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RECENT ADVANCES IN IRON OXIDE NANOPARTICLES FOR DIAGNOSTIC, THERAPEUTIC AND BIOMEDICAL APPLICATIONS

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Abstract

Iron oxide nanoparticles (IONPs) have emerged versatile nanomaterials that has a high potential in the biomedical sciences because of its magnetic characteristics, biocompatibility, and straightforward functionalization of the surface. This review is an overview of the recent developments in the diagnostic and therapeutic uses of the IONPs with special reference to the magnetic resonance imaging (MRI), targeted drug delivery, and magnetic hyperthermia. Superparamagnetic iron oxide nanoparticles (SPIONs) have been shown to be performing outstandingly as T2 MRI contrast agents to allow enhanced imaging of diseased tissues. Moreover, functionalized IONPs are also useful as the vectors of chemotherapeutic drugs and natural bioactive agents in order to enable the stimuli-responsive release of drugs and magnetically directed drug delivery. IONPs have also been identified as promising cancer hyperthermia that employs their property of producing localized heat in the presence of an alternating magnetic field and thermoablation. Moreover, new uses in biosensing, gene delivery, and tissue regeneration, discussed, and main issues associated with in vivo behavior, safety, and clinical translation.

1. Introduction

Nanotechnology has become one of the most disruptive disciplines in contemporary science, with unparalleled possibilities as far as innovation is concerned, in medicine, biology, chemistry and materials science [1]. The iron oxide nanoparticles (IONPs) are one of the many types of nanomaterials considered in such not only biomedical but also biotechnological applications because of their magnetic characteristics, biocompatibility, and structural flexibility. Their size, surface chemistry and magnetic behavior have been precisely manipulated allowing the creation of multifunction platforms that can be

used in disease diagnosis, therapy and monitoring to overcome critical challenges [2]. IONPs, especially superparamagnetic iron oxide nanoparticles (SPIONs) are superparamagnetic at the nanoscale that is, they are highly magnetized when a magnetic field is applied to them but not when the field is removed. This character would be a very desirable property of the biomedical applications of the property; this helps in reducing aggregation of the particles and the chances of embolism after the systemic administration of the property is done. In addition, iron is a crucial component of the human body, and iron oxide-containing materials can be absorbed by the body and processed into natural iron deposits, which is why IONPs are more naturally biocompatible than most other inorganic nanomaterials [3-5].

The increasing attention to IONPs is explained by the outstanding opportunities in diagnostic imaging, targeted medicine, magnetic hyperthermia, and diverse other biomedical applications [6]. The proper and prompt identification of diseases has been one of the pillars in the field of diagnostic medicine to enable successful treatment and better patient outcomes. One of the most potent non-invasive imaging modalities to date is the Magnetic Resonance Imaging (MRI) which has a high soft tissue contrast and spatial resolution without ionizing radiation. The sensitivity of MRI, however, is usually based on the application of contrast agents that help in increasing the degree of signal differentiation between normal and pathological tissues [7-10]. The limitations of traditional contrast agents include short circulation, lack of specificity as well as possible toxicity, and this has prompted the need to identify safer and more effective options. In this respect, SPIONs have proved to be very useful MRI contrast agents especially in T2-weighted imaging. The SPIONs are used to induce local magnetic field in homogeneities which cause the transverse relaxation of the protons in the water surrounding streamlining the appearance of better contrast and improving the lesion detectability [11]. Notably, they are nanoscale, which means that they can effectively interact with biological systems and circulate in the bloodstream upon proper surface modification. In addition to this, this preferential accumulation in tumor tissues of IONPs due to the Enhanced Permeation and Retention (EPR) effect has made them potential tools to be used in the imaging of cancer in the future [12]. The vasculature involved in tumors is generally loose and poorly structured, allowing nanoparticles to accumulate passively in the tumor microenvironment to create improved imaging contrast and allow easier visualization of the tumor morphology and progression. In addition to passive targeting, there is a large variety of synthetic and natural ligands that can be coated onto the surface of IONPs in order to accomplish active targeting and better biological behavior. Polyethylene glycol (PEG), dextran, chitosan, and polyvinyl alcohol functionalization helps to increase the colloidal stability, increase the blood circulation time and decrease the immune recognition. Also, conjugation with targeting ligands including folic acid, peptides, or antibodies helps to provide specificity dramatically as receptor-mediated uptake by cancer cells is possible. The functionality of IONPs is further extended to have inherent antioxidant, anti-inflammatory and anticancer effects through incorporation of natural bioactive compounds such as polyphenols and phytochemicals. The advances have contributed to the rise of the theranostic nanoplatforms, which integrate diagnostic imaging and therapeutic capabilities into one platform [13-15]. The therapeutic promise of IONPs is also very strong. Magnetic nanoparticles-based targeted delivery of drugs is a potent approach to circumvent the drawbacks of traditional chemotherapy (systemic toxicity, low bioavailability, and non-selective distribution). With the help of an external magnetic field IONPs can be loaded with chemotherapeutic drugs, natural compounds or genetic material and directed to a disease site. This method enhances the level of drug at the target site and reduces exposure to healthy tissues therefore reducing drug side effects [16]. Moreover, therapeutic payloads release can be highly regulated using stimuli-responsive systems, such

as pH, enzyme, temperature, or heating with magnetic fields.

Magnetic hyperthermia is one of the most innovative applications of IONPs as a therapeutic treatment method that is minimally invasive and takes advantage of the fact that magnetic nanoparticles can produce localized heat when subjected to an alternating magnetic field. The high sensitivity of cancer cells to high temperatures is particularly caused by the abnormal metabolism of cancer cells and their low heat dissipation ability [17-20]. Mild hyperthermia may cause apoptosis and make tumor cells sensitive to chemotherapy and radiotherapy whereas higher temperatures may lead to irreversible thermal ablation and necrosis. The combination of magnetic hyperthermia with drug delivery and MRI has even intensified the presence of IONPs as multifunctional therapeutic agents that can be applied as simultaneous treatment and monitoring agents. Along with imaging and cancer therapy, IONPs have proven to have great potential in a wide variety of other biomedical applications. They are cellular labeling and magnetic separation as a diagnostic and detoxification, magnetofection as an improved gene delivery, tissue repair and regeneration using stem cell guidance and tracking, and biosensing platforms as the detection of disease biomarkers.

