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Nanomaterials for Cancer Therapy

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Abstract*: Cancer is one of the worst diseases in the world. Nanotechnology, being a novel technology, has recently been widely used in cancer therapy through diagnostics, imaging, and theranostics. Cancer is a disease with a complex pathology. Here are some examples of nanomaterials utilized in cancer therapy, along with their associated properties. Current chemotherapy has issues such as lack of selectivity, cytotoxicity, induction of multidrug resistance, and stem-like cell development. Nanomaterials are materials with optical, magnetic, and electrical properties that are unique to the nanoscale (1-100 nm). Nanomaterials utilized in cancer therapy are categorized into numerous types. Furthermore, as new multidrug resistance pathways are discovered and explored, nanoparticles are being studied more closely. In this thorough review, we have summarized the current understanding and effort in this field to pave the path for physicians to accelerate the implementation* of hybrid modes of treatments by leveraging the usage of diverse nanoparticles.

Keywords: Nanoparticles, Nanotechnology, Cancer therapy, Polymeric materials

I. INTRODUCTION

Cancer is widely regarded as the result of gene alterations [1]. Cancer is a broad word for a group of diseases distinguished by uncontrolled, random cell division and invasiveness. Over the past many years, extensive efforts have been made to identify numerous cancer risk factors [2]. However, the interaction between malignancies and the immune system is more than just an antagonistic relationship; it also includes a complicated process of tumor growth, metastasis, invasion, and recurrence, which can lead to resistance to existing immunotherapeutic medications [3]. Nanotechnology is a relatively young branch of scientific inquiry that studies the structure, properties, and behavior of materials smaller than a few hundred nano meters (Ferrari 2005).). Nanotechnology has recently sparked great interest in cancer therapies because to its enormous potential to provide a fresh paradigm for overcoming the limitations of traditional chemotherapeutic drugs [4]. Targeted drug delivery was significantly improved by the specific binding of nano ligands conveying the drug to tumor cell surface receptors. Coupling the nanoparticles with drug-carrying polymers (such as poly lactic-co glycolic acid—PLGA) improved drug absorption and increased toxicity to tumor cells [5]. Understanding smart nanoparticles necessitates a variety of views, including those that overlap. In this example, a smart nanoparticle can be thought of as a toolbox [6].]. Photothermal, magnetic, and neutron-capture systems. Unfortunately, the use of nanomaterials as carriers of therapeutic compounds has some drawbacks that preclude these therapeutic systems from practical use [7]. Thus, discovering new, improved, safer, and more targeted medicines is critical for cancer patients. In recent decades, numerous techniques to cancer treatment have arisen that go beyond typical chemotherapy. Advanced technology, including genomic methods, [8]. The combination of biology with nanotechnology has been heralded as a significant technical advance with a wide range of applications, including diagnostic devices, biosensing, drug delivery systems, and customized therapeutic therapies [9]. Given the variety of colloidal nanoparticles available, systematic classification is difficult, and various attempts have been made. Therefore, nano particles can be classed based on their form, average size, chemical composition, and Among other characteristics, the technique of preparation is mentioned [10]. Nanoparticles have various advantages over small-molecule medications, including a longer circulation period and better distribution to specific locations. Once an NP reaches the body, it interacts with the host's immune system before being swallowed by mononuclear phagocyte cells. The interaction of nanoparticles with immune cells can cause immunological repression or immune activation, which can improve or lessen the therapy benefits of nanoparticles [11]. Nanoparticles are atomic groupings of matter that range in size from 1 to 100 nano meters. Research into inorganic nanoparticles and their interactions with biological systems is in the early phases, with the goal of determining their response and tuning them to desired qualities by functionalisation [12]. In this study, we detail the recent successes in the development of the the use of nanomaterials in cancer therapies, with a focus on synthetic processes, therapeutic agent delivery, and tumor imaging, includes inorganic nanomaterials such as carbon nanotubes, silica NPs, gold NPs, magnetic NPs, and quantum dots, as well as emerging organic nanomaterials such as polymeric micelles, liposomes, dendrimers, and so on [14].

II. NANOTECHNOLOGY USED IN CANCER THERAPY

Characteristics of nanomaterials [1].

