Review

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Review

Current Development of Bio-Inspired Nanoparticles in Cancer Theragnostics

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Abstract: The introduction of cancer therapeutics and nanotechnology has resulted in a paradigm shift from conventional therapy to precision medicine. Nanotechnology, an interdisciplinary field with a focus on biomedical applications, holds immense promise in bringing about novel approaches for cancer detection, diagnosis, and therapy. The past decade has witnessed significant research and material applications related to nanoparticles (NPs). NPs differ from small-molecule drugs as they possess unique physicochemical characteristics, such as a large surface-to-volume ratio, enabling them to penetrate live cells efficiently. Traditional cancer therapies, such as chemotherapy, radiation therapy, targeted therapy, and immunotherapy, have limitations, such as cytotoxicity, lack of specificity, and multiple drug resistance, which pose significant challenges for effective cancer treatment. However, nanomaterials have unique properties that enable new therapeutic modalities beyond conventional drug delivery in the fight against cancer. Moreover, nanoparticles (1-100 nm) have numerous benefits, such as biocompatibility, reduced toxicity, excellent stability, enhanced permeability and retention effect, and precise targeting, making them ideal for cancer treatment. The purpose of this article is to provide consolidated information on various bio-inspired nanoparticles that aid in cancer theragnostics.

Keywords: nanoparticles; quantum dots; radioisotopes; liposomes; micelles; nanobubbles; theranostics; therapeutics; toxicity

1. Introduction

Nowadays, cancer is a second biggest cause for death amongst humans [1]. The World Health Organization estimates that cancer caused more than 10 million deaths globally in 2022, which equates to 1 in 6 fatalities [2]. Lung, skin, colorectal, breast, prostate and stomach cancers are the most prevalent types of cancer, and they are listed chronologically from highest to lowest cancer case numbers [3]. Cancer research has made significant strides, but a cure is still many years away [4].

Theragnostic is a new biomedical procedure that combines diagnosis and treatment into one step. Targeting particular (diseased) tissues or cells with precision in order to improve the accuracy of diagnostic and therapeutic procedures is a distinctive aim of theranostics [5]. Theragnostic' main goal is to combine critical phases of medical care, like diagnosis and therapy, in order to speed up, make care safer, and improve outcomes [6]. Drug delivery using nanoparticles is a successful method for overcoming the difficulties of on the loose drug administration [7]. The chargeless chemotherapeutic agents have very slight bioavailability and, by activating various efflux mechanisms in cancer cells, cause drug resistance. Drug delivery using nanoparticles is advantageous for suppressing various drug resistance phenomena in cancer cells [8]. In contrast to small molecules, which enter cells through diffusion, receptor-mediated endocytosis is how nanoparticles are internalised [9]. The procedure enables the drug to be released from the lysosomal compartments by nanocarriers [10].

With each passing year, cancer's global toll rises and is quickly overtaking all other causes of death. Natural compounds appear to be an option with fewer side effects than chemotherapy, though their bioavailability is still a concern. Chemotherapy plays an important role but causes side effects.

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Quantum dots (QDs) with a bioinspired design derived from plant sources exhibit promising drug delivery and anti-cancer potential with minimal toxicity [11–14]. QDs are widely used in many different applications and can be specifically used for bio-imaging and drug delivery in cancer therapy due to their well-known optical activity. Additionally, using bioinspired QDs as a delivery system for anti-cancer drugs is less studied [15].

Liposomes were first employed in few simple experiments, like the photochemistry of biological membranes, and are now mainly known for their amazing prospectus in the controlled release of a wide variety of drugs [16]. Liposomes used to be used to load a variety of PSs for the photodynamic cancer therapy due to their many benefits and potentials. Combining photochemistry and photo physics, the multidisciplinary field of photodynamic therapy (PDT) has enormous potential for use in cancer treatment [17]. To create cytotoxic and reactive oxygen species as well as subsequently oxidise light-exposed tissues, PDT uses a photosensitizing agent (PS) and light. Available PSs are still far away from being an ideal therapy, despite the many benefits of PDT and the tremendous progress made in this area, due to its low permeability, side effects, non-specific phototoxicity, hydrophobicity, weak bioavailability, and propensity for self-aggregation [18–20]. PS can be enclosed in such small liposomes, a cutting-edge drug delivering system that has shown to improve drug permeability into the biological membranes and load both the lipophilic agents and hydrophobic, to get around these restrictions. To increase the effectiveness of delivery, liposomes can be covered with targeting agents [21].

Drug delivery systems have been a main area of focus for pharmaceutical research from the start. In the current technological era of nanocarriers, polymeric micelles, also known more commonly as just PMs, have emerged as multifunctional nanoparticles that have shown promise in a number of scientific fields [22]. Due to their enhanced retention and permeability, which enable them to change the release profile of the integrated pharmacological substances and concentrate them in the target zone, they are much better suited for the poorly soluble medications. PMs are anticipated to be a treatment option which is super successful for the cancer therapy in the coming time due to their amazing biocompatibility, enhanced permeability, very less toxicity to healthy cells, and ability to solubilize in their micellar core, several types of drugs [23–27]. They can assemble in the tumour microenvironment (TME) thanks to their nano size and the EPR effect. Additionally, PMs are used as "smart drug carriers," which makes them target particular cancer sites by using several stimuli, enhancing the specificity and effectiveness of targeted drug delivery which is micelle-based [28,29].

