International Journal on Science and Technology (IJSAT)
E-ISSN: 2229-7677 ● Website: www.ijsat.org ● Email: editor@ijsat.org

# A Review article on Lipid nanoparticles for targeting Anti - Tumor Drugs

**Bhakti Pandey[1], Anubhuti Ananta[2], Anubhuti Mishra Kartik Choudhary[3], Kashish Dayal[4]**

[1,2,3,4]IIMT college of pharmacy, Knowledge Park III, Greater Noida, Uttar Pradesh 201310

**Abstract**

Researchers were always coming up with new nanotechnologies to fill in gaps in the right delivery of therapeutic medications and imaging agents for Tumor therapy and diagnostics. Lipid nanoparticles, or LNPs, are acceptable particulates that are extracted from different lipids and other biochemical compounds. Their overall function is to dissolve biological barriers, or biobarriers, which enables LNPs to collect again in a specific location outside of disease-target cells for responsive therapeutics. LNPs are roughly 100 nm in size. The majority of substances with significant medicinal applications were either poisonous or insoluble in aqueous solutions, or they were unstable both chemically and physiologically. Lipid-based nanoparticles, or LBNPs, are among the most promising medication delivery systems for bioactive organic molecules. Because of its current use in chemotherapy, some chemotherapeutics have a stronger antitumor impact, revolutionizing Tumorcurement. LBNPs offer excellent temporal and thermal stability, maximum load potential, ease of preparation, low manufacturing costs, and large manufacturing output since they may be produced utilizing naturally existing sources. Additionally, combining chemotherapeutic medications with LNPs decreases curement resistance, minimizes toxicities associated with active therapeutic dosages, and increases drug concentrations in tumor cells while decreasing concentrations in normal tissue. LBNPs have been extensively researched for their potential to cureTumor, both in vivo and in vitro, with promising results in certain clinical studies. An overview of the several LBNP varieties that have been created recently, as well as their uses and contributions to various Tumorlikes, are given in this paper.

**Keywords:** -Nanotechnologies, Lipid Nanoparticles, Tumor therapy, Diagnostics, Medication delivery system, Lipid-based nanoparticles.

## 1. Introduction

A like of disease known as a tumor is characterized by abnormal cell growth that can spread to other cells or bodily parts. Out of more than 100 different types of Tumor, it is one of the deadliest (1). Fifteen percent of Tumors in developing countries are caused by infections with Epstein-Barr viruses, H. pylori, hep C, hpv, hbv, and HIV (2). These factors work, at least partially, by changing the genes within a cell. Before Tumor begins, several genetic changes are often required (3). In 5–10% of instances, inherited genetic defects are the cause of Tumor(4). Medical testing and a variety of symptoms & indicators may assist in identifying Tumor. After that, it would typically be investigated further by diagnostic imaging and confirmed by a biopsy (5). Roughly 90.5 million people had Tumor diagnoses in 2015 (6). In 2019,

there were around 18 million new cases reported annually (7). It was held accountable for over 8.8 million fatalities annually (8). The four general types of Tumor in males are colorectal, stomach, lung, and prostate Tumor(9).

The four general types of Tumor in women are colorectal, lung, cervical, and breast Tumor(9). If all new Tumor cases had been included, skin Tumors other than melanoma would have accounted for around 40% of Tumor cases per year (10,11). Except for Africans, who are more likely to get non-Hodgkin Tumor, acute lymphoblastic and brain Tumor seem to be the most general in children (12). It seems that "fat" is another word for "lipid." Lipids seem to be a substance that dissolves in alcoholic, (C2H5)2O, and chcl3 solutions but are insoluble in water (13). A vital component of human cells is lipids. Plant and animal cells were mostly made up of lipids, proteins, and Cx (H2O)y.

Lipids include cholesterol and triglycerides. Lipids enter the system quickly and stay there. It is crucial to the makeup of cells and acts as a reference for energy. lipids that have combined with another like of chemical molecule to form a complex. Lipids may be classified as either amphiphilic or aquaphobic small molecules. Their amphiphilic nature allows us to develop a variety of structures in aquatic environments, such as membranes, huge uniflagellar liposomes, and vesicles. Figure 1 displays the structure of SLN, liposomes, and lipid emulsion.

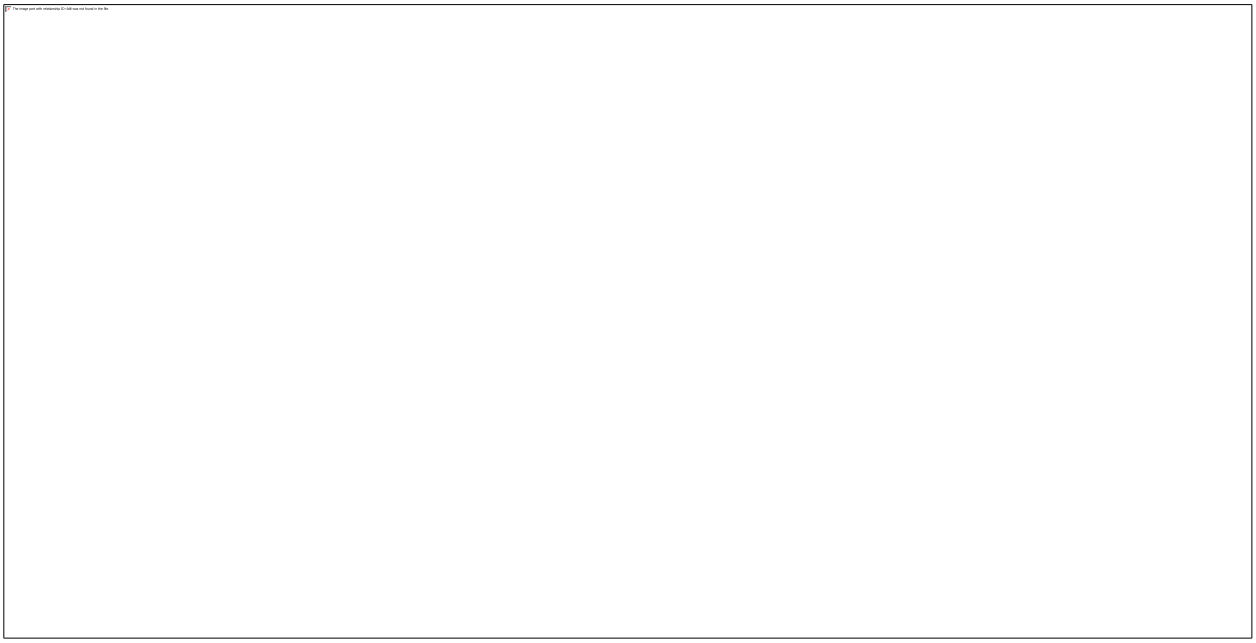

**Figure 1:- Schematic representation of the general configuration of solid lipid nanoparticles, which are superior than lipid emulsions and liposomes.**

Since the start of the pharmaceutical era, lipids have drawn a lot of interest due to their biocompatibility as transporters. Their very hydrophobic nature results in little oral absorption (14). Due to the unfulfilled desire to broaden the spectrum of uses for these carriers, they were encased in colloidal delivery systems and were not used in propulsion systems until 1900 (15–18). When developing nanoparticle-based delivery systems, lipid nanoparticles were shown to be more benefitsous than polymeric nanoparticles, and this is why they are often used in drug delivery (19). These lipid-based carrier systems are also known as "Nano safe" carriers as LNPs are composed of physiologic and/or biodegradable lipids (20).

Solid lipid nanoparticles (SLNs), which were created in the early 1990s, are a very effective LNP synthesis (21). This delivery approach was established because of the benefitss of earlier carriers such as liposomes, emulsifiers, and polymeric nanoparticles (22). The features that set apart SLNs from liposomes include the absence of polar compounds, the GRAS quality of all formulations, and the viability of the manufacturing processes and leveling-up process (23).