Medical nanotechnology makes use of nanoscale materials, which typically range in size from 1-100 nm. These materials are used to design and produce medicinal medications and devices. As the size reduces to the nanoscale, various new optical, magnetic, and electrical properties emerge, distinguishing nanomaterials from standard macromolecules. Typical nanomaterials feature several common characteristics: high surface-to-volume ratio, increased electrical conductivity, superparamagnetic activity, spectral shift of optical absorption, and unique unusual fluorescence features. [1]

Liposome-modified nanomaterials [3]

Liposomes are a new type of medication carrier that has been intensively studied in cancer treatment. Liposomes are closed vesicles with an interior aqueous phase composed of lipid bilayers, which have made major contributions to drug carrier biocompatibility, biodegradability, cytotoxicity, immunogenicity, and so on. Small single vesicles, multilamellar vesicles, and big monomolecular vesicles are the three most common forms of cysts [3].

Nanoparticles with characteristics : [11]

1. Carbon-based nanoparticles have excellent physiochemical properties, such as strong penetration into cell membranes and high surface area. Excellent physiochemical features, including high-level penetration across the cell membrane, high surface area, and high drug loading capacity[11].
2. Ceramic nanoparticles have high biocompatibility [11].
3. Magnetic nanoparticles play a significant role in detecting and protecting metastatic breast cancer [11].
4. Polymeric nanoparticles are surrounded by polymer shells [11].
5. Lipid-based nanoparticles are more biocompatible and have lower toxicity compared to inorganic nanoparticles [11].

Polymeric nanoparticles [1].

Nanoparticles' components have evolved throughout time. Initially, nanoparticles were made from nonbiodegradable polymers such as polymethyl methacrylate (PMMA), polyacrylamide, polystyrene, and polyacrylates.[1]

Organic nanomaterials for cancer treatment [14].

Natural or synthetic polymer-formed organic-based nanomaterials have been widely exploited in cancer therapy due to their superior features such as biological compatibility and degradability. They can be classified into five types: polymeric micelles, polymeric NPs, liposomes, dendrimers, and polymer-drug conjugates [14].

Nanomaterials for cancer treatment [1].

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Fig: A [1]

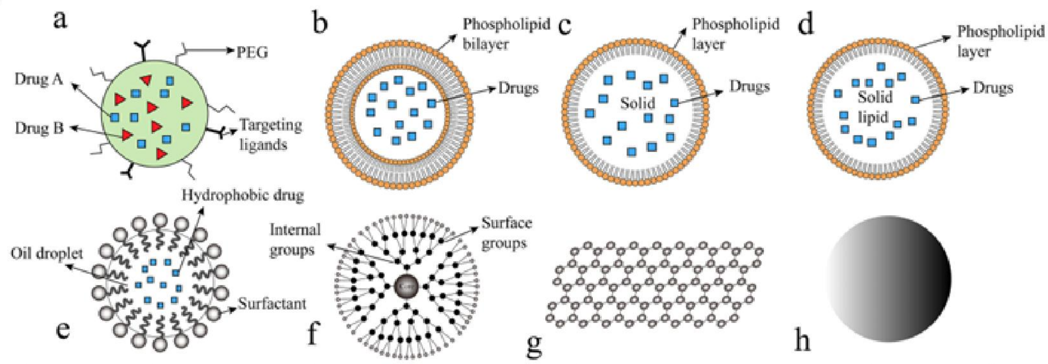

Fig. 1 Categories of nanomaterials applied in cancer treatment. **a** Nanoparticles. **b** Liposomes. **c** Solid lipid nanoparticles. **d** Nanostructured lipid carriers. **e** Nanoemulsions. **f** Dendrimers. **g** Graphene. h Metallic nanoparticles. PEG, poly(ethylene glycol)

III. SYNTHESIS OF NPS : [2,9,11]

The nanoparticles vary in shape, size, and structure. Several synthesis approaches are used to achieve this goal. These methods can be broadly divided into two basic categories:

1) The bottom-up method

2) The top-down approach.

