Review Article
The Magnetic Nanomaterial Biofunctions in Cancer Diagnosis and Therapy

Xuefeng Bian,1 Ting Guo,2 Ji Zhang,1 Jianguo Xia,1 Xiaqian Feng,2 Fujin Wang,2 Mei Lin,3 and Weizhong Tian1

1Imaging Department, Taizhou People’s Hospital Affiliated to Nantong University, Taizhou 225300, China
2Institute of Clinical Medicine, Taizhou People’s Hospital Affiliated to Nantong University, Taizhou 225300, China
3Clinical Medical Laboratory, Taizhou People’s Hospital Affiliated to Nantong University, Taizhou 225300, China

Correspondence should be addressed to Mei Lin; l_mei@163.com and Weizhong Tian; jstztwz@163.com
Xuefeng Bian and Ting Guo contributed equally to this work.

Received 9 March 2021; Accepted 5 May 2021; Published 2 June 2021

Academic Editor: Luis Jesús Villarreal-Gómez

Copyright © 2021 Xuefeng Bian et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Magnetic nanomaterials have recently emerged; they are characterized by small particle size, superparamagnetism, and surface modification ease [4]. Magnetic nanoparticles can be employed in different aspects, combined with biomolecules, fluorescent probes, and antitumor drugs; currently, they are used as magnetic resonance contrast agents, targeted drug delivery, and in magnetic fluid hyperthermia [5]. The Fe3O4 core/shell/crown functional magnetic nanomaterials have achieved good therapeutic results in bladder cancer in vitro [6]. The gadolinium-doped iron oxide nanoparticles (GdIO NPs) showed good potential in magnetic resonance imaging and achieved promising results in breast cancer treatment in vitro [7]. The superparamagnetic PEG-modified La1-xSrxFn3 (LSMO) magnetic nanoparticles exhibited favorable potency in magnetic resonance imaging and tumor magnetic fluid hyperthermia [8].

Herein, concerning the recent research on magnetic nanomaterials in tumor therapy, the preparation, characterization, and diagnostic applications of various magnetic nanomaterials and their cancer diagnosis and therapy applications are briefly reviewed.

1. Introduction

Cancer remains the second most common cause of death, and its morbidity and mortality are increasing in China; this is mainly because most tumor onset is subtle and challenging to be detected in the early stage [1]. Most diagnosed cancer patients are already in advanced and late stages; this hinders curative treatment. Besides, the primary cancer treatment includes surgery, chemotherapy, and radiotherapy [2]. However, the complete removal of the tumor tissue through surgical treatment is intractable. Various side effects and adverse reactions often accompany radiotherapy and chemotherapy. Moreover, tumors could evolve metastasis and drug resistance during progression or recurrence, which dramatically reduces the subsequent treatment effect [3]. Therefore, it is pivotal to identify new cancer treatments and prognostic methods.

The magnetic nanomaterial has newly emerged; they are characterized by small particle size, superparamagnetism, and surface modification ease [4]. Magnetic nanoparticles can be employed in different aspects, combined with biomolecules, fluorescent probes, and antitumor drugs; currently, they are used as magnetic resonance contrast agents, targeted drug delivery, and in magnetic fluid hyperthermia [5]. The Fe3O4 core/shell/crown functional magnetic nanomaterials have achieved good therapeutic results in bladder cancer in vitro [6]. The gadolinium-doped iron oxide nanoparticles (GdIO NPs) showed good potential in magnetic resonance imaging and achieved promising results in breast cancer treatment in vitro [7]. The superparamagnetic PEG-modified La1-xSrxFn3 (LSMO) magnetic nanoparticles exhibited favorable potency in magnetic resonance imaging and tumor magnetic fluid hyperthermia [8].

Herein, concerning the recent research on magnetic nanomaterials in tumor therapy, the preparation, characterization, and diagnostic applications of various magnetic nanomaterials and their cancer diagnosis and therapy applications are briefly reviewed.
2. Preparation and Characterization of Magnetic Nanomaterials

2.1. Preparation of Magnetic Nanomaterials. Fe3O4 and γ-Fe2O3-based nanoparticles are currently applicable in living organisms; this nanoparticle composition is beneficial as the iron-containing cells can maintain the intracellular environment’s stability by absorbing, storing, and excreting iron atoms [9]. Also, iron can be easily removed from the body, allowing a comparatively large iron dose since the oxidative stress reaction is absent. Iron oxide nanoparticles are high safe [10]. Preparing magnetic nanomaterials are divided into physical and chemical approaches; this includes grinding, ultrasonic, and plasma methods. Currently, the preparation methodology includes hydrothermal synthesis, sol-gel, and forced hydrolysis and thermal decomposition [11].

2.1.1. The Coprecipitation Method. The coprecipitation is a convenient and straightforward method to obtain iron oxide particles; this is achieved by adding an alkaline solution to a salt solution of iron (Fe2+/Fe3+) in an inert gas atmosphere at room temperature. Its preponderance is that large amounts of iron oxide nanoparticles can be synthesized one time. However, the size of the magnetic nanomaterials obtained by the coprecipitation method is challenging to control, where the particle diameter distribution is relatively dispersed and tricky to be consolidated [12].