2. Principle of cancer theranostics

Increased imaging capabilities and diagnostics have made it possible to identify cancers earlier and more thoroughly [30]. Recently, these methods have expanded into theranostics, in which contrast agents that are typically used for the imaging have been combined with therapeutics in order to diagnose and treat cancers simultaneously in a patient-specific manner [31].

Nanoparticles (NPs) play a wide range of roles in cancer diagnosis and have a number of advantages over other traditional methods of delivering chemotherapeutic drugs. Delivering drugs to the target tissue, or cells, or organs is more precise as well as effective with NPs, and the risk of side effects is reduced. With less drug removal from the system, NPs deliver drugs to tumour areas in passive and active modes [32]. The biodistribution of chemotherapy drugs in the body as well as the effectiveness of nanocarriers are significantly influenced by the size and surface properties of nanoparticles [33].

Phospholipids/surfactants are the primary constituents of self-assembled vesicular nanoparticles (NPs), which show promising potential for the nanomedicine as novel biomedical nanocarriers. The two most common vesicle subcategories in recent decades, liposomes and noisome, have been utilised extensively in the treatment of cancer [34,35].

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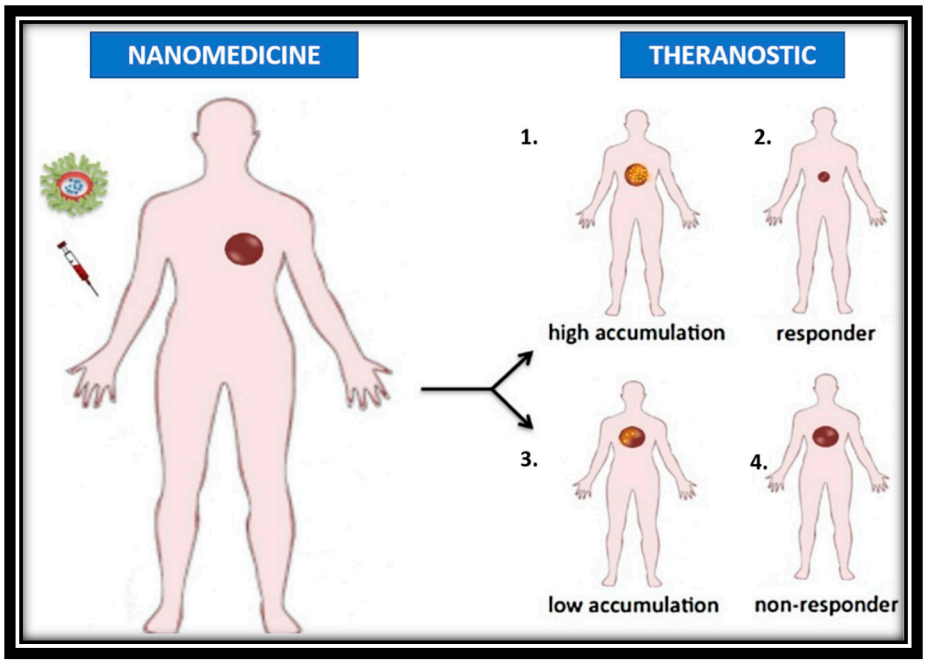

Figure 1. The way in which nanoparticles in their own way effect the body to treat cancer.

3. Application of cancer theranostics

Drugs are more easily accessible in the cellular core, where they activate apoptotic signals for cell death, than in the peripheral cytoplasm, where they are less likely to activate efflux mechanisms [36]. As a result of their cellular internalisation mechanisms, nano-drug delivery systems are less likely than free drugs to result in multiple drug resistance [37]. Another crucial fact is the capability of the nanocarriers to be surface-modified with additional ligands to provide active cancer cell targeting, straightforward internalisation, and organelle-specific drug targeting [38].

Two-dimensional black phosphorus nanosheets (BPNSs), which have recently attracted a lot of interest, are best suited for theranostic nanomedicine. They are becoming more and more sought-after as a potential replacement for the graphene-based nanomaterials used in biomedical applications, in part because of qualities like drug loading efficiency, biocompatibility, electrical, optical, thermal and phototherapeutic characteristics [39–41].

Cancer immunotherapies aim to amplify the immune system's capacity to detect and combat cancer. Cancer immunotherapies try to "teach" the immune system to recognise and eliminate cancerous cells in the tumour microenvironment (TME) [42]. In order to improve cancer immunotherapies, nanomedicine-based delivery are crucial. These strategies either increase the anti-tumour response of the immune system or lessen their periodic side effects [43].

