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Original Article

Magnetically Loaded Drug Delivery System: A Review

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ABSTRACT

Various new drug delivery systems have been developed with different routes of administration to achieve controlled and targeted drug delivery. Magnetic microcarriers, including magnetic microspheres, magnetic liposomes, magnetic nanoparticles, magnetic resealed erythrocytes, and magnetic emulsion, are among these systems.Targeted medication delivery, imaging, and bio separation technology all make extensive use of magnetic micro/nanoparticles and molecular magnetic labels.This project will cover a variety of subjects, including the magnetic targeting principle, the mechanism of magnetic targeted drug delivery, magnetic microcarriers, and the application of magnetism in targeted drug delivery. using producing high concentrations of pharmaceuticals without damaging healthy surrounding tissue, magnetically targeted drug delivery using particle carriers is an effective technique for delivering medications to localised disease areas, such as tumours. As contrast agents and drug reservoirs that are activated by a magnet placed outside the body, magnetic microspheres and nanospheres can also be employed for non-targeted applications. This project will cover The historical and contemporary uses of magnetic microspheres, as well as the hurdles that must be overcome for the effective and advantageous use of magnetic carriers in clinical practise.

Keywords: Magnetic nanoparticles, Magnetic Microcarriers, Drug Delivey, Drug Targetting

INTRODUCTION

For years delivering therapeutic compounds to target site has posed a significant challenge to treat many diseases. Traditional drug application methods are limited in their effectiveness, poor bio distribution, and lack of selectivity. Drug delivery systems (DDSs) are engineered technologies designed to address these limitations by enabling targeted drug delivery and controlled release of therapeutic agents. Controlled Drug Delivery System can transport drugs to the site of action, reducing undesirable side effects while protecting the drug from degradation or clearance and increasing drug concentration in target tissues [1,2]. As a result, lower drug doses are required, making this modern form of therapy particularly important when there is a discrepancy between a drug's dose or concentration and its therapeutic results or toxic effects. Drug targeting involves delivering drugs exclusively to specific receptors, organs, or other parts of the body. The delivery of drugs is crucial for treating diseases, and it is important from both commercial and scientific perspectives. The method of drug delivery can significantly impact the drug's effectiveness.

Magnetic nanoparticles (MNPs) have garnered significant interest due to their distinct optical, electronic, magnetic, and physicochemical properties. Their small size makes them suitable for nano-engineering of surfaces and production of functional nanostructures. As a result, MNPs have a wide range of potential applications in various fields such as biomedicine, materials science, and electronics.

Currently, numerous MNPs are undergoing early clinical trials, and some formulations have already received clinical approval for medical imaging and therapeutic purposes. Examples include LumirenVR and GastromarkVR for bowel imaging, and Feridex I.V. VR and EndoremVR for liver and spleen imaging, among others. These approved formulations have shown promising results, making them potential candidate [3,4]. Magnetic drug targeting is a technique used to deliver chemotherapeutic agents to specific targets, such as tumors. This is achieved by using magnetic nanoparticles (also known as ferrofluids) that are attached to the agents, and an external magnetic field that is directed towards the target. This approach aims to concentrate the drug at

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the desired location to increase its effectiveness while reducing the risk of side effects [5]. This article can cover the principles of magnetic targeting, the mechanism of magnetic targeted drug delivery, the advantages and disadvantages of magnetic targeting, magnetic microcarriers, the applications of magnetism in targeted drug delivery, and some alternative fields.

AIM AND OBJECTIVES:

The aim of this review paper is to provide a comprehensive overview of magnetically loaded drug delivery systems, focusing on the current state-of-the-art research and development in the field. This review will cover various aspects of magnetically loaded drug delivery systems, including their working principle, targeting mechanism, design, advantages, disadvantages, applications, limitation etc.

ADVANTAGES OF MDDS:

- **Targeted delivery:** Magnetic targeting can deliver drugs directly to the site of the disease, such as a tumor, while sparing healthy tissue, reducing the side effects of drugs, and improving therapeutic efficacy.
- **Controlled release:** Magnetically loaded drug delivery systems allow for controlled drug release, leading to improved drug efficacy, reduced toxicity, and increased patient compliance.
- **Flexibility:** Magnetic targeting can be adapted to different body parts, organs, and tissues, making it a versatile drug delivery platform.
- **Non-invasive:** Magnetic targeting does not require invasive procedures, making it less traumatic than other drug delivery methods.
- **Efficiency:** Magnetically loaded drug delivery systems have high drug-loading capacity and offer a fast and efficient drug delivery.