The flexibility of IONPs is due to their high surface area, functionalization capability and high magnetic responsiveness that in combination allows adapting these particles to wide biomedical demands [21-25]. In spite of these promising developments, a range of critical factors should be considered, in order to achieve successful clinical translation of IONP-based technologies. The particle size, shape, surface chemistry and magnetic characteristics have to be carefully regulated to obtain the best biodistribution, long circulation and efficient cellular uptake. Surface coatings are important in aggregation prevention, opsonization reduction, and macrophage-phagocytic system clearance reduction. Although IONPs are, in general, assumed to be non-toxic, the biodegradation levels, long-term toxicity, and their interactions with complex biological systems are to be thoroughly assessed [26].

In the future, IONP research can be viewed as the future of green synthesis, further functionalization schemes, and more permanently integrated theranostic devices. Greater insight into the nature of nano- bio interactions coupled with the ability to manufacture scalably and have a well-defined regulatory pathway will be essential to the translation of laboratory-scale innovations into clinically approved products. The purpose of this review is to give a general review of diagnostic, therapeutic and emerging biomedical uses of iron oxide nanoparticles, and also to give special attention on surface functionalizational strategies, natural compound incorporation and the challenges and opportunities of the clinical translation of such nanoparticles [27-30].

1.1. Diagnostic Application

1.1.1. Magnetic Resonance Imaging (MRI)

The Magnetic Resonance Imaging (MRI) is non-invasive diagnostic test that is very powerful and is necessary in the present medical imaging processes particularly when it comes to visualizing the soft tissues and also in the detection of pathological processes such as cancer at early stage. Clinical diagnosis is being widely applied through MRI because it is highly spatially resolute and best tissue contrast without having to use ionizing radiations thus diminishing the harmful impacts of its regular repeated uses [31]. However, conventional MRI can require administration of contrast agents to improve the difference between normal and abnormal tissues. In this connection, nanoparticles of iron oxide, especially superparamagnetic iron oxide nanoparticles (SPIONs) are now able to be highly useful as MRI contrast agents. The primary mechanism of action of the SPIONs is the ability to be used as a T2 contrast agent because it produces the local magnetic field inhomogeneity, which will accelerate the transverse relaxation of the surrounding water protons. This leads to steep signal loss in T2 weighted images, hence contrast increase and enhancement of lesion sensitivity. The magnetic properties, particle size,

surface chemistry, and crystallinity are high-dependence factors that IONPs use to determine their relaxivity and image ability. Appropriate surface manipulation can enable SPIONs to be useful in the interaction with biological systems due to their small nanoscale size and be long circulated in the bloodstream. The primary advantage of IONPs in the imaging of cancer is the potential to be concentrated in favor of the tumor tissues via the Enhanced Permeability and Retention (EPR) effect. Tumor vasculature is typically maladaptive and highly leaky and lacks lymphatic clearance and therefore nanoparticles can accumulate passively in the tumor microenvironment. It is passive targeting which increases the contrast of tumors in MRI significantly allowing easier visualization of the tumor limits, size and progression. In addition, the IONPs can be targeted in order to escape the rapid clearance by the reticuloendothelial system (RES) that further enhances their uptake in tumors. IONPs can be functionalized using either natural or synthetic ligands (polymers, biomolecules and phytochemicals) to improve specificity and biological behavior. Surface coatings, which enhance colloidal stability, biocompatibility and time of circulation are made of polyethylene glycol (PEG), dextran and chitosan. Active targeting active conjugation of ligands such as folic acid that bind folate receptors which are surface expressed on most of the cancer cells can be attained [32-35]. In fact, folate- and quercetin-coated IONPs have been reported to exhibit enhanced MRI contrast and, concurrently, exhibit anti-prolliferative property towards cancer cells and, therefore, they are likely to be used as theranostic agents, i.e., the materials that can be used as diagnostic and treatment agents. Similarly, (M)IONPs carrying multiple functionalities covalently functionalized with gold, curcumin, lipoic acid and glutathione have also shown good MRI contrast properties at reduced cytotoxicity to normal cells [36]. It has been reported that these nanocomposites possess spectacular growth inhibiting properties on the glioma cells signifying that these nanocomposites are used along with the imaging and targeted destruction of cancerous cells. Increasing biomedical applications of IONPs through incorporation of bioactive molecules can enhance the efficiency of targeting besides conferring anti-oxidant, anti-inflammatory and anti-cancer action. Besides the use of IONPs in cancer diagnostics, MRI is actively used today to investigate many other diseases. The studies of diabetes use the IONPs to visualise the pancreatic inflammation and trace the immune cell invasion into the pancreatic islets of Langerhans. The IONPs are applied in cardiovascular medicine to determine the presence of atherosclerotic plaques through the detection of atherosclerotic plaques in cardiovascular disorders which is initially diagnosed by locating these macrophages [37]. Besides, IONPs are also being researched to visualize neuroinflammation, liver fibrosis, and to track stem cells, so it demonstrates their utility as an instrument of more advanced diagnostics. In general, introduction of IONPs in MRI is a significant milestone in diagnostic imaging. The attraction is because they have a tunable magnetic property, functionalization capability and biocompatibility that can make them good candidates in the next generation contrast agent. With the improvement of research and clinical translation, there is a lot of promise in IONP-based MRI contrast agents to improve the diagnosis of diseases, monitoring of the efficacy of the treatment and personalized medicine [38].