Recently, tumor nanotechnology has been created as a possible Tumor therapy approach for the delivery of antiTumor drugs (24). With sizes ranging from 1 to 1000 nm, nanoparticles improve the selectivity of antiTumor drugs and their therapeutic bioavailability (25). Figure 2 illustrates the several nanoparticles (NPs) and nanotech approaches to Tumortherapies that have lately been reported. Electronically confined symmetric intensity distribution, wide excitation spectrum, and unique optical properties make semiconductor quantum dots (QDs) a promising versatile material system for biological applications. A fascinating new class of fluorescent components in semiconductor QDs. They are used in applications such as biosensing, biolabeling, and bioimaging. QDs are more effective than regular fluorophores. They are less photobleached, brighter, and more controllable in terms of fluorescence intensity. A single light source may excite different colored QDs, which have narrow emission spectra and large absorption spectra. For screening cell receptors, the aforementioned QDs seem to be the best option. It is necessary to modify the surface of QDs using different biological materials to produce efficient fluorescence probes (26).

We highlight the lipid-based nanoformulations (Figure 2) among the many others used in Tumorcurement since significant advancements in preparation and alternative compositions have been made in recent years. Lipid nanosystems may be chemically modified to avoid immune system detection or to improve drug availability. These may 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) (27). It may be possible to use nanoparticle medications in addition to conventional therapy modalities to improve patient response.

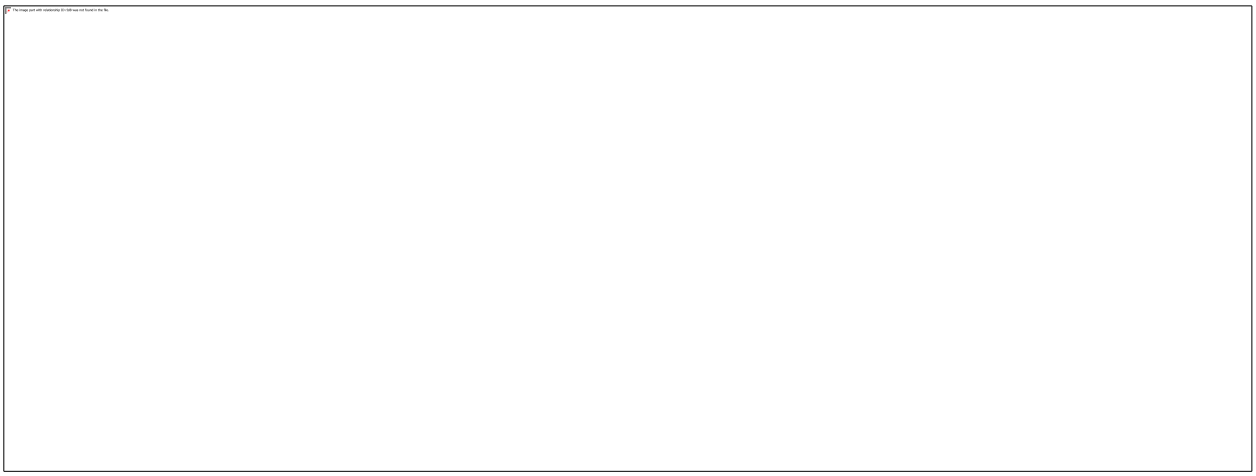

**Figure 2:- Several tools based on nanotechnology are used in the curement of Tumor.**

Many antitumor medications have previously been examined in nano-formulations. A number of these medications have also been studied in clinical trials and/or are available commercially for use in medicine (28).

## 2. Solid lipid nanoparticle

The hard size range for them is 1–1000 nanometers. Particle sizes typically range from 150 to 300 nanometers. Solid submicronic colloidal nanocarriers (SLNs) vary in size from 1 to 1000 nm. The majority of the particles range in size from 150 to 300 nm. Polymeric nanoparticles, for example, are drug delivery techniques that provide a framework for controlled releases (29). The solid SLN matrix enables them to combine the benefitss of polymeric nanoparticles, liposomes, and micronized emulsifiers by limiting medicine movement and providing im stability (30). Additionally, testing reveals that SLNs were very beneficial in several areas, including the avoidance of using organic solvents during manufacture, potential scaling (31), and the inclusion of both lipophilic and hydrophilic medications in sizable amounts (32). The liquid lipid (oil) in an oil-in-water emulsion is changed to a solid lipid (or possibly a mixture of solid lipids) to form SLNs. The fact that SLNs are solid at body temperature as well as ambient temperature is a crucial characteristic (33). These drug delivery systems consist of solid lipids ranging from 0.1 to 30% (w/w) distributed in an aqueous medium. Solid-form lipids, such as complex glyceride blends, free fatty acids, free fatty alcohols, and even wax (usually well-known physiological lipids), make up the majority of SLNs (34). Using more intricate structures is also possible (35).

### 2.1. Limitations of SLN and ways to overcome

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

### 2.2.Drug deterioration caused by high-pressure

Drug degradation primarily results from alterations in molecular size and structure. Additionally, consistent high pressure has been proven to reduce the molecular weight of polymers. Although multiple investigations affirm that the majority of bioactive metabolites are not adversely affected by drug degradation induced by high-pressure homogenization, larger molecular weight compounds or those with extended chain lengths exhibit greater susceptibility compared to smaller spherical molecules. Nevertheless, incorporating high molecular weight substances such as albumin, dextrose, and DNA into solid lipid nanoparticles (SLNs) demands a distinct approach due to their heightened vulnerability to breakage.

### 2.3.Drug incorporation and lipid crystallization

Lipid crystallization is a further important consideration. Researchers have been examining the connection between pharmaceutical administration and cholesterol modification over the last ten years. It is well-known that lipid alterations are studied. X-ray and differential scanning calorimetric measurements are the main techniques used. However, research on large amounts of lipids has provided the bulk of the data. Lipid particle characteristics are thus influenced by drug inclusion and lipid crystallization. The prevalence of supercooled melts, the occurrence of numerous lipid modifications, the shape of lipid nanodispersions, and gelation processes are all significant factors to take into account when addressing drug capture inside SLNs.

### 2.4. Multiple coexisting colloidal species

Despite being an important issue to solve, researchers have not given much attention to the cohabitation of several nanoparticles inside SLNs. Surfactants are integrated into the lipid inside as well as its surface. Heterogeneous micelles must be taken into account in systems stabilized by glycocholate/lecithin and similar ones. Micelles, liposomes, and mixed micelles can dissolve medications, making them suitable for use as alternative therapeutic inclusion targets. For example, hydrolytic drugs break down more quickly in dissolved water and interface localized molecules than in lipid-based compounds. Increasing the matrix thickness naturally lowers the drug's diffusion coefficient within the transporter, which is why SLNs are expected to work better than lipid nanoemulsions. Good delivery mechanisms need complete transparency on the in vitro and in vivo fate of the bits.

## 3. Nanostructured carriers of lipid

SLNs have several significant drawbacks despite their efficiency and protection, such as a greater moisture concentration, low drug content due to crystalline shape, drug ejection during preservation, and the possibility of polymorphism transitions and particle growth during storage. To meet these restrictions, the Solid Lipid Nanoparticles organization must be altered.

The invention of a "2nd gen" of LNPs, the NLCs, around the turn of the century, was the result of ongoing research (29). The first NLC ideas were then created by Dr. Rimpler of Wedemark, Germany. These were Nano repair Q10 cream, Nano repair Q10 serum, and Nano lipid CLR restore from ChemischesLaboratorium in Berlin, Germany. Solid Lipid Nanoparticles are expected to be at the forefront of nanotechnology innovation due to their wide range of potential applications and the short period between discovery and commercial launch (36). Although medication loading with aquaphilic molecules is quite low, the available data indicates that SLNs & NLCs were perfect for the integration of lipophilic compounds (37). According to preliminary studies on the subject, only very potent aquaphilic medications with low levels of effectiveness may be completely integrated into the solid lipid matrix (38).