2.1.2. Sol-Gel and Forced Hydrolysis Techniques. In the sol-gel approach, molecular precursors in the solution are hydroxylated and condensed to obtain the initial nanoparticle solution. The initial solution is further condensed and set to be polymerized to obtain a three-dimensional wet gel of the metal oxide network. The wet gel characteristics are highly dependent on the structural treatment of the sol preparation. The method has advantages: materials can be customized, the size of particles is homogenous, and the reaction temperature is relatively low [13]. The γ-Fe2O3 nanoparticles obtained by the sol-gel method can be embedded in an inert, inorganic, and transparent silica matrix with high-temperature resistance. Sugimoto et al. reported that nanostructured oxides with various structures and compositions could be obtained following different preparation conditions, precursor properties, ion source, and pH [14].

2.1.3. Thermal Decomposition Method. Thermal decomposition is a commonly used approach in the biomedical field to prepare precise nanoparticles. This method helps control the nanoparticles’ size and morphology and control the yield [15]. Recently, there are two main types of thermal decomposition: first, oxidizing the metal carbonyl precursor in the air after or during thermal decomposition [16]. The second is precursor decomposition with a cationic metal without a reducing agent [17]. Many small-sized monodisperse nanomagnetic crystals can be synthesized by dissolving metal-organic compounds in a high-boiling organic solvent with stable surfactant and thermal decomposition. Sun et al. discovered the broad applications of the organometallic precursors of acetyl-acetone; these precursors included iron, manganese, and nickel acetylacetonate [18]. The surfactants used in this approach are usually fatty acids, oleic acid, and hexadecyl-amine [19]. Hyeno et al. have experimentally demonstrated that decomposing organometallic compound precursors by thermal decomposition with surfactant can achieve small and even nanoparticles with good crystallinity and dispersibility. The ratio of organometallic compound precursors, solvents, surfactants, temperature, time, and oxidation are all keys to control the nanoparticles diameter and morphology accurately [20]. This approach has a significant drawback as the final product is organic soluble nanoparticles, limiting its application in the biological field. Moreover, the produced nanoparticles by thermal decomposition often require further surface treatment, and the reaction process is intricate and requires high temperature [21].

2.1.4. Hydrothermal Synthesis Method. In this method, the reaction needs to be done in a reactor or autoclave under high pressure and temperature, 2000 psi, 200°C, respectively. Laurent used the hydrothermal approach in the preparation of Fe3O4 nanoparticles [22]. Different nanoparticles have been prepared by hydrothermal synthesis as it has better crystallinity over other techniques. However, different hydrothermal synthesis conditions may cause different particle crystallinities and affect their magnetism. The well-crystallized nanoparticles are thinner, have a narrower surface layer and cation distribution space, and their superparamagnetic relaxation is low.

2.1.5. Microemulsion. The water molecules have a spherical shape in the water-in-oil microemulsion and are surrounded by the surfactant molecules. The microemulsions can function as cages to produce nanoparticles, reducing the average particle size during collision and aggregation [23]. Thus, the nanoparticles’ size can be controlled and adjusted by changing the size of water droplets, determined by the molar ratio of water to surfactant. This method can be used to control the size of the synthesized nanomaterial within a specific range. However, since the nanoparticles’ size and shape generally vary within a relatively large range, the produced nanoparticles may be spherical, rectangular, or tubular [24]. Besides, compared with other methods, such as thermal decomposition and coprecipitation, the nanoparticles prepared by the microemulsion technique are less efficient, and the synthesis process is too complicated. Therefore, the microemulsion approach is mainly used in the laboratory.

2.2. Characterization and Detection of Magnetic Nanomaterials. The nanomaterials are initially characterized by their size and shape; these are crucial indicators to validate their production process. The transmission electron microscopy and high-resolution transmission electron microscopy are used to determine the nanomaterials’ size and shape, and they require an ultrathin specimen. Their output data comprises grouped diffracted beams called a phase-contrast image (Figure 1) [25].

The crystal characteristics of the magnetic nanomaterial can also be detected by 40Kv, 30mA-Cu Kα X-ray. The unique iron peak in the diffraction pattern demonstrates the irons as magnetic nanomaterials [26]. Ge and S used X-
ray diffraction to analyze the crystalization of magnetic nanoparticles in a powder state; they demonstrated that the magnetic nanoparticles without copolymer have six diffraction peaks at 2θ, 30.1, 35.4, 42.9, 52.7, 57.5, and 62.7 (Figure 2), indicating the presence of iron oxide at the corresponding peak [27].

The nanomaterial’s magnetism is another critical characteristic. It is typically measured by a vibrating sample magnetometer, which can detect their magnetization changes with different field intensities. The nanomaterial’s magnetism turns from the high baseline value to zero upon decreasing the applied field intensity. In that case, the iron oxide magnetic nanoparticles can be detected as a single crystal from the altered magnetic direction.

The chemical composition of the magnetic nanomaterials’ functional ligands and polymers is determined using Fourier transform infrared spectroscopy. Bhattarai et al. detected a strong light emission from iron oxide nanoparticles in the low-frequency region (below 800 cm⁻¹) by Fourier transform infrared spectroscopy. Stabilizing the magnetic nanoparticles using cystic chitosan exhibited an alteration in the modified chitosan’s infrared spectrum due to the interaction with iron oxide nanoparticles [28]. This amide change of the light corresponding band spectrum from high energy to low energy indicates the nitrogen linkage of iron oxide nanoparticles to the modified chitosan.