1.2. Therapeutic Applications

1.2.1. Targeted Drug Delivery

Targeted drug delivery systems are considered to be one of the most promising and researched areas of therapeutic use of iron oxide nanoparticles (IONPs). IONPs are versatile surfaces that can carry numerous therapeutic agents, such as chemotherapeutic drugs, natural phytochemicals, genes, and proteins because of their unique magnetic properties, nanoscale size, and their ability to be easily surface functionalized. The use of external magnetic field can also be used to direct and focus these functionalized IONPs at a particular pathological point, e.g., tumor, to increase therapeutic effectiveness. The target nature of this method greatly enhances the concentration of the drug in

the area of the disease and decreases systemic distribution and consequently off-target toxicity and the side effects that are usually found with traditional chemotherapy [39].

IONP-based nanocarriers are usually internalized into the cell through endocytosis, phagocytosis or receptor-mediated endocytosis depending on the particle size, surface charge and type of surface ligands. Depending on the targeting moieties of interest, e.g. folic acid, peptides, antibodies, or polysaccharides, further functionalization of these nanoparticles can be used to improve selective uptake by cancer cells, which overexpress certain receptors. When taken up, the nanoparticles are normally localized in endosomes or lysosomes, and an environmental change can stimulate controlled drug release, e.g. acidic pH or enzymatic activity. The release of the drug could be accurately controlled by stimuli-responsive releases, such as pH-sensitive, temperature-sensitive, redox-responsible, or enzyme-sensitive releases. Tumor tissues usually have acidic micro surroundings and high levels of enzymes than normal tissues hence they are the best targets of such controlled delivery strategies. Alternating magnetic fields also may be used to produce localized heating (magnetothermal effect) which further accelerates drug release and therapeutic activity [40].

Other studies have shown how natural bioactive compounds could be successfully delivered using systems based on IONPs. An example is IONPs conjugated with diosgenin, a saponin of steroid, which is a derivative of the plant Dioscorea bulbifera that has been demonstrated to have excellent anticancer properties by inducing apoptosis and inhibiting cell proliferation in breast cancer cells. On the same note, IONPs loaded with curcumin, especially those that have been modified with biocompatible polymers like chitosan have shown controlled and sustained drug release kinetics and increased cytotoxicity to lung cancer cells. Chitosan can also be used to enhance drug loading in addition to offering the ability to release drugs under acidic tumor conditions through pH-sensitive behavior. Functionalized phytic acid and chitosan IONPs have also been shown to possess high inhibitory effects against the proliferation of colon cancer cells with pH-controlled drug release ensuring that there is minimal drug leakage when in physiological conditions [41]. Moreover, IONPs conjugated with polyphenols isolated out of Vitis vinifera or plant extracts out of Couroupita guianensis have demonstrated strong cytotoxic action towards diverse types of cancer cells at appreciably reduced dosages than the free extracts. This increased activity is explained by increase in cellular absorption, prevention of bioactive compounds degradation, and prolonged intracellular release. One of the most significant issues in drug delivery targets, specifically in brain tumor therapy, is to overcome the blood-brain barrier (BBB), which limits most therapeutic agents to the central nervous system. Recent reports have shown that properly engineered IONPs, particularly ones that are smaller in size say in the range of about 10 to 20 nm, do penetrate or bypass the BBB upon an external magnetic field. The defective and porous vasculature of the brain tumors also contributes to the nanoparticle accumulation in the intracranial locations. Surface modification with ligands or surfactants in combination with magnetic targeting, has demonstrated encouraging outcomes in improving the delivery of drugs to brain tumors with reduced neurotoxicity. Altogether, the use of IONP-based targeted drug delivery systems is a rather versatile and efficient treatment approach. They are the best candidates of personalized and precision medicine due to their capacity to integrate magnetic targeting, controlled drug release and surface functionalization. Further development and progress in nanoparticle engineering and biological targeting are also anticipated to increase their clinical use in the treatment of cancer and the treatment of other complex diseases [42-45].

1.2.2. Magnetic Hyperthermia and Thermoablation

The magnetic hyperthermia is the new and least invasive mode of therapy which employs the heat produced by the iron oxide nanoparticles (IONPs) when subjected to alternating magnetic

field (AMF). In this technique, the IONPs are initially concentrated at the tumor location either by passive targeting (Enhanced Permeation and Retention effect), active targeting with ligands or by magnetic guidance. When an AMF is applied, the nanoparticles lose electromagnetic energy as heat via other processes like Néel and Brownian relaxation losses. This localized heat production increases the temperature of the tumor to a therapeutic level causing selective destruction of the cancer cells without damaging the adjacent healthy tissues [46].

The high temperature is also known to be more sensitive to cancer cells compared to normal cells, which have a changed metabolism, poor vascularization as well as limited heat dissipation capacity. Mild hyperthermia, usually in the temperature span of 42- 45 o C, may provoke apoptosis, disrupt protein folding, deviate the DNA repair pathway, and prevent tumor angiogenesis. Once elevated temperatures of around 50 o C or more are attained, the treatment changes into thermoablation whereby cells undergo irreversible cellular damage, membrane rupture, and necrotic cell death. This thermal destruction within a controlled manner is what makes magnetic hyperthermia especially appealing to the treatment of solid tumors that are resistant to conventional therapy [47].

In combination therapy with radiotherapy or chemotherapy, magnetic hyperthermia is often used because heat will make tumor cells more sensitive to these therapies. Hyperthermia enhances the penetration of drugs and radiosensibility as well as this process boosts blood flow and oxygenation in the tumor microenvironment. Also, heat can disrupt the tumor cell membranes leading to increased intracellular absorption of chemotherapeutic agents leading to synergistic effectiveness of anticancer effects at reduced doses of drugs. IONPs particularly offer the benefit of being hyperthermiaable, highly magnetic responsive biocompatible tunable heaters. The heat generation capacity of the IONPs is determined by the particle size, shape, magnetic anisotropy, concentration and surface coating. IONPs constituted in an optimized form have shown great specific absorption rates (SAR) and can be heated efficiently at relatively low levels of magnetic fields, which is safe to use in a clinical setting. Significant tumor volume reduction as well as extended survival following IONP-mediated magnetic hyperthermia treatment has been reported in vivo in a large number of studies and in animal models [48-53].