## 4. Medical application of SLN

### 4.1.Tumor chemoimmunotherapy

A drug known as tumor chemoimmunotherapy combines the beneficial effects of immunotherapy with chemotherapy. Chemotherapy often involves the use of both novel molecularly targeted therapies and conventional cytotoxic medications. Conversely, immunotherapy is a relatively new line of Tumorcurement that uses the patient's immune system to combat Tumor cells. Immune checkpoint inhibitors, Tumor vaccines, adoptive cell therapy, and cytokine curements are among the things that are employed.

### 4.2. Lipid-based nanoparticles for Tumor immunotherapy

Nanotechnology has drawn a lot of attention in Tumorcurement because of its unique benefitss(39). For example, polymeric micelles, lipid-based, gold, and inorganic nanoparticles are all examples of

nanoparticles. Nanoparticles are widely used in the transportation of therapeutics, such as hydrophilic or hydrophobic small molecules, proteins, and genetic materials for chemotherapeutic agents. By employing active targeting strategies like specific ligands or passively focusing methods like the EPR impact, such nanoparticles may deliver therapeutic medications to certain cells (40).

Particularly lipid-based nanoparticles offer enticing pharmacological & multifunctional qualities, including the capacity to frighten both aquaphilic and aquaphobic medicines and biocompatibility and biodegradability (41–43). Furthermore, by modifying the surface or lipid components, lipid-based nanoparticles' surface properties may be easily modified. Some of them are included in Table 1 and are now undergoing preclinical trials. Examples of these include liposomes, nanodiscs, and hybrid lipid-based nanoparticles.

**Table 1:- Various types of novel drug delivery method for cancer.**

| Composition | Chemotherapy | Type of Tumor | Mode of operations | References |
|---|---|---|---|---|
| PEGylatedliposomes | Doxorubicin | BreastTumor | i.v. | (44) |
| Charge-reversalcellpenetratingpeptide-modifiedliposomes | Paclitaxel | Melanoma | i.v. | (45) |
| pH-responsiveliposomes | Mitoxantrone | BreastTumorandrenalTumor | i.v. | (46) |
| Enzyme/pHdual-sensitivemicelle-liposomes | Paclitaxel | MetastaticbreastTumor | i.v. | (47) |
| Thermo-sensitiveexosome-liposomehybridnanoparticles | Docetaxel | Metastaticperitonealcarcinoma | i.v. | (48) |
| Lipid-coatedcalciumnanoparticles | Zoledronate | LungTumor | i.v. | (49) |
| Liposome-coatedmesoporoussilicananoparticles | All-transretinoicacid þdoxorubicin | Melanoma | i.v. | (50) |
| HDL-Nanodisc | Doxorubicin | ColorectalTumor | i.v. | (51) |
| | DocetaxelColon | carcinomas | Intra-tumoral | (52) |

**4.3.Liposomes**

Liposomes are nanosized particles that have shown increases in directed payload distribution and biocompatibility with little 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 outside surface and a wet center that may include compounds that are aquaphilic. Through interactions with chemical linkers on the liposomal surface or charge-charge interactions, a variety of therapeutic substances may be encapsulated into liposomes. One of the most potent nanotech pharmaceuticals for cureingTumor is liposomes, which enable the administration of both lipid and water-soluble therapeutic agents while retaining efficacy. While PEGylated liposomal DOX (Doxil®) was the first nano-drug ap by the Food and Drug Administration in 1995, the FDA has authorized the use of over six liposomal medications for the curement of Tumor. Based on liposomes' efficacy in chemotherapy, liposomes were used as one of the most alluring targeted delivery systems in chemo-immunotherapy. Although liposomes have shown considerable promise in clinical applications, their limited accumulation and penetration into the tumor interstitial space considerably reduces their therapeutic effectiveness (53). Liposomes are the first and most studied nanocarriers for Tumor medication delivery.

### 4.4.Nano disc

Membrane scaffolding proteins (MSP) are a pair of amphipathic proteins that filter the hydrophobic edge of a phospholipid bilayer, creating nanodiscs, a synthetic model membrane system. Apolipoprotein A1 (apoA1), the main building block of high-density lipoproteins (HDL), is elevated in certain nanodiscs. Compared to liposomes and micelles, the geometry of nanodiscs is similar to discoidal HDL, which mimics a more natural habitat. This biomimicking delivery approach seems to work better in immunotherapy. A comprehensive study on nanodisc-based chemoimmunotherapy was conducted by Schwendeman's group. Initially, they created an HDL-mimicking nano-disc and used an adjuvant (CpG) and neoantigen (Ag peptide) to adhere it to draining lymph nodes. Up to 47 times more neoantigen-specific CTLs were induced by the nano-disc than by solubilized vaccinations and 31 times more than by the clinical trial adjuvant. These results validated a new and effective approach to Tumor immunotherapy (54).

### 4.5.Lipid hybrid-based nanoparticles

Flexible-configured lipid-based hybrid nanoparticles are attractive for chemoimmunotherapy. Multiple lipid-coated inorganic nanoparticles are being created 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) (51). During chemo-immunotherapy, a lipid component of hybrid nanoparticles is also used as a dose form. To enhance Tumor-localized chemoimmunotherapy, Zhang et al. created TCNs for the synchronized bio-distribution and selective delivery of SF & IMD-0354 to malignant cells & TAMs (55).

## 5. Tumorcurement applications

BreCcurement makes use of a large and diverse class of nanoparticles called Lipid-Based NPs (LBNPs) in particular (56). Apart from their variety, liposomes are used extensively due to their excellent biocompatibility and capacity to encapsulate a variety of cargo. Many studies are now using LBNPs, and some of them (like Doxil® and Abraxane®) have already received licenses for BreCcurement(8). The

most recent significant developments in the use of LBNPs in the management of the most prevalent Tumor types are covered in this section.

### 5.1.Tumor of the bowel

Due to its high mortality rate (bowel Tumor is the second largest cause of death) and the recent rise in occurrence, bowel Tumor is a serious health issue (57,58). LBNPs provide a potential means of enhancing current therapies, especially in cases of advanced colorectal Tumor when monoclonal antibodies (cetuximab, trastuzumab, and bevacizumab) or chemotherapy (5-FU alone or in conjunction with other medications) are not working. A 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 a 5-FU thermosensitive gel-mediated microemulsion (ME).

A complex device based on Pickering emulsions (PE) was created by Low et al. (59). It is composed of a magnetic cellulose nanocrystal that has been loaded with CUR and may release medication in a controlled manner when subjected to an external magnetic field. This method prevented HCT116 cells from developing in both monolayer and multicellular spheroids. Moreover, lipopolysaccharide (LPS) from attenuated Salmonella bacteria coated with DOX-thermosensitive liposomes and high-intensity focused ultrasonic waves were employed by Ektate et al. (60) 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. To improve CRC curement, liposome characterization is also being used. Consequently, Moghimipour et al. 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 created by Kaseem et al. ; in HCT-116 cells, these niosomes reduce the IC50 of the free drug by 16 times(61,62).

### 5.2.Tumor of the stomach

It is the fifth most generalTumor in the world and the leading cause of Tumor-related death (57). The only stomach Tumor that can be cureed with surgery is if it hasn't progressed to any lymph nodes. Curement for severe stomach Tumor should include combination chemotherapy, which has serious side effects.