These techniques are further categorized into several subclasses based on reaction conditions and operation

Fig.2 [2]

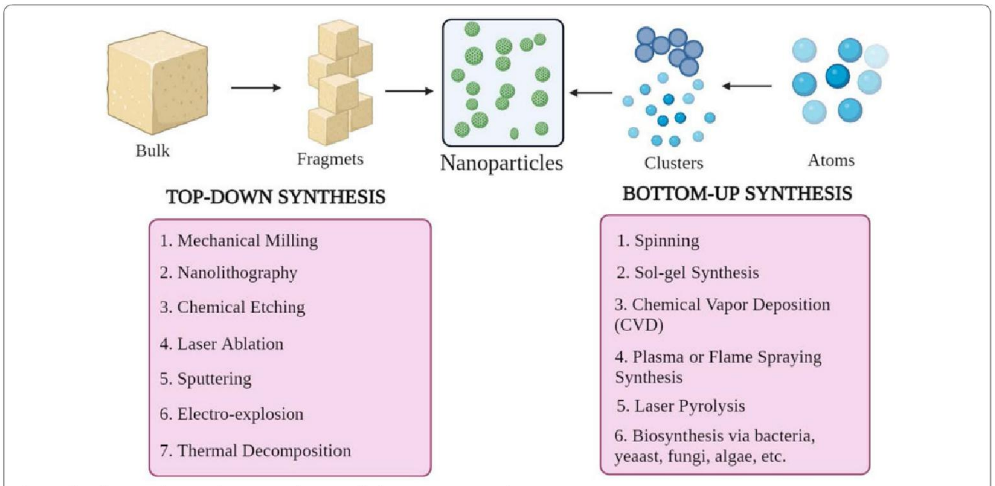

Fig. 2 Classification of NP synthesis **a** top-down and **b** bottom-up approaches

Bottom-up Approach [2, 9]

This process includes creating material from atoms to clusters to NPs, i.e., from simpler substances, and is thus known as the constructive method. Commonly used methods include the bottom-up approach [2, 9].

This process includes creating material from atoms to clusters to NPs, i.e., from simpler substances, and is thus known as the constructive method. Spinning, solgel synthesis, chemical vapor deposition (CVD), plasma or flame spraying synthesis, laser pyrolysis, and biosynthesis are some of the most popular processes.

Chemical vapor deposition (CVD). The chemical vapor deposition method deposits a thin film onto a substrate through the chemical reaction of the gaseous substrate. This reaction is commonly carried out at Use a sealed jar with a pressure higher than the boiling point of the solvent (9).

The top-down approach [2,9,11]

It is sometimes referred to as the destructive approach, as it reduces bulk material or substance in order to produce NPs. A bigger molecule is divided into smaller pieces, which are then transformed into NPs. Mechanical milling, nanolithography, chemical etching, laser ablation, sputtering, electrical explosion, and thermal decomposition are among the methods used [2].

Lithography -Nanomaterials are synthesized by a concentrated electron beam. This technique is roughly divided into two categories: masked lithography and maskless lithography. In microfabrication, lithography is used to pattern part of a thin film using the bulk substrate [9].

Mechanical milling-Mechanical milling is one of the top-down ways for producing different nanoparticles. Milling seeks to reduce particle size and combine them in an inert atmosphere. Plastic deformation controls particle shape and fracture, as well as particle size, while cold welding increases particle size and influences mechanical milling. This process is simple, low-cost, and can create nanoparticles of varying sizes. [9]

Laser ablation is a popular process for creating nanomaterials such as semi conductors, metal nanoparticles, nanowires, composites, and ceramic carbon nanotubes using various solvents. In this method, a laser beam is directed toward a metal solution. Because of the high laser intensity, the precursor evaporates, followed by nucleation and development of of a plasma plume, which results in the formation of nanoparticles.[9]

Nanomaterials can be created using either synthetic methods or renewable technologies. Synthetic processes include chemical vapor deposition, thermal decomposition, hydrothermal synthesis, solvothermal synthesis, pulsed laser ablation, temperature, combustion, Nanomaterials can be created using either synthetic methods or renewable technologies. Chemical vapor deposition, thermal breakdown, hydrothermal synthesis, solvothermal synthesis, pulsed laser ablation, templating, combustion, microwave synthesis, and gas phase synthesis are some synthetic processes [11].