A key strength of this modality is that it can be integrated with targeted drug delivery systems and result in multifunctional or theranostic platforms. As an example, folate and curcumin-coated IONPs have demonstrated successful tumor targeting with folate receptor-mediated uptake and fast attaining of hyperthermia temperatures with AMF exposure. Localized heating in such systems not only causes the death of tumor cells but it also increases the rate of drugs release which leads to increased efficacy of the therapeutic process [54-59].

The green-synthesized IONPs with natural compounds and plant-derived polyphenols have become more and more popular owing to enhanced biocompatibility and other biological functions. IONPs coated or synthesized with polyphenols of cinnamon and vanilla, and epigallocatechin gallate (EGCG) of green tea have been shown to exhibit effective heating behavior and antioxidant and anticancer activity. Naturally functionalized IONPs have been also successfully used in integrative applications with magnetic hyperthermia, controlled drug delivery, and magnetic resonance imaging (MRI), and are therefore prospective multifunctional nanoplatforms [60]. Moreover, magnetic hyperthermia can be remotely and precisely controlled in space and time because the heat is only produced in the accumulation location of the nanoparticle when the external magnetic field is applied. This makes it less toxic in the system and should there be a need to administer the treatment again. As nanoparticles engineering, optimization of magnetic field and clinical safety testing progress, IONP-mediated magnetic hyperthermia and thermoablation is likely to become a prominent part of the future cancer treatment plans, especially in the context of personalized and precision medicine [61-63].

1.3. Other Biomedical Applications

In addition to imaging and cancer therapy, iron oxide nanoparticles (IONPs) have been widely used in a large variety of biomedical fields because they are magnetic responsive, surface modifiable, and biocompatible. They can be used in a wide variety of applications as a diagnostic, separation technology, regenerative medicine, gene delivery and biosensing tool and thus have far more applications than on traditional therapeutic platforms [64].

1.3.1. Cellular Labeling, Separation, and Detoxification

IONP can be functionalized with the help of surface-derivatizing ligands (antibodies, peptides, aptamers) and be used to selectively target target cells, such as cancer cells, bacteria, viruses, or circulating tumor cells (CTCs). When labeled, such cells are easily extracted out of complicated biological fluids by the application of an external magnetic field. The usage of this magnetic separation method is common in cell sorting, in the purification of blood, in diagnosis tests, and in the detection of pathogens. IONPs can also be customized to target toxins, heavy metals and bacterial endotoxins of biological fluids in detoxification procedures and thus are quickly removed and enhance patient safety in clinical practice including septicemia [65].

1.3.2. Magnetofection and Gene Delivery

Magnetofection is a new technology of delivering genes that capitalizes on the magnetic properties of IONPs in order to increase the transfection efficiency of nucleic acids. DNA, RNA or small interfering RNA (siRNA) can be electrostaticaly bound to ions of polyethyleneimine (PEI), chitosan or poly-L-lysine via an ionic interaction with the polymer cationic surface. These complexes are then quickly drawn to the cell surface under the influence of an external magnetic field and the uptake into the cell is greatly enhanced. Magnetofection has been shown to be more beneficial in delivery of genes, lower dose, and less cytotoxic than conventional methods of transfection, and is used to deliver genes in vitro and in vivo in cancer gene therapy and regenerative medicine [66].

1.3.3. Tissue Repair and Regeneration

IONPs are becoming more and more important to tissue engineering and regenerative medicine. IONP-labeled stem cells can be directed to injury sites in the body (bone defects, areas of cardiac infarction or neural damage, etc.) by magnetic force, enhancing cell localization and therapeutic outcome. Also, IONPs make it possible to monitor the migration, survival of transplanted cells and their integration in real-time with MRI, which clinicians can use to monitor the success of organ transplants. IONPs are also being considered in tissue soldering and wound healing, in which magnetic heating can be used to strengthen tissue adhesion and repair without causing too much damage to the adjacent tissues [67-69].

1.3.4. Biosensing and Diagnostic Platforms

The application of IONPs in biosensing is extensively used because of the high surface area, the ability to functionalize them, and the amplification of signals of magnetism. They are important elements in immunoassays, enzyme based detection and magnetic biosensors in sensitive and selective detection of proteins, enzymes, nucleic acids and disease biomarkers. IONP based biosensors have been shown to be sensitive, fast in response and have low detection limits which ensure their use in early disease detection, point of care testing, and environmental monitoring [70].

1.3.5. Critical Considerations for In Vivo Application

To achieve an effective in vivo application of IONPs, a proper balance of physicochemical and biological characteristics of these nanoparticles is to be carefully optimized to guarantee their safety, efficacy, and clinical applicability.

1.3.6. Size and Shape

The biodistribution, circulation time and cellular uptake of particles depend on the critical determinant of particle size. The sizes of IONPs

between 10 and 100 nm are normally optimal as anything below 5 nm gets easily filtered out by the renal system whereas anything that is beyond 200 nm will be absorbed by the spleen and liver. Besides size, particle shape (spherical, cubic, or rod-like) is also a factor in determining magnetic behavior and biological interactions which affect circulation and therapeutic performance [71].

1.3.7. Surface Coating and Functionalization

The bare IONPs are hydrophobic in nature, and readily form aggregates in a physiological solution, which results in rapid opsonization and clearance by the macrophage-phagocytic system (MPS) [61]. Surface coating of the biocompatible polymers like polyethylene glycol (PEG), dextran, chitosan, polyvinyl alcohol (PVA) or naturally present polyphenols is thus necessary. These coatings enable steric stabilization, enhance colloidal stability, lower immune recognition and prolong blood circulation time. In addition, functional coatings provide reactive sites in which conjugating targets can be made (targeting ligands, therapeutic agents, or imaging probes), which facilitates active targeting and multifunctionality [72].