To improve patient responses, novel medicines based on nano formulation are now being investigated. Liposomes were widely used in GC curement, either on their own or in conjunction with substances such as SATB1 siRNA/CD44 antibodies (63), Arg-Gly-Asp peptides (64), or DNA complex formation (65). When SGC7901 cells expressing large amounts of integrin 51 were implanted into malignant cells of any animal, their usage im drug deposition 51 (64). Additionally, liposomes demonstrated im targeting precision and demonstrated an 80% reduction in SATB1 gene expression in CD44 þ GC beginning cells (63). Moreover, liposomes recognized GC MKN-45P cells that were disseminated peritoneally, which reduced their accumulation in the liver. According to preliminary research utilizing SLNs in GC (66), etoposide (VP16) exhibited enhanced activity in SGC-7901 cells, leading to higher growth inhibition, cell arrests in the G2/M stage (17.13 percent), and mitochondria-involved apoptosis.

An SLN was created by Li et al. (70) to be used with miR-542-3p, ATRA, and sorafenib. This technique had a synergistic effect on MGC-803 cells and enhanced the uptake of both antiTumor medications.

### 5.3.Tumor of the breast

It is the primary cause of death for women and is going through major changes as a consequence of NP progress, most notably in the curement of Tumor that has spread. NEs preloaded with DOX and bromo tetra trandrine (W198, P-glycoprotein (P-gp) inhibitor) have been analyzed throughout the tolerant MCF-7/ADR Tumor cell. This led to an increase in DOX's cellular uptake and deposition in Tumor cells. Conversely, DOX decreased heart and gastrointestinal damage (67). On the other hand, clinical trials assessed compositions based on DOX-liposomes.

Recently, PLD and lapatinib have been used to determine the optimal combination of both medications at the greatest tolerable dose for HER2-positive BreC patients (stage Ib) (68). Additionally, a phase 3 experiment including the combination of Myocet with either vinorelbine (MV) or cyclophosphamide (CM) in patients with Tumor has been created (69).

Another like of LBNP used in BreC research is SLNs. A technique for combining PTX with derivatized DNA delivery with such a pH-sensitive ligand was proposed by Yu et al. (70). This method reduces the volume of the tumor in vivo and lowers the amount of PTX that is deposited in all other organs. In addition, Garg et al. (71)created 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.

### 5.4.Glands Tumor

NEs, liposomes, and solid-lipid NPs (SLNs) (PrC) are the main LBNPs that are currently being researched as possible prostate Tumor therapeutic options. Recently, Ahmad et al. (72)created an oil-in-water NE that contains a therapeutic toxoid agent connected to an omega-3 fatty acid. 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 reduction in tumor growth in rats carrying tumors. Similar antitumor effects were seen in PC-3 cells when catechin extract (flavanols with antiTumor properties) was fed into NE (73). PEG-folate-targeted oleeuropein liposomes were used to cure 22Rv1 PrC cells in terms of liposomes.

These nanoplatforms im the survival, bioavailability, and apoptosis of 22Rv1 cells in in vivo models (74). By combining the method with the application of radiation, Hua et al. (75) also produced NPs that include diverse liposomes loaded with docetaxel and a gold nanorod, exhibiting 100% inhibition of PrC cell growth. Additionally, there are several applications in all other forms of Tumor, such as pancreatic, liver, lung, and nervous system Tumors. Many changes have been made recently, and freshly created nanoparticles are being used to cureTumor.

## 6. Recent research in this field

### 6.1.Chondroitin/Lactoferrin-dual functionalized pterostilbene-solid lipid nanoparticle

For women, breast Tumor continues to be the primary cause of Tumor-related death. Thus, research into cutting-edge curement strategies—including phytotherapeutics—is essential. One phytochemical compound that shows promise in the fight against breast Tumor is pterostilbene (PTS). Some significant issues that impair PTS functioning include poor solubility, limited bioavailability, and chemical instability. This work presents the synthesis of new PTS-loaded solid lipid nanoparticles via ultrasonication. As an active-targeting strategy, dual-functionalization using lactoferrin (Lf) and chondroitin-sulfate was used. The effectiveness of CS/Lf/PTS-SLNs was confirmed in an orthotopic Tumor model by in vivo anti-tumor efficacy, which resulted in a 2.4-fold reduction in tumor development when compared to PTS-solution. In comparison to PTS-solution. Additionally, CS/Lf/PTS-SLNs had a greater anti-tumorigenic impact in comparison to PTS-solution, as shown by an immunohistochemistry experiment. According to our research, CS/Lf/PTS-SLNs represent a potentially useful nano platform for phytotherapeutic targeted breast Tumorcurement(76).

### 6.2.Im Anti-Tumor activity of encapsulated geraniol into a biocompatible lipid nanoparticle

Plant and herb essential oils include GOH, and linear monoterpene alcohol with a variety of pharmacological characteristics, including antiTumor potential. To create effective carrier systems, GOH stability, administration, and bioavailability under physiological settings should be enhanced due to its low water solubility and volatility. To enhance its antiTumor efficacy, GOH was encapsulated into nanostructured lipid carriers (NLC) using a new technique. A Zeta potential of around −10 mV, a mean size of 110 nm, a polydispersity index (PDI) of less than 0.2, and a GOH encapsulation effectiveness of 95% was attained in the very stable and sparsely dispersed NLC/GOH. Wide- and small-angle X-ray scattering investigations indicate that the crystalline structure of NLC altered after GOH incorporation. After 24 hours, there was a higher in vitro release of GOH from NLC under an acidic pH (tumoral environment). The NLC/GOH was shown to be safe for use with blood components, to interact preferentially with human serum albumin over plasmatic opsonins, and to adsorb a thin layer of serum proteins in vitro. After 24 hours, an effective time-dependent cellular absorption of NLC/GOH was shown in A549 cells. Following GOH encapsulation into NLC, there was a 1.8–3.2 fold increase in the loss of A549 cell viability, along with an increase in mitochondrial membrane depolarization and cell death. When tested on A549 cells, highly cytotoxic quantities of NLC/GOH were shown to be non-toxic to WI-38 cells, which are normal lung fibroblasts. Last but not least, the inhibition of A549 cell migration induced by free GOH was enhanced by GOH nanoencapsulation within NLC(77).

### 6.3. Lipid Nanoparticle (LNP) enables mRNA Delivery

Since COVID-19 mRNA vaccines have proven successful in preventing and cureing a variety of illnesses, messenger RNA (mRNA) has drawn a lot of interest (78-85). mRNA must penetrate the target cells and express enough proteins to fulfill the therapeutic goal. As a result, creating efficient distribution methods is essential and required. Since many mRNA-based curements have either received approval or are undergoing clinical trials, lipid nanoparticles (LNPs) are a unique tool that have expedited mRNA use in humans. The main topic of this review is mRNA-LNP-mediated antiTumorcurement. It highlights current issues and potential prospects for this area of study, reviews

exemplary curement techniques in Tumor, and describes the primary development tactics of mRNA-LNP formulations. It is believed that these signals will assist in advancing the use of mRNA-LNP technology in Tumorcurement(78).

### 6.4.Targeted solid lipid nanoparticle formulation for colon Tumorcurement

There are several pharmacological consequences linked to thymol. However, its application has been restricted due to drawbacks such as high volatility, poor bioavailability, and low solubility in water.(86-89) To increase the effectiveness of thymol, the current work synthesized and characterized solid lipid nanoparticles (SLNs) loaded with thymol. Atomic force microscopy (AFM), differential scanning calorimetry (DSC), and Fourier-transformed infrared spectroscopy (FT-IR) were used to analyze thymol-loaded solid-liquid nanoparticles (SLNs). A hemolysis test and cytotoxicity investigation were also carried out (90-95). A prolonged release of the substance was seen in vitro. Additionally, thymol-loaded SLNs showed greater cytotoxicity than thymol-free SLNs, and the hemolysis data demonstrated SLNs' blood biocompatibility.(96-100) SLNs, being nanocarriers, provide a novel way to enhance thymol's effectiveness in Tumor therapy(79).

