REVIEW ARTICLE

A Comprehensive Review of Advances in Nanoparticle-Based Cancer Therapy

Abdellateif Okkod*, Sunith Reddy

Center for Pharmaceutical Science, Jawaharlal Nehru Technological University, Hyderabad, Telangana, India.

Received: 15th January, 2024; Revised: 08th March, 2024; Accepted: 25th April, 2024; Available Online: 25th June, 2024

ABSTRACT

A promising method for treating different kinds of cancer is cancer therapy based on nanoparticles. The goal of this thorough analysis is to present a summary of the most current developments in cancer treatment using nanoparticles and discuss the different kinds of nanoparticles and how they might be used to enhance therapeutic efficacy and deliver anticancer medications. These include mesoporous dendritic silica nanospheres, gold nanoparticles, and chitosan nanoparticles. The review stresses the significance of stability and dynamic interfaces in attaining effective drug administration and addresses the difficulties related to medication release and degradation in nanoparticle-based therapy. Moreover, it investigates the immune reactions, such as dendritic cell maturation and immune response activation, that are brought on by nanoparticle-based therapy. Overall, this thorough analysis highlights the promise of these cutting-edge strategies for enhancing the effectiveness of cancer treatment and offers insightful information about the developments in nanoparticle-based cancer therapy. The information provided in this study contributes to the growing corpus of information in the field of nanomedicine and suggests future avenues for investigation and development of treatments utilizing nanoparticles to treat cancer.

Keywords: Nanoparticles, Drug delivery, Targeted treatment, Polymeric nanoparticles, Gold nanoparticles, Nanocarriers.

International Journal of Drug Delivery Technology (2024); DOI: 10.25258/ijddt.14.2.72

How to cite this article: Okkod A, Reddy S. A Comprehensive Review of Advances in Nanoparticle-Based Cancer Therapy. International Journal of Drug Delivery Technology. 2024;14(2):1077-1089.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Uncontrolled rapid cell proliferation that results in aberrant cells, known as cancer cells, is among the most dangerous disorders. The World Health Organization (WHO) claims around ten million cancer-related deaths reported in 2022, with an approximated 18.1 M of cancer patients globally.[1] The three types of cancer that have the highest global death rates are breast cancer (2.26 M fatalities), lung cancer (2.21 M), and prostate cancer (1.41 million).[2] Since 1970, the US government has spent more than $100 billion on cancer research, with little improvement with regard to patient survival. After heart disorders, Globally, cancer ranks among the leading causes of death.[3] Treatments for cancer include radiation therapy and, surgery, and chemotherapy. The current chemotherapies are administered *via* traditional oral or intravenous.[4,5] Because passive drug targeting of tumors is made easier by the use of nanotechnology systems, there are significant chances for the creation of new therapies. This increases drug permeability and retention and improves the pharmacokinetic/co-dynamic features of medications.[6] Polymers, liposomes, and solid lipid nanoparticles are just a few of the drug carriers that have seen increased use in recent years due to their effectiveness in treating cancers, capacity to increase medication stability, and lack of harmful side effects.[7–10] Nanoparticles, ranging from 1 to 1500 nm in diameter, encompass a diverse array of materials used to improve traditional therapeutic delivery methods. They have proven effective in delivering proteins, hydrophobic and hydrophilic small molecules, and nucleic acids, overcoming barriers to intracellular delivery and trafficking that were previously challenging with conventional administration methods.[11,12] Nanocarrier-based drug delivery systems are a focal point of medical research because of their substantial potential for practical application. These systems are particularly relevant in the field of oncology, where they enable the imaging, diagnosis, and treatment of cancer. Well-engineered nanoparticles facilitate the delivery of drugs or agents to specific cell types within target organs through mechanisms such as active targeting or passive targeting, specifically through increased permeability and retention.[13,14] Additionally, nanoparticles have proven their capacity to improve tissue drug levels and cellular absorption, which can improve site-directed drug delivery. Therapeutics that are encapsulated in nanoparticles may enable

*Author for Correspondence: okkod50@gmail.com

flexible administration, enhance the stability and solubility of active ingredients, and provide protection from hydrolytic or enzymatic destruction. Extravasation of the active into off-target locations frequently prevents systemic administration of high dosages of medication, increasing toxicity and undesirable effects.[15,16] Nanoparticles may be designed with smart systems that aim at a particular tissue or region of the vasculature in order to facilitate transport across cell membranes. Such focused delivery techniques can increase uptake by particular cell types and circumvent problems with biodistribution first-pass metabolism.[17] and can provide a more persistent, localized, low-dose distribution by establishing a depot for the payloads, which may help reduce systemic negative effects, this is particularly helpful for medications that exhibit strong therapeutic impacts but whose preclinical or clinical testing was previously stopped due to systemic toxicity.[18] Using nanoparticles for therapeutic administration frequently also results in improved drug functioning and aesthetics.[19] The cellular uptake routes of phagocytosis, micropinocytosis, and clathrin- or caveolin-mediated endocytosis are all impacted by the size of nanoparticles.[20] The field of biomedical applications uses a range of forms, such as nanoparticles, nanocarriers, nano biosensors, nano vaccines, nanoshells, and nanorobotics.[21] Theoretically, using nanoparticles for delivery can improve cytotoxic drug tolerability, boost retention in tumor sites through EPR, and reduce the need for extensive surgical reconstructions. Nanoparticles are also routinely delivered topically and transdermally. Delivery on a topical basis is difficult because the thick layer of corneum necessitates either using a skin surface that is already injured for nanoparticle absorption and delivery or creating micropores for NP administration.[22]

NPs in Lung Cancer Treatment

Due to their poor utilization of traditional chemotherapeutics that are susceptible to destruction by the stomach's acidic environment and by circulatory enzymes. Lung cancer research is causing agony for scientists. Additionally, the barriers in the body prevent cancer medications from reaching their objectives. As a result, subjecting patients to adverse outcomes "hurts normal cells." For cancer patients, the adverse effects of tumor medications add another layer of crisis to an existing crisis. Since the patient experiences the negative effects of cancer medications in addition to the illness itself, conventional cancer medications are among the worst at treating lung cancer and provide a fictitious feeling of safety.[23] Cancer medications without nanoparticles rapidly pass through the kidneys and are withdrawn from the body. [24] Among all cancer forms, Lung cancer ranks as the leading cause of cancer-related deaths, contributing to a quarter of all cancer fatalities. Each year, lung cancer mortality exceeds those of prostate, breast, and colon cancers combined. These statistics urge scientists to find a solution to save the lives of cancer patients.[25] Nanoparticles occupy the center stage in the treatment of lung cancer. Furthermore, they have a chance to reduce the side effects of traditional cytotoxic medications,

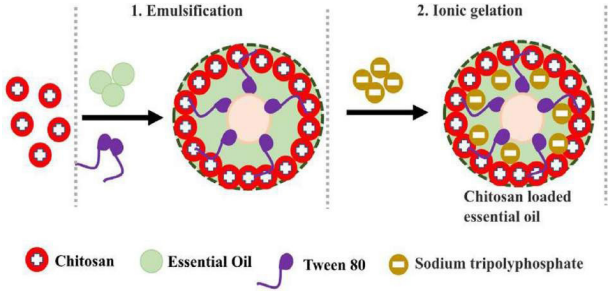

Figure 1: shows the emulsification and ionic gelation procedures used to create essential oil-loaded chitosan nanoparticles.[28]

which would be extremely beneficial to cancer patients. However, a significant difficulty is that many nanoparticle kinds are designated as alien by the body. Essentially, they were confined within the liver, where they perished. In contrast, natural nanoparticles face reduced absorption by immune cells in the liver, allowing them to traverse the liver barrier more effectively.[26] Due to limited research on Fav's effects on lung cancer cells, scientists utilized a solid lipid nanoparticle formulation (Fav-SLNps) to examine the cytotoxicity, proliferation, necrosis, autophagy traits, and cellular uptake of Fav nanoparticles in an A549 cell model.[27] As shown in Figure 1 Chitosan-infused essential oils were acquired, and their qualities and ability to combat biofilm formation were initially evaluated.[28]

The control cells have been demonstrated to be clear, smooth, and of their original size and form (Figure 2). According to a recent paper, AO/EB serves as a potent fluorescent dye suitable for marking damaged regions in cancer cells. Plant essential oils exhibit notable efficacy in eliminating cancer cells at escalating concentrations, and when paired with chitosan, their effectiveness against cancer cells was evidenced by the substantial increase in damaged cells. This finding has been recently established As appear in Figure 2.[29] It was extremely efficient to work with chitosan-based nanoparticles loaded with cinnamaldehyde on cancer cells. It validated the current outcome. Similarly,[30] in a fluorescent microscope utilizing Rodhamine123, necrotic lesions, nucleus part deformation, and uneven structure were observed. According to the results, the chitosan-infused essential oils were found to be remarkably efficient in combating A549 lung cancer cells.[31] Lately, the anticancer effects of chitosan-infused essential oils have been noted, and they have a more damaging effect than essential oils. Furthermore, anti-lung cancer effects.[32]