1.3.8. Biodegradation and Toxicity

IONPs are considered to be safe because of the normal metabolism of iron in the body, which involves incorporation of iron in hemoglobin, ferritin or other iron-storage proteins. According to toxicological experiments, cytotoxic effects are generally noted to appear at high concentrations (>100 μg/mL) [73]. To a large extent, the character of the surface coating will serve to control toxicity, biodegradation rate and inflammatory reactions. Well-designed IONPs have low long-term toxicity and are readily eliminated by the normal iron metabolism mechanisms [74].

Conclusion

The iron oxide nanoparticles are a strong and multifunctional platform of next-generation biomedical uses. They have proved to be of definite advantage over the traditional methods of operation especially in cancer diagnosis and treatment because they have been incorporated into diagnostic imaging, targeted drug delivery, and magnetic hyperthermia. Their stability, targeting efficiency, and therapeutic performance have been enhanced greatly with surface functionalization approaches such as using polymers and natural bioactive compounds. Although the preclinical results are encouraging, difficulties in the field of controlled synthesis, long-term biocompatibility, biodistribution, and large-scale production are the major obstacles to translating into clinical applications. Future studies are required on green synthesis, progressive multifunctional coating, and insightful knowledge on nano- bio interactions. It has been anticipated that the generation of integrated theranostic IONP-based systems will be critical in individualized and precision medicine that will be able to bridge the gap between diagnosis, therapy and real-time monitoring of treatment.

References

Ramsden, J.J. Global Nanotechnology. In Applied Nanotechnology; Elsevier: Amsterdam, The Netherlands, 2018; pp. 245–254.

Feynman, R.P. There's plenty of room at the bottom [data storage]. J. Microelectromech. Syst. 1992, 1, 60–66.

Taniguchi, N. On the Basic Concept of Nanotechnology. Proc. Int. Conf. Prod. Eng. 1974, 2, 18–23.

Mitchell, M.J.; Billingsley, M.M.; Haley, R.M.; Wechsler, M.E.; Peppas, N.A.; Langer, R. Engineering precision nanoparticles for drug delivery. Nat. Rev. Drug Discov. 2021, 20, 101–124.

Bobo, D.; Robinson, K.J.; Islam, J.; Thurecht, K.J.; Corrie, S.R. Nanoparticle-Based Medicines: A Review of FDA-Approved Materials and Clinical Trials to Date. Pharm. Res. 2016, 33, 2373–2387.

Arias, L.S.; Pessan, J.P.; Vieira, A.P.M.; De Lima, T.M.T.; Delbem, A.C.B.; Monteiro, D.R. Iron Oxide Nanoparticles for Biomedical Applications: A Perspective on Synthesis, Drugs, Antimicrobial Activity, and Toxicity. Antibiotics 2018, 7, 46.

Manshian, B.B.; Jiménez, J.; Himmelreich, U.; Soenen, S.J. Personalized medicine and follow-up of therapeutic delivery through exploitation of quantum dot toxicity. Biomaterials 2017, 127, 1–12.

Karimi, Z.; Karimi, L.; Shokrollahi, H. Nano-magnetic particles used in biomedicine: Core and coating materials. Mater. Sci. Eng. C 2013, 33, 2465–2475.

Savliwala, S.; Chiu-Lam, A.; Unni, M.; Rivera-Rodriguez, A.; Fuller, E.; Sen, K.; Threadcraft, M.; Rinaldi, C. Magnetic Nanoparticles; Gubin, S.P., Ed.; Wiley: Hoboken, NJ, USA, 2020.

Yazdani, F.; Fattahi, B.; Azizi, N. Synthesis of functionalized magnetite nanoparticles to use as liver targeting MRI contrast agent. J. Magn. Magn. Mater. 2016, 406, 207–211.

Martín, M.J.; Azcona, P.; Lassalle, V.; Gentili, C. Doxorubicin delivery by magnetic nanotheranostics enhances the cell death in chemoresistant colorectal cancer-derived cells. Eur. J. Pharm. Sci. 2021, 158, 105681.

Mehrasbi, M.R.; Mohammadi, J.; Peyda, M.; Mohammadi, M. Covalent immobilization of Candida antarctica lipase on core-shell magnetic nanoparticles for production of biodiesel from waste cooking oil. Renew. Energy 2017, 101, 593–602.

Wang, J.; Jiang, L.-H.; Zhou, Y.; Ye, B.-C. Enhanced biodegradation of di-n-butyl phthalate by Acinetobacter species strain LMB-5 coated with magnetic nanoparticles. Int. Biodeterior. Biodegrad. 2017, 116, 184–190.

Muñoz de Escalona, M.; Sáez-Fernández, E.; Prados, J.C.; Melguizo, C.; Arias, J.L. Magnetic solid lipid nanoparticles in hyperthermia against colon cancer. Int. J. Pharm. 2016, 504, 11–19.

Horst, M.F.; Coral, D.F.; Fernández van Raap, M.B.; Alvarez, M.; Lassalle, V. Hybrid nanomaterials based on gum Arabic and magnetite for hyperthermia treatments. Mater. Sci. Eng. C 2016, 74, 443–450.

Tietze, R.; Lyer, S.; Dürr, S.; Struffert, T.; Engelhorn, T.; Schwarz, M.; Eckert, E.; Göen, T.; Vasylyev, S.; Peukert, W.; et al. Efficient drug-delivery using magnetic nanoparticles—Biodistribution and therapeutic effects in tumour bearing rabbits. Nanomed. Nanotechnol. Biol. Med. 2013, 9, 961–971.

Mohmood, I.; Lopes, C.B.; Lopes, I.; Tavares, D.S.; Soares, A.M.V.M.; Duarte, A.C.; Trindade, T.; Ahmad, I.; Pereira, E. Remediation of mercury contaminated saltwater with functionalized silica coated magnetite nanoparticles. Sci. Total Environ. 2016, 557–558, 712–721.