3. Surface Modification of Magnetic Nanomaterials

The magnetic nanomaterial surface modification alleviates its cytotoxicity and improves their biocompatibility and binding capability to active molecules or compounds. Therefore, magnetic nanomaterial surface modification promotes it as a powerful tool in the biomedical field [29]. The main purpose of surface modification includes improving the stability of magnetic nanomaterials in vitro and in vivo and also minimizing residual magnetism. During the nanomaterial surface modification, the provided functional group on the surface enables further derivatization and enhances the solubility in various solvents, thereby broaden their applications [30]. Different nanomaterial surface modifications determine their antifouling property and hydrodynamic size; they also
Table 1: Commonly used surface modification materials for magnetic nanoparticles.

| Material                          | Properties                                      | Application                                                                 |
|----------------------------------|-------------------------------------------------|----------------------------------------------------------------------------|
| Dextran [70]                     | Good biocompatibility and biodegradability       | Stabilize the colloidal solution and increase the time of nanomaterial circulation in the blood |
| Polyethylene glycol (PEG) [71]   | With good hydrophilicity, it does not cause an immune response and antigen-antibody reaction | Reduce the phagocytosis time of nanomaterials by macrophages and increase the circulation time of nanomaterials in the blood |
| Polyvinyl alcohol (PVA) [72]     | Good hydrophilicity, biocompatibility, superior film, and gel-forming ability | Improve the stability of the colloidal solution |
| Polyacrylic acid [73]            | Good water solubility                           | Improve the biocompatibility of nanomaterials and help nanomaterials adhering |
| Oleic acid, lauric acid, Dodecylphosphoric acid, cetylphosphonic acid, hexadecylphosphonic acid, alkanesulfonic acid, various phosphates, etc. | With good biocompatibility, it is safe and nontoxic. Although soluble in water, it can be soluble in various organic solvents. | Improve the stability and biocompatibility of nanomaterials |
| Silica [75]                      | Good biocompatibility, safe and nontoxic, chemically stable | The nanomaterials are prevented from degrading and coagulating in the organism, making it easier to connect functional groups |
| Gold [76]                        | Biocompatibility, optical, and magnetic properties for biological applications | Improve the stability of magnetic nanoparticles and maintain the magnetic moment of magnetic nanomaterials |
| Carbon [77]                      | Stable chemical properties, good thermal stability, and good biocompatibility | Improve the stability of magnetic nanomaterials, improve the oxidation resistance and acid resistance of magnetic nanoparticles |

play an important role in their biokinetics and biodistribution in vivo [31]. For instance, the nanomaterial’s overall particle size must be significantly small to avoid being engulfed by the reticuloendothelial system (RES), a vital nonspecific immune system formed by macrophages residing in tissues and relatively large to avoid kidney clearance. Besides, proper surface modification can reduce the magnetic nanomaterials’ surface toxicity and enable them to be enriched in specific regions, a prerequisite in tumor diagnosis and targeted therapy [32]. Furthermore, the appropriate nanomaterials’ surface modification exhibits precision characteristics when coated with targeting ligands such as proteins, peptides, antibodies, or other small molecules. This unique conjugation of the magnetic nanomaterial to specific ligands promotes identifying certain molecular markers on the surface of malignant cells, allowing the magnetic nanomaterials to be specifically enriched in the tumors, providing a strong basis for their use in tumor diagnosis and treatment [33]. Moreover, magnetic nanomaterial-small molecule coupling can increase the affinity between the magnetic nanomaterials and the corresponding surface receptors of malignant cells. For instance, folic acid receptors are overexpressed in different human tumors, including ovarian, lung, breast, endometrial, kidney, and colon cancer. The recent applicable materials in surface modification include high molecular polymers, surfactants, and inorganic coatings. See Table 1 for details [34].

4. Magnetic Nanomaterials Applications in Tumor Diagnosis

4.1. Magnetic Nanomaterial Applications in Magnetic Resonance Imaging. Magnetic resonance imaging (MRI) is a widely used noninvasive medical diagnostic technique. MR image has unique advantages in diagnosing various tumors such as liver cancer, cervical cancer, ovarian cancer, glioma, and other tumors [35]. Magnetic resonance imaging uses radio frequency (RF) electromagnetic waves to motivate nuclear materials with nonzero spins in a magnetic field—to generate nuclear magnetic resonance (NMR). The induction coil detection technology is used to obtain tissue relaxation information and proton density information (acquisition resonance signal). Finally, mathematical image reconstruction has been used in different techniques to construct magnetic resonance images [36]. During NMR imaging, the RF pulses are stopped to transmit the resonated hydrogen atom in the body. The relaxation process aims to restore the high energy nucleus to equilibrium, and the time experienced by this process is called the relaxation time. The relaxation time is divided into T1 and T2, where T1 is called longitudinal relaxation time, and T2 is called transverse relaxation time [37]. The currently used contrast agents are divided into T1 inhibitors such as paramagnetic metal ions Gd3+, Mn2+, etcetera, and
T2 inhibitors, including superparamagnetic and ferromagnetic substances. Due to the efficient magnetism of the magnetic nanomaterials, they have been broadly utilized in magnetic resonance imaging research. The superparamagnetic iron oxide (SPIOs) nanomaterials are famously used in MRI imaging; they significantly enhance the contrast of T2WI images. Currently, Dao et al. reported the use of nanoparticle alloys such as FePt and MnZrFe as MRI contrast agents [38].