Bismuth and gold nanostructures were utilized to convey the anticancer drug doxorubicin (DOX), aiding in its effective transportation to tumor locations and its controlled release with sensitivity to pH, targeting lung cancer cells in human subjects. This innovative method markedly amplifies the therapeutic advantages of cancer treatment, demonstrated both in laboratory studies and in living organisms. The newly devised chemo-photothermal synergistic therapy exceeds the effectiveness of either photothermal therapy or chemotherapy in isolation. These nanostructures act as carriers for medication and agents for photothermal treatment.[33] To treat lung cancer,

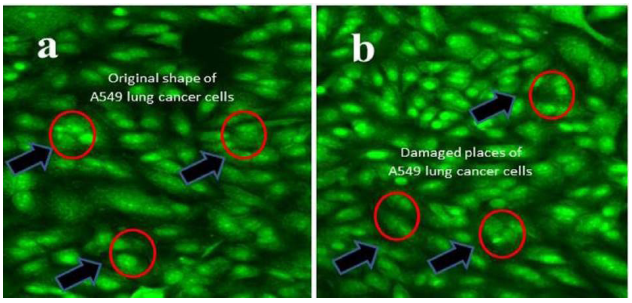

Figure 2: Observing variations in inner membrane morphology using AO/EB fluorescent dyes through fluorescence microscopy. As a result, the untreated control (a) and chitosan-loaded essential oils (b) retained their original morphology.[29]

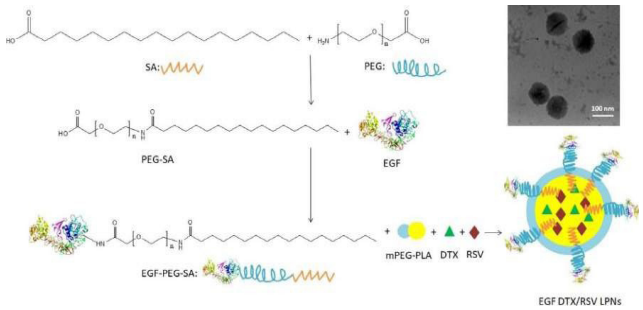

Figure 3: Overcoming multi-drug resistance with EGFR-targeted LPNs: EGF-modified nanoparticles Deliver DTX and RSV to tumor cell mitochondria.[34]

a method of drug delivery employs lipid-polymer hybrid nanoparticles that contain docetaxel and resveratrol. These nanoparticles are designed to target the endothelial growth factor receptor and respond to reactive oxygen species. Additionally, EGF-PEG-SA was utilized to produce EGF-modified DTX and RSV co-encapsulated LPNs, as illustrated in Figure 3.[34] The efficacy of targeted nanocarriers in treating non-small cell lung cancer (NSCLC) was demonstrated using amodiaquine, an FDA-approved anti-malarial drug known as 4-[(7-chloroquinolin-4-yl) amino]-2-[(diethylamino) methyl] phenol (AQ). The formulated nanoparticles (NPs) were analyzed for their physical and chemical properties, revealing favorable particle size and surface charge, which facilitated efficient cellular uptake. The effectiveness of targeted AQ-loaded NPs in fighting cancer was compared to that of their non-targeted counterparts.[35]

NPs Prepared for Bladder Cancer

Bladder cancer (BCa) is a common urinary tract ailment, ranking as the tenth most prevalent oncological disease worldwide in terms of incidence.[36] Cystoscopy, urine cytology, and imaging are now used to identify bladder cancer, with cystoscopy serving as the gold standard for (BCa) diagnosis.[37] Smoking is among the many danger factors for bladder cancer. Additional risk factors include genetics and gender, exposure to chemicals at work, radiation therapy (such as external radiation therapy for gynecological cancers), dietary choices, metabolic diseases, bladder schistosomiasis, and recurrent urinary tract infections.[38,39] It is anticipated that genetics will play a part in the development of bladder cancer, and recent discoveries of molecular subtypes and genetic alterations have made this an active area of study and potential therapeutic use.[40] We typically do a comprehensive bladder cancer detection procedure, which involves urinary cytology, and cystoscopy biopsy, and imaging when patients present with hematuria, difficult urination, and symptoms of distant tumors (back or pelvic discomfort).[41] Biomedical uses of nanosystems with certain physicochemical characteristics, such as tiny size effects, large surface areas, high reactive capacity, and quantum effects, are referred to as nanomedicine.[42] One of the many nanotechnologies utilized in medicine is nanocarrier systems for drug delivery, and due to their superior translational value, they have attracted a lot of scientific attention. Well-designed nanoparticles can carry chemicals or pharmaceuticals to specific cell types within target organs using active or passive targeting (enhanced permeability and retention), allowing for imaging, diagnostics, and cancer treatment.[43] Numerous nano drugs are authorized for use in BCs clinical studies, such as pegylated liposomal doxorubicin (PLD), liposomal doxorubicinPLZ4-coated paclitaxel-loaded micelles (PPM), ONM-100, genexol PM, and ferumoxtran-10 (USPIO), this drug particle loaded with liposome, micelles and magnetic nanoparticle.[44]

NPs Prepared for Skin Cancer

Skin, as a critical physical and immunological barrier, demands special consideration when administering nanoparticle drugs. The skin's immunological richness is attributed to immune cell types that include skin-resident as well as skin-homing T cells, which are lymphoid cells that are innate, Langerhans' cells within the epidermis, dermal dendrites, and others.[45] The stratum corneum layer, which is made up of a large structure of dried-out, decomposing keratinocytes within an ordered lipid layer, serves as the major barrier to the entry of NPs aimed at attacking the skin. NPs can be tailored to act in harmony with the environment based on the method of administration and amount of targeting required, for example, whenever administered locally *via* transdermal dispersion or when injected directly into the site.[46] Nanostructures have gained substantial attention in a variety of therapeutic fields, particularly treatment for cancer, because of its ability to interact on materials ranging from one to a thousand nm.[47] Nanoscale substances have particular chemical and physical characteristics that significantly benefit the treatment of cancer. Several nanomaterials, including microfibers, nanosuspension, nanoemulsions, and nonclay, have effectively cured skin cancer.[48-50] Still, when compared to other kinds of nanomaterials, NPs have shown astounding superiority.[51] However, the utilization of nanotechnology in cancer treatment is substantial. Regulatory agencies such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have approved several treatments. Examples include doxil (a liposomal formulation of doxorubicin), abraxane® (nanoparticles containing paclitaxel). On caspar (a polymer-protein conjugate with L-asparaginase), Marqibo (a liposomal

formulation of vincristine), onivyde (a liposomal formulation of Irinotecan), and vyxeos (a liposomal formulation of cytarabine/daunorubicin), all of which have received FDA approval. Additionally, nanotherm (iron oxide nanoparticles) and hensify (hafnium oxide nanoparticles) have been endorsed by the EMA. These treatments are tailored for various cancers, including breast cancer, ovarian cancer, non-small cell lung carcinoma, sarcoma, glioblastoma, pancreatic cancer, leukemia, multiple myeloma, and various other conditions, with the exception of skin cancer.[52-54] To overcome the toxicity barrier and develop an effective NP-based cancer therapy paradigm, several researchers and pharmaceutical firms are still working hard. In light of this, the current study offers a quick overview of a number of cancer forms, including lung, bladder, and skin cancer. The following article thoroughly examines the scope of nanotechnology and the several kinds of NPs utilized in cancer treatment, including polymer, inorganic, and lipid-based NPs, also discuss the benefits and drawbacks. of these therapy options, making it a state-of-the-art review.

Types of Nanocarriers

In the biomedical business, the use of nanoparticle medicine delivery devices has lately increased. Various kinds of nanocarriers have been developed to meet specific needs in clinical research. Nanoparticles used in nanocarrier-assisted medication delivery systems include liposomal, polymeric, magnetic, and gold nanoparticles, as well as mesoporous silica nanoparticles. Table 1 gives a brief overview of the advantages and disadvantages of nanomaterials employed in cancer therapy or diagnosis preparation.