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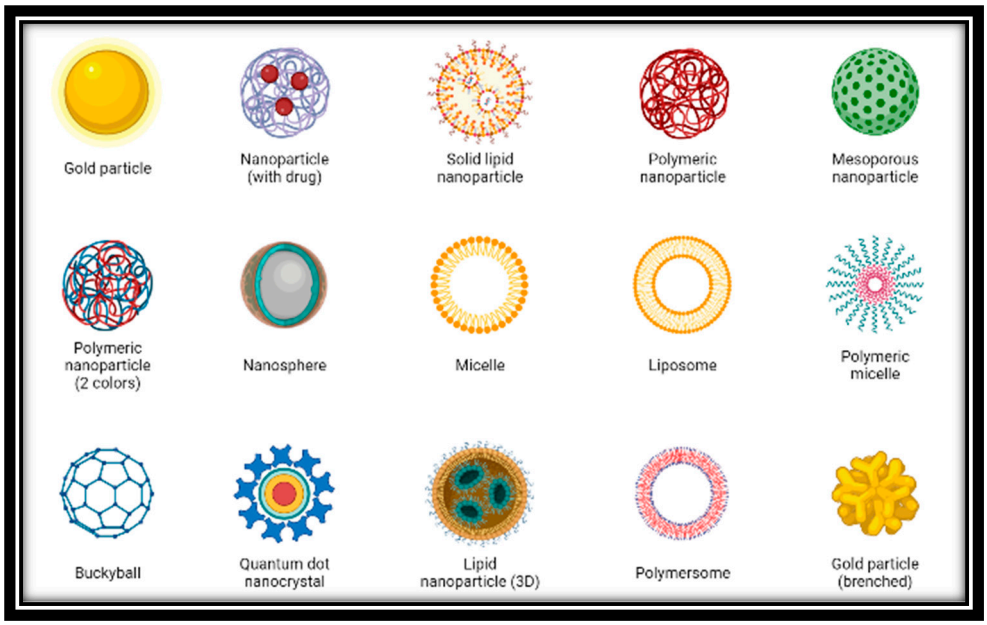

Figure 2. These are some of the nano-particles which are being used in cancer theragnostics.

Table 1. The table below represents different nanoparticles being used in cancer therapy:.

Contrast Agent	Drug used	Applications
Gold	DOX	Diagnosis, tumour targeting and PTT
Silica	Pyro pheophorbide (HPPH), DOX	Drug carrier, X-ray/CT imaging, Photodynamic therapy
Manganese oxide	siRNA	MRI plus RNA delivery
CNTs	DNA plasmid, DOX, PTX	Diagnosis, DNA and drug delivery
QDs	DOX, MTX	Imaging, therapy and sensing
Iron oxide	siRNA, DOX, docetaxel	Targeting, MRI and therapy

3.1. Quantum dots

Small semiconducting particles or nanocrystals known as quantum dots have extremely small diameters. They were initially found in 1980 [44]. The unbelievably high surface-to-volume ratios of these dots contribute to their unusual electronic properties, which are intermediate between those of discrete molecules and bulk semiconductors [45,46]. Fluorescence, where the nanocrystals can produce distinct colours depending on the size of the particles, is the most noticeable effect of this. The quantum dot is a type of nanoparticle with dimensions between tens of nanometers and a few hundredths of a nanometer, which are smaller than those of a typical nanoparticle. The quantum dot can be used in a multiple fields, including solar cells, light-producing diodes, lasers, and biomedical applications because the quantum mechanical behaviour associated with it exhibits various optical and electronic properties [47].

Due to their unusual properties, such as their small size, high surface area, photoluminescence, chemical stability, simple synthesis, and potential for functionalization, carbon quantum dots (CQDs) have attracted a lot of attention recently [48]. They are fluorescent carbon nanostructures with a size of less than 10 nm. Curiously, the scientific community has recently opted to use biomass precursors rather than chemical compounds to prepare CQDs. These biomass sources turn waste into useful materials while being cheap, accessible, environmentally friendly, and abundant [49,50]. Because of technological developments, we can detect tumours at the cellular level, making it simpler to study variations in the transcriptional gene and its genetic factors. Ideal chemotherapy is viewed as a non-specific therapy with the ability to kill healthy cells and harm a person's systemically. Therefore, creating new technologies is now an urgent necessity. Semiconductor particles known as QDs have

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sizes between 2 and 10 nanometers. Many researchers are interested in QDs, for their distinctive qualities, like their small size, extensive surface area, charges in the surface, and precise targeting. The numerous nanocarriers include well-known QD-based drug carriers. Enhancing solubility, extending time for retention, and minimising the negative effects of loaded medications are all benefits of using QDs as a delivery method [32]. Zero-dimensional carbon-based nanomaterials have shown clear structural and functional advantages for the use of nanotheranostics: (I) Several luminescent models, like the PL, thermally activated delayed fluorescence (TADF), phosphorescence, hemiluminescence, etc., can be achieved by CDs and used for a variety of bioimaging models; (II) Compared to other imaging probes, CDs exhibit excellent biocompatibility and photostability, making them suitable for use as in vivo real-time imaging agents; Near-infrared (NIR) emission, in particular, is tunable in (III) CDs and is applicable for tissue imaging alongside deep penetration; (IV) CDs have demonstrated very unique properties, like blood-brain barrier (BBB) penetration and novel cell targeting, which is extraordinarily advantageous for imaging; (V) CDs demonstrate clearable behaviour in living organisms, which is great for long term imaging [51–62].

Even though research on quantum dots (QD) nano-transporters is still ongoing, they have not yet made their benefits known to the public. There have already been a few beneficial developments as a result of the discovery of QDs [63]. The application of QD shows conversion in natural imaging and photography has shown incredibly amazing suitability in bio-imaging, the creation of novel drugs, the delivery of targeted genes, biosensing, as well as photodynamic therapy and diagnosis. The current review set out to prove the value of QD in the detection and management of cancer [64,65].