4.2. Magnetic Nanomaterial Applications in PET-CT Imaging. Positron emission computed tomography (PET-CT) is a commonly used noninvasive clinical examination in the tumor diagnosis and prognosis. The chelated 2-fluoro-2-deoxy-D-glucose (18F-FDG) with small molecules or antibodies is a commonly used contrast agent [39]. In recent preclinical studies, the radioactive-labeled magnetic nanoparticles have been proved very promising in cancer diagnosis. It has three significant advantages compared with traditional imaging techniques: (1) the magnetic nanoparticles labeled with radioactive tracer possess precision targeting due to the EPR effect, (2) magnetic nanoparticles have a high surface to volume ratio, allowing the use of high-density radioactive labels, and (3) obtainable complementary multimodal imaging, for instance, utilizing different radionuclides nanoparticles in integrated imaging [40]. Pratt et al. found that chelating radionuclides on the surface of small and biocompatible magnetic nanoparticles improved the accuracy and specificity of early tumor diagnosis, also using the advantages of PET scan of displaying the changes in tissue functions [41].

4.3. Biofluorescence Imaging. Bioluminescence imaging obtains optical images given fluorescence characteristics changes. At the cellular level, fluorescent nanomaterials act as fluorescent probes enter the cells in both active transport and passive diffusion due to their small size; at the organism level, the nanoparticles enter the bloodstream, then exuded and enriched in the tumor lesion due to the high permeability of tumor blood vessels. CL et al. combined magnetic nanoparticles with fluorescent materials to prepare magnetic fluorescent nanocomposites that are both superparamagnetic and fluorescent. When the magnetic fluorescent nanocomposites are introduced into living cells, the fluorescence can be traced and controlled to be enriched at the desired location upon applying an external magnetic field, which dramatically improves the efficiency of cell imaging [42].

4.4. Hybrid Imaging Model. Different imaging techniques comprise certain advantages and disadvantages, and yet, there is no ideal technique. A single imaging technique cannot guarantee optimal performance in different cases. Nevertheless, hybrid imaging can integrate the advantages of several techniques to address the inherent limitations of a single imaging technique [43]. For instance, PET-CT is a renowned sensitive tumor diagnostic tool, while MRI can provide more anatomical information through high-resolution images [44]. Therefore, combining these two imaging techniques can provide higher sensitivity and more detailed anatomical information in tumor diagnosis. Nanomaterials can possess precision targeting properties through surface modification and could be used as contrast agents in imaging technology. Tracking the contrast agent’s enrichment in the body helps determine surgery scope and facilitate the procedure, i.e., employing fluorescence imaging. It can also ensure whether tumor tissues are entirely removed or not, i.e., performing MRI analysis. Besides, the tumors’ occurrence and progression can be tracked and identified, i.e., utilizing PET-CT [45]. The recent hybrid imaging techniques are MRI/fluorescence imaging and PET-CT/MR imaging [46]. Therefore, diagnosis accuracy can be improved, and better cancer therapeutics can be developed.

5. Magnetic Nanomaterial Applications and Research in Tumor Therapy

Recently, radiotherapy and (or) chemotherapy are commonly used as initial treatment combined with surgery [47]. However, different factors, including genetic alterations, could promote tumor drug resistance by dysfunctioning the cellular transport mechanisms and reducing drug efficiency and cellular detoxification capability. These adverse effects restrict the administrated drug dosage to patients [48].

5.1. Magnetic Nanomaterial Applications as Drug Carriers. With the vigorous development of the nanotechnology, has more and more attention has been paid to nanocarriers. Nanoparticles have good biocompatibility and less immune reaction, coupling with other ligands or antibodies after easily into the organization or the specific antigen specificity and cell surface receptors, or be swallowed up by the target cell into the cell, the DNA of the implementation of transhipment. It is also released in cells with high gene transfer efficiency [49]. Magnetic nanoparticles, especially paramagnetic and superparamagnetic ferrite nanoparticles, have become an objective material in drug carriers’ development [50]. The ferrite nanoparticles are primarily made of iron-containing particles or other active ingredients containing iron. It has been proven that ferrite nanoparticles exhibit decent biocompatibility and can be entirely metabolized. Moreover, it has robust and distinct drug-loading capabilities. Various antibodies, antigens, small molecules, polypeptides, and active proteins can be loaded on the modified nanoparticles’ surface. Different examples can present the mode of action of the modified nanoparticles; for instance, through the antigen-antibody reaction in the body or under the guidance of an external magnetic field, these targeted antigen-loaded nanoparticles are enriched in the tumor lesions, concentrating the accumulation of the antibodies to the target tumor cells to achieve the optimal therapeutic potential [51]. Recently, the nanoparticle preparation process is relatively mature. A complex combination of tumor suppressor genes, antitumor monoclonal antibodies, and antitumor drugs such as doxorubicin, paclitaxel, and cisplatin, can be integrated to establish a distinct advantageous microcarrier system that possesses magnetism, bioapplicability, and capability to cross the blood-brain barrier. Following the previously mentioned basis of establishing microcarrier systems,
the “three-stage carrier rocket theory” is proposed to provide a basis for tumor-targeted therapy [52]. Magnetic nanomaterials are proposed in the 1970s as carriers in targeted therapeutics, which has been recently shown as an ideal application [53]. For instance, the MNP-HP-CP complex has been synthesized using magnetic nanoparticles (MNPs) coated with heparin (HP) and embedded with cisplatin (CP) by solvent evaporation and emulsification crosslinking. The MNP-HP-CP complex intake by human ovarian cancer cells CP70 promoted cell apoptosis [54]. These findings proved the feasibility of magnetic nanomaterials as drug carriers. It has also been shown that this magnetic nanomaterial composite is biocompatible, minimally cytotoxic, and sustains the release of cisplatin [55].