Liposome based nanocarrier

Liposomes are intracellular drug delivery devices composed of phospholipids and cholesterol that develop into a lipid bilayer surrounding an aqueous core. In the first decade of the 1960s, a British scientist named "Bangham" proposed the concept of a liposome. Since then, liposomes have been widely used as a nanocarrier for medication delivery in a variety of biological applications.[74] Liposomes are often made from phospholipids that include phosphatidylserine, phosphatidylinositol, phosphatidylcholine (or lecithin), phosphatidylglycerol, phosphatidylethanolamine (or cephalin), others. In an aqueous environment, these phospholipids self-assemble to form lipid bilayers, which create one or more water-filled compartments. Furthermore, cholesterol is used to improve the stability of bilayers in body fluids, preventing drugs from being released prematurely.[75] The capability of liposomes in the delivery of anticancer medicines has been extensively studied thus far as shown in Table 2. Thermosensitive, ultrasound-sensitive-sensitive and, enzyme-triggered, magnetic field-sensitive, and ligand-targeted liposomes are the six primary categories of liposomes.[76] The modified liposomes have shown promising infusion chemotherapy outcomes, and the majority of the liposomes now employed for tumor infusion chemotherapy are ligand-targeted. Enhanced clinical use of nanocarriers resulted in the FDA's initial approval of doxil, a liposomal medication containing the anticancer medicine adriamycin hydrochloride.[77]

Polymeric based nanocarriers

The macromolecules known as polymers are made up of

Table 1: Advantages and Disadvantages of Various Nanocarriers in Cancer Treatment

Type of nanocarriers	*Merits*	*Demerits*	*References*
Liposome	Bioavailability is high providing protection for the medications they contain large capacity for medication loading excellent biocompatibility wide drug adaptability	High cost Quick clearance Inaccurate accumulation	55-57
Polymer nanocarriers such as microemulsions, nanogels, micelles and chitosan	Hydrophilicity degradability and biocompatibility prolonged touch with the skin surface; High effectiveness of medicine delivery absorbed quickly by cells; Mucoadhesive easily soluble in enzymes minor toxicity the reduction of the skin barrier impact stable thermodynamics enhancing stability and loading capacity concentrating drugs on tumor tissue.	Controlling medication release and degradation are challenging duties quick clearance Lack of stability creating a dynamic oil/water interface that functions in microemulsions The characteristics of chitosan nanoparticles *in-vivo* are influenced by several chitosan-based delivery strategies.	58-68
Metal gold nanoparticles	Easy preparation Size and distribution that are under control Excellent biocompatibility Effective surface modification	Producing stable NPs might require charge and size Possibility of toxicity	69
Metal silica nanoparticles	Stability and biocompatibility wide surface area High pore volume Easy surface functionalization modification	High cost premature medication release Large-scale synthesis is challenging	70-71
Magnetic nanoparticles	Biological compatibility and biodegradability The potential of heat treatment magnetic properties	A rapid aggregation large surface energy toxic outcome	72-73

Table 2: Efficacy of Nanoparticle Drug Carriers

Type of NPs	*Drug loaded*	*Carrier*	*Impact and mechanism*	*References*
SLN, nanostructured lipid carriers	P0 P2	Liposome	NLCs demonstrated the ability to release P0 and P2 under regulated conditions and provide protection against UVB-mediated degradation.	78
Nanostructured lipid carriers	Quercetin	Prevention liposome	The generated photoprotective formulations *in-vivo* SPF were markedly raised by the addition of NLCs to quercetin without altering the number of UV filters. improved impact on the barrier to skin hydration	79
SLNs	5-Fluorouracil resveratrol	Liposome	Studying the mechanisms that improve skin permeability, evaluating dermatokinetics, and thoroughly examining the effects of the optimal formulation on skin- enhanced medication distribution and penetration into the dermal layer of skin	80
Diamino LNPs	IL12 mRNA IL27 mRNA	Liposome	DAL-LNPs are efficient at delivering mRNA to cause the production of cytokines. I.T. administration resulted in slower tumour development, more lymphocytes infiltrating the tumour, and higher levels of cytokine expression.	81
Cationic lipids	DNA vaccine encoding melanoma tumor-associated antigen (pCMV-MART1)	Liposome	research on melanoma vaccination studies on tumour regression and cytokine release from transfected mice's splenocytes in coculture demonstrate the effectivenessof the anticancer treatment.	82
SLNs	Curcumin Resveratrol	Liposome	In a skin- binding investigation employing snake skin, more than 70% of curcumin resveratrol SLNs were locally attached to the skin. Treatment of localized melanoma with curcumin resveratrol SLNs	83
SLNs	Oil of *Zataria multiflora* (ZMSLN)	Liposome	The majority of EOs are hydrophobic. When loaded onto nanocarriers, EOs performed better.	84

repeating subunits. Control release, timings, biocompatibility, Selected polar and non-polar release. are characteristics of polymeric drug delivery vehicles.[85]

Several chemotherapeutic drugs are currently incorporated in polymeric nano-delivery systems with the goal of increasing antitumor activity, inhibiting metastasis, and lowering doses that work and side responses. Polymers can encapsulate medications or bind them to their surfaces.[86] New design options for these nanocarriers have piqued researchers' imaginations as nanotechnology has advanced. Potential options for achieving the regulated release of medicines at specific places include stimuli-responsive polymers. Chitosan, gels, nanoemulsions, and micelles are popular polymer-carriers for nano-drug delivery.

- *Chitosan*

Naturally occurring nanoparticles, particularly chitosan, are effective, affordable, and environmentally safe sources for nanocarriers are among polymeric nanoparticles. A polymer that is not harmful, biodegradable, and has biocompatible qualities is chitosan.[87] Applications include imaging, screening, and treatment technology have grown as a result of the increasing usage of chitosan nanoparticles as pharmaceutical agents and medication carriers.[88] They are thought to be a successful slow-release medication delivery method. These hold hope regarding prospective cancer treatments using drug delivery devices, both passively (cancer targeting based on increased permeability and long-lasting retention impacts) and actively (receptor-mediated or provoked cancer targeting). Even with all of the advantages, there are still problems that need to be fixed. For instance, the different chitosan-based delivery techniques have an effect on the *in-vivo* properties of chitosan nanoparticles. It is possible to practically investigate the limited reactivity of biological serum with blood cells (especially at very high concentrations of NPs) and its weak colloidal stability through a variety of tests in order to create optimized NPs that are exactly appropriate for *in-vivo* drug delivery systems. [89] If we can create nanoparticles in the future with effective surface changes, these issues will be amenable to solution.

- *Gels*

Hydrogel is A polymeric structure that has been used in medical applications according to its softness, mobility, biological compatibility, and significant tensile strength, particularly for enhanced drug administration compared to traditional formulations.[90] Polymeric nanogels function more therapeutically and reduce the adverse effects of the therapy when employed as drug carriers since they can modify the dosage of the medication by stimuli such as temperature or light in order to minimize the odor of the medicine.[91] In order to construct smart transporters of nanogels which can trigger release, this is critical for cancer treatment, imaging, and protein-based drug delivery, the present direction of nanogel research is focused on developing multi-stimulus response systems.[92] Due to the limits of current production techniques, hybridized nanogels are not completely used. However, they still have a vital role in the future growth of numerous medical equipment, including controlled or slow-release

medication delivery systems, due to their enormous potential.[93] Researchers discovered a potential drug delivery strategy for these materials by mixing polymers, metals, and additional functional polymers to form nanogels. The most frequent particles employed in hybridized nanogels today include golden nanoparticles, carbon-based substances, liposomes, tiny quantum dots, and metallic nanoparticles.[94]

- *Micelles*

Micelles are created when amphiphilic polymers with hydrophobic tails and hydrophilic heads self-assemble.[95], In addition to being able to make hydrophobic medications more soluble and stable, polymeric micelles may also be designed to be the right size to delay premature drug elimination and transit more safely *via* the most refined circulatory systems.[96] Polymers that are sensitive to a variety of stimuli, including changes in pH, temperature, and the presence of light as an external stimulus, have been produced because stimulation sensitivity can significantly boost the drug delivery effectiveness of nanocarrier systems. These multifunctional micelles demonstrate more encouraging outcomes for the intracellular transport of pharmaceuticals.[97] However, micelles also have drawbacks, such as low loading capacity, lack of physical stability *in-vivo*, and poor solubility of tiny particle-size micelles. These issues need to be researched further and remedied. The creation of various micelle forms is still a key area of investigation for micelles in the future since these shapes may be advantageous for applications involving targeted drug administration [98]

- *Nanoemulsions*

The ingredients of a nanoemulsion are an o/w combination, a ternary surfactant, and a quaternary co-surfactant if required. The result is a stable dispersion of droplets.[99] It benefits

Table 3: provides a quick review of the latest polymeric-based nanoparticle

Type of NPs	*Drug loaded*	*Carrier*	*Impact and mechanism*	*Referencees*
Eudragit RS 100 as polymeric wall and medium-chain triglyceride or vitamin E as oil core	Benzofuroazepine	Polymer	Tested various materials for encapsulating testing of the sunscreen's irritating capabilities in capsules	104
PEGylated hyaluronic acid nanogel (NI-MAHA-PEG nanogel)	IL-12	Polymer	Drug release research has shown that environment- responsive NP increases drug release in a hypoxic environment. IVIS dispersion of NPs was shown. Show NP anticancer effectiveness.	105
PLA-HPG	PLA-HPG	Polymer	Slides coated with poly-l- lysine were used to demonstrate the particle stickiness. time course research that showed medication retention in the intertumoral cavity Ability to combat the *in-vivo* SCC model	106
Pegylated platinum NPs	Doxorubicin	Metal Polymer	To test a material's biocompatibility, *in-vitro* cell viability assays and *ex vivo* CEA assays are used. The incubation of tumour particles following injection with H&E was done to examine the expression of SOX2 and KI67, as well as to assess the *in-vitro* antitumor impact. To confirm treatment delivery, a TUNEL test with tumour apoptosis is performed	107
Folic acid cholesterol-sodium alginate NPs	Metformin-Doxorubicin	Polymer	Anti-melanoma effects were seen when NPs were delivered into xenograft melanoma tumours. It was discovered that FCA NP-loaded metformin plus doxorubicin caused melanoma cells to undergo PAN-optosis both *in-vitro* and *in-vivo*.	108
mPEG-bePLGA	Cyanine IR-768, photosensitizer Daunorubicin	Polymer	Polymeric micelles' mitochondria-targeting abilities strong phototoxic effects were generated *in-vitro* as a result of efficient singlet oxygen production.	109
PEI	CpG	Polymer	To demonstrate *in-vitro* production of an immune response, dendritic cell maturation and an ELISA investigation of the supernatant were performed. evaluated the intertumoral immunological l response	110
Dermatan sulfate chitosan nanocarrier (naturalglycosaminogl ycan)	SN38 (camptothecin chemotherapeutic)	Polysacc haride de	The EPR effect spreads SN38/DCNP to the tumor, where it binds to CD146 on the surface of melanoma cells. Particles showed pH- pH-activated degradability. TUNEL test is also used to detect *in-vivo* tumour effectiveness	111

