and protection, such as a greater moisture concentration (70–99.9%), inadequate drug content due to crystalline form, drug ejection during preservation, and the possibility of polymorphism transitions and particle growth while storing. To meet these restrictions, the Solid Lipid Nanoparticles organization must be altered. The invention of a "2nd gen" of LNPs, the NLCs, at the turn of the millennium was the result of ongoing research.[10]

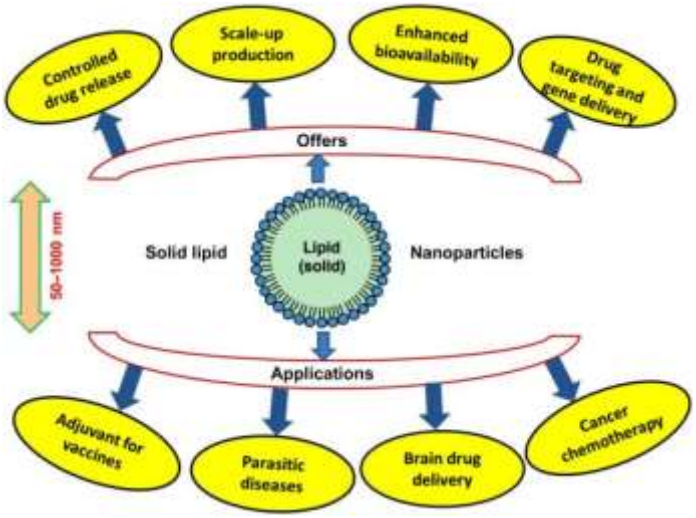

Figure 4: The Benefits and uses of SLN are depicted schematically. Adopted from.[10]

Solid Lipid Nanoparticles are expected to be at the forefront of nanotechnology innovation due to their wide range of potential applications and the short time span between discovery and commercial launch. Information now available indicates that, although medication loading with aquaphilic molecules is quite low, SLNs and NLCs were perfect for the integration of lipophilic compounds. Subsequent studies on the subject indicate that only highly potent aquaphilic medications with relatively small amounts of efficacy might be completely integrated into the solid lipid matrix.[10]

4. Medical Applications Of SLN

4.1. Cancer Chemoimmunotherapy

A drug known as tumor chemoimmunotherapy combines the beneficial effects of immunotherapy with chemotherapy. Chemotherapy typically involves the use of both novel molecularly targeted treatments and such conventional cytotoxic medications. Conversely, immunotherapy is a relatively new form of cancer treatment that uses the patient's own immune system to combat the cancerous cells. Immune checkpoint inhibitors, cancer vaccines, adoptive cell therapy, and cytokine treatments are among the things that are used.[11]

4.2. Nanoparticles Based On Lipids In Cancer Immunotherapy

Nanotechnology has drawn a lot of interest in cancer therapy because of its unique advantages. In order to carry therapeutics, such as small molecules (either hydrophilic or hydrophobic), proteins, and genetic materials for chemotherapeutic agents, nanoparticles, for example, such as polymeric micelles, lipid-based nanoparticles, gold nanoparticles, and

inorganic nanoparticles, are commonly used. By employing active targeting strategies like specific ligands or passively focusing techniques like the EPR impact, such nanoparticles can deliver therapeutic medications to particular cells. Particularly lipid-based nanoparticles have enticing pharmacological & multifunctional qualities, including the capacity to frighten both aquaphilic and aquaphobic medicines and biocompatibility and biodegradability.[12]

Additionally, lipid components or surface modifications can easily modify the surface properties of lipid-based nanoparticles. Some of those are currently in preclinical trials; some are included in Table 1 and include liposomes, nanodiscs, and hybrid lipid-based nanoparticles.[13]

4.3. Liposomes

Liposomes are nanosized particles that have demonstrated increases in directed payload distribution and biocompatibility with minimal injury. They are mostly made of cholesterol and phospholipids. Amphiphilic phospholipids self-assemble into a circular lipid bilayer shape with its lipid soluble ends, enclosing water-insoluble medications. On the other hand, the water-soluble head of phospholipids forms both an exterior surface and a watery center that may contain chemicals that are aquaphilic. Through interactions with chemical linkers on the liposomal surface or charge–charge interactions, a variety of therapeutic substances can be encapsulated into liposomes. One of the most successful uses of nanotechnology in the treatment of cancer is liposomes, which enable the administration of both lipid and water-soluble medicinal medicines while preserving effectiveness.[14]

Table 1: Lipid based nanoparticles in clinical trials.