3.2. Liposomes

By increasing drug efficacy and enhancing cell type-specific delivery, liposomes have amazing benefits that could strengthen immune responses and cancer immunotherapy [66]. Liposomes are lipid-based nanoparticles that have a high potential for enhancing cancer immunotherapies because they can incorporate and/or associate a variety of cancer drug molecules [67]. Liposomes can be used for a variety of immunotherapeutic cancer treatments, such as vaccination or checkpoint blockade, making them very flexible. Low-molecular-weight anticancer drugs, immunomodulators, and antigens are frequently delivered using these mechanisms [68,69].

Anticancer agents have been formulated as liposomal formulations to increase anti-tumor efficacy by rising deposition of tumour drug, reducing toxicity of drug by avoiding critical normal tissues, and extend drug circulating lifetime [70]. The clinical application of micro- and nanoparticulate formulations and its development, alongwith the combination of the novel agents with conventional medications and therapies of standard-of-care, still present challenges inspite of clinical approval of chemotherapeutics which are multiple liposome-based [71]. Control over drug biodistribution, encapsulated drug release rates, and target cell uptake are all factors that need to be optimised. Several liposome-based goods have been authorised or put on the market. To improve liposomes' therapeutic indices for applications in oncology, antineoplastic agent classes have been added. Anthracyclines, analogues of platinum, camptothecins, vinca alkaloid, and antimetabolite are a few of them. Many liposomal anticancer medications are either clinically approved or in late stage clinical development [72–75].

There are a number of factors to consider when contrasting the traits of the drug and the liposome carrier. Before it can be approved, a drug must first show promise in treating the chosen tumour type [76]. A number of cancers have been successfully treated using anthracyclines and vinca alkaloids, two common examples [77]. The drug must be loaded into the liposome carrier adequately and effectively in order for the drug to be commercially viable [78]. To deliver a dose that is pharmacologically active in the proper quantity of carrier lipids, the carrier must have enough drug in it. Third, while the drug is being transported steadily by the carrier in the bloodstream, the drug must be released from the carrier at the tumour site at the appropriate rate. The release rate of agents which are chemotherapeutic to be encompassed into the carrier is significantly influenced by the physicochemical properties of the agent [79,80] .

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3.3. Radioisotopes

A radioisotope is an atom that is unique in that it has the ability to emit radiation. As a result of internal changes in unstable, or radioactive, atoms, radiations are waves or particles that are sent out in all directions [81]. For the large-scale development, high-current medical systems producing enhanced yields of radioisotopes, experimental thick target yields and functions of excitation—i.e., cross sections of isotope production that depend on energy—are crucial [82,83].

Radiation therapy is a commonly used treatment for various types of brain tumors in almost every setting [84]. Nonetheless, it may not be a viable option or may pose an unacceptable risk for patients with aggressive and/or recurrent tumors. Recurrent tumors are highly aggressive, and administering repeated therapeutic courses through reirradiation may result in a significantly higher risk of local tissue damage while decreasing efficacy [85]. This is due to limitations in dosing and target coverage. Copper is a bioelement that is a cofactor for many enzymes and is involved in many major biochemical processes, though excessive amounts of copper encourage the growth of cancer cells. Understanding and utilising the copper radioisotope's biochemical pathways in oncogenesis are necessary for the continued development of radiopharmaceuticals based on these radioisotopes. Based on their emissions, energies, and half-lives, five of the copper radioisotopes have attracted interest for use in nuclear medicine because they can be produced with pharmaceutical-grade quality [86–90].

In modern medicine, accelerator-produced radioisotopes are frequently used for imaging, cancer therapy, and therapy and diagnostic combination(theragnostics) [91]. A number of radioisotope-based treatments are in advanced stages of clinical trials, which may pave the way for a strong demand for specific accelerator systems devoted to radioisotope production [92]. Although cyclotrons are the industry standard, we explore different options here using linear accelerators. Linacs have the advantage of modularity, compactness, and lower beam loss with less shielding needed when compared to cyclotrons [93]. Considerable attention has been given to the development of nanocarrier systems for drug delivery that utilize chitosan, which is a linear chain polysaccharide derived from the chitin of arthropods and occurs naturally. This non-toxic, biodegradable, and biocompatible polymer was combined with specific radioisotopes for diagnostic and therapeutic purposes. (64Cu, 68Ga, 90Y, 153Sm, 166Ho and 177Lu) [94]. By using the ionotropic gelation method, radiolabelled chitosan was transformed into nanoparticles. In epithelial lung cancer cells, the surrogate nanoparticles' cell uptake and cytotoxicity were assessed. The intrinsically radiolabelled nanoparticles had a high in vivo stability, according to biodistribution studies carried out on healthy C57BL/6 mice– it is shown in the figure given below [95].