Although paclitaxel is an essential drug in ovarian cancer treatment, its high administered dose may cause severe allergic reactions and dramatically limits its therapeutic effect [56]. On the other hand, the polyethylene glycol- (PEG-) triethoxysilane (APTES)- (PA-) modified magnetic nanomaterial packed with paclitaxel and doxorubicin precisely delivered the paclitaxel and doxorubicin to tumor cells, alleviating adverse side effects and sustaining the drug concentration in the tumor tissue [57] and increasing the therapeutic effect of paclitaxel.

5.2. Magnetic Nanomaterial Applications in Tumor Hyperthermia. Tumor hyperthermia refers to heat augmentation tumor treatment. Tumor hyperthermia is renowned as the fifth therapeutic approach after surgery, radiotherapy, chemotherapy, and immunotherapy [58]. It employs physical energy to elevate a particular or whole-body heat so that the tumor tissue temperature rises to a certain level and duration. Within specific time and temperature, tumor cells die without affecting healthy cells due to the different temperature tolerance between healthy and tumor cells [59]. When the temperature range is 40–42°C, the tumor cell fluidity is enhanced, the structure is weakened, and the viability is lost. High temperature injuriously affects the tumor cells’ endoplasmic reticulum, lysosomal membrane, and mitochondrial membrane, promoting cell death. The high temperature also inhibits the polymerase and ligase activity, repressing the synthesis of nucleic acids. Besides, the tumors’ surrounding blood vessels are characterized by abundant blood flow, abnormal vascular structure, twisted blood vessel shape, and high blood flow resistance and enable blood vessel thrombosis or occlusion. During hyperthermia, healthy and tumor tissues’ temperature increases; however, because of the optimal blood circulation in healthy tissues rather than tumor tissues, the heat poorly dissipated and eventually rises, killing tumor cells. Jordan et al. reported the unprecedented use of magnetic nanoparticles in tumor hyperthermia and proposed magnetic fluid hyperthermia (MFH) conceptualization [60]. The magnetism and adequate water solubility of magnetic fluids fostered its uses in clinical applications. Applying an external alternating magnetic field (AMF) over magnetic nanoparticles converts the magnetic energy into heat and steadily increases local tumor tissue temperature, thereby suppressing tumor cell growth [61]. Studies have shown that compared to paclitaxel cytotoxicity under normal body temperature, 30 minutes of constant heating at 43°C can significantly increase paclitaxel cytotoxicity by 10-100 times [62]. Secord et al. reported that the PEG-modified liposome nanoparticle-adriamycin complex combined with abdominal hyperthermia exhibited better precision, outcome, and drug uptake in tumor tissues [63].

5.3. Magnetic Nanomaterial Applications in Photodynamic Tumor Therapy. Photodynamic therapy is a new therapeutic technique that combines photosensitizer with the corresponding illuminant to destroy tumor tissue through selective photodynamic reactions [64]. The photosensitizer is the key for photodynamic therapy. Conventional photosensitizers include porphyrins, chlorin, and bacteriochlorin/phthalocyanines. However, due to low hydrophilicity and possible aggregation, traditional photoactive molecules are limited in biomedical applications. It is thus urgent to improve the photosensitizers’ water solubility and biocompatibility [65].

The emergence of nanomaterials provides a new aspect in developing photoactive molecules. They can be used as new carriers for photoactive molecules and improving the photosensitizers’ biocompatibility. Moreover, the self-targeting nanomaterial enables sufficient photosensitizer enrichment in the tumor tissue, improving tumor therapeutic effects, and reducing the photosensitizer’s adverse effects [66]. Recently, gold nanomaterials, carbon-based nanomaterials, and silica nanomaterials are the major substances in photodynamic therapy. These nanomaterials have a high drug-loading capacity and can efficiently boost tumor photothermal therapy [67]. Besides, photodynamic therapy, chemotherapy, hyperthermia, and other tumor therapies can be integrated by constructing multifunctional nanomaterials to achieve multitherapeutic synergy, which is favorable in cancer treatment [68].

6. Prospect

The constant nanotechnology and magnetic nanomaterial development have made significant progress in cancer diagnostics and therapeutics. Magnetic nanomaterials are widely used in MRI/PET-CT imaging, antitumor drug carriers, magnetic fluid hyperthermia, and different fields. However, their application remains preclinical and yet to be applicable in clinical trials [69]. Primarily, we need a comprehensive study on the multifunctional magnetic nanomaterials’ biosafety, distribution, long-term toxicity, synthesis, elemental composition, size, surface modification, and metabolism in vivo. With the rapid development of magnetic nanomaterials, nanotechnology, and biotechnology, magnetic nanomaterials can be widely used in cancer diagnosis and treatment in the future.

7. Conclusion

Magnetic nanoparticles not only have the general characteristics of nanoparticles but also have magnetic properties, which have become the research focus in the field of nanomedicine in recent years. Magnetic nanoparticles are widely
used in biomedicine, drug gene delivery, magnetic resonance imaging, molecular probe, tumor detection, tumor therapy, and other fields due to their unique properties. With the development of nanotechnology, magnetic nanoparticles will be more widely used in tumor diagnosis and treatment.

Conflicts of Interest
The authors declare that they have no conflict of interest in this work.

Authors’ Contributions
Xuefeng Bian and Ting Guo contributed equally to this work.

Acknowledgments
The work is financially supported by the National Natural Science Foundation of China (81517197), Social Development Plan of Taizhou, China (TS202004), the National Science Foundation of Nanjing University of Chinese Medicine (XZR2020093), China, Taizhou People’s Hospital Medical Innovation Team Foundation, China (CXTDA201901), and Scientific Research Foundation of Taizhou People’s Hospital, China (ZL202023).