Composition	Chemotherapy	Immunotherapy	Type of Cancer	Mode of Operations
Liposomes				
PEGylated liposomes	Doxorubicin	Alendronate	Breast cancer	i.v.
Charge-reversal cell penetrating peptide-modified liposomes	Paclitaxel	PD-L1 antibody	Melanoma	i.v.
pH-responsive liposomes	Mitoxantrone	Indoximod	Breast cancer and renal cancer	i.v.
Enzyme/pH dual-sensitive micelleliposomes	Paclitaxel	HY19991	Metastatic breast cancer	i.v.
Hybrid lipid-based nanoparticles				

Thermo-sensitive exosome-liposome hybrid nanoparticles	Docetaxel	GM-CSF	Metastatic peritoneal carcinoma	i.v.
Lipid-coated calcium nanoparticles	Zoledronate	Zoledronate	Lung cancer	i.v.
Liposome-coated mesoporous silica nanoparticles	All-trans retinoic acid + doxorubicin	IL-2	Melanoma	i.v.
Nano discs				
HDL-Nano disc	Doxorubicin	αPD-1	Colorectal cancer	i.v.
Docetaxel Colon	Cholesterol modified	CpG	carcinomas	Intra-tumoral

The FDA has authorized the use of more than six liposomal medications for the treatment of cancer, despite the fact that PEGylated liposomal DOX (Doxil®) was the first nano-drug to get FDA approval in 1995. Developing on the success of liposomes in chemotherapy, liposomes were employed as one of the most attractive targeted delivery systems in chemo-immunotherapy. Despite their considerable potential in clinical settings, liposomes are the most studied and first developed nanocarriers for the delivery of cancer drugs. However, their limited ability to accumulate and permeate the interstitial space within tumors severely limits the effectiveness of chemotherapy.[15]

4.4. Nano Disc

A phospholipid bilayer with the hydrophobic edge filtered by two amphipathic proteins known as membrane scaffolding proteins (MSP) is the basis of nano discs, a synthetic model membrane system. Higher-density lipoproteins' (HDL) main component, increased apolipoprotein A1 (apoA1), is the MSP in some nanodiscs. Comparable to discoidal HDL, the structure of nano discs mimics a more natural habitat than that of liposomes and micelles. This biomimicking delivery strategy seems more effective in immunotherapy. The substantial research on nano disc-based chemoimmunotherapy by Schwendeman's group is now complete. First, an HDL-mimicking nano-disc was made and a neoantigen (Ag peptide) and adjuvant (CpG) were applied to draining lymph nodes. In comparison to solubilized vaccinations, the nano-disc stimulated up to 47-fold more neoantigen-specific CTLs and 31-fold more than the clinical trial adjuvant. These results supported a new, effective cancer immunotherapy approach.[16]

4.5. Nanoparticles Based On A Hybrid Of Lipids

Flexible-configured lipid-based hybrid nanoparticles are attractive for chemoimmunotherapy. Multiple lipid-coated inorganic nanoparticles are being developed towards an efficient therapeutic dose. For chemo-immunotherapy, Kong et al. synthesized lipid-coated biodegradable hollow mesoporous silica nanoparticles (dHMLB) with co-encapsulated all-trans retinoic acid (ATRA). During chemo-immunotherapy, a lipid component of hybrid nanoparticles is also used as a dose form. To enhance cancer-localized chemoimmunotherapy, Zhang et al. developed TCNs for the synchronized bio-distribution and selective administration of SF & IMD-0354 to malignant cells & TAMs.[17]

5. Applications In Cancer Therapy

Particularly significant in BreC therapy are Lipid-Based NPs (LBNPs), a broad and diverse family of nanoparticles. However, liposomes are commonly used due to their high biocompatibility and capacity to encapsulate a variety of cargos, even aside from their diversity. Many studies are currently using LBNPs, and some of them (like Doxil® and Abraxane®) have a history of BreC treatment licenses. The most recent significant developments in LBNP therapy for the most prevalent cancer types are covered in this section.