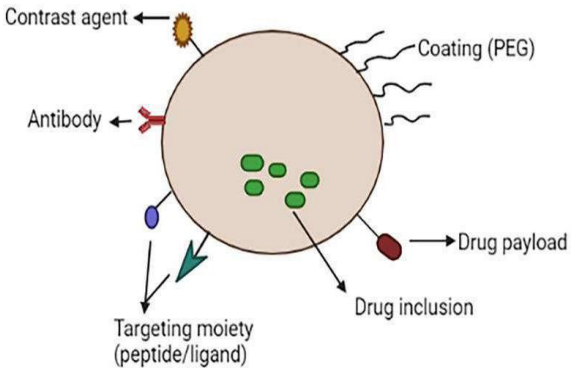

Figure 4: Diagrammatic depiction of multipurpose carbon nanotubes

from regulated drug release, improved drug stability, and a solution to the hydrophobic drug water solubility issue.[100] Nanoemulsions offer the Advantage of enhanced solubility and absorption of moderately bioavailable chemicals over liposomal nanoparticles, which greatly prolongs the period that a drug remains in the body.[101] Co-surfactants assist microemulsions in producing a more adaptable and dynamic layer by lowering the tension of a surfactant film.[102] Using viscous microemulsions as drug delivery systems, gemcitabine and cisplatin's ability to penetrate bladder endothelial tissue is increased, strengthening their combined anticancer effects. The findings point to microemulsions as a potentially effective intravesical medication delivery method.[103] However, there are still certain problems with nanoemulsions that require attention. First, the delivery of cancer drugs is severely hampered by targeted nanoemulsions. Second, in order to interact with tumor tissue, nanoemulsions must be able to bypass the mononuclear phagocytic system & renal clearance biological barrier. Table 3 provides a quick review of the latest polymeric-based nanoparticle

Metallic based nanocarriers

The production of metallic-based nanoparticles is a cost-effective, environmentally benign, and non-toxic technique.[112] A biomolecule of plants, algae, microbes, etc. is required for the nanoparticles made biologically.[113] In this kind of synthesis, The biomolecules in the extraction process oxidize and reduce metal ions to form metal nanoparticles, which begins through a reaction between salts of noble metals.[114] The varieties of biomolecules present in the removed components have an impact on the size, stability, and formation of the produced particles. In several arewas, such as biotechnology, chemicals, cosmetics, and healthcare products, metallic nanoparticles are in high demand. Of all the nanomaterials used in the biomedical industry, metallic nanoparticles are thought to be among the best.[115] Mesoporous silica nanoparticles, silver nanocarriers, diagnostic procedures. Many different metal nanoparticles are utilized to treat different forms of cancer. NP-based medications have demonstrated promising outcomes in anticancer therapy and, are less toxic and have lower drug resistance. Gold nanoparticles and carbon nanotubes are the primary nanocarrier-based nanoparticles employed in cancer treatment or chemical drugs

- *Silver nanocarriers*

Of all the metallic nanoparticles utilized in the biomedical industry, considered to be among the best nanomaterials are silver nanoparticles.[116] By impeding numerous signaling cascades involved in the etiology and development of malignancies, silver nanoparticles slow the spread of tumor cells.[117,118] Silver nanoparticles have been demonstrated in numerous studies to be capable of killing human cancer cells with minimal harm to healthy cells. Nonetheless, physical, chemical, and biologically produced silver nanoparticles are frequently used because they are less costly and hazardous.[119,120] A straightforward, high-yield reduction procedure is all that is required for green manufacture of silver nanoparticles using plant extracts.[121] Reducers, caps, and stabilizers are provided by the bioactive components found in plant extracts. Plant extracts contain phenolics, proteins, polysaccharides, flavones, amino acids, alkaloids, and proteins that function as capping and reducing agents.[122] A novel method of treatment for cancer was made possible by the usage of silver nanoparticles.[123]

- *Gold nanoparticles*

Due to its novel uses in cancer treatment, including medication delivery, tumor identification, and photothermal agents, gold nanoparticles are among the several nanocarriers created for use in nanomedicines that have attracted current scientific attention.[124] In addition to efficiently absorbing visible, ultraviolet, and near-infrared light and releasing energy in the form of heat, gold nanoparticles also have low toxicity, high stability, simple synthesis, and conjugation properties to specific biomolecules, making them excellent nanoplatforms for photothermal and immunotherapy, radiotherapy, and drug delivery.[125,126] Many chemotherapy medications, such as 5-fluorouracil (5-FU) and paclitaxel (PTX), have been effectively conjugated with AuNPs to reduce the pharmaceutical dose and, consequently, the side effects of the treatment.[127] There are only a fewer clinical trials examining gold nanoparticles for cancer detection and treatment, despite the fact that gold nanoparticles have demonstrated potentially helpful qualities in numerous preclinical investigations. Additionally, no medicines containing gold nanoparticles have been successfully employed in clinical practice yet.[128,129]

- *Carbon nanotubes*

Carbon nanotubes are cylindrical molecules based on carbon that can be used as nanocarriers in cancer treatment. Graphene sheets are formed into a smooth cylinder and wrapped with an excellent diameter as tiny as 1-nm, aspect ratio, lengths as long as several micrometers, and the option to be open-ended to create carbon nanotubes.[130] Two varieties of carbon nanotubes exist: first is MWCNTs or multi-walled carbon nanotubes, and the second is SWCNTs, or single-walled carbon nanotubes. SWCNTs have a small diameter, flexibility, and imaging potential. MWCNTs, however, in contrast, are made of nested graphene cylinders and offer a large surface area that makes endohedral filling very effective.[131] Among various

Table 4: Efficacy of Various Metal-Based Nanoparticles in Cancer Therapy

Type of NPs	*Drug loaded*	*Carrier*	*Impact and mechanism*	*References*
Ag NPs	Silver	Metal (silver)	Ag NPs work well to stop UVB-induced skin damage.	137
Ziziphus jujubea fruit extract	Cerium oxide	Metal (cerium)	Excellent UV protection, cerium oxide nanoparticles are harmless to cells at concentrations less than 400 µg/mL after 24 hours.	138
Ziziphus jujubea fruit extract	Cerium oxide	Metal (cerium)	SPF w40-exhibited cerium oxide nanoparticles behave non-toxically on lung cells at doses less than 500 µg/mL.	139
Nanocomposite made with the sol-gel technique	TiO2/Zn2TiO4/Ag	Metal	When compared to TiO2 NPs, the nanocomposite was found to have a	140
Gold NPs	Gold	Metal (gold)	Gold nanoparticles (NPs) are photostable and a viable substitute for inorganic sunscreen chemicals. They adhere to the green chemistry principles and are both economical and environmentally beneficial.	141
AgNP- and BSA-loaded hydrogel film	(BSA) bovine serum albumin	Metal (silver)	The BSA/AgNP gel film's bioadhesiveness was evaluated against pig skin. A study using photosensitizers was conducted both *in-vitro* and *in-vivo.* The mice's tumor sections treated with PTT at 50°C showed a notable reduction in cancer cells.	142
Lecithin, cholesterol, and calcium chloride	Oncolytic virus Ad5	Metal and Membrane	tested the *in-vivo* effectiveness, safety, precision, and mechanism of Lipo-CapeAd5 in combination with PD-1 inhibitors Immune cell invasion into cancer identified	143
Mesoporous dendritic silica nanospheres	Erianin	Metal (silica)	Research on cellular absorption, *in-vitro* release, and cellular proliferation were conducted. Determined *in-vitro* apoptosis Using a western blot, the cytoplasmic calcium content was determined. Porcine skin penetration and skin retention research conducted	144
Polyglycerol- coated iron oxide	Doxorubicin and chlorin e6 (Ce6) conjugated to PEG	Metal (iron) and polymer	The cells treated with NP showed a significant nuclear existence of gH2AX staining. DAMP articulation and/or output were measured. Tumors *in-vivo* were exposed to radiation and NP. After removing the tumors, type 1 macrophage activation markers and DAMP expression was examined.	145
Gold nanoparticles	Sorafenib (multi-kinase inhibitor)	Metal (gold)	Analyze perfusion, permeability, and hypoxia in tumor blood vessels. Neoangiogenesis using CD31 staining reduced vascular development was seen when VEGF was delivered and regulated. Tumor vascular normalization with treatment and tested tumor mesenchymal transition	146

carbon-based nanoparticles and spherical nanoparticles, carbon nanotubes attracted more interest because of their unique characteristics, which include high cargo loading, ultra-high aspect ratio, and intracellular bioavailability. Figure 4 depicts this schematic illustration of multifunctional CNTs.[132]