Martín, M.J.; Gentili, C.; Lassalle, V. In vitro Biological Tests as the First Tools to Validate Magnetic Nanotheranostics for Colorectal Cancer Models. ChemMedChem 2020, 15, 1003–1017. Pharmaceutics 2022, 14, 204 21 of 25

Verma, R.; Asthana, A.; Singh, A.K.; Prasad, S.; Susan, M.A.B.H. Novel glycine-functionalized magnetic nanoparticles entrapped calcium alginate beads for effective removal of lead. Microchem. J. 2017, 130, 168–178.

Gong, Y.; Wang, L.; Liu, J.; Tang, J.; Zhao, D. Removal of aqueous perfluorooctanoic acid (PFOA) using starch-stabilized magnetite nanoparticles. Sci. Total Environ. 2016, 562, 191–200.

Wang, P.; Wang, X.; Yu, S.; Zou, Y.; Wang, J.; Chen, Z.; Alharbi, N.S.; Alsaedi, A.; Hayat, T.; Chen, Y.; et al. Silica coated Fe3O4 magnetic nanospheres for high removal of organic pollutants from

wastewater. Chem. Eng. J. 2016, 306, 280–288.

Khodadadi Yazdi, M.; Zarrintaj, P.; Hosseiniamoli, H.; Mashhadzadeh, A.H.; Saeb, M.R.; Ramsey, J.D.; Ganjali, M.R.; Mozafari, M. Zeolites for theranostic applications. J. Mater. Chem. B 2020, 8, 5992–6012.

Ur Rahman, H., Khan, E., Muhammad, M., Khan, M., Ahmad Bhat, M., Shahzada Khan, G., & Ali, N. (2024). Antioxidant and Antibacterial Screening and Hg (II) Sensing, Activities of Cu (II) pyridine-2, 6-dicarboxylate Complexes. *ChemistryOpen*, *13*(10), e202400089.

Brueckl, H.; Shoshi, A.; Schrittwieser, S.; Schmid, B.; Schneeweiss, P.; Mitteramskogler, T.; Haslinger, M.J.; Muehlberger, M.; Schotter, J. Nanoimprinted multifunctional nanoprobes for a homogeneous immunoassay in a top-down fabrication approach. Sci. Rep. 2021, 11, 6039.

Medinger, J.; Nedyalkova, M.; Lattuada, M. Solvothermal Synthesis Combined with Design of Experiments—Optimization Approach for Magnetite Nanocrystal Clusters. Nanomaterials 2021, 11, 360.

Petropoulos, A.E.; Schaffer, B.K.; Cheney, M.L.; Enochs, S.; Zimmer, C.; Weissleder, R. MR Imaging of Neuronal Transport in the Guinea Pig Facial Nerve: Initial Findings. Acta Otolaryngol. 1995, 115, 512–516.

Muhammad, M., Ilyas, M., Khan, M., Khan, Q., & Ismail, M. (2025). Spectrofluorimetric Analysis of Honey Samples for Quantification of Riboflavin: Statistical Evaluation of External Factors. *Journal of Political Stability Archive*, *3*(4), 139-158.

Nedyalkova, M.; Donkova, B.; Romanova, J.; Tzvetkov, G.; Madurga, S.; Simeonov, V. Iron oxide nanoparticles—In vivo/in vitro biomedical applications and in silico studies. Adv. Colloid Interface Sci. 2017, 249, 192–212.

Caizer, C.; Rai, M. (Eds.) Magnetic Nanoparticles in Human Health and Medicine; Wiley: Hoboken, NJ, USA, 2021.

Conde, J.; Dias, J.T.; GrazÃo, V.; Moros, M.; Baptista, P.V.; de la Fuente, J.M. Revisiting 30 years of biofunctionalization and surface chemistry of inorganic nanoparticles for nanomedicine. Front. Chem. 2014, 2, 48.

Sikorski, A.F.; Toporkiewicz, M.; Meissner, J.; Matusewicz, L.; Czogalla, A. Toward a magic or imaginary bullet? Ligands for drug targeting to cancer cells: Principles, hopes, and challenges. Int. J. Nanomed. 2015, 10, 1399.

Ramzy, L.; Nasr, M.; Metwally, A.A.; Awad, G.A.S. Cancer nanotheranostics: A review of the role of conjugated ligands for overexpressed receptors. Eur. J. Pharm. Sci. 2017, 104, 273–292.

Ali, A., Rahman, H.U., Awaiz, H., Jamal, I., Nabi, B., Ullah, W., Khan, M., Shah, M.A., Gul, S., Farid, F. and Shoaib, M.M., The Search for Extraterrestrial Life Through Chemistry.

Mou, X.; Ali, Z.; Li, S.; He, N. Applications of Magnetic Nanoparticles in Targeted Drug Delivery System. J. Nanosci. Nanotechnol. 2015, 15, 54–62.

Shen, Z.; Wu, H.; Yang, S.; Ma, X.; Li, Z.; Tan, M.; Wu, A. A novel Trojan-horse targeting strategy to reduce the non-specific uptake of nanocarriers by non-cancerous cells. Biomaterials 2015, 70, 1–11.

Funkhouser, J. Revolution, Reinventing pharma: The theranostic. Curr. Drugs Discov. 2002, 2, 17–19.

Naud, C.; Thébault, C.; Carrière, M.; Hou, Y.; Morel, R.; Berger, F.; Diény, B.; Joisten, H. Cancer treatment by magneto-mechanical effect of particles, a review. Nanoscale Adv. 2020, 2, 3632–3655.

Alalwiat, A. A., Khan, M., Khan, I., Ahmad, I., Ballal, S., Sharma, G. C., ... & Bajaber, M. A. (2025). Removal of pendimethalin from aqueous samples using peanut shell biochar-Fe3O4 magnetic composite; adsorption studies, thermodynamic and kinetics. *Journal of the Australian Ceramic Society*, 1-11.