5.1. Bowel Cancer

Due to its high mortality rate (bowel cancer is the second largest cause of death) and recent rise in incidence, bowel cancer is a serious health concern. LBNPs offer a potential means of enhancing current therapies, especially in advanced colorectal cancer patients who are not responding well to chemotherapy (5-FU alone or in combination with other medications) or monoclonal antibodies (cetuximab, trastuzumab, and bevacizumab). Thermosensitive gel-mediated 5-FU microemulsion (ME) was able to increase Caco-2 permeability and cell absorption, as well as its accumulation in rectal tissue in vivo, in contrast to the 5-FU ME. Low & Associates developed a complex apparatus based on Pickering emulsions (PE) that has a magnetic cellulose nanocrystal loaded with CUR and can release medication in a controlled manner when subjected to an external magnetic field.[18] This method prevented the growth of HCT116 cells in both monolayer and multicellular spheroids. Additionally it used high-intensity focused ultrasonic waves in conjunction with lipopolysaccharide (LPS) from attenuated Salmonella bacteria coated with DOX-thermosensitive liposomes to activate macrophages in the tumor environment. This strategy was able to improve DOX

internalization and decrease tumor formation in vivo by altering the fluidity of the membrane. Characterization of liposomes is also being used to improve CRC treatment. Consequently, used FoA to increase the absorption of 5-FU in CT-26 cells, hence decreasing its IC50 and decreasing the volume of the tumor. Imatinib mesylate (IM)-containing niosomes were developed to decrease the IC50 of the free drug in HCT-116 cells by a factor of 16.[19]

5.2. Stomach Cancer

It is the world's fifth most common cancer and the primary cause of cancer-related death. Surgery alone could be used to treat stomach cancer that hasn't progressed to the lymph nodes. Combination chemotherapy, which has serious side effects, should be used to treat severe stomach cancer.[20] Current research is looking into new medicines that use nano formulation to improve patient responses. In GC treatment, liposomes were widely used, either on their own or in conjunction with substances such as Arg-Gly-Asp peptides, SATB1 siRNA/CD44 antibodies, or DNA complex formation. Their application improved drug deposition in malignant cells of any animal transplanted with SGC7901 cells that had strong integrin 51 expression. antibodies against SATB1 siRNA/CD44, or in the assembly of DNA complexes.[21] When SGC7901 cells expressing large levels of integrin 51 were implanted into malignant cells of any animal, their use improved drug deposition 51. Additionally, liposomes demonstrated improved targeting precision and demonstrated an 80% reduction in SATB1 gene expression in CD44 þ GC beginning cells.[22] Moreover, liposomes suppressed the accumulation of GC MKN-45P cells in the liver by recognizing and distributing them throughout the peritoneum. In SGC-7901 cells, etoposide (VP16) boosted growth inhibition, caused cell arrests in the G2/M stage (17.13 percent), and triggered mitochondria-involved apoptosis, according to preliminary investigations utilizing SLNs in GC. For use in combination with ATRA, sorafenib, and miR-542-3p, Li et al. developed an SLN. By using this strategy, both anticancer medications were better absorbed and had a synergistic effect on MGC-803 cells.[23]

5.3. Breast Tumour

As the primary cause of death for women, it is undergoing substantial changes due to the introduction of NPs, most notably in the management of metastatic cancer. NEs preloaded with DOX and bromo tetra trandrine (W198, P-glycoprotein (P-gp) inhibitor) have been analyzed throughout the tolerant MCF-7/ADR cancer cell. This led to an increase in DOX cellular uptake and deposition in cancer cells. Conversely, DOX decreased heart and

gastrointestinal damage. On the other hand, clinical trials assessed compositions based on DOX liposomes.[24]

Recently, PLD and lapatinib have been used to determine the optimal combination of both treatments at the greatest tolerable dosage for HER2-positive BreC patients (stage Ib). Additionally, a phase 3 experiment including the combination of Myocet with either vinorelbine (MV) or cyclophosphamide (CM) in patients with cancer has been created. Another kind of LBNP used in BreC research are SLNs. A technique for combining PTX with derivatized DNA delivery with such a pH-sensitive ligand was proposed. This method reduces the volume of the tumor in vivo and lowers the amount of PTX that is deposited in all other organs. Moreover, developed a fucose-methotrexate SLN that, in contrast to free methotrexate, which accumulates throughout the kidney, liver, and spleen, accumulated preferentially in tumor tissue as soon as two hours after therapy.[25]