Mesoporous silica nanoparticles

Mesoporous silica nanoparticles have attracted attention from researchers due to their amazing potential as nanocarriers for imaging and cancer treatment,.[133] due to their wide surface area, high pore volume, consistent pore size distribution, superior biocompatibility, and additional surface modification to modify the surface features of the nanoparticles.[134] According to the study, MSNs show promise as medicine delivery and biomedical imaging carriers. Additionally, medications can be added to the mesoporous material to create long-lasting drug release.[135] Mesoporous silica nanoparticles have formerly been the subject of much research, and despite this, doctors still do not routinely employ them in the clinic for cancer treatment or drug delivery, primarily because of cost concerns.[136] Table 4 provides a quick review of the latest metallic-based nanoparticle

CONCLUSION AND FUTURE WORK PERSPECTIVES

In conclusion, there is a lot of promise for changing the course of treatment for a variety of cancer types with nanoparticle-based cancer therapy. Improved therapeutic efficacy, less systemic toxicity, and tailored drug administration have all been made possible by developments in nanoparticle composition and design. Utilizing several nanoparticle forms, including mesoporous dendritic silica nanospheres, gold nanoparticles, and chitosan nanoparticles, has shown promise in controlling tumor vascular growth and delivering anticancer medications.

However, there are still issues with cancer therapy based on nanoparticles that need to be resolved. More study is necessary to enhance the stability and dynamic surfaces of nanoparticles, which are critical for attaining efficient drug administration. Furthermore, to properly grasp the impact of the immunological responses, more investigation is necessary.

The development of more effective drug release mechanisms, the enhancement of nanoparticle stability, and the investigation of novel targeting strategies should be the main areas of future effort in nanoparticle-based cancer therapy. Personalized cancer treatment has a lot of potential thanks to the mixing of various nanoparticle kinds and the incorporation of therapeutic and imaging functions. To assess the safety and effectiveness of nanoparticle-based treatments in human patients, it is also crucial to move these investigations from preclinical to clinical trials.

Finally, it should be noted that the field of nanoparticle-based cancer therapy is one that is fast developing and has enormous promise to transform cancer treatment. In the end, improved patient outcomes in the fight against cancer will result from ongoing research and development in this field, which will also progress nanomedicine.

REFERENCES

1. Kapoor D, Sharma S, Verma K, Bisht A, Sharma M, Singhai NJ, et al. Quality-by-design-based engineered liposomal nanomedicines to treat cancer: an in-depth analysis. Nanomedicine. 2022;17(17):1173-89.
2. Cancer. Available from: https://www.who.int/health-topics/cancer#tab=tab_1. Accessed 2020 Jul 29.
3. Amin H, Osman SK, Mohammed AM, Zayed G. Gefitinib-loaded starch nanoparticles for battling lung cancer: Optimization by full factorial design and in vitro cytotoxicity evaluation. Saudi Pharm J. 2023;31(1):29-54.
4. Caglar HB, Baldini EH, Othus M, Rabin MS, Bueno R, Sugarbaker DJ, et al. Outcomes of patients with stage III non-small cell lung cancer treated with chemotherapy and radiation with and without surgery. Cancer. 2009;115(18):4156-66.
5. Jonna S, Reuss JE, Kim C, Liu SV. Oral chemotherapy for treatment of lung cancer. Front Oncol. 2020;10:793.
6. Lee MS, Dees EC, Wang AZ. Nanoparticle-Delivered Chemotherapy: Old Drugs in New Packages. Oncology (Williston Park). 2017;31(3):198-208.
7. Tulbah AS, Pisano E, Scalia S, Young PM, Traini D, Ong HX. Inhaled simvastatin nanoparticles for inflammatory lung disease. Nanomedicine. 2017;12(20):2471-85.
8. Tulbah AS, Gamal A. Design and characterization of atorvastatin dry powder formulation as a potential lung cancer treatment. Saudi Pharm J. 2021;29(12):1449-57.
9. Tulbah AS, Pisano E, Landh E, Scalia S, Young PM, Traini D, et al. Simvastatin nanoparticles reduce inflammation in LPS-stimulated alveolar macrophages. J Pharm Sci. 2019;108(12):3890-7.
10. Tulbah AS. Inhaled atorvastatin nanoparticles for lung cancer. Curr Drug Deliv. 2022;19(10):1073-82.
11. Huang W, Xing Y, Zhu L, Zhuo J, Cai M. Sorafenib derivatives-functionalized gold nanoparticles confer protection against tumor angiogenesis and proliferation via suppression of EGFR and VEGFR-2. Exp Cell Res. 2021;406(1):112633.
12. Chang J, Yu B, Saltzman WM, Girardi M. Nanoparticles as a Therapeutic Delivery System for Skin Cancer Prevention and Treatment. JID Innov. 2023;100197.
13. de la Torre P, Pérez-Lorenzo MJ, Alcázar-Garrido Á, Flores AI. Cell-based nanoparticles delivery systems for targeted cancer therapy: Lessons from anti-angiogenesis treatments. Molecules. 2020;25(3):715.
14. Li X, Chen L, Luan S, Zhou J, Xiao X, Yang Y, et al. The development and progress of nanomedicine for esophageal cancer diagnosis and treatment. Semin Cancer Biol. 2022 Nov;86:873-85.
15. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015;33(9):941-51.
16. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2021;20(2):101-24.
17. Cheng CJ, Tietjen GT, Saucier-Sawyer JK, Saltzman WM. A holistic approach to targeting disease with polymeric nanoparticles. Nat Rev Drug Discov. 2015;14(4):239-47.
18. Dehelean CA, Marcovici I, Soica C, Mioc M, Coricovac D, Iurciuc S, et al. Plant-derived anticancer compounds as new perspectives in drug discovery and alternative therapy. Molecules. 2021;26(4):1109.
19. Suh HW, Lewis J, Fong L, Ramseier JY, Carlson K, Peng ZH, et al. Biodegradable bioadhesive nanoparticle incorporation of broad-spectrum organic sunscreen agents. Bioeng Transl Med. 2019;4(1):129-40.
20. Xu E, Saltzman WM, Piotrowski-Daspit AS. Escaping the endosome: assessing cellular trafficking mechanisms of non-viral vehicles. J Control Release. 2021;335:465-80.
21. Prasad SB, Yashwant, Aeri V. Formulation and Evaluation of the Microsphere of Raupya Bhasma for Colon-targeted Drug Delivery. International Journal of Pharmaceutical Quality Assurance. 2022;13(3):286-289.
22. Tadros AR, Romanyuk A, Miller IC, Santiago A, Noel RK, O'Farrell L, et al. STAR particles for enhanced topical drug and vaccine delivery. Nat Med. 2020;26(3):341-7.
23. Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, et al. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. Genes Dis. 2022.
24. Peterson LL, Hurria A, Feng T, Mohile SG, Owusu C, Klepin HD, et al. Association between renal function and chemotherapy-related toxicity in older adults with cancer. J Geriatr Oncol. 2017;8(2):96-101.
25. Bade BC, Cruz CS. Lung cancer 2020: epidemiology, etiology, and prevention. Clin Chest Med. 2020;41(1):1-24.
26. Chen W, di Carlo C, Devery D, McGrath DJ, McHugh PE, Kleinsteinberg K, et al. Fabrication and characterization of gefitinib-releasing polyurethane foam as a coating for drug-eluting stent in the treatment of bronchotracheal cancer. Int J Pharm. 2018;548(2):803-11.
27. Tulbah AS. In vitro bio-characterization of solid lipid nanoparticles of favipiravir in A549 human lung epithelial cancer cells. J Taibah Univ Med Sci. 2023;18(5):1076.
28. Rajivgandhi G, Stalin A, Kanisha CC, Ramachandran G, Manoharan N, Alharbi NS, et al. Physiochemical characterization and anti-carbapenemase activity of chitosan nanoparticles loaded