### 6.5. Targeted Asialoglycoprotein for the treatment HCC

Asialoglycoprotein receptors have been employed for liver-targeted delivery and HCC treatment because they are substantially expressed on hepatocytes. Targeted BTZ distribution to HCC hasn't been documented, however. As a targeted agent, N-SALB with a Gal moiety was created for this investigation, and FT-IR and NMR investigations verified its structure. The development of BTZ-loaded N-SALB surface-modified SLNs aimed to deliver BTZ to HCC cancer cells. The average particle size of the Gal-SLNs/BTZ was 116.3 nm, with a PDI of 0.210 and a zeta potential of -13.8 mV. Their spherical, nanometer-sized shape was revealed via TEM investigation. The capacity for EE and DL was 84.5% and 1.6%, respectively. According to release tests, BTZ that was injected into the SLNs was gradually released at a pH of 7.4 over the course of 72 hours. N-SALB-targeted nanoparticles exhibited a much greater intracellular uptake in HepG2 cells by flow cytometry analysis compared to non-targeted nanoparticles. The MTT test cytotoxicity analysis demonstrated acceptable biocompatibility for all lipid formulations. All formulations showed concentration-dependent cytotoxicity, with N-SALB-targeted nanoparticles showing the greatest cytotoxicity against HepG2 cells. When comparing N-SALB-targeted nanoparticles to non-targeted nanoparticles, the greatest proportion of apoptosis was observed. Ultimately, targeted nanoparticle accumulation in the tumor was shown to be much greater than non-targeted nanoparticle accumulation, according to biodistribution tests conducted on HepG2 carrying nude mice.(101)

### 6.6. Treatment for pancreatic cancer

One of the most deadly cancers is pancreatic cancer, which has no symptoms in its early stages. The head, neck, and pancreas are the sites of genesis for 60%–70% of pancreatic malignancies. For 75%–80% of patients, the diagnosis of pancreatic cancer is made too late, usually at the metastatic stage, making it very difficult for the patients to survive. Although surgical resection, radiation therapy, chemotherapy, CT scans, MRIs, and other modern diagnostic and therapeutic techniques are widely used, they have a poor survival rate and a number of drawbacks. Potential options for earlier diagnosis

and more effective therapy include nanotechnological methods or medication delivery systems using nanoparticles. Among the several nanoparticle drug delivery technologies, solid lipid-based nanoparticles (SLNs) are widely used in cancer therapies. This chapter illustrates the benefits of SLNs on pancreatic cancer as well as how drugs are delivered to the disease using SLNs and their production methods.(102)

**Conclusion**

Lipid-based nanoparticles are a broad and diverse class of substances that have been used to cure a number of illnesses, Tumor being the most general. Because of their exceptional biocompatibility and flexibility, liposomes are now the most often used lipid-based nanoparticles; nevertheless, SLNs and NLCs have recently become more well-liked.However, research on these particular nanoparticles is not the main emphasis; instead, a number of publications highlight cutting-edge methods for employing lipid-based nanoparticles to cure other types of Tumor. 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. One's primary benefits can be the use of biomaterials, components, and manufacturing methods that are safe for the environment. 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 deemed essential to create standardized procedures for evaluating the potential risks associated with the ingestion of nanomaterials and the related regulatory framework. Melanoma therapy, like other nanosized drug carriers, is a significant area of research for which SLNs can be used. This may also indicate a high level of funding for the field as well as the suitability of nanostructures for the delivery of cytotoxic drugs because of the direct and indirect attacks that are triggered by malignant cellular level. Nevertheless, the use of lipid nanoparticles is beneficial in several medicinal fields.Unfortunately, more study, more effort, and more financial facilities are needed before SLN/NLC may be shown to be therapeutically helpful in real-world situations. Currently, the scarcity of SLNs that have progressed to clinical trials indicates that it will take a few years for these discoveries to reach the domestic or global pharmaceutical market.

**Reference**

1. J.C. Underwood, S.S. Cross, General and Systematic Pathology, Elsevier heath science, Amsterdam, Netherlands, 2009.
2. Tumor, World Health Organization, 12 September 2018.
3. World Tumor Report 2014, World Health Organization, 2014. Chapter 1.1.
4. H. Rehder. Family Tumor syndromes, Hered. Tumor. 2009;41–86.
5. How Is Tumor Diagnosed?, American Tumor Society, 29 January 2013.
6. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet [Internet]. 2016 Oct;388(10053):1459–544. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673616310121
7. Sciacovelli M, Schmidt C, Maher ER, Frezza C. Metabolic Drivers in Hereditary Tumor

Syndromes. Annu Rev Tumor Biol [Internet]. 2020 Mar 9;4(1):77–97. Available from: https://www.annualreviews.org/doi/10.1146/annurev-Tumorbio-030419-033612
8. GBD 2015 Mortality and Causes of Death, Collaborators, Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015,.
9. World Tumor Report 2014, World Health Organization, 2014. Chapter 1.1. Archived from the original on 12 July 2017.
10. Dubas LE, Ingraffea A. Nonmelanoma Skin Tumor. Facial Plast Surg Clin North Am [Internet]. 2013 Feb;21(1):43–53. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1064740612001447
11. Cakir BÖ, Adamson P, Cingi C. Epidemiology and Economic Burden of Nonmelanoma Skin Tumor. Facial Plast Surg Clin North Am [Internet]. 2012 Nov;20(4):419–22. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1064740612000818
12. World Tumor Report, World Health Organization 2014, 2014 pp. Chapter 1.3. Archived from the original on 12 July 2017.
13. IUPAC, Compendium of Chemical Terminology, second ed., The “Gold Book”, 1997. Online corrected version: (2006–) “lipids”.
14. Tang J, Sun J, He Z-G. Self-Emulsifying Drug Delivery Systems: Strategy for Improving Oral Delivery of Poorly Soluble Drugs. Curr Drug ther [Internet]. 2007 Jan 1;2(1):85–93. Available from: http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1574-8855&volume=2&issue=1&spage=85
15. Humberstone AJ, Charman WN. Lipid-based vehicles for the oral delivery of poorly water soluble drugs. Adv Drug Deliv Rev [Internet]. 1997 Apr;25(1):103–28. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0169409X96004942
16. Kuentz M. Lipid-based formulations for oral delivery of lipophilic drugs. Drug Discov Today Technol [Internet]. 2012 Jun;9(2):e97–104. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1740674912000145
17. Patel AR, Velikov KP. Colloidal delivery systems in foods: A general comparison with oral drug delivery. LWT - Food Sci Technol [Internet]. 2011 Nov;44(9):1958–64. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0023643811001307
18. Pouton CW, Porter CJH. Formulation of lipid-based delivery systems for oral administration: Materials, methods and strategies. Adv Drug Deliv Rev [Internet]. 2008 Mar;60(6):625–37. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0169409X07003109
19. MÃ¼ller R. Solid lipid nanoparticles (SLN) for controlled drug delivery â€“ a review of the state of the art. Eur J Pharm Biopharm [Internet]. 2000 Jul 3;50(1):161–77. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0939641100000874
20. Pardeike J, Hommoss A, Müller RH. Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. Int J Pharm [Internet]. 2009 Jan;366(1–2):170–84. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378517308006996
21. Gasco MR. Method for producing solid lipid microspheres having a narrow size distribution, U.S. Patent No. 5 250 (1993) 236.
22. R.H. Müller JSL. Medication Vehicles Made of Solid Lipid Particles (Solid Lipid Nanospheres SLN), 1996.