IV. NANOPARTICLES IN CANCER THERAPY :[1,2,3,5,10,11,14].

Nano-emulsions-Nano emulsions (NE) are colloidal nanoparticles composed of aqueous phase, emulsifying agents, and oil. The size of a nanoemulsion ranges from 10 to 1000 nm. Nano emulsions are widely utilized drug nanocarriers, which are typically solid spheres with amorphous and lipophilic surfaces that exhibit negative charge [1].

Metallic materials - Metallic elements are vital components of the living body, playing a role in practically every life function. Many new products have emerged in nanomaterials that mix metallic elements with traditional therapeutic method and these goods exploit the activity of metallic elements in living organisms to improve the flaws of the original therapeutic methods, such as Zhang etal [3].

Metal and metal oxide nanoparticles, polymeric micelles, polymer/lipids, and other conjugates. The remaining medications are based on metals and metal oxides, polymeric micelles, polymer lipids, and other conjugates, and are undergoing various phases of approval or trials. Platinum is one of the most utilized metals for the delivery of anticancer medicines; cisplatin was the first to be used as an anti-cancer medication, followed by a number of additional chemicals. Platinol, along with picoplatin, carboplatin, sebriplatin, ormaplatin, oxaliplatin, aroplatin, enloplatin, satraplatin, zeniplatin, miboplatin, satraplatin, and iproplatin, was licensed by the FDA for combination therapy for a number of malignancies [5].

Gold nanoparticles, along with their equivalents, have shown exceptional potential in improving cancer cell susceptibility to radiation therapy. When these nanoparticles are precisely targeted to neoplastic foci, they enhance the absorption of radiation energy, exacerbating cellular damage[10].

Solid Lipid Nanoparticles (SLN) are colloidal nanocarriers (1–100 nm) composed of a phospholipid monolayer, emulsifier, and water[10].

Nanoparticles such as **gold, silver, silica, magnetics, and iron oxide** are employed in cancer diagnostics because of their quick detection time and low cost. In addition, They have fewer adverse effects than chemical-based therapies and radiation. Electrochemical biosensors are simple, inexpensive, and effective for cancer detection. Functionalization can boost nanoparticles' cancer detection capacities. For example, in order to detect breast adenocarcinoma cells, cancer antibodies were coupled with polyethylene glycol (PEG). This antibody PEG complex was subsequently attached to the nanoparticle surface via a sulfur-containing group at the PEG linker's distal end [11].

Fig.C [11]

Table 5. Application of magnetic nanoparticles in cancer detection and screening.

Type of Nanoparticle	Cancer Cells	Applications
Magnetic gold nanoparticles	Breast cancer checks	ELISA-based detection of breast cancer, specifically for HER2 breast cancer patients.
Magnetic nanoparticles	Liver cancer cells	Enhanced detection of liver cancer cells (in vitro)
Magnetic nanoparticles	Brain cancer cells	Magnetic nanoparticles as contrast agents in the diagnosis and treatment of cancer (in vivo)
Surface-modified magnetic nanoparticles	Colon cancer cells	For colon cancer cell theranostics (in vitro)
Superparamagnetic iron oxide nanoparticles	Pancreatic cancer cells	Pancreatic cancer diagnosis using MRI and potential for early diagnosis through targeted strategies

Polymeric nanoparticles

Polymeric nanoparticles (PNPs) are characterized as "colloidal macromolecules" having a distinct structural architecture produced by various monomers [2]. PEG is the most commonly employed in the construction of the hydrophilic shell, which can aid to stabilize and protect the carriers from degradation by minimizing unspecific interactions in vivo [14].

Fig. C [14]