Aegle marmelos essential oil against K. pneumoniae through DNA fragmentation assay. Surf Interfaces. 2021;23:100932.
29. Barrera-Martínez CL, Padilla-Vaca F, Liakos I, Meléndez-Ortiz HI, Cortez-Mazatan GY, Peralta-Rodríguez RD. Chitosan microparticles as entrapment system for trans-cinnamaldehyde: Synthesis, drug loading, and in vitro cytotoxicity evaluation. Int J Biol Macromol. 2021;166:322-32.
30. Almanaa TN, Alharbi NS, Ramachandran G, Chelliah CK, Rajivgandhi G, Manoharan N, et al. Anti-biofilm effect of Nerium oleander essential oils against biofilm forming Pseudomonas aeruginosa on urinary tract infections. J King Saud Univ Sci. 2021;33(2):101340.
31. Farrag NS, Shetta A, Mamdouh W. Green tea essential oil encapsulated chitosan nanoparticles-based radiopharmaceutical as a new trend for solid tumor theranosis. Int J Biol Macromol. 2021;186:811-9.
32. Yee Kuen C, Galen T, Fakurazi S, Othman SS, Masarudin MJ. Increased cytotoxic efficacy of protocatechuic acid in A549 human lung cancer delivered via hydrophobically modified-chitosan nanoparticles as an anticancer modality. Polymers (Basel). 2020;12(9):1951.
33. Ouyang R, Zhang Q, Cao P, Yang Y, Zhao Y, Liu B, et al. Efficient improvement in chemo/photothermal synergistic therapy against lung cancer using Bi@ Au nano-acanthospheres. Colloids Surf B Biointerfaces. 2023;222:113116.
34. Song Z, Shi Y, Han Q, Dai G. Endothelial growth factor receptor-targeted and reactive oxygen species-responsive lung cancer therapy by docetaxel and resveratrol encapsulated lipid-polymer hybrid nanoparticles. Biomed Pharmacother. 2018;105:18-26.
35. Parvathaneni V, Shukla SK, Kulkarni NS, Gupta V. Development and characterization of inhalable transferrin functionalized amodiaquine nanoparticles–Efficacy in Non-Small Cell Lung Cancer (NSCLC) treatment. Int J Pharm. 2021;608:121038.
36. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. Breast. 2022;66:15-23.
37. Xiong Y, Song X, Kudusi, Zu X, Chen M, He W, Qi L. Oncogenic GBX2 promotes the malignant behaviors of bladder cancer cells by binding to the ITGA5 promoter and activating its transcription. Funct Integr Genomics. 2022;22(5):937-50.
38. Witjes JA, Bruins HM, Cathomas R, Compérat EM, Cowan NC, Gakis G, et al. European Association of Urology guidelines on muscle-invasive and metastatic bladder cancer: summary of the 2020 guidelines. Eur Urol. 2021;79(1):82-104.
39. Saginala K, Barsouk A, Aluru JS, Rawla P, Padala SA, Barsouk A. Epidemiology of bladder cancer. Med Sci (Basel). 2020;8(1):15.
40. Babjuk M, Burger M, Capoun O, Cohen D, Compérat EM, Escrig JL, et al. European Association of Urology guidelines on non–muscle-invasive bladder cancer (Ta, T1, and carcinoma in situ). Eur Urol. 2022;81(1):75-94.
41. Compérat E, Amin MB, Cathomas R, Choudhury A, De Santis M, Kamat A, et al. Current best practice for bladder cancer: a narrative review of diagnostics and treatments. Lancet. 2022.
42. Wang L, Yang D, Lv JY, Yu D, Xin SJ. Application of carbon nanoparticles in lymph node dissection and parathyroid protection during thyroid cancer surgeries: a systematic review and meta-analysis. Onco Targets Ther. 2017;10:1247-60.
43. Li X, Chen L, Luan S, Zhou J, Xiao X, Yang Y, et al. The development and progress of nanomedicine for esophageal cancer diagnosis and treatment. Semin Cancer Biol. 2022 Nov;86:873-85.
44. Zhang C, Zhao J, Wang W, Geng H, Wang Y, Gao B. Current advances in the application of nanomedicine in bladder cancer. Biomed Pharmacother. 2023;157:114062.
45. Nguyen AV, Soulika AM. The dynamics of the skin's immune system. Int J Mol Sci. 2019;20(8):1811.
46. Krishnan V, Mitragotri S. Nanoparticles for topical drug delivery: Potential for skin cancer treatment. Adv Drug Deliv Rev. 2020;153:87-108.
47. Gowda BJ, Ahmed MG, Chinnam S, Paul K, Ashrafuzzaman M, Chavali M, et al. Current trends in bio-waste mediated metal/metal oxide nanoparticles for drug delivery. J Drug Deliv Sci Technol. 2022;71:103305.
48. Mehan N, Kumar M, Bhatt S, Saini V. A current review on drug loaded nanofibers: interesting and valuable platform for skin cancer treatment. Pharm Nanotechnol. 2020;8(3):191-206.
49. Naves LB, Dhand C, Venugopal JR, Rajamani L, Ramakrishna S, Almeida L. Nanotechnology for the treatment of melanoma skin cancer. Prog Biomater. 2017;6:13-26.
50. Peixoto D, Pereira I, Pereira-Silva M, Veiga F, Hamblin MR, Lvov Y, et al. Emerging role of nanoclays in cancer research, diagnosis, and therapy. Coord Chem Rev. 2021;440:213956.
51. Kaur H, Kesharwani P. Advanced nanomedicine approaches applied for treatment of skin carcinoma. J Control Release. 2021;337:589-611.
52. Barenholz Y. Doxil®—The first FDA-approved nano-drug: Lessons learned. J Control Release. 2012;160(2):117-34.
53. Lobo C, Lopes G, Silva O, Gluck S. Paclitaxel albumin-bound particles (abraxane™) in combination with bevacizumab with or without gemcitabine: Early experience at the University of Miami/Braman Family Breast Cancer Institute. Biomed Pharmacother. 2007;61(9):531-3.
54. Akram D, Ahmad S, Sharmin E, Ahmad S. Silica reinforced organic–inorganic hybrid polyurethane nanocomposites from sustainable resource. Macromol Chem Phys. 2010;211(4):412-9.
55. De Leo V, Maurelli AM, Giotta L, Catucci L. Liposomes containing nanoparticles: preparation and applications. Colloids Surf B Biointerfaces. 2022;112737.
56. Kim EM, Jeong HJ. Liposomes: biomedical applications. Chonnam Med J. 2021;57(1):27.
57. Filipczak N, Pan J, Yalamarty SSK, Torchilin VP. Recent advancements in liposome technology. Adv Drug Deliv Rev. 2020;156:4-22.
58. Rajput R, Narkhede J, Naik J. Nanogels as nanocarriers for drug delivery: A review. Admet DMPK. 2020;8(1):1-15.
59. Maddiboyina B, Desu PK, Vasam M, Challa VT, Surendra AV, Rao RS, et al. An insight of nanogels as novel drug delivery system with potential hybrid nanogel applications. J Biomater Sci Polym Ed. 2022;33(2):262-78.
60. Korzhikov-Vlakh V, Tennikova T. Nanogels Capable of Triggered Release. In: Tunable Hydrogels: Smart Materials for Biomedical Applications. 2021:99-146.
61. Sivanesan I, Gopal J, Muthu M, Shin J, Mari S, Oh J. Green synthesized chitosan/chitosan nanoforms/nanocomposites for drug delivery applications. Polymers. 2021;13(14):2256.
62. Pal K, Bharti D, Sarkar P, Anis A, Kim D, Chałas R, et al. Selected applications of chitosan composites. Int J Mol Sci. 2021;22(20):10968.
63. Souto EB, Cano A, Martins-Gomes C, Coutinho TE, Zielińska