23. Doktorovova S, Souto EB, Silva AM. Nanotoxicology applied to solid lipid nanoparticles and nanostructured lipid carriers – A systematic review of in vitro data. Eur J Pharm Biopharm [Internet]. 2014 May;87(1):1–18. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0939641114000472
24. Bor G, Mat Azmi ID, Yaghmur A. Nanomedicines for Tumor therapy: current status, challenges and future prospects. Ther Deliv [Internet]. 2019 Feb;10(2):113–32. Available from: https://www.future-science.com/doi/10.4155/tde-2018-0062
25. Gulino A. Nanoparticle-based delivery of small interfering RNA: challenges for Tumor therapy. Int J Nanomedicine [Internet]. 2012 Jul;3637. Available from: http://www.dovepress.com/nanoparticle-based-delivery-of-small-interfering-rna-challenges-for-ca-peer-reviewed-article-IJN
26. Fatima I, Rahdar A, Sargazi S, Barani M, Hassanisaadi M, Thakur VK. Quantum Dots: Synthesis, Antibody Conjugation, and HER2-Receptor Targeting for Breast Tumor Therapy. J Funct Biomater [Internet]. 2021 Dec 16;12(4):75. Available from: https://www.mdpi.com/2079-4983/12/4/75
27. R. Rama A, Jimenez-Lopez J, Cabeza L, Jimenez-Luna C, C. Leiva M, Perazzoli G, et al. Last Advances in Nanocarriers-Based Drug Delivery Systems for Colorectal Tumor. Curr Drug Deliv [Internet]. 2016 Aug 1;13(6):830–8. Available from: http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1567-2018&volume=13&issue=6&spage=830
28. Alavi M, Hamidi M. Passive and active targeting in Tumor therapy by liposomes and lipid nanoparticles. Drug Metab Pers Ther [Internet]. 2019 Mar 26;34(1). Available from: https://www.degruyter.com/document/doi/10.1515/dmpt-2018-0032/html
29. H. Muller R, Shegokar R, M. Keck C. 20 Years of Lipid Nanoparticles (SLN & NLC): Present State of Development & Industrial Applications. Curr Drug Discov Technol [Internet]. 2011 Sep 1;8(3):207–27. Available from: http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1570-1638&volume=8&issue=3&spage=207
30. Kathe N, Henriksen B, Chauhan H. Physicochemical characterization techniques for solid lipid nanoparticles: principles and limitations. Drug Dev Ind Pharm [Internet]. 2014 Dec 25;40(12):1565–75. Available from: http://www.tandfonline.com/doi/full/10.3109/03639045.2014.909840
31. TEERANACHAIDEEKUL V, MULLER R, JUNYAPRASERT V. Encapsulation of ascorbyl palmitate in nanostructured lipid carriers (NLC)—Effects of formulation parameters on physicochemical stability. Int J Pharm [Internet]. 2007 Aug 1;340(1–2):198–206. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378517307002682
32. Jaiswal P, Gidwani B, Vyas A. Nanostructured lipid carriers and their current application in targeted drug delivery. Artif Cells, Nanomedicine, Biotechnol [Internet]. 2016 Jan 2;44(1):27–40. Available from: https://www.tandfonline.com/doi/full/10.3109/21691401.2014.909822
33. Lima AM, Pizzol CD, Monteiro FBF, Creczynski-Pasa TB, Andrade GP, Ribeiro AO, et al. Hypericin encapsulated in solid lipid nanoparticles: Phototoxicity and photodynamic efficiency. J Photochem Photobiol B Biol [Internet]. 2013 Aug;125:146–54. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1011134413001164

34. Wissing S., Kayser O, Müller R. Solid lipid nanoparticles for parenteral drug delivery. Adv Drug Deliv Rev [Internet]. 2004 May;56(9):1257–72. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0169409X04000456
35. H. Svilenov CT. Solid lipid nanoparticles - a promising drug delivery, Nanomedicine. Nanomedicine. 2009;187–237.
36. Iqbal MA, Md S, Sahni JK, Baboota S, Dang S, Ali J. Nanostructured lipid carriers system: Recent advances in drug delivery. J Drug Target [Internet]. 2012 Dec 29;20(10):813–30. Available from: http://www.tandfonline.com/doi/full/10.3109/1061186X.2012.716845
37. ALMEIDA A, SOUTO E. Solid lipid nanoparticles as a drug delivery system for peptides and proteins☆. Adv Drug Deliv Rev [Internet]. 2007 Jul 10;59(6):478–90. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0169409X07000439
38. Almeida AJ, Runge S, Müller RH. Peptide-loaded solid lipid nanoparticles (SLN): Influence of production parameters. Int J Pharm [Internet]. 1997 Apr;149(2):255–65. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378517397048850
39. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for Tumor therapy. Nat Nanotechnol [Internet]. 2007 Dec;2(12):751–60. Available from: https://www.nature.com/articles/nnano.2007.387
40. Zafar A, Alruwaili NK, Imam SS, Alharbi KS, Afzal M, Alotaibi NH, et al. Novel nanotechnology approaches for diagnosis and therapy of breast, ovarian and cervical Tumor in female: A review. J Drug Deliv Sci Technol [Internet]. 2021 Feb;61:102198. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1773224720314878
41. Ramishetti S, Kedmi R, Goldsmith M, Leonard F, Sprague AG, Godin B, et al. Systemic Gene Silencing in Primary T Lymphocytes Using Targeted Lipid Nanoparticles. ACS Nano [Internet]. 2015 Jul 28;9(7):6706–16. Available from: https://pubs.acs.org/doi/10.1021/acsnano.5b02796
42. Khan A, Imam SS, Aqil M, Ahad A, Sultana Y, Ali A, et al. Brain Targeting of Temozolomide via the Intranasal Route Using Lipid-Based Nanoparticles: Brain Pharmacokinetic and Scintigraphic Analyses. Mol Pharm [Internet]. 2016 Nov 7;13(11):3773–82. Available from: https://pubs.acs.org/doi/10.1021/acs.molpharmaceut.6b00586
43. Khan A, Aqil M, Imam SS, Ahad A, Sultana Y, Ali A, et al. Temozolomide loaded nano lipid based chitosan hydrogel for nose to brain delivery: Characterization, nasal absorption, histopathology and cell line study. Int J Biol Macromol [Internet]. 2018 Sep;116:1260–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0141813018317124
44. Shmeeda H, Amitay Y, Gorin J, Tzemach D, Mak L, Stern ST, et al. Coencapsulation of alendronate and doxorubicin in pegylated liposomes: a novel formulation for chemoimmunotherapy of Tumor. J Drug Target [Internet]. 2016 Dec 7;24(9):878–89. Available from: https://www.tandfonline.com/doi/full/10.1080/1061186X.2016.1191081
45. Li M, Yang Y, Xu C, Wei J, Liu Y, Cun X, et al. Tumor-Targeted Chemoimmunotherapy with Immune-Checkpoint Blockade for Enhanced Anti-Melanoma Efficacy. AAPS J [Internet]. 2019 Mar 11;21(2):18. Available from: http://link.springer.com/10.1208/s12248-018-0289-3
46. Mei K-C, Liao Y-P, Jiang J, Chiang M, Khazaieli M, Liu X, et al. Liposomal Delivery of Mitoxantrone and a Cholesteryl Indoximod Prodrug Provides Effective Chemo-immunotherapy in Multiple Solid Tumors. ACS Nano [Internet]. 2020 Oct 27;14(10):13343–66. Available from: https://pubs.acs.org/doi/10.1021/acsnano.0c05194