5.4. Glandular Carcinoma

At the moment, NEs, liposomes, and solid-lipid NPs (SLNs) (PrC) are the main LBNPs being researched as possible therapeutic approaches for prostate cancer. Recently, developed an oil-in-water NE that contains a medicinal drug connected to an omega-3 fatty acid that is toxoid. When compared to AbraxaneTM, NE is more effective in reducing the toxoid IC50 of PPT2 cell types by a factor of twelve, allowing for a greater decrease in tumor size in rats carrying tumors. Similar antitumor effects were observed in PC-3 cells when NE was loaded with catechin extract (flavanols with anticancer properties). In terms of liposomes, PEG-folate-targeted-oleuropein-liposomes were applied to 22Rv1 PrC cells. These nanoplatforms improved the survival, oleuropein bioavailability, and apoptosis of 22Rv1 cells in in vivo models .also produced NPs with a gold nanorod and diverse liposome loaded with docetaxel, exhibiting 100% inhibition of PrC cell growth by combining the method with radiation. Additionally, there are several applications in all other forms of cancer, such as pancreatic, liver, lung, and nervous system cancers. Many changes have been made recently, and freshly created nanoparticles are being used to treat cancer.[26]

5.5 Liver Cancer

A primary liver cancer, hepatocellular carcinoma (HCC) is one of the most prevalent cancers in the world. Since the 1990s, HCC has been the primary cause of China's second-highest cancer-related death rate. Globally, HCC has the third-highest mortality rate among all cancer-related disorders. The liver is the most common organ where tumor metastases arise in

addition to original malignancies. Stabilized lipid coated lipoplexes were proposed by Bartsch et al. (2004) to transport antisense oligonucleotide (AS-ODN) to liver endothelial cells both in vitro and in vivo.[27]

5.6 Lung Cancer

One of the main causes of death in the globe is lung cancer. "Non-small cell lung cancers" (NSCLCs) are adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma, which together account for the majority of lung malignancies. Surgery is usually the first line of treatment for patients with early-stage NSCLC; 5-year survival rates vary from 25% to 80%, depending on the disease stage. The inability of current lung cancer treatments to cure scattered tumors at a level of toxicity that is tolerable has resulted in low success rates. changes in the p53 gene are typically responsible for lung malignancies. These changes can result in increased drug resistance, decreased ability to repair mutations, increased tumor angiogenesis, cell proliferation, and suppression of apoptosis. Therefore, gene therapy is an alternate approach that has demonstrated potential in the treatment of lung cancer. Viral and non-viral vectors are the two primary types of vectors used in gene delivery. Concerns about viral vectors' immunogenicity and toxicity have sparked a lot of interest in non-viral gene delivery techniques.[28]

Biodegradable nanoparticles have demonstrated their superiority over other non-viral vectors due to their enhanced stability and regulated release capabilities. Generally, there are two types of nanoparticles used in gene delivery systems: cationic and anionic nanoparticles. In order to create stable polymer/lipids-DNA complexes, cationic nanoparticle systems take use of the ionic interaction between cationic polymers and anionic plasmid DNA. Solid lipid nanoparticles (SLNs), which are cationic lipid formulations, are becoming more and more popular as promising colloidal carrier systems. It was suggested that p53 gene/cationic lipid complexes could be used as an alternative to viral delivery systems in the treatment of early endobronchial carcinoma. Cationic lipids have a lower efficacy than viral vectors, but they might be more advantageous when administered over an extended period of time to several tumor sites spread across the bronchial epithelium. Furthermore, the majority of nonviral gene delivery strategies under consideration exhibit little immunogenicity.[29]