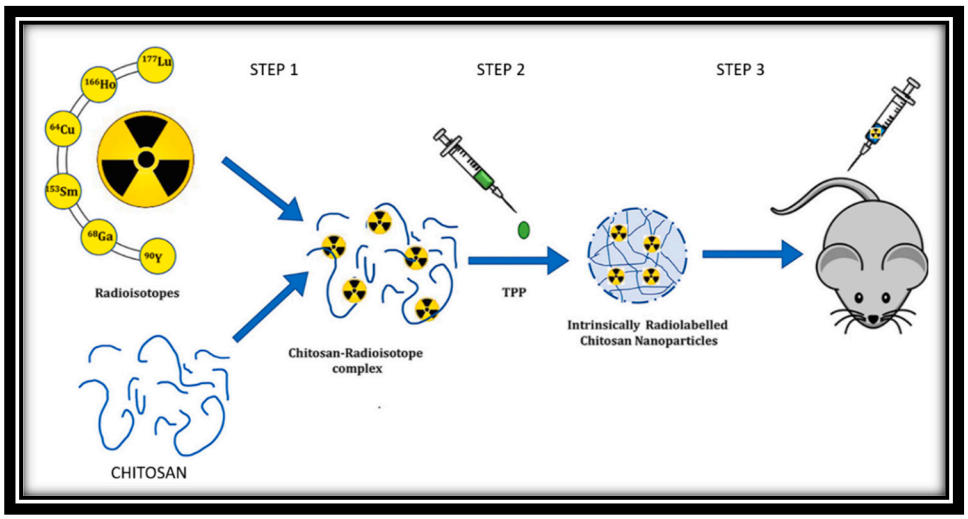

Figure 3. Radioisotope biodistribution on healthy C57BL/6 mice.

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3.4. Micelles

Polymeric micelles have emerged as a popular option for delivering chemotherapeutic agents that are difficult to dissolve to cancer patients in pre-clinical studies [96]. These micelles are formed by the self-assembly of amphiphilic polymers and can be customized with different polymeric combinations to achieve optimal loading, stability, systemic circulation, and delivery to the target cancer tissues [97]. Moreover, the surface of the nanocarriers can be modified with additional ligands to facilitate active cancer cell targeting, internalization, and organelle-specific drug targeting. Polymeric micelles offer several advantages over other types of nanoparticles. They are formed by amphiphilic polymers that self-assemble in an aqueous environment, and different polymeric building blocks can be used to achieve the desired hydrophobic/lipophilic balance, size, drug loading capacity, micellization ability, and stability in the systemic circulation [98].

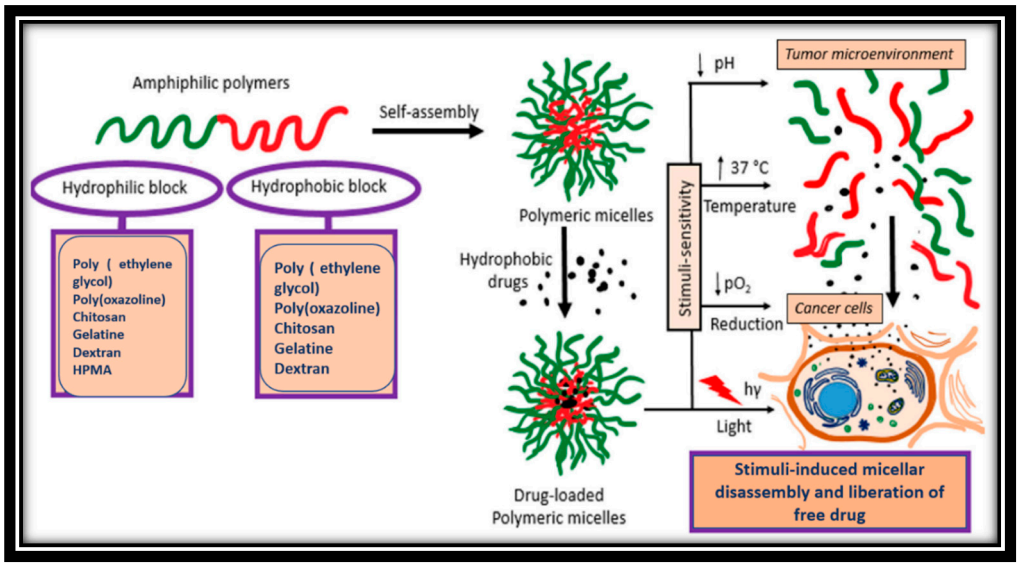

Figure 4. The figure shows the use of polymeric micelles in cancer therapy.

Compared to other drug delivery methods, micelles have an advantage due to their small size, which enables them to extravasate more effectively through leaky vasculature. The hydrophilic polymeric coating on their surface also enables them to evade detection by the reticuloendothelial system during circulation [99]. Furthermore, micelles can be directed towards the tumor site by chemically conjugating tumor-homing ligands onto their surface [100].

Micelles are nanoparticles that self-assemble when amphiphilic block copolymers are dissolved in specific solvents at concentrations above the critical micelle concentration (CMC). In recent years, nanosized delivery systems like micelles have gained attention due to their improved in vivo stability, ability to protect entrapped drugs, release kinetics, ease of cellular penetration, and increased therapeutic efficacy [101].

Various immune cell types, such as effector T cells, regulatory T cells, dendritic cells, natural killer (NK) cells, myeloid-derived suppressor cells (MDSCs), and tumour-associated macrophages, play important roles in triggering and enhancing the immune response against tumors. Recent studies have shown the development of several methods, including cancer vaccines, antibodies, and immune-stimulating adjuvants, to trigger potent anti-tumor immunity against aberrant cancer cells. These approaches are enhancing the current anti-tumor immunity and reinvigorating an immunosuppressive tumor microenvironment [102–105].

3.5. Nanobubbles

Nanobubbles, which are gas-filled cavities in aqueous solutions, have distinctive features attributed to their low internal pressure and surface tension resulting from the charged gas/liquid interface [106]. To induce cell death in the tumour lymph node by delivering particles, DOX

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medications are loaded into magnetic PLGA microbubbles that contain perfluorocarbon gas. The results indicate that this approach can be utilized to improve lymphatic targeting and mitigate tumour metastasis [107].