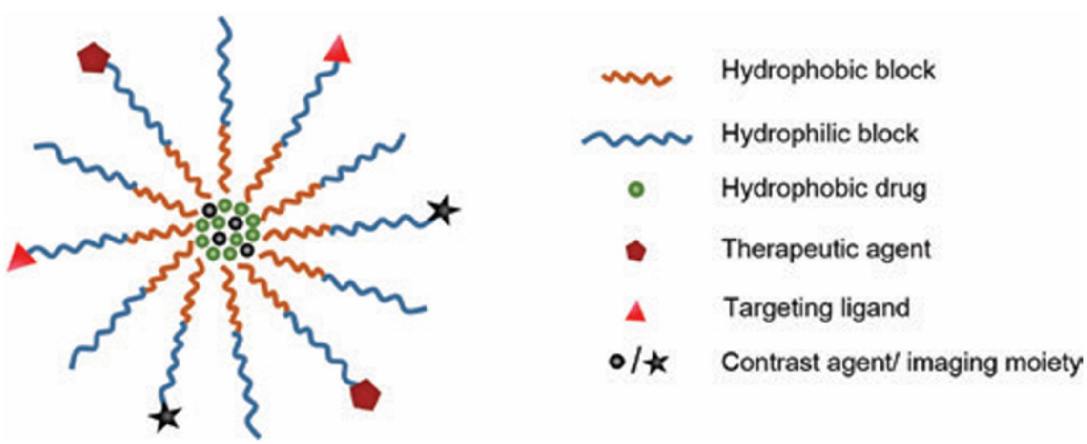

Figure 2: Schematic of optimized polymeric micelle for anticancer therapy, bearing targeting ligands, contrast agents or imaging moieties and therapeutic drugs.

V. DRUG TARGETING TECHNIQUES IN CANCER THERAPY [2,5].

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NPs are known to cross the BBB. NPs are now delivered by a variety of methods, including the EPR effect, targeted ultrasound, pep tide-modified endocytosis, and transcytosis. Glutathione PEGylated liposomes encapsulated with methotrexate demonstrated enhanced methotrexate absorption in rats [2].

Fig . E [5]

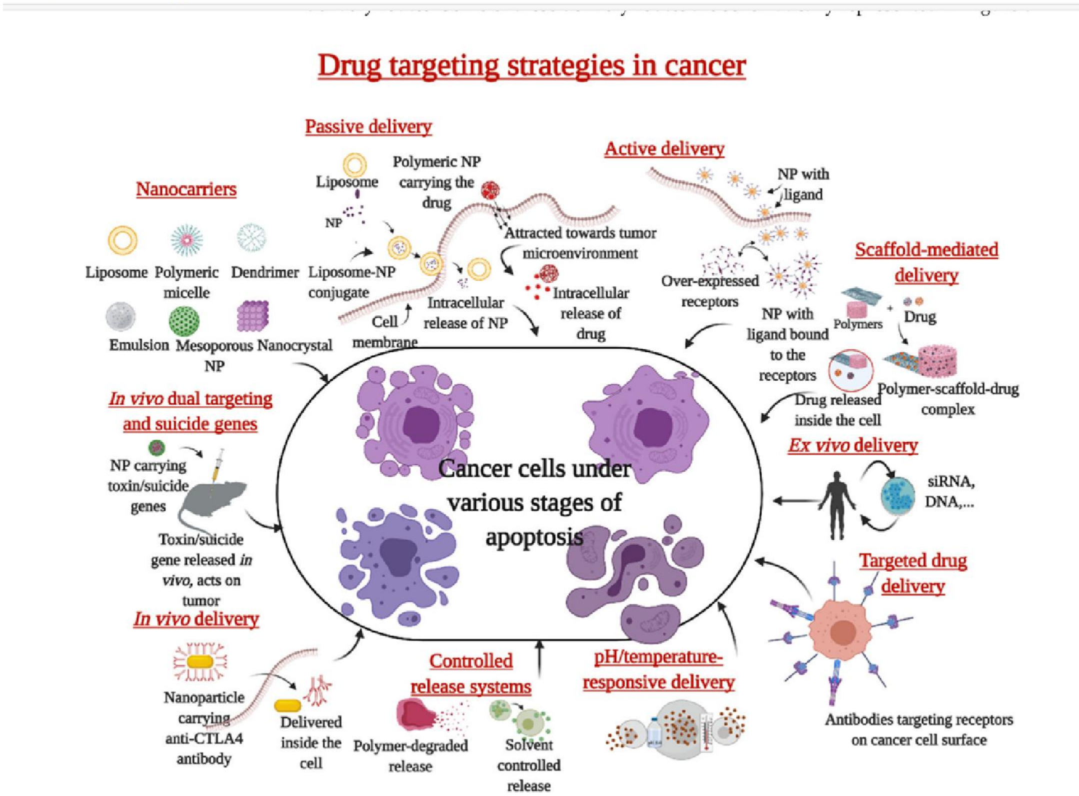

Figure 6. Schematic representation of the drug targeting strategies followed to deliver therapeutic molecules to cancer cells. The various modes of drug delivery ensure that the drug is effectively delivered to the cells of interest and thus, unwanted damage to normal cells can be minimized.