Sindhwani, S.; Syed, A.M.; Ngai, J.; Kingston, B.R.; Maiorino, L.; Rothschild, J.; MacMillan, P.; Zhang, Y.; Rajesh, N.U.; Hoang, T.; et al. The entry of nanoparticles into solid tumours. Nat. Mater. 2020, 19, 566–575.

Duli ´nska-Litewka, J.; Łazarczyk, A.; Hałubiec, P.; Szafra ´nski, O.; Karnas, K.; Karewicz, A. Superparamagnetic Iron Oxide Nanoparticles—Current and Prospective Medical Applications. Materials 2019, 12, 617.

Petryk, A.A.; Giustini, A.J.; Ryan, P.; Strawbridge, R.R.; Hoopes, P.J. Iron oxide nanoparticle hyperthermia and chemotherapy cancer treatment. In Energy-based Treatment of Tissue and Assessment V; Ryan, T.P., Ed.; International Society for Optics and Photonics: Bellingham, WA, USA, 2009; p. 71810N.

Nabavinia, M.; Beltran-Huarac, J. Recent Progress in Iron Oxide Nanoparticles as Therapeutic Magnetic Agents for Cancer Treatment and Tissue Engineering. ACS Appl. Bio Mater. 2020, 3, 8172–8187.

Talluri, S.; Malla, R.R. Superparamagnetic Iron Oxide Nanoparticles (SPIONs) for Diagnosis and Treatment of Breast, Ovarian and Cervical Cancers. Curr. Drug Metab. 2020, 20, 942–945.

Kralj, S.; Makovec, D. Magnetic Assembly of Superparamagnetic Iron Oxide Nanoparticle Clusters into Nanochains and Nanobundles. ACS Nano 2015, 9, 9700–9707.

Zhang, Y.; Yang, M.; Portney, N.G.; Cui, D.; Budak, G.; Ozbay, E.; Ozkan, M.; Ozkan, C.S. Zeta potential: A surface electrical characteristic to probe the interaction of nanoparticles with normal and cancer human breast epithelial cells. Biomed. Microdevices 2008, 10, 321–328.

Dheyab, M.A.; Aziz, A.A.; Jameel, M.S.; Noqta, O.A.; Khaniabadi, P.M.; Mehrdel, B. Simple rapid stabilization method through citric acid modification for magnetite nanoparticles. Sci. Rep. 2020, 10, 10793.

Gupta, R.; Sharma, D. Biofunctionalization of magnetite nanoparticles with stevioside: Effect on the size and thermal behaviour for use in hyperthermia applications. Int. J. Hyperth. 2019, 36, 301–311.

Khan, M., Ahmad, I., Khan, S., Zeb, A., Elsadek, M. F., Patel, S., ... & Rahman, H. U. (2024). Molecularly imprinted polymer for the selective removal of direct violet 51 from wastewater: synthesis, characterization, and environmental applications. *Journal of Polymer Engineering*, *44*(10), 760-775.

Khan, S., Khan, M., Rahman, H. U., AbdelGawwwad, M. R., & Elsadek, M. F. (2025). Exploring Riboflavin Quantification in Honey via Spectrofluorimetry: A Statistical Examination of Influential Extrinsic Variables. *Current Analytical Chemistry*, *21*(3), 253-262.

Yang, C.; Xiong, F.; Wang, J.; Dou, J.; Chen, J.; Chen, D.; Zhang, Y.; Luo, S.; Gu, N. Anti-ABCG2 monoclonal antibody in combination with paclitaxel nanoparticles against cancer stem-like cell activity in multiple myeloma. Nanomedicine 2014, 9, 45–60.

Hayashi, K.; Nakamura, M.; Sakamoto, W.; Yogo, T.; Miki, H.; Ozaki, S.; Abe, M.; Matsumoto, T.; Ishimura, K. Superparamagnetic Nanoparticle Clusters for Cancer Theranostics Combining Magnetic Resonance

Imaging and Hyperthermia Treatment. Theranostics 2013, 3, 366–376.

Thapa, B.; Diaz-Diestra, D.; Beltran-Huarac, J.; Weiner, B.R.; Morell, G. Enhanced MRI T 2 Relaxivity in Contrast-Probed Anchor-Free PEGylated Iron Oxide Nanoparticles. Nanoscale Res. Lett. 2017, 12, 312.

Dabbagh, A.; Hedayatnasab, Z.; Karimian, H.; Sarraf, M.; Yeong, C.H.; Madaah Hosseini, H.R.; Abu Kasim, N.H.; Wong, T.W.; Rahman, N.A. Polyethylene glycol-coated porous magnetic nanoparticles for targeted delivery of chemotherapeutics under magnetic hyperthermia condition. Int. J. Hyperth. 2019, 36, 104–114.

Nurudeen, S., Khan, S., Khan, M., Ali, A., Fawy, K. F., Marwani, H. M., ... & Bajaber, M. A. (2025). A comprehensive review on medicinal applications of iodine. *Reviews in Inorganic Chemistry*, (0).

Gaspar, M.M.; Radomska, A.; Gobbo, O.L.; Bakowsky, U.; Radomski, M.W.; Ehrhardt, C. Targeted Delivery of TransferrinConjugated Liposomes to an Orthotopic Model of Lung Cancer in Nude Rats. J. Aerosol Med. Pulm. Drug Deliv. 2012, 25, 310–318.

Diaz-Diestra, D.; Morell, G.; Tu, K.; Jadwisienczak, W.M.; Weiner, B.R.; Beltran-Huarac, J.; Santiago-Medina, C.; Kumar, N.; Thapa, B. T1- and T2-weighted Magnetic Resonance Dual Contrast by Single Core Truncated Cubic Iron Oxide Nanoparticles with Abrupt Cellular Internalization and Immune Evasion. ACS Appl. Bio Mater. 2018, 1, 79–89.