5.7 Brain Tumor

SLN is among the most well-characterized lipid-based nanoscale compounds created for the delivery of drugs to brain tumors. Solid physiological lipids are micro-emulsified or homogenized at high pressure to create these nanoparticles. Though the precise process by which SLNs traverse the BBB and BTB remains unclear, endothelial cells' endocytosis of SLNs is thought to be the mediator of internalization. The adsorption of circulating plasma proteins to the surface of the SLN is assumed to promote the process of endocytosis. Drugs can be loaded and shielded from degradation by the lipid matrix of SLN. Depending on the SLN's surface coating and the lipids that make up its composition, the unloading of medications within target tumor tissues can also be managed.[30] The transportation of medications across the blood-brain barrier was achieved, in particular, by coating the nanoparticles with polysorbate (Tween) surfactants. Brain tumor identification, both preoperatively and intraoperatively, could be revolutionized by SLN. According to estimates, the annual incidence of primary brain tumors in the US is roughly 43,800. Ever since it was suggested to use nanotechnology for glioma imaging. The use of nanodevices in brain tumor diagnosis and treatment has grown significantly in recent years. Many other ways to target nanoparticles have been described, including as peptides, cytokines, medications, antibodies, and ferromagnetic compounds.[31] When given systemically, the reticuloendothelial system quickly removes nanoparticles. This procedure entails the opsonization of nanoparticles, macrophage phagocytosis, and hepatic and splenic absorption. The reticuloendothelial system's ability to clear nanoparticles can be hindered in part by hydrophilic molecules adhering to their surface. However, often used substances like pluronic or polyethylene glycol that are used to provide a hydrophilic coating might also be pro-inflammatory or immunogenic. The harmful effect of nanoparticles (about 200 nm) on cerebral endothelial cells showed that passage of the BBB was conceivable, however this was refuted in another investigation for identical nanoparticles (about 300 nm). Additionally, a different kind of nanoparticle did not exhibit this impact. medication transport into the brain required a physical bond between the medication and the nanoparticles. Additionally, studies of manganese in various brain regions have demonstrated that additional SLN, such as manganese oxide, translocate to the brain via the olfactory route.[32]

5.8 Nanoparticle And Quantum Dot For Cancer Treatment

By using nanotubes, liposomes, dendrimers, and polymers, the application of nanoparticles in cancer research has recently enhanced medication transport, targeting, and diagnostics. A

sophisticated substitute for the conventional bioimaging instruments, other nanoparticles, including quantum dots, have outstanding photophysical characteristics. As a tool for biomedical and bioanalytical imaging, quantum dots represent one of the fastest-growing nanotechnology products. Application in different biological models is appropriate due to their superior photophysical and occasionally multifunctional surfaces.[33] There are now intriguing uses for semiconductor quantum dots and nanoparticles made of metals, lipids, or polymers in the early detection and treatment of cancer. Cadmium-containing semiconductors are a common component of quantum dots, which have special optical properties. Although toxicity of such quantum dots to humans and living cells has not yet been thoroughly studied, cadmium poses a possible risk. It is therefore of great interest to look for less hazardous materials with comparable targeting and optical capabilities.[34]

Over the past few decades, there hasn't been much of a change in the prognosis for patients with malignant gliomas, despite advancements in neurosurgery and radiation therapy. To minimize tissue damage during cancer treatment, precise delivery of ionizing radiation is essential .The development of photosensitizing quantum dots to produce radicals upon absorption of visible light has been the subject of some study recently. Despite the safety of visible light, this method is only effective for treating superficial tumors. Future developments in quantum nanotechnology may completely change a number of facets of brain tumor diagnosis and treatment.[35]

5.9 Radionuclide Nanoparticles For Cancer Treatment

Additionally, highly effective radiation therapy is being made possible by nanotechnology. For example, injecting single doses of an atomic nanogenerator at kilobecquerel (nanocurie) levels into mice with solid prostate carcinoma or disseminated human lymphoma has been shown to induce tumor regression and prolong survival without causing toxicity in a significant portion of the animal population. In a different study, it was demonstrated that when near infrared light is applied to metal nanoshells with adjustable optical resonance, tumor cells suffer irreversible thermal damage. The majority of small molecules used in targeted radionuclide therapy clinical trials today—such as antibodies and smaller peptides—are used for both targeting and delivery, or the pair biotin/avidin that has been radiolabeled .Improved internal radionuclide therapy could be achieved by employing various carrier materials, such as liposomes, dendrimers, and other structures with diameters on the order of

several nanometers, that have larger radioactive loading and differ in their in vivo behavior.[36]