VI. THE ADVANTAGES OF NANOPARTICLES IN CANCER THERAPY

The pH-sensitive drug delivery device can deliver medications to the acidic TME. Similarly, temperature sensitive NPs release medications at the target region in response to temperature variations induced by sources such as magnetic fields and ultrasonic waves. Furthermore, the "physicochemical characteristics" of NPs, such as shape, size, molecular mass, and surface chemistry, play a vital role in the targeted drug delivery system [2].Using nanoparticles as contrast agents in imaging can improve penetration power, acquisition speed, and specificity/sensitivity.Surface-Enhanced Raman Scattering (SERS) combined with nanoparticles has numerous advantages, including the ability to detect multiple forms of cancer simultaneously and observe prolonged tumors in vivo[5]. There are numerous advantages of utilizing smart nanoparticles for ratio-metric distribution of synergistic medication combinations for cancer treatment in clinical settings. For example, smart nanoparticle-based synergistic drug combination delivery can modify the pharmacokinetics and biodistribution of ratio metric medicine combinations administered in free solution [6].Nanomaterials are the optimal choice for controlled drug delivery, diagnostics, and imaging. It promotes therapeutic efficacy by increasing sensitivity, light absorption, drug half-life, solubility, and assuring long-term drug release [13].

SOME OTHER NANOMATERIALS & METHODS USED IN CANCER THERAPY:

Palladium-based nanomaterials Compared to other intensively studied noble nanomaterials, such as Au and Ag nanostructures [21], research on biomedical applications of Pd-based nanomaterials began later, owing to the optical absorption of Pd NPs being primarily located in the UV-Vis region, which received less favorable attention.[15]

Bimetallic nanomaterials Many methods for the synthesis of BMNs are documented, and some products can be produced by different methods because to similarities in basic physics. [16].**Ferroptosis** is a new type of programmed cell death that is predicted to play an essential role in cancer treatment.[17]

Metal sulfide nanoparticles (MeSNs) are a novel type of metal-containing nanomaterials made up of metal ions and sulfur molecules.[18] .Injectable hydrogels for the transport of nanoparticles. This approach uses photoresponsive nanostructures Photoresponsive drugs are delivered intravenously, collect at the tumor site, and when exposed to near infrared (NIR, 750-1000 nm) light, cause a local temperature increase, leading in the death of cancer cells.[19] Silicon nanoparticles are an important class of nanomaterials with significant potential for technologies such as energy, catalysis, and biotechnology, due to their numerous distinctive qualities, including biocompatibility, abundance, and unique electrical, optical, and mechanical capabilities, among others. [20] Hybrid materials are defined as composites consisting of at least two constituents, usually organic and inorganic, at the nanometer or molecular level. They have a surprising long history, dating back to the emergence of paints made from inorganic and organic components thousands of years ago.[21**].**

Copper-based nanomaterials (Cu-based NMs) have good biocompatibility and Many biomedical researchers have been drawn to these unique features. Cu-based nanomaterials are among the most extensively researched materials in cancer treatment. [22] .Silicon nanoparticles are an important class of nanomaterials with significant potential for technologies like energy, catalysis, and biotechnology, due to their numerous distinctive qualities, including biocompatibility, abundance, and unique electrical, optical, and mechanical capabilities, among others. [20] Photobiomodulation (PBM) is an alternative and traditional medical approach that uses low-intensity light sources, such as lasers or light-emitting diodes (LEDs), to treat a variety of disorders.[23] .Biodegradable Organic Nanomaterials Inorganic nanoparticles function as innovative platforms for bridging the gap between medicines and therapeutic targets. They have been widely employed in cancer theranostics because of their natural physicochemical qualities, which include exceptional optical, thermal, and magnetic features, as well as their good performance in targeted drug administration, controlled drug release, and imaging capability [24]. Nanotechnology-based medication delivery devices have opened up new opportunities in this field by minimizing these restrictions. 5. For example, nanoformulations improve the elimination half-life of medications and preserve them in circulation for a longer period of time [25].