References
[1] Global Burden of Disease Cancer Collaboration, "Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017," *JAMA Oncology*, vol. 5, no. 12, pp. 1749–1768, 2019.

[2] P. Muller, S. Walters, M. P. Coleman, and L. Woods, "Which indicators of early cancer diagnosis from population-based data sources are associated with short-term mortality and survival?," *Cancer Epidemiology*, vol. 56, pp. 161–170, 2018.

[3] I. Lilenthal and N. Herold, "Targeting molecular mechanisms underlying treatment efficacy and resistance in osteosarcoma: a review of current and future strategies," *International Journal of Molecular Sciences*, vol. 21, no. 18, p. 6885, 2020.

[4] M. Aflori, "Smart nanomaterials for biomedical applications—a review," *Nanomaterials (Basel)*, vol. 11, no. 2, p. 396, 2021.

[5] S. Caspani, R. Magalhães, J. P. Araújo, and C. T. Sousa, "Magnetic Nanomaterials as Contrast Agents for MRI," *Materials*, vol. 13, no. 11, p. 2586, 2020.

[6] Y.-P. Wang, Y.-T. Liao, C.-H. Liu et al., "Trifunctional Fe3O4/CaP/alginate core–shell–corona nanoparticles for magnetically guided, pH-responsive, and chemically targeted chemotherapy," *ACS Biomaterials Science & Engineering*, vol. 3, no. 10, pp. 2366–2374, 2017.

[7] N. D. Thorat, R. A. Bohara, S. A. M. Tofail et al., "Superparamagnetic Gadolinium Ferrite Nanoparticles with Controllable Curie Temperature - Cancer Theranostics for MR-Imaging-Guided Magneto-Chemotherapy," *European Journal of Inorganic Chemistry*, vol. 2016, pp. 4586–4597, 2016.

[8] N. D. Thorat, R. A. Bohara, and V. Malgras, "Multimodal Superparamagnetic Nanoparticles with Unusually Enhanced Specific Absorption Rate for Synergetic Cancer Therapeutics and Magnetic Resonance Imaging," *ACS Applied Materials & Interfaces*, vol. 8, no. 23, pp. 14656–14664, 2016.

[9] H. Shimoshige, Y. Nakajima, H. Kobayashi et al., "Formation of Core-Shell Nanoparticles Composed of Magnetite and Samarium Oxide in Magnetospirillum magneticum Strain RRS-1," *PLoS one*, vol. 12, no. 1, p. e0170932, 2017.

[10] A. P. Plan Sangnier, S. Preveral, A. Curcio et al., "Targeted thermal therapy with genetically engineered magnetite [email protected]: Photothermia is far more efficient than magnetic hyperthermia," *Journal of Controlled Release*, vol. 279, pp. 271–281, 2018.

[11] P. Yañez-Sedeño, A. González-Cortés, S. Campuzano, and J. M. Pingarrón, "Multimodal/Multifunctional Nanomaterials in (Bio)electrochemistry: Now and in the Coming Decade," *Nanomaterials*, vol. 10, no. 12, p. 2556, 2020.

[12] J. Wojnarowicz, T. Chudoba, and W. Lojkowski, "A review of microwave synthesis of zinc oxide nanomaterials: reactants, process parameters and morphologies," *Nanomaterials (Basel)*, vol. 10, no. 6, p. 1086, 2020.

[13] E. Barrios, D. Fox, Y. Y. L. Sip et al., "Nanomaterials in Advanced, High-Performance Aerogel Composites: A Review," *Polymers*, vol. 11, no. 4, p. 726, 2019.

[14] H. J. Deng and Z. L. Lei, "Preparation and characterization of hollow Fe3O4@SiO2@PEG-PLA nanoparticles for drug delivery," *Composites: Part B*, vol. 54, pp. 194–199, 2013.

[15] D. W. Ye, Y. Li, and N. Gu, "Magnetic labeling of natural lipid encapsulations with iron-based nanoparticles," *Nano Research*, vol. 11, no. 6, pp. 2970–2991, 2018.

[16] H. Lee, J. Han, H. Shin, H. Han, K. Na, and H. Kim, "Combination of chemotherapy and photodynamic therapy for cancer treatment with sonoporation effects," *Journal of Controlled Release*, vol. 283, pp. 190–199, 2018.

[17] J. Lu, J. Sun, F. Li et al., "Highly Sensitive Diagnosis of Small Hepatocellular Carcinoma Using pH-Responsive Iron Oxide Nanocluster Assemblies," *Journal of the American Chemical Society*, vol. 140, no. 32, pp. 10071–10074, 2018.

[18] T. Ojha, V. Pathak, Y. Shi et al., "Pharmacological and physical vessel modulation strategies to improve EPR-mediated drug targeting to tumors," *Advanced Drug Delivery Reviews*, vol. 119, pp. 44–60, 2017.

[19] K. Mylkie, P. Nowak, P. Rybczynski, and M. Ziegler-Borowska, "Polymer-Coated Magnetite Nanoparticles for Protein Immobilization," *Materials*, vol. 14, no. 2, p. 248, 2021.

[20] H. Jiang, H. Wu, Y. L. Xu, J. Z. Wang, and Y. Zeng, "Preparation of galactosylated chitosan/tripolyphosphate nanoparticles and application as a gene carrier for targeting SMMC7721 cells," *Journal of Bioscience and Bioengineering*, vol. 111, no. 6, pp. 719–724, 2011.