A, Silva AM. Microemulsions and nanoemulsions in skin drug delivery. Bioengineering. 2022;9(4):158.
64. Rehman AU, Anton N, Bou S, Schild J, Messaddeq N, Vandamme TF, et al. Tunable functionalization of nano-emulsions using amphiphilic polymers. Soft Matter. 2021;17(7):1788-95.
65. Al-Adham IS, Jaber N, Al-Remawi M, Al-Akayleh F, Al-Kaissi E, Ali Agha AS, et al. A review of the antimicrobial activity of thermodynamically stable microemulsions. Lett Appl Microbiol. 2022;75(3):537-47.
66. Tawfik SM, Azizov S, Elmasry MR, Sharipov M, Lee YI. Recent advances in nanomicelles delivery systems. Nanomaterials. 2020;11(1):70.
67. Majumder N, Das NG, Das SK. Polymeric micelles for anticancer drug delivery. Ther Deliv. 2020;11(10):613-635.
68. Wan Z, Zheng R, Moharil P, Liu Y, Chen J, Sun R, et al. Polymeric micelles in cancer immunotherapy. Molecules. 2021;26(5):1220.
69. D'Acunto M, Cioni P, Gabellieri E, Presciuttini G. Exploiting gold nanoparticles for diagnosis and cancer treatments. Nanotechnology. 2021;32(19):192001.
70. Rastegari E, Hsiao YJ, Lai WY, Lai YH, Yang TC, Chen SJ, et al. An Update on Mesoporous Silica Nanoparticle Applications in Nanomedicines. Pharmaceutics. 2021;13:1067.
71. Mohamed Isa ED, Ahmad H, Abdul Rahman MB, Gill MR. Progress in mesoporous silica nanoparticles as drug delivery agents for cancer treatment. Pharmaceutics. 2021;13(2):152.
72. Khan AU, Chen L, Ge G. Recent development for biomedical applications of magnetic nanoparticles. Inorg Chem Commun. 2021;134:108995.
73. Lu C, Han L, Wang J, Wan J, Song G, Rao J. Engineering of magnetic nanoparticles as magnetic particle imaging tracers. Chem Soc Rev. 2021;50(14):8102-8146.
74. Chavda VP, Vihol D, Mehta B, Shah D, Patel M, Vora LK, et al. Phytochemical-loaded liposomes for anticancer therapy: an updated review. Nanomedicine. 2022;17(8):547-568.
75. Šturm L, Poklar Ulrih N. Basic methods for preparation of liposomes and studying their interactions with different compounds, with the emphasis on polyphenols. Int J Mol Sci. 2021;22(12):6547.
76. Padmasree M, Vishwanath BA. Comparison of In-vitro Release Study of PEGylated and Conventional Liposomes as Carriers for the Treatment of Colon Cancer. International Journal of Pharmaceutical Quality Assurance. 2022;13(2):204-207.
77. Li F, Qin Y, Lee J, Liao H, Wang N, Davis TP, et al. Stimuli-responsive nano-assemblies for remotely controlled drug delivery. J Control Release. 2020;322:566-592.
78. Daré RG, Costa A, Nakamura CV, Truiti MC, Ximenes VF, Lautenschlager SO, et al. Evaluation of lipid nanoparticles for topical delivery of protocatechuic acid and ethyl protocatechuate as a new photoprotection strategy. Int J Pharm. 2020;582:119336.
79. Felippim EC, Marcato PD, Maia Campos PMBG. Development of photoprotective formulations containing nanostructured lipid carriers: sun protection factor, physical-mechanical and sensorial properties. AAPS PharmSciTech. 2020;21:1-14.
80. Iqubal MK, Iqubal A, Imtiyaz K, Rizvi MMA, Gupta MM, Ali J, et al. Combinatorial lipid-nanosystem for dermal delivery of 5-fluorouracil and resveratrol against skin cancer: Delineation of improved dermatokinetics and epidermal drug deposition enhancement analysis. Eur J Pharm Biopharm. 2021;163:223-239.
81. Liu JQ, Zhang C, Zhang X, Yan J, Zeng C, Talebian F, et al. Intratumoral delivery of IL-12 and IL-27 mRNA using lipid nanoparticles for cancer immunotherapy. J Control Release. 2022;345:306-313.
82. Moku G, Vangala S, Gulla SK, Yakati V. In vivo targeting of DNA vaccines to dendritic cells via the mannose receptor induces long-lasting immunity against melanoma. ChemBioChem. 2021;22(3):523-531.
83. Palliyage GH, Hussein N, Mimlitz M, Weeder C, Alnasser MHA, Singh S, et al. Novel curcumin-resveratrol solid nanoparticles synergistically inhibit proliferation of melanoma cells. Pharm Res. 2021;38(5):851-871.
84. Valizadeh A, Khaleghi AA, Roozitalab G, Osanloo M. High anticancer efficacy of solid lipid nanoparticles containing Zataria multiflora essential oil against breast cancer and melanoma cell lines. BMC Pharmacol Toxicol. 2021;22(1):1-7.
85. Ilyas RA, Sapuan SM. The preparation methods and processing of natural fibre bio-polymer composites. Curr Org Synth. 2019;16(8):1068-1070.
86. Gagliardi A, Giuliano E, Venkateswararao E, Fresta M, Bulotta S, Awasthi V, et al. Biodegradable polymeric nanoparticles for drug delivery to solid tumors. Front Pharmacol. 2021;12:601626.
87. Wang W, Meng Q, Li Q, Liu J, Zhou M, Jin Z, et al. Chitosan derivatives and their application in biomedicine. Int J Mol Sci. 2020;21(2):487.
88. Shanmuganathan R, Edison TNJI, LewisOscar F, Kumar P, Shanmugam S, Pugazhendhi A. Chitosan nanopolymers: an overview of drug delivery against cancer. Int J Biol Macromol. 2019;130:727-736.
89. Narmani A, Jafari SM. Chitosan-based nanodelivery systems for cancer therapy: Recent advances. Carbohydr Polym. 2021;272:118464.
90. Jhawat V, Gulia M, Maddiboyina B, Dutt R, Gupta S. Fate and applications of superporous hydrogel systems: a review. Curr Nanomed. 2020;10(4):326-341.
91. Maddiboyina B, Desu PK, Vasam M, Challa VT, Surendra AV, Rao RS, et al. An insight of nanogels as novel drug delivery system with potential hybrid nanogel applications. J Biomater Sci Polym Ed. 2022;33(2):262-278.
92. Gholap A, Tapkir A, More A, Kore P, Bagade P, Nale P, Patil A, Nagure A, Dadas A, Khamkar K. Formulation and Evaluation of Antiaging Ointment Containing Microencapsulated Turmeric and Jojoba Oil. International Journal of Drug Delivery Technology. 2023;13(4):1297-1304.
93. Maddiboyina B, Desu PK, Vasam M, Challa VT, Surendra AV, Rao RS, et al. An insight of nanogels as novel drug delivery system with potential hybrid nanogel applications. J Biomater Sci Polym Ed. 2022;33(2):262-278.
94. Maddiboyina B, Hanumanaik M, Nakkala RK, Jhawat V, Rawat P, Alam A, et al. Formulation and evaluation of gastro-retentive floating bilayer tablet for the treatment of hypertension. Heliyon. 2020;6(11).
95. Li X, Cao C, Wei P, Xu M, Liu Z, Liu L, et al. Self-assembly of amphiphilic peptides for recognizing high furin-expressing cancer cells. ACS Appl Mater Interfaces. 2019;11(13):12327-12334.
96. Majumder N, Das NG, Das SK. Polymeric micelles for anticancer drug delivery. Ther Deliv. 2020;11(10):613-635.
97. Ghosh B, Biswas S. Polymeric micelles in cancer therapy: State of the art. J Control Release. 2021;332:127-147.
98. Perumal S, Atchudan R, Lee W. A review of polymeric micelles and their applications. Polymers. 2022;14(12):2510.