Silicon-based nanomaterials with unique characteristics have gained a lot of attention in recent years, indicating significant promise for a variety of biological and medicinal applications. [26] .Nanomedicines make use of nanoscale or nanostructured materials in medicines for specific medicinal applications. In this study, we illustrate the current developments of various nanomedicines for liver cancer by providing chosen instances in different stages. [27] Gold nanoparticles have been explored for many years to induce PDT because of some of their promising qualities, such as high surface areas, strong biocompatibility, and rapid surface modification via gold-thiol chemistry. [28] .According to World Health Organization data for 2020, there are approximately 19 million new cancer diagnoses and 10 million cancer-related deaths worldwide. Despite massive improvements in cancer detection and treatment over the last few decades—such as more precise diagnostic procedures and more tailored therapy methods—many problems persist [29]. One example is doxorubicin (DOX), one of the most used chemotherapy drugs, which promotes apoptosis of fast dividing cells while destroying several normal body cells that divide rapidly under normal conditions. [30] .Furthermore, carbon-based NPs encapsulated within CNTs can greatly increase ultrasonic signal amplitude and echo duration, resulting in better imaging results. [31] .In turn, the adoption of enzyme therapy has been extended beyond the use in genetic disorders and is currently being investigated in the treatment of a plethora of other diseases, such as cancer treatments [32] .Early cancer diagnosis is expected to reduce the death rate. The most common procedures for cancer detection are magnetic resonance imaging (MRI) and computed tomography (CT scan) [33]. Furthermore, by both passive and active targeting, these nanocarriers can preferentially concentrate in tumors' leaky vasculature via the increased permeation and retention (EPR) effect. More than two dozen nanomedicine formulations have previously been approved for therapeutic use, while others are currently in clinical testing [34].The application of nanomaterials in cancer theranostics is garnering enormous attention as a result of advancements in nanobiotechnology [35]. A sequence of biological events must be initiated, repeated, and increased in the cancer-immunity cycle in order to elicit an efficient antitumor immune response. [36] One study revealed that copper sulfide (CuS) nanoparticle-based medication delivery was effective in cancer treatment. Cancer cells' three basic metabolic pathways are regulated by many carcinogenic signaling mechanisms. These metabolicpathways include metabolism of lipids, amino acids, and glucose. [38] **Cisplatin** (Cis) was the first platinum-based medicine licensed by the US FDA for the treatment of malignancies, including ovarian. [39] However, although cancer immunotherapy has been proved to be durable and successful in treating tumors, only a small fraction of patients (about 10%) get a favorable clinical response [40]. Functional inorganic nanomaterials, typically metal and semiconductor nanostructures, as emerging panaceas, have piqued the curiosity of many due to their non-invasive penetrating capacity, multifunctionality, improved biocompatibility, and other properties. [41] Nanotherapeutic technologies can circumvent various difficulties presented by traditional cancer therapy. [42] fungi, algae, yeast, plant viruses, bacteria, and plants, as well as other natural resources, have been widely used as reducing/capping agents in the greener synthesis of nanomaterials [43]. The unique and active role of nano biomaterials with amplified characteristics is constantly being explored in order to reduce harmful practices and adverse effects. [44]. Above mentioned data provides information on various types of nanomaterials used in cancer therapy with its action.

VII. CONCLUSION

Cancer treatments based on these distinct features have been extensively investigated. In general, different nanomaterials can have their surfaces modified, and in many circumstances, standard anti-tumor chemical medicines can be loaded into distinct nanocarriers. Because they can be tuned to target specific cells and tissues, nanoparticles have shown great promise in cancer diagnosis and treatment. However, successfully translating NP-based medicines to the clinic presents a number of problems. Some of these structures have already been used in vivo, in vitro, and in clinical translation due to their relevant features for cancer therapies, such as size- and surface-dependent properties, versatility in synthesis and surface modification, diverse functionalities, and modification to improve biocompatibility. There are already Some innovative nanomaterial-based structures approved for cancer therapy are commercially available, including Abraxane, Doxil, and Embosphere, among others. Despite the numerous benefits, the successful translation of nanomaterial-based medicines into clinical practice faces numerous problems and hurdles, including biocompatibility, pharmacokinetics, and in vivo targeting efficacy.

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