[21] P. Pradhan, J. Giri, F. Rieken et al., "Targeted temperature sensitive magnetic liposomes for thermo-chemotherapy," *Journal of Controlled Release*, vol. 142, no. 1, pp. 108–121, 2010.

[22] S. Laurent, D. Forge, M. Port et al., "Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications," *Chemical Reviews*, vol. 108, no. 6, pp. 2064–2110, 2008.

[23] M. Kumagai, T. K. Sarma, H. Cabral et al., "Enhanced in vivo magnetic resonance imaging of tumors by PEGylated iron-oxide-gold core-shell nanoparticles with prolonged blood circulation Properties," *Macromolecular Rapid Communications*, vol. 31, no. 17, pp. 1521–1528, 2010.
G. Wang, S. Gao, R. Tian et al., “N-hexanoyl chitosan stabilized magnetic nanoparticles: implication for cellular labeling and magnetic resonance imaging,” J. Nanobiotechnology, vol. 6, no. 1, pp. 1–11, 2008.

S. R. Bhattacharai, R. B. Kc, S. Y. Kim et al., “Facile Hydrothermal Synthesis of Iron Oxide Nanoparticles with Tunable Magnetic Properties,” The Journal of Physical Chemistry C, vol. 113, no. 31, pp. 13593–13599, 2009.

S. Ge, X. Shi, K. Sun et al., “Theranostic hyaluronic acid–iron micellar nanoparticles for magnetic-field/enhanced in vivo cancer chemotherapy,” Chem Med Chem, vol. 13, no. 1, pp. 78–86, 2018.

J. K. Lewis, J. C. Bischof, I. Braslavsky et al., "The Grand Challenges of Orga..." Cryobiology, vol. 72, no. 2, pp. 169–182, 2016.

Y. B. Zhou, Z. M. Tang, C. L. Shi, S. Shi, Z. Qian, and S. Zhou, "Polyethyleneimine functionalized magnetic nanoparticles as a potential non-viral vector for gene delivery," Journal of Materials Science-Materials in Medicine, vol. 23, no. 11, pp. 2697–2708, 2012.

F. Fan, J. Sun, B. Chen et al., “Rotating magnetic field-controlled fabrication of magnetic hydrogel with spatially disk-like microstructures,” Science China Materials, vol. 61, no. 8, pp. 1112–1122, 2018.

H. Shokrollahi and A. Khorramdin, “Magnetic resonance imaging by using nano-magnetic particles,” Journal of Magnetism and Magnetic Materials, vol. 369, no. 11, pp. 176–183, 2014.

X. Shi, S. H. Wang, S. D. Swanson et al., “Dendrimer–Functionalized Shell-crosslinked Iron Oxide Nanoparticles for In Vivo Magnetic Resonance Imaging of Tumors,” Advanced Materials, vol. 20, no. 9, pp. 1671–1678, 2008.

J. Park, N. R. Kadasala, S. A. Abouelmagd et al., “Polymer–iron oxide composite nanoparticles for EPR-independent drug delivery,” Biomaterials, vol. 101, pp. 285–295, 2016.

A. H. Rezayan, M. Mousavi, S. Kheirouj, G. Ameobadegy, M. S. Ardestani, and J. Mohammadnejad, “Monodisperse magnetite (Fe3O4) nanoparticles modified with water soluble polymers for the diagnosis of breast cancer by MRI method,” Journal of Magnetism and Magnetic Materials, vol. 420, no. 15, pp. 210–217, 2016.

T. J. Daou, G. Pourroy, J. M. Greneche, A. Bertin, D. Felder-Flesch, and S. Begin-Colin, “Water soluble dendronized iron oxide nanoparticles,” Dalton Transactions, vol. 23, pp. 4442–4449, 2009.

Z. Liu, S. Tabakman, K. Welsher, and H. Dai, “Carbon nanotubes in biology and medicine: In vitro and in vivo detection, imaging and drug delivery,” Nano Research, vol. 2, no. 2, pp. 85–120, 2009.
[54] J. Xiong, “SALL4: Engine of Cell Stemness,” Current Gene Therapy, vol. 14, no. 5, pp. 400–411, 2014.

[55] Z. Shen, T. Chen, X. Ma et al., “Multifunctional Theranostic Nanoparticles Based on Exceedingly Small Magnetic Iron Oxide Nanoparticles for T1-Weighted Magnetic Resonance Imaging and Chemotherapy,” ACS Nano, vol. 11, no. 11, pp. 10992–11004, 2017.

[56] S. S. Zeng, T. Yamashita, M. Kondo et al., “The transcription factor SALL4 regulates stemness of EpCAM-positive hepatocellular carcinoma,” Journal of Hepatology, vol. 60, no. 1, pp. 127–134, 2014.

[57] C. Wu, Y. Shen, M. Chen, K. Wang, Y. Li, and Y. Cheng, “Recent Advances in magnetic nanomaterial-based microtransduction for cell fate regulation,” Advanced Materials, vol. 30, no. 17, p. 1705673, 2018.

[58] M. Fiorillo, A. F. Verre, M. Iliut et al., “Graphene oxide selectively targets cancer stem cells, across multiple tumor types: Implications for non-toxic cancer treatment, via “differentiation-based nano-therapy,” Oncotarget, vol. 6, no. 6, pp. 3553–3562, 2015.