47. Lang T, Liu Y, Zheng Z, Ran W, Zhai Y, Yin Q, et al. Cocktail Strategy Based on Spatio-Temporally Controlled Nano Device Improves Therapy of Breast Tumor. Adv Mater [Internet]. 2019 Feb 5;31(5). Available from: https://onlinelibrary.wiley.com/doi/10.1002/adma.201806202
48. Wang G, Wu B, Li Q, Chen S, Jin X, Liu Y, et al. Active Transportation of Liposome Enhances Tumor Accumulation, Penetration, and Therapeutic Efficacy. Small [Internet]. 2020 Nov 8;16(44). Available from: https://onlinelibrary.wiley.com/doi/10.1002/smll.202004172
49. Lv Q, Cheng L, Lu Y, Zhang X, Wang Y, Deng J, et al. Thermosensitive Exosome–Liposome Hybrid Nanoparticle-Mediated Chemoimmunotherapy for Im Curement of Metastatic Peritoneal Tumor. Adv Sci [Internet]. 2020 Sep 29;7(18). Available from: https://onlinelibrary.wiley.com/doi/10.1002/advs.202000515
50. relay drug delivery for amplifying antitumor efficiency. Biomaterials 2018, 185, 205–218. [CrossRef] 138 X. Zang, J. Zhou, X. Zhang, D. Chen, Y. Han, X. Chen, Dual-targeting tumor cells and tumor associated macrophages with lipid coated calcium zoledronat.
51. Kong M, Tang J, Qiao Q, Wu T, Qi Y, Tan S, et al. Biodegradable Hollow Mesoporous Silica Nanoparticles for Regulating Tumor Microenvironment and Enhancing Antitumor Efficiency. Theranostics [Internet]. 2017;7(13):3276–92. Available from: http://www.thno.org/v07p3276.htm
52. Kuai R, Yuan W, Son S, Nam J, Xu Y, Fan Y, et al. Elimination of established tumors with nanodisc-based combination chemoimmunotherapy. Sci Adv [Internet]. 2018 Apr 6;4(4). Available from: https://www.science.org/doi/10.1126/sciadv.aao1736
53. Scheetz LM, Yu M, Li D, Castro MG, Moon JJ, Schwendeman A. Synthetic HDL Nanoparticles Delivering Docetaxel and CpG for Chemoimmunotherapy of Colon Adenocarcinoma. Int J Mol Sci [Internet]. 2020 Mar 5;21(5):1777. Available from: https://www.mdpi.com/1422-0067/21/5/1777
54. Kuai R, Ochyl LJ, Bahjat KS, Schwendeman A, Moon JJ. Designer vaccine nanodiscs for personalized Tumor immunotherapy. Nat Mater [Internet]. 2017 Apr 26;16(4):489–96. Available from: https://www.nature.com/articles/nmat4822
55. Wang T, Zhang J, Hou T, Yin X, Zhang N. Selective targeting of tumor cells and tumor associated macrophages separately by twin-like core–shell nanoparticles for enhanced tumor-localized chemoimmunotherapy. Nanoscale [Internet]. 2019;11(29):13934–46. Available from: http://xlink.rsc.org/?DOI=C9NR03374B
56. García-Pinel B, Porras-Alcalá C, Ortega-Rodríguez A, Sarabia F, Prados J, Melguizo C, et al. Lipid-Based Nanoparticles: Application and Recent Advances in TumorCurement. Nanomaterials [Internet]. 2019 Apr 19;9(4):638. Available from: https://www.mdpi.com/2079-4991/9/4/638
57. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global Tumor statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 Tumors in 185 countries. CA Tumor J Clin [Internet]. 2018 Nov 12;68(6):394–424. Available from: https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21492
58. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global Tumor incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Tumor [Internet]. 2019 Apr 15;144(8):1941–53. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ijc.31937
59. Low LE, Tan LT-H, Goh B-H, Tey BT, Ong BH, Tang SY. Magnetic cellulose nanocrystal

stabilized Pickering emulsions for enhanced bioactive release and human colon Tumor therapy. Int J Biol Macromol [Internet]. 2019 Apr;127:76–84. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0141813018351390

60. Ektate K, Munteanu MC, Ashar H, Malayer J, Ranjan A. Chemo-immunotherapy of colon Tumor with focused ultrasound and Salmonella-laden temperature sensitive liposomes (thermobots). Sci Rep [Internet]. 2018 Aug 30;8(1):13062. Available from: https://www.nature.com/articles/s41598-018-30106-4
61. Moghimipour E, Rezaei M, Ramezani Z, Kouchak M, Amini M, Angali KA, et al. Folic acid-modified liposomal drug delivery strategy for tumor targeting of 5-fluorouracil. Eur J Pharm Sci [Internet]. 2018 Mar;114:166–74. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0928098717306772
62. Kassem MA, El-Sawy HS, Abd-Allah FI, Abdelghany TM, El-Say KM. Maximizing the Therapeutic Efficacy of Imatinib Mesylate–Loaded Niosomes on Human Colon Adenocarcinoma Using Box-Behnken Design. J Pharm Sci [Internet]. 2017 Jan;106(1):111–22. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0022354916415790
63. Yang F, Zheng Z, Zheng L, Qin J, Li H, Xue X, et al. SATB1 siRNA-encapsulated immunoliposomes conjugated with CD44 antibodies target and eliminate gastric Tumor-initiating cells. Onco Targets Ther [Internet]. 2018 Oct;Volume 11:6811–25. Available from: https://www.dovepress.com/satb1-sirna-encapsulated-immunoliposomes-conjugated-with-cd44-antibodi-peer-reviewed-article-OTT
64. DING J, FENG M, WANG F, WANG H, GUAN W. Targeting effect of PEGylated liposomes modified with the Arg-Gly-Asp sequence on gastric Tumor. Oncol Rep [Internet]. 2015 Oct;34(4):1825–34. Available from: https://www.spandidos-publications.com/10.3892/or.2015.4142
65. Wonder E, Simón-Gracia L, Scodeller P, Majzoub RN, Kotamraju VR, Ewert KK, et al. Competition of charge-mediated and specific binding by peptide-tagged cationic liposome–DNA nanoparticles in vitro and in vivo. Biomaterials [Internet]. 2018 Jun;166:52–63. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0142961218301522
66. Wang J, Zhu R, Sun X, Wang T, Liu H, Wang S-L. Intracellular uptake of etoposide-loaded solid lipid nanoparticles induces an enhancing inhibitory effect on gastric Tumorthrough mitochondria-mediated apoptosis pathway. Int J Nanomedicine [Internet]. 2014 Aug;3987. Available from: http://www.dovepress.com/intracellular-uptake-of-etoposide-loaded-solid-lipid-nanoparticles-ind-peer-reviewed-article-IJN
67. Cao X, Luo J, Gong T, Zhang Z-R, Sun X, Fu Y. Coencapsulated Doxorubicin and Bromotetrandrine Lipid Nanoemulsions in Reversing Multidrug Resistance in Breast Tumor in Vitro and in Vivo. Mol Pharm [Internet]. 2015 Jan 5;12(1):274–86. Available from: https://pubs.acs.org/doi/10.1021/mp500637b
68. Rocca A, Cecconetto L, Passardi A, Melegari E, Andreis D, Monti M, et al. Phase Ib dose-finding trial of lapatinib plus pegylated liposomal doxorubicin in advanced HER2-positive breast Tumor. Tumor Chemother Pharmacol [Internet]. 2017 May 24;79(5):863–71. Available from: http://link.springer.com/10.1007/s00280-017-3279-8
69. LORUSSO V, GIOTTA F, BORDONARO R, MAIELLO E, DEL PRETE S, GEBBIA V, et al. Non-pegylated liposome-encapsulated doxorubicin citrate plus cyclophosphamide or vinorelbine

in metastatic breast Tumor not previously cureed with chemotherapy: A multicenter phase III study. Int J Oncol [Internet]. 2014 Nov;45(5):2137–42. Available from: https://www.spandidos-publications.com/10.3892/ijo.2014.2604