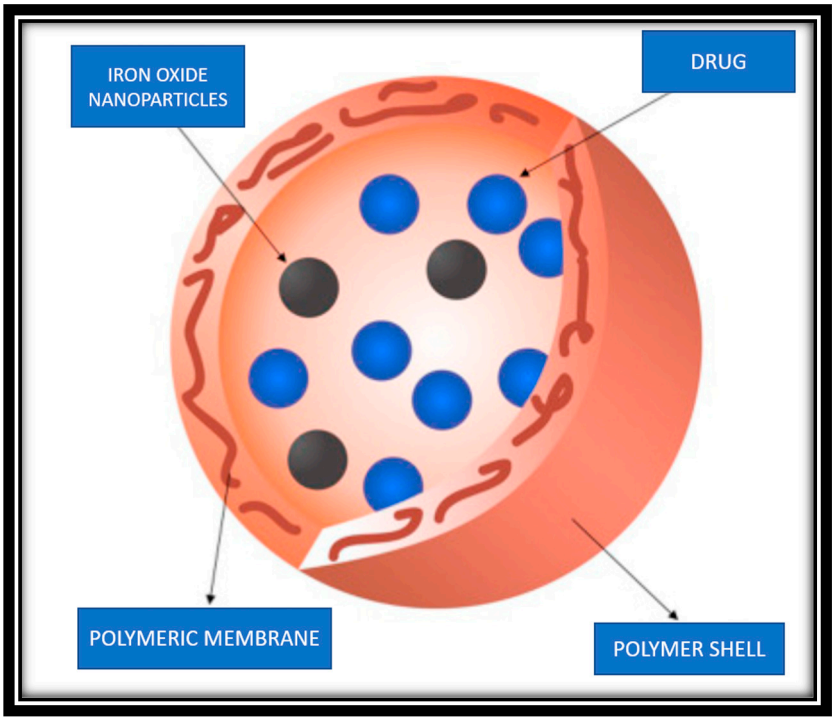

Figure 5. Schematic diagram of a magnetic nano capsule which encapsulates the therapeutic agent.

There are several ways to create plasmonic nanobubbles, including (1) using extracorporeal cell processing systems for gene therapy, monitoring, and eliminating cancer cells from bone marrow and blood; (2) detecting and eliminating residual cancer cells and microtumours on thin surfaces and in surgical beds during surgery; and (3) detecting and ablating residual cancer cells and metastases in deep tissues [108–110].

In the field of oncology, microbubbles (MBs) and nanobubbles (NBs) can serve as contrast agents that can be modified to meet theragnostic requirements [111]. Thanks to the integration of nanotechnology with the biomedical sector, theranostic development has progressed rapidly, with numerous products currently in various stages of regulatory pre-clinical and clinical trials. MB and NB platforms stand out from other delivery systems due to their ability to perform traditional theranostic functions, as well as to enhance tissue permeation and deliver gas therapeutics, such as oxygen, to the tumoral architecture [112–115].

3.6. Diagnosis using cancer theranostics

Nanoparticle-based therapy has been suggested as a potential solution for overcoming Multi Drug Resistance in various types of cancer, including breast cancer, ovarian cancer, and prostate cancer [116]. The intersection of nanotechnology and medicine has opened up a new phase in cancer treatment, and further exploration of this field is needed. This review explores current challenges, future research directions, and the underlying principles of using the nano-carrier system in cancer therapy [117,118].

Nanotheragnostic is seen as a promising strategy for combating cancer by slowing down cancer progression during the initial diagnostic procedure, reducing the overall cancer burden and making the ensuing anticancer therapy easier [119]. Developing a molecular therapy system that can circulate undetected in the bloodstream, identify the target, and efficiently deliver drugs or silence genes is a significant challenge. Nanotechnology is essential for creating new types of nanotherapeutics that can provide efficient treatments with minimal side effects and high specificity [120,121].

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Nanomedicine combines life sciences with nanoscience, nanoengineering, and nanotechnology to produce useful findings for healthcare. Nanotechnology-based drug delivery systems and nanoimaging agents are of great interest in medicine and pharmacy [122]. The simultaneous integration of diagnosis and treatment is known as "theragnostic." The ideal nanotheranostic system should have long-lasting circulation in the body, adequate release behavior, tissue target specificity and penetration, imaging capability, and a high target to background ratio [123].

Polymeric nanoparticles, carbon-based nanomaterials, lipid-based nanovesicles, protein-based nanostructures, dendrimers, ceramic nanostructures, metallic inorganic nanocarriers, and graphene quantum dots are some of the technologies used to create theranostic nanomedicines. Magnetic nanoparticles (MNPs) are of particular interest due to their inherent magnetic properties, which enable them to be used as contrast agents in magnetic resonance imaging as well as a therapeutic system in conjunction with hyperthermia. MNPs also function effectively as drug carriers for specific therapeutic regimens [124,125].

Researchers are exploring more cost- and environmentally-conscious large-scale technologies, including the environmentally friendly biological process known as “green synthesis” [126]. AuNPs are being synthesized using plants' secondary metabolites, which has several advantages over traditional physical and chemical synthesis, including cost effectiveness, energy efficiency, and biocompatibility. Biological approaches, particularly the plant-based synthesis of metal nanoparticles, are considered the best course of action due to their environmental and in vivo safety and simplicity in synthesis [127].