[59] Z. Wang, J. Tan, C. McConville et al., “Poly lactic-co-glycolic acid controlled delivery of disulfiram to target liver cancer stem-like cells,” Nanomedicine: Nanotechnology, Biology and Medicine, vol. 13, no. 2, pp. 641–657, 2017.

[60] H. Sun, S. He, B. Wen, W. Jia, E. Fan, and Y. Zheng, “Effect of Biejiajian Pills on Wnt signal pathway molecules β-catenin and GSK-3β and the target genes CD44v6 and VEGF in hepatocellular carcinoma cells,” Nan Fang Yi Ke Da Xue Xue Bao, vol. 34, no. 10, pp. 1454–1458, 2014.

[61] Y.-Y. Lu, J.-J. Wang, X.-K. Zhang, W.-B. Li, and X.-L. Guo, “1118-20, an indazole diarylurea compound, inhibits hepatocellular carcinoma HepG2 proliferation and tumour angiogenesis involving Wnt/β-catenin pathway and receptor tyrosine kinases,” Journal of Pharmacy and Pharmacology, vol. 67, no. 10, pp. 1393–1405, 2015.

[62] Z. Gao, Y. Hou, J. Zeng et al., “Tumor Microenvironment-triggered Aggregation of Antiphagocytosis99mTc-Labeled Fe3O4nanoprobe for enhanced tumor imaging in vivo,” Advanced Materials, vol. 29, no. 24, p. 1701095, 2017.

[63] X. Ke, Y. Zhao, X. Lu et al., “TQ inhibits hepatocellular carcinoma growth within vitroandin vivobioactivity repression of Notch signaling,” Oncotarget, vol. 6, pp. 32610–32621, 2015.

[64] R. Dhanasekaran, I. Nakamura, C. Hu et al., “Activation of the transforming growth factor-β/SMAD transcriptional pathway underlies a novel tumor-promoting role of sulfatase 1 in hepatocellular carcinoma,” Hepatology, vol. 61, no. 4, pp. 1269–1283, 2015.

[65] H. Zhang, X. L. Liu, Y. F. Zhang et al., “Magnetic nanoparticles based cancer therapy: Current status and applications,” Science China. Life Sciences, vol. 61, no. 4, pp. 400–414, 2018.

[66] M. Niederberger, “Multiscale nanoparticle assembly: From particulate precise manufacturing to colloidal processing,” Advanced Functional Materials, vol. 27, no. 47, p. 1703647, 2017.

[67] L. Deng, J. H. Stafford, S.-C. Liu et al., “SDF-1 Blockade Enhances Anti-VEGF Therapy of Glioblastoma and Can Be Monitored by MRI,” Neoplasia, vol. 19, no. 1, 2016.

[68] Y. Li, Y. Deng, X. Tian et al., “Multi-pronged design of light-triggered nanoparticles to overcome cisplatin resistance for efficient ablation of resistant tumor,” ACS Nano, vol. 9, no. 10, pp. 9626–9637, 2015.

[69] L. P. Singh, S. K. Srivastava, R. Mishra, and R. S. Ningthoujam, “Multifunctional hybrid nanomaterials from water dispersible CaF2Eu3+, Mn2+and Fe3O4for luminescence and hyperthermia application,” Journal of Physical Chemistry C, vol. 118, no. 31, pp. 18087–18096, 2014.

[70] H. Unterweger, L. Dészí, J. Matuszak et al., “Dextran-coated superparamagnetic iron oxide nanoparticles for magnetic resonance imaging: evaluation of size-dependent imaging properties, storage stability and safety,” International Journal of Nanomedicine, vol. 13, pp. 1899–1915, 2018.

[71] M. Ebadi, S. Bullo, K. Buskaran, M. Z. Hussein, and S. Fakurazi, “Synthesis and properties of magnetic nanothermoplastics coated with polyethylene glycol/5-fluorouracil/layered double hydroxide,” International Journal of Nanomedicine, vol. 14, pp. 6661–6678, 2019.

[72] A. Krzywicka and E. Migiel, “Silver-polystyrene (Ag/PS) nanocomposites doped with polyvinyl Alcohol (PVA)-fabrication and bactericidal activity,” Nanomaterials (Basel), vol. 10, no. 11, p. 2245, 2020.

[73] J. Lojk, V. B. Bregar, M. Rajh et al., “Cell type-specific response to high intracellular loading of polycrylic acid-coated magnetic nanoparticles,” International Journal of Nanomedicine, vol. 10, pp. 1449–1462, 2015.

[74] A. Rajan, M. Sharma, and N. K. Sahu, “Assessing magnetic and inductive thermal properties of various surfactants functionali- sed Fe3O4 nanoparticlest for hyperthermia,” Scientific Reports, vol. 10, no. 1, p. 15045, 2020.

[75] J.-H. Lee, S.-M. You, K. Luo, J.-S. Ko, A.-H. Jo, and Y.-R. Kim, “Synthetic ligand-coated starch magnetic microbeads for selec- tive extraction of food additive silicon dioxide from commercial processed food,” Nanomaterials (Basel), vol. 11, no. 2, p. 532, 2021.

[76] T. Nguyen, F. Mammeri, and S. Ammar, “Iron Oxide and Gold Based Magneto-Plasmonic Nanostructures for Medical Applications: A Review,” Nanomaterials, vol. 8, no. 3, p. 194, 2018.

[77] X. Yuan, X. Zhang, S. Lu, Y. Wei, and X. Wei, “Cellular Toxicity and Immunological Effects of Carbon-based Nanomateri- als,” Particle and Fibre Toxicology, vol. 16, no. 1, 2019.