70. Yu D, Li W, Zhang Y, Zhang B. Anti-tumor efficiency of paclitaxel and DNA when co-delivered by pH responsive ligand modified nanocarriers for breast Tumorcurement. Biomed Pharmacother [Internet]. 2016 Oct;83:1428–35. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0753332216309933
71. Garg NK, Singh B, Jain A, Nirbhavane P, Sharma R, Tyagi RK, et al. Fucose decorated solid-lipid nanocarriers mediate efficient delivery of methotrexate in breast Tumor therapeutics. Colloids Surfaces B Biointerfaces [Internet]. 2016 Oct;146:114–26. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0927776516303824
72. Ahmad G, El Sadda R, Botchkina G, Ojima I, Egan J, Amiji M. Nanoemulsion formulation of a novel taxoid DHA-SBT-1214 inhibits prostate Tumor stem cell-induced tumor growth. Tumor Lett [Internet]. 2017 Oct;406:71–80. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0304383517304810
73. Chen B-H, Tsai YJ. Preparation of catechin extracts and nanoemulsions from green tea leaf waste and their inhibition effect on prostate Tumor cell PC-3. Int J Nanomedicine [Internet]. 2016 May;1907. Available from: https://www.dovepress.com/preparation-of-catechin-extracts-and-nanoemulsions-from-green-tea-leaf-peer-reviewed-article-IJN
74. Nassir AM, Ibrahim IAA, Md S, Waris M, Tanuja, Ain MR, et al. Surface functionalized folate targeted oleuropein nano-liposomes for prostate tumor targeting: In vitro and in vivo activity. Life Sci [Internet]. 2019 Mar;220:136–46. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0024320519300669
75. Hua H, Zhang N, Liu D, Song L, Liu T, Li S, et al. Multifunctional gold nanorods and docetaxel-encapsulated liposomes for combined thermo- and chemotherapy. Int J Nanomedicine [Internet]. 2017 Oct;Volume 12:7869–84. Available from: https://www.dovepress.com/multifunctional-gold-nanorods-and-docetaxel-encapsulated-liposomes-for-peer-reviewed-article-IJN
76. Aly S, El-Kamel AH, Sheta E, El-Habashy SE. Chondroitin/Lactoferrin-dual functionalized pterostilbene-solid lipid nanoparticles as targeted breast Tumor therapy. Int J Pharm [Internet]. 2023 Jul;642:123163. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378517323005835
77. Rodenak-Kladniew B, Gambaro R, Cisneros JS, Huck-Iriart C, Padula G, Castro GR, et al. Enhanced antiTumor activity of encapsulated geraniol into biocompatible lipid nanoparticles against A549 human lung Tumor cells. J Drug Deliv Sci Technol [Internet]. 2023 Feb;80:104159. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1773224723000114
78. Zong Y, Lin Y, Wei T, Cheng Q. Lipid Nanoparticle (LNP) Enables mRNA Delivery for Tumor Therapy. Adv Mater [Internet]. 2023 Dec;35(51). Available from: https://onlinelibrary.wiley.com/doi/10.1002/adma.202303261
79. Moghimipour E, Abedini M, Handali S. Targeted Solid Lipid Nanoparticles Formulation for Colon TumorCurement and Cytotoxicity Assessment Using HT29 Cell Line. Jundishapur J Nat Pharm Prod [Internet]. 2023 May 6;18(2). Available from: https://brieflands.com/articles/jjnpp-135987.html
80. Granot-Matok, Y., Kon, E., Dammes, N., Mechtinger, G. & Peer, D. Therapeutic mRNAdelivery to

leukocytes. J. Control. Release 305, 165–175 (2019).
81. Kon, E. et al. Resveratrol enhances mRNA and siRNA lipid nanoparticles primary CLL celltransfection. Pharmaceutics 12, 520 (2020).
82. Tombácz, I. et al. Highly efficient CD4+ T cell targeting and genetic recombination usingengineered CD4+ cell-homing mRNA-LNPs. Mol. Ther. 29, 3293–3304 (2021).
83. Hayward, S. L., Wilson, C. L. & Kidambi, S. Hyaluronic acid-conjugated liposomenanoparticles for targeted delivery to CD44 overexpressing glioblastoma cells.Oncotarget 7, 34158–34171 (2016).
84. Yong, S. B. et al. Dual-targeted lipid nanotherapeutic boost for chemo-immunotherapy ofTumor. Adv. Mater. 34, e2106350 (2022).
85. Kampel, L. et al. Therapeutic inhibitory RNA in head and neck Tumor via functionaltargeted lipid nanoparticles. J. Control. Rel. 337, 378–389 (2021).
86. Kedmi, R. et al. A modular platform for targeted RNAi therapeutics. Nat. Nanotechnol. 13,214–219 (2018).
87. Weinstein, S. et al. Harnessing RNAi-based nanomedicines for therapeutic gene silencingin B-cell malignancies. Proc. Natl Acad. Sci. USA 113, E16–E22 (2016).
88. Kandela, I., Chou, J. & Chow, K. Registered report: coadministration of a tumor-penetratingpeptide enhances the efficacy of Tumor drugs. Elife 4, e06959 (2015).
89. Sugahara, K. N. et al. Tissue-penetrating delivery of compounds and nanoparticles intotumors. Tumor Cell 16, 510–520 (2009).
90. Alberici, L. et al. De novo design of a tumor-penetrating peptide. Tumor Res. 73,804–812 (2013).
91. Scodeller, P. et al. Precision targeting of tumor macrophages with a CD206 bindingpeptide. Sci. Rep. 7, 14655 (2017).
92. Sofias, A. M. et al. Tumor targeting by αvβ3-integrin-specific lipid nanoparticles occursvia phagocyte hitchhiking. ACS Nano 14, 7832–7846 (2020).
93. Kheirolomoom, A. et al. In situ T-cell transfection by anti-CD3-conjugated lipidnanoparticles leads to T-cell activation, migration, and phenotypic shift. Biomaterials281, 121339 (2022).
94. Houdaihed, L., Evans, J. C. & Allen, C. Dual-targeted delivery of nanoparticlesencapsulating paclitaxel and everolimus: a novel strategy to overcome breast Tumorreceptor heterogeneity. Pharm. Res. 37, 39 (2020).
95. Bae, Y. H. Drug targeting and tumor heterogeneity. J. Control. Rel. 133, 2–3 (2009).
96. Muro, S. Challenges in design and characterization of ligand-targeted drug deliverysystems. J. Control. Rel. 164, 125–137 (2012).
97. Hartmann, L. C. et al. Folate receptor overexpression is associated with poor outcome inbreast Tumor. Int. J. Tumor121, 938–942 (2007).
98. Herdt, D. et al. The occurrence of MET ectodomain shedding in oral Tumor and itspotential impact on the use of targeted therapies. Tumors 14, 1491 (2022).
99. Miller, M. A. et al. Reduced proteolytic shedding of receptor tyrosine kinases is apost-translational mechanism of kinase inhibitor resistance. Tumor Discov. 6, 383–399(2016).
100. Athauda, G. et al. c-Met ectodomain shedding rate correlates with malignant potential.Clin. Tumor Res. 12, 4154–4162 (2006).
101. F. Mostafaei et al., “Enhanced intracellular accumulation and cytotoxicity of bortezomib against liver cancer cells using N-stearyl lactobionamide surface modified solid lipid nanoparticles,” Int. J. Pharm., vol. 649, p. 123635, Jan. 2024, doi: 10.1016/j.ijpharm.2023.123635.

102. D. Ghosh, G. Dutta, A. Chatterjee, A. Sugumaran, G. Chakrabarti, and S. Manickam, “Solid lipid nanoparticle-based drug delivery for pancreatic cancer,” in Recent Advances in Nanocarriers for Pancreatic Cancer Therapy, Elsevier, 2024, pp. 267–295.