99. Hunter SJ, Armes SP. Pickering emulsifiers based on block copolymer nanoparticles prepared by polymerization-induced self-assembly. Langmuir. 2020;36(51):15463-15484.
100. György C, Hunter SJ, Girou C, Derry MJ, Armes SP. Synthesis of poly (stearyl methacrylate)-poly (2-hydroxypropyl methacrylate) diblock copolymer nanoparticles via RAFT dispersion polymerization of 2-hydroxypropyl methacrylate in mineral oil. Polym Chem. 2020;11(28):4579-4590.
101. Du Z, Li Q, Li J, Su E, Liu X, Wan Z, et al. Self-assembled egg yolk peptide micellar nanoparticles as a versatile emulsifier for food-grade oil-in-water Pickering nanoemulsions. J Agric Food Chem. 2019;67(42):11728-11740.
102. Shanmuganathan R, Edison TNJI, LewisOscar F, Kumar P, Shanmugam S, Pugazhendhi A. Chitosan nanopolymers: an overview of drug delivery against cancer. Int J Biol Macromol. 2019;130:727-736.
103. Chen TY, Tsai MJ, Chang LC, Wu PC. Co-delivery of cisplatin and gemcitabine via viscous nanoemulsion for potential synergistic intravesical chemotherapy. Pharmaceutics. 2020;12(10):949.
104. Prado VC, Sari MHM, Borin BC, do Carmo Pinheiro R, Cruz L, Schuch A, et al. Development of a nanotechnological-based hydrogel containing a novel benzofuroazepine compound in association with vitamin E: An in vitro biological safety and photoprotective hydrogel. Colloids Surf B Biointerfaces. 2021;199:111555.
105. Zhan X, Teng W, Sun K, He J, Yang J, Tian J, et al. CD47-mediated DTIC-loaded chitosan oligosaccharide-grafted nGO for synergistic chemo-photothermal therapy against malignant melanoma. Mater Sci Eng C. 2021;123:112014.
106. Hu JK, Suh HW, Qureshi M, Lewis JM, Yaqoob S, Moscato ZM, et al. Nonsurgical treatment of skin cancer with local delivery of bioadhesive nanoparticles. Proc Natl Acad Sci. 2021;118(7)
107. Mukherjee S, Kotcherlakota R, Haque S, Bhattacharya D, Kumar JM, Chakravarty S, et al. Improved delivery of doxorubicin using rationally designed PEGylated platinum nanoparticles for the treatment of melanoma. Mater Sci Eng C. 2020;108:110375.
108. Song M, Xia W, Tao Z, Zhu B, Zhang W, Liu C, et al. Self-assembled polymeric nanocarrier-mediated co-delivery of metformin and doxorubicin for melanoma therapy. Drug Deliv. 2021;28(1):594-606.
109. Tokarska K, Lamch Ł, Piechota B, Żukowski K, Chudy M, Wilk KA, et al. Co-delivery of IR-768 and daunorubicin using mPEG-b-PLGA micelles for synergistic enhancement of combination therapy of melanoma. J Photochem Photobiol B Biol. 2020;211:111981.
110. Xu Y, Ma S, Si X, Zhao J, Yu H, Ma L, et al. Polyethyleneimine-CpG Nanocomplex as an In Situ Vaccine for Boosting Anticancer Immunity in Melanoma. Macromol Biosci. 2021;21(2):2000207.
111. Li S, Zhang F, Yu Y, Zhang Q. A dermatan sulfate-functionalized biomimetic nanocarrier for melanoma targeted chemotherapy. Carbohydr Polym. 2020;235:115983.
112. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, Wang Y, et al. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. Front Mol Biosci. 2020;7:193.
113. Al-Zahrani SA, Bhat RS, Al Rashed SA, Mahmood A, Al Fahad A, Alamro G, et al. Green-synthesized silver nanoparticles with aqueous extract of green algae Chaetomorpha ligustica and its anticancer potential. Green Process Synth. 2021;10(1):711-721.
114. Włodarczyk R, Kwarciak-Kozłowska A. Nanoparticles from the cosmetics and medical industries in legal and environmental aspects. Sustainability. 2021;13(11):5805.
115. Ssekatawa K, Byarugaba DK, Kato CD, Wampande EM, Ejobi F, Nakavuma JL, et al. Green strategy–based synthesis of silver nanoparticles for antibacterial applications. Front Nanotechnol. 2021;3:697303.
116. Yesilot S, Aydin C. Silver nanoparticles; a new hope in cancer therapy? East J Med. 2019;24(1).
117. Sayed R, Sabry D, Hedeab G, Ali HH. In vitro characterization and evaluation of silver nanoparticles cytotoxicity on human "liver and breast" cancer cells versus normal melanocytes. Egypt J Histol. 2019;42(3):755-766.
118. Xu L, Wang YY, Huang J, Chen CY, Wang ZX, Xie H. Silver nanoparticles: Synthesis, medical applications and biosafety. Theranostics. 2020;10(20):8996.
119. Daghestani M, Al Rashed SA, Bukhari W, Al-Ojayan B, Ibrahim EM, Al-Qahtani AM, et al. Bactericidal and cytotoxic properties of green synthesized nanosilver using Rosmarinus officinalis leaves. Green Process Synth. 2020;9(1):230-236.
120. Rizwana H, Alwhibi MS, Aldarsone HA, Awad MA, Soliman DA, Bhat RS. Green synthesis, characterization, and antimicrobial activity of silver nanoparticles prepared using Trigonella foenum-graecum L. leaves grown in Saudi Arabia. Green Process Synth. 2021;10(1):421-429.
121. Jadoun S, Arif R, Jangid NK, Meena RK. Green synthesis of nanoparticles using plant extracts: A review. Environ Chem Lett. 2021;19:355-374.
122. Naikoo GA, Mustaqeem M, Hassan IU, Awan T, Arshad F, Salim H, et al. Bioinspired and green synthesis of nanoparticles from plant extracts with antiviral and antimicrobial properties: A critical review. J Saudi Chem Soc. 2021;25(9):101304.
123. Saravanan M, Vahidi H, Medina Cruz D, Vernet-Crua A, Mostafavi E, Stelmach R, et al. Emerging antineoplastic biogenic gold nanomaterials for breast cancer therapeutics: a systematic review. Int J Nanomedicine. 2020;3577-3595.
124. Barani M, Hosseinikhah SM, Rahdar A, Farhoudi L, Arshad R, Cucchiarini M, et al. Nanotechnology in bladder cancer: diagnosis and treatment. Cancers. 2021;13(9):2214.
125. Yafout M, Ousaid A, Khayati Y, El Otmani IS. Gold nanoparticles as a drug delivery system for standard chemotherapeutics: A new lead for targeted pharmacological cancer treatments. Sci Afr. 2021;11
126. Sharifi M, Attar F, Saboury AA, Akhtari K, Hooshmand N, Hasan A, et al. Plasmonic gold nanoparticles: Optical manipulation, imaging, drug delivery and therapy. J Control Release. 2019;311:170-189.
127. Kang MS, Lee SY, Kim KS, Han DW. State of the art biocompatible gold nanoparticles for cancer theragnosis. Pharmaceutics. 2020;12(8):701.
128. Kaur R, Singh J, Avti PK, Kumar V, Kumar R. Anisotropic Gold Nanoparticles Synthesized using Litchi chinensis Leaf Extract and their Effect on Breast Cancer. International Journal of Drug Delivery Technology. 2023;13(4):1131-1138.
129. Yang Y, Zheng X, Chen L, Gong X, Yang H, Duan X, et al. Multifunctional gold nanoparticles in cancer diagnosis and treatment. Int J Nanomedicine. 2022;2041-2067.
130. Ahmed W, Elhissi A, Dhanak V, Subramani K. Carbon nanotubes: Applications in cancer therapy and drug delivery research. In: Emerging nanotechnologies in dentistry. William

Andrew Publishing; 2018. p. 371-389.
131. Jampilek J, Kralova K. Advances in drug delivery nanosystems using graphene-based materials and carbon nanotubes. Materials. 2021;14(5):1059.
132. Kiran AR, Kumari GK, Krishnamurthy PT. Carbon nanotubes in drug delivery: Focus on anticancer therapies. J Drug Deliv Sci Technol. 2020;59:101892.
133. Barabadi H, Vahidi H, Mahjoub MA, Kosar Z, Damavandi Kamali K, Ponmurugan K, et al. Emerging antineoplastic gold nanomaterials for cervical cancer therapeutics: a systematic review. J Cluster Sci. 2020;31:1173-1184.
134. Kenchegowda M, Rahamathulla M, Hani U, Begum MY, Guruswamy S, Osmani RAM, et al. Smart nanocarriers as an emerging platform for cancer therapy: A review. Molecules. 2021;27(1):146.
135. Castillo RR, Lozano D, Vallet-Regí M. Mesoporous silica nanoparticles as carriers for therapeutic biomolecules. Pharmaceutics. 2020;12(5):432.
136. Porrang S, Davaran S, Rahemi N, Allahyari S, Mostafavi E. How advancing are mesoporous silica nanoparticles? A comprehensive review of the literature. Int J Nanomedicine. 2022;1803-1827.
137. Ho YY, Sun DS, Chang HH. Silver nanoparticles protect skin from ultraviolet b-induced damage in mice. Int J Mol Sci. 2020;21(19):7082.
138. Miri A, Akbarpour Birjandi S, Sarani M. Survey of cytotoxic and UV protection effects of biosynthesized cerium oxide nanoparticles. J Biochem Mol Toxicol. 2020;34(6)
139. Miri A, Beiki H, Najafidoust A, Khatami M, Sarani M. Cerium oxide nanoparticles: green synthesis using Banana peel, cytotoxic effect, UV protection and their photocatalytic activity. Bioprocess Biosyst Eng. 2021;44(9):1891-1899.
140. Torbati TV, Javanbakht V. Fabrication of TiO2/Zn2TiO4/Ag nanocomposite for synergic effects of UV radiation protection and antibacterial activity in sunscreen. Colloids Surf B Biointerfaces. 2020;187:110652.
141. Rizzi V, Gubitosa J, Fini P, Nuzzo S, Agostiano A, Cosma P. Snail slime-based gold nanoparticles: An interesting potential ingredient in cosmetics as an antioxidant, sunscreen, and tyrosinase inhibitor. J Photochem Photobiol B Biol. 2021;224:112309.
142. Amatya R, Hwang S, Park T, Chung YJ, Ryu S, Lee J, et al. BSA/silver nanoparticle-loaded hydrogel film for local photothermal treatment of skin cancer. Pharm Res. 2021;38:873-883.
143. Ji W, Li L, Zhou S, Qiu L, Qian Z, Zhang H, et al. Combination immunotherapy of oncolytic virus nanovesicles and PD-1 blockade effectively enhances therapeutic effects and boosts antitumour immune response. J Drug Target. 2020;28(9):982-990.
144. Mo C, Lu L, Liu D, Wei K. Development of erianin-loaded dendritic mesoporous silica nanospheres with pro-apoptotic effects and enhanced topical delivery. J Nanobiotechnology. 2020;18(1):1-14.
145. Li TF, Xu HZ, Xu YH, Yu TT, Tang JM, Li K, et al. Efficient delivery of chlorin e6 by polyglycerol-coated iron oxide nanoparticles with conjugated doxorubicin for enhanced photodynamic therapy of melanoma. Mol Pharm. 2021;18(9):3601-3615.
146. Huang W, Xing Y, Zhu L, Zhuo J, Cai M. Sorafenib derivatives-functionalized gold nanoparticles confer protection against tumor angiogenesis and proliferation via suppression of EGFR and VEGFR-2. Exp Cell Res. 2021;406(1):112633