Kim, D.; Lee, H.; Kwon, S.; Choi, H.; Park, S. Magnetic nano-particles retrievable biodegradable hydrogel microrobot. Sens. Actuators B Chem. 2019, 289, 65–77.

Mahmoudi, M.; Simchi, A.; Imani, M.; Shokrgozar, M.A.; Milani, A.S.; Häfeli, U.O.; Stroeve, P. A new approach for the in vitro identification of the cytotoxicity of superparamagnetic iron oxide nanoparticles. Colloids Surf. B Biointerfaces 2010, 75, 300–309.

Curcio, A.; Silva, A.K.A.; Cabana, S.; Espinosa, A.; Baptiste, B.; Menguy, N.; Wilhelm, C.; Abou-Hassan, A. Iron Oxide Nanoflowers @ CuS Hybrids for Cancer Tri-Therapy: Interplay of Photothermal Therapy, Magnetic Hyperthermia and Photodynamic Therapy. Theranostics 2019, 9, 1288–1302.

Kumar, A.; Jena, P.K.; Behera, S.; Lockey, R.F.; Mohapatra, S.; Mohapatra, S. Multifunctional magnetic nanoparticles for targeted delivery. Nanomed. Nanotechnol. Biol. Med. 2010, 6, 64–69.

Ben Djemaa, S.; David, S.; Hervé-Aubert, K.; Falanga, A.; Galdiero, S.; Allard-Vannier, E.; Chourpa, I.; Munnier, E. Formulation and in vitro evaluation of a siRNA delivery nanosystem decorated with gH625 peptide for triple negative breast cancer theranosis. Eur. J. Pharm. Biopharm. 2018, 131, 99–108.

Khan, M., Din, I. U., Aslam, M., Huma, M., Batool, F., Jan, M., ... & Rahman, H. U. (2025). Synthesis and characterization of Cu (II), Zn (II), Cd (II), and Mn (II) Complexes with heterocyclic N-donor ligands and carboxylic acid derivatives and their antibacterial activity. *Global Research Journal of Natural Science and Technology*.

Sakono, N.; Nakamura, K.; Ohsima, T.; Hayakawa, R.; Sakono, M. Tyrosinase-mediated Peptide Conjugation with Chitosan-coated Gold Nanoparticles. Anal. Sci. 2019, 35, 79–83.

Naha, P.C.; Hsu, J.C.; Kim, J.; Shah, S.; Bouché, M.; Si-Mohamed, S.; Rosario-Berrios, D.N.; Douek, P.; Hajfathalian, M.; Yasini, P.; et al. Dextran-Coated Cerium Oxide Nanoparticles: A Computed Tomography Contrast Agent for Imaging

the Gastrointestinal Tract and Inflammatory Bowel Disease. ACS Nano 2020, 14, 10187–10197.

Hao, H.; Ma, Q.; He, F.; Yao, P. Doxorubicin and Fe3O4 loaded albumin nanoparticles with folic acid modified dextran surface for tumor diagnosis and therapy. J. Mater. Chem. B 2014, 2, 7978–7987.

Comes Franchini, M.; Baldi, G.; Bonacchi, D.; Gentili, D.; Giudetti, G.; Lascialfari, A.; Corti, M.; Marmorato, P.; Ponti, J.; Micotti, E.; et al. Bovine Serum Albumin-Based Magnetic Nanocarrier for MRI Diagnosis and Hyperthermic Therapy: A Potential Theranostic Approach Against Cancer. Small 2010, 6, 366–370.

Alalwiat, A. A., Khan, M., Khan, I., Ahmad, I., Ballal, S., Sharma, G. C., ... & Bajaber, M. A. (2025). Correction: Removal of pendimethalin from aqueous samples using peanut shell biochar-Fe3O4 magnetic composite; adsorption studies, thermodynamic and kinetics. *Journal of the Australian Ceramic Society*, *61*(4), 1625-1625.

Chertok, B.; Moffat, B.A.; David, A.E.; Yu, F.; Bergemann, C.; Ross, B.D.; Yang, V.C. Iron oxide nanoparticles as a drug delivery vehicle for MRI monitored magnetic targeting of brain tumors. Biomaterials 2008, 29, 487–496.

Ungureanu, B.S.; Teodorescu, C.-M.; Săftoiu, A. Magnetic Nanoparticles for Hepatocellular Carcinoma Diagnosis and Therapy. J. Gastrointest. Liver Dis. 2016, 25, 375–383.

Jan, Mubark, Madiha Aslam, Kalim Ullah, Malik Muhammad Shoaib, Habib Ur Rahman, Talha Mahmood, Akhtar Ali et al. "A Novel Cyclohexyl-Naphthyl Bis-Hydrazone Schiff Base: Synthesis, Characterization and Antibacterial Activity." *Global Research Journal of Natural Science and Technology* 3, no. 1 (2025).

Mu, Q.; Wang, H.; Zhang, M. Nanoparticles for imaging and treatment of metastatic breast cancer. Expert Opin. Drug Deliv. 2017, 14, 123–136.

Bhise, K.; Sau, S.; Alsaab, H.; Kashaw, S.K.; Tekade, R.K.; Iyer, A.K. Nanomedicine for cancer diagnosis and therapy: Advancement, success and structure–activity relationship. Ther. Deliv. 2017, 8, 1003–1018.

Wilhelm, S.; Tavares, A.J.; Dai, Q.; Ohta, S.; Audet, J.; Dvorak, H.F.; Chan, W.C.W. Analysis of nanoparticle delivery to tumours. Nat. Rev. Mater. 2016, 1, 16014.

Kar, S.; Gajewicz, A.; Puzyn, T.; Roy, K. Nano-quantitative structure–activity relationship modeling using easily computable and interpretable descriptors for uptake of magnetofluorescent engineered nanoparticles in pancreatic cancer cells. Toxicol. In Vitro 2014, 28, 600–606.