Hydroxyapatite nanoparticles (HAp NPs) have shown great promise for enhanced cancer therapy due to their chemical structure, which provides excellent opportunities for loading and delivering a wide variety of anticancer drugs in a sustained, prolonged, and targeted manner. HAp NPs can also be modified by incorporating specific therapeutic elements into their composition, providing a strategy for delivering advanced anticancer effects [128].

BP nanomaterials have been used for managing various types of cancer due to their excellent optical characteristics and drug loading capability. Two-dimensional BP nanosheets are particularly suitable for theranostic nanomedicine due to their excellent biocompatibility and low toxicity, efficient drug loading from their large surface area, improved photothermal conversion efficiency, and high performance in photodynamic cancer therapy. BP materials also have excellent electrochemical catalytic activity and can be used as electrochemical biosensors. However, preventing BP nanomaterials' degradation in water is a significant obstacle to their biomedical application [129,130].

4. Clinical trials of cancer theranostics

Clinical trials have revealed the use of magnetic materials having very intriguing properties, as well as usage of nanometric materials in the form o carriers and releasers of fluorescent molecules and therapeutic agents [131]. When compared to free molecular cargo, these nano formulations have a number of benefits, including improved drug solubility, bioavailability, stability, and tumour specificity. In some instances, tumour multidrug resistance has also decreased, which has improved treatment efficiency by lowering drug dosage and averting potential side effects [132].

Gold nanoparticles are being investigated as effective tools for treating cancer, with studies being conducted to explore their potential as drug carriers, contrast agents, photothermal agents, and radiosensitizers. In 2004, the National Cancer Institute, the USFDA, and the National Institute of Standards and Technology collaborated to establish the Nanotechnology Characterisation Laboratory (NCL), which is responsible for conducting pre-clinical characterisation and standardisation of nanomaterials intended for cancer therapeutics. The NCL has tested more than 180 nanomaterials to date, conducting physicochemical in vitro and in vivo characterisation. A pilot study of AuroShell® particles for photothermal therapy is currently underway, involving the intravenous administration of the particles to 15 patients with recurrent or resistant head and neck cancer. After the patients receive the AuroShell particles, they may undergo one or more interstitial

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illuminations using an 808-nm laser. Neutron-activated analysis will be used in post-treatment biopsies to evaluate the uptake of nanoparticles in tumours [133–135].

There are several methods for thermal therapy using nanoparticles, including infrared light absorption, radio frequency ablation, and magnetic heating [136]. Two of these methods are currently undergoing human clinical trials, and they have shown to be highly effective in animal models. Exogenous absorbers can be used to heat the tumour site while minimising damage more precisely to healthy tissue and enabling non-invasive therapy [137]. Nanoparticles can frequently be engineered to produce local heating at the site of a tumour. Additionally, nanoparticles may present a chance to create versatile platforms for combined imaging and therapy [138,139].

Table 2. Few projects being supported by European Commission's Seventh Framework programme that use iron oxide nanoparticles or imaging methods is given below:.

PROJECT	CONSORTIUM	AIM
Vibrant	10 groups	Contrast agent for pancreatic beta-cell imaging in diabetes Mellitus type I
Magnifyco	11 groups	Magnetic nanoparticles have the potential to be used theranostically to treat ovarian cancer.
SaveMe	19 groups	Nano core platforms to advance cancer treatment and diagnosis
NAD	19 groups	Alzheimers' treatment
Namdiatream	22 groups	Molecular biomarker and detection
Multifun	15 groups	Breast and pancreatic cancer early detection using iron oxide nanoparticles with cancer stem cells
Nanomagdye	8 groups	Iron oxide nanoparticles as a new contrast agent in cancer patients' lymph node imaging

In 25 patients who went through HIFU and TACE together from 32 HCCs, as well as 46 HCCs from 32 patients who underwent TACE alone, Clinical Trail retrospectively reviewed the tumour responses. The TACE+HIFU group's mean follow-up observation lasted an average of 31 months, while the TACE group's lasted an average of 33 months. Amongst 25 patients, 18 men and 7 women—were in the TACE+HIFU group, and out of 32 there were 23 men and 9 women—were in the TACE group. The average age of the TACE+HIFU group was 57 years (range: 44–67 years), while the average age of the TACE group was 65 years (range: 43–89 years).

Table 3. The table below shows tumour responses from this trial [140].

Responses	TACE group (n=32)	TACE+HIFU group (n=25)
SD	4(13%)	5(20%)
CR	9(28%)	5(20%)
PD	17(53%)	13(52%)
PR	2(6%)	2(8%)
Disease control rate	15/32(47%)	12/25(48%)

5. Limitations and challenges

To implement the concept of "safe-by-design", guidelines have been developed by regulatory agencies and scientists to assess the toxicological characteristics of nanomaterials. However, combining nanotechnology with other technologies can be difficult due to the frequent emergence of new materials [141]. It is essential to focus on and address the toxicity of various types of QDs as numerous types of them are being produced. Each QD type possesses a unique set of physical and chemical properties, influenced by its structure and geometry, which can impact the probability of toxicity [142,143].