5.10 Magnetic Nanoparticles For Cancer Treatment

As the next generation of magnetic resonance imaging (MRI) contrast agents, magnetic nanoparticles (MNPs) are being intensively studied as drug delivery vehicles with specific targeting. MNPs have been thoroughly tested as therapeutic tools for the targeted administration of drugs by magnetic drug targeting and active targeting by attaching high affinity ligands. Using a mouse xenograft model, Huh et al. (2005) recently reported the utilization of superparamagnetic iron oxide (SPIO) nanoparticles for cancer in vivo detection. The nanoparticles in this study were coupled to the cancer-targeting antibody herceptin. SPIO nanoparticles were used by Harisinghani et al. (2003) in human prostate cancer patients to identify minor lymph node metastases. In this instance, dextran coating was applied to the nanoparticles to help them stay in the bloodstream and gradually enter the lymph nodes, where macrophages absorb them. MNPs have been thoroughly studied as MRI contrast agents to enhance solid tumor detection, diagnosis, and treatment planning. Lesions as small as 2-3 mm can now be distinguished by clinical imaging of liver cancers and metastases using the reticulo-endothelium system-mediated absorption of SPIOs. The improvement of brain tumor boundary delineation and tumor volume quantification is another clinical use of ultra superparamagnetic iron oxide MNPs under assessment.[37]

5.11 Future Trends

Because of the effective integration of active ingredients and the associated advantages, SLN make up a desirable colloidal drug carrier system. Even though the majority of technological advancements have been on delivering individual chemotherapeutic medicines to tumors, it is becoming more and more obvious that an integrative strategy may be more effective than a reductionist one. Platforms based on nanotechnology can fill a special need in this market by allowing multimodal distribution with a single application. SLNs can be used to target drugs, however the drug must release once it reaches the desired sick spot in the body. Therefore, biodegradable nanoparticle formulations are required for drug delivery since the medicine must be released and transported in order to be effective. It's interesting to note that until recently, pharmaceutical sciences did not recognize that carrier systems themselves may offer hazards to patients. Instead, they were using nanoparticles to lessen the toxicity and adverse effects of medications. However, we think that more and more treatments and diagnostics

based on nanotechnology will certainly make their way into clinical practice over the course of the next few years.

Figure 5: Studying with solid lipid nanoparticles for drug carriers: benefits, present obstacles, and limits. Adopted from.[38]

6. CONCLUSION

Lipid-based nanoparticles are an extensive and diverse class of substances that have been used to cure a number of illnesses, the most common of which being cancer. These days, liposomes are the most commonly used lipid. Based Nanoparticles due to their superior biocompatibility and flexibility; yet, SLNs and NLCs have recently become more well-liked. However, research on these particular nanoparticles is not the main focus; instead, a number of publications highlight cutting-edge methods for employing lipid-based nanoparticles to treat other types of cancer. A portion of it has already advanced to the next level and started new jobs in clinical research. In the last ten years, SLNs and nanostructured lipid carriers have drawn a lot of attention as potential drug delivery (nano)systems.

Using biomaterials could be one's primary advantage, as it's environmentally Figure 5: Advantages, current challenges, and limitations of investigating solid lipid nanoparticles as therapeutic carriers. Taken from[38] safe production methods and components (Figure 5). But it definitely should be emphasized that thorough clinical and environmental safety investigation has to be completed before these systems are mass produced and distributed. It is thought that standardized procedures for evaluating the risks associated with the use of nanomaterials and the related regulatory framework must be established. Similar to other Because of the direct and indirect attacks caused by malignant cellular level, melanoma therapy, an important research area in which SLNs can be used, may also represent both a high level of funding in the field as well as the appropriateness of nanostructures for such delivering of cytotoxic drugs. However, the use of lipid nanoparticles is beneficial in many

clinical fields. Unfortunately, more study, more effort, and working capital facilities are needed before SLN/NLC may be demonstrated to be therapeutically helpful in real-world situations. As of right now, the scarcity of SLNs that have progressed to medical research indicates that it will take at least a few years before such advancements reach the national or international stage. pharmaceutical industry.[39]

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