Even though the majority of CDs show low toxicity, there are still many people who are worried about the risk of using CDs in therapeutic applications. On the one hand, various animal studies have shown that CNTs and other members of the carbon family of nanomaterials can be ingested by

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macrophages, causing inflammation and damage to the respiratory system [144]. Numerous reports have been made about the novel cytotoxicity in some types of CDs, including their toxicity upon ROS generation and toxicity upon dose. As a result, there still need to be more worries and studies about the risk of CDs for applications in clinic therapy [145].

In anti-cancer studies, QDs are frequently combined with various nanoparticles for imaging purposes to monitor drug targeting and release. There have been instances where QDs enhanced the drug's activity, but these studies with anti-cancer phytochemicals are uncommon. Effects of QDs are cytotoxic. Heavy metals continue to be a health concern even though coating the core helps to reduce the toxic effects of QDs [146].

Current research in nanomedicine is facing an exciting challenge with the development of imaging and therapeutics using nanostructure-based systems [147]. The reason being that a single platform must include multiple nanocarriers and active agents to enhance therapy, imaging, and controlled drug release. Traditional methods of diagnosis and treatment, particularly for cancer, are associated with unfavorable outcomes such as serious side effects, drug resistance, high drug clearance rate, drug distribution to healthy tissues, and low drug concentration reaching diseased cells [148–150].

Theranostic nanomedicines have the ability to overcome the body's defenses, achieve systemic circulation, and deliver both diagnostic agents and drugs to the targeted location at the cellular and molecular levels for treating and diagnosing diseases. Compared to conventional therapy, theranostic nanomedicines offer numerous advantages such as high cellular drug uptake, minimal side effects, and high drug release. Different nanocarriers used in nanotheranostics are capable of accumulating high drug concentrations at the intended site of action while having minimal toxic effects on healthy tissues.

6. Discussion

For addressing novel genomic biomarkers that alert cancer cells and do so with increased sensitivity, nanotechnology-based systems hold great promise for enabling early detection of genome/genetic alterations that are the root cause of cancer. Nanoscale structures and emerging technologies have been combined to deliver to the target site with fewer side effects. Based on the experience gained so far, it is obvious that the next step in successfully implementing nanotheranostics in clinics is the body's response to the nanoconjugates.

The increasing prevalence of cancer necessitates the use of contrast agents to provide the highest sensitivity for detecting tumors and offering early treatment options. As a result, research focus on developing contrast agents can have a significantly positive impact on society in the long run. Moreover, iron oxide nanoparticles' theranostic potential for upcoming cancer treatments is demonstrated by the recent approval of NanoTherm for hyperthermia. Iron oxide nanoparticles can offer new and effective treatment options for cancers that previously had limited treatment options, both as a contrast agent and by enhancing drug delivery. In response to the removal of some iron oxide nanoparticle products from development, regulatory agencies have implemented a range of safety measures to ensure the safe and efficient basic and clinical development of iron oxide nanoparticles.

It is easy to assume that combining TACE therapy with other treatments will be more effective in treating non-advanced medium-sized tumors, as TACE monotherapy has been successful in treating advanced-stage disease. Preliminary results suggest that TACE+HIFU combination therapy is more effective than TACE alone in treating non-advanced HCCs that are 5 cm or smaller. However, randomized controlled studies comparing TACE+HIFU with other traditional treatments are necessary to support this claim.

In the realm of personalized medicine, the "all-in-one" approach to developing theranostic agents is showing great promise. Such agents can aid in the early detection and monitoring of a patient's cancer.

Administering anticancer agents over a longer period of time can increase their therapeutic effectiveness. While this approach is currently only applicable to imaging methods, faster and more

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accurate diagnostic techniques are being developed using multiple emulsion and Janus-like particle preparation techniques. Ongoing research aims to find a permanent cure for cancer, with the hope that the illness can soon be identified and effectively treated at an early stage.

7. Conclusion

Copper radioisotopes are ideal candidates for theranostic applications because they can be used as diagnostic and therapeutic partners (for example, 61Cu and 67Cu) or to take advantage of 64Cu's dual emissions. In the latter scenario, real-time therapy follow-up offers patients significant advantages.

Despite the potential of cancer immunotherapies, there are still numerous obstacles that must be addressed before they can be broadly applied in clinical settings. One issue is that certain immunotherapies have short half-lives and require large dosages, which can cause off-target toxicities and severe side effects, such as cytokine release and vascular leakage syndromes, in some patients. Furthermore, the effectiveness of cancer immunotherapies is limited to a small percentage of patients, with response rates ranging from 10-30% depending on the type of cancer.

Promising systems for use in the detection and treatment of cancer include theranostic nanogels. These systems' high degree of adaptability enables the combination of various therapeutic agents and imaging modalities for improved theranostic functions. The creation of multifunctional theranostic nanogels has become a popular method for enhancing the diagnostic accuracy of imaging tests and the therapeutic efficacy of administered therapies. In particular, nanogels make a significant contribution to the creation of new theranostic platforms for several medical applications.

Nanocarrier systems have the ability to enhance drug delivery, primarily due to their responsiveness to stimuli. Polymeric micelles, which can react to different stimuli such as pH changes, temperature, light incidence, and reductive environmental conditions, have been created. Polymeric micelles hold promise as a drug delivery option for cancer treatment as a result of their improved drug loading capability, simple scale-up methods, and better understanding of their fate in the biological system, enabling them to move from laboratory settings to the bedside of patients.

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