DISADVANTAGES OF MDDS:

- **Limited penetration:** The magnetic field may not penetrate deep tissues or may be blocked by certain materials, making it difficult to reach deep-seated tumors or other disease sites.
- **Technical challenges:** Magnetically loaded drug delivery systems require specialized equipment and expertise, which may increase the cost and complexity of the treatment.
- **Magnetic field effects:** The magnetic field used for targeting may cause unwanted effects on other tissues or organs, which could lead to adverse reactions or unintended consequences.
- **Magnetic materials safety concerns:** There are some safety concerns associated with the use of magnetic materials, such as potential toxicity, biocompatibility, and biodistribution.
- **Regulatory hurdles:** Magnetically loaded drug delivery systems may face regulatory hurdles related to safety, efficacy, and approval, which could delay their widespread use in clinical settings.

PRINCIPLE:

Magnetic drug delivery through particulate carriers is an effective technique for delivering drugs to a specific area of disease. It allows for the achievement of high concentrations of chemotherapeutic or radiological agents near the target site, such as a tumor, without causing toxic effects to normal tissue or the entire body. In this approach, a drug or therapeutic radioisotope is bound to a magnetic compound, injected into the bloodstream, and then stopped with a powerful magnetic field in the target area [6]. The drug is slowly released from the magnetic carriers or confers a local effect, such as irradiation from radioactive microspheres or hyperthermia with magnetic nanoparticles. This approach enables the replacement of large amounts of freely circulating drug with much lower amounts of drug targeted magnetically to localized disease sites, resulting in increased localized drug levels. Magnetic carriers receive their magnetic responsiveness to a magnetic field from incorporated materials, such as magnetite, iron, nickel, cobalt, neodymium-iron-boron, or samarium-cobalt. Magnetic carriers are classified by size, with ferrofluids at the lower end, colloidal iron oxide solutions. Encapsulated magnetite particles in the range of 10-500 nm are known as magnetic nanospheres, and any magnetic particles just below 1-100 nm are magnetic microspheres. Magnetic liposomes are also included in the discussion of magnetic carriers [7]. The principle of magnetic targeting, involves injecting a drug or therapeutic radioisotope bound to a magnetic compound into a patient's bloodstream, stopping it with a powerful magnetic field in the target area, and releasing it in a controlled manner. The magnetic

fields are considered safe for biological systems and adaptable to any part of the human body. Up to 60% of an injected dose can be deposited and released in a controlled manner in selected non-reticuloendothelial organs (i.e., not in the liver/spleen/bone marrow) [8].

Magnetic Drug Targeting:

Mechanism:

Magnetic theory can be a complex topic, as different metals and metal oxides exhibit various forms of magnetism and respond to magnetic forces in unique ways.Magnetism is the atomic or subatomic response of a material to an applied magnetic field, where the dipole moment and magnetic field are created by the electron spin and charge.When multiple dipoles combine, they create a magnetic field of measurable intensity.Magnetic materials are composed of small regions known as magnetic domains, which orient themselves in the presence of an external magnetic field.[9] Magnetic materials are classified into six main types, including paramagnetic, superparamagnetic, ferromagnetic, diamagnetic, antiferromagnetic, and ferrimagnetic materials.[10] Among these, superparamagnetic materials are particularly attractive for magnetic targeted drug delivery systems (MTDDS) due to their significant properties. MTDDS is one of the most promising strategies for delivering drugs to specific sites in the body. Compared to traditional techniques, MTDDS are highly efficient and quick-impact, and can reduce the toxicity and other adverse side effects in non-target regions by concentrating drugs in target sites [11]. To achieve magnetic targeting, a drug or therapeutic radionuclide is bound to a magnetic compound, introduced into the body, and then concentrated in the target area by means of a magnetic field (using an internally implanted permanent magnet or an externally applied field). The particles then release the drug or give rise to a local effect, with drug release occurring through mechanisms requiring enzymatic activity or changes in physiological conditions such as pH, osmolality or temperature. Drug release can also be magnetically triggered from the drug-conjugated magnetic NPs. [12] Magnetic carriers receive their magnetic responsiveness to a magnetic field from incorporated materials such as magnetite, iron, nickel, cobalt, neodymium–iron–boron, or samarium cobalt [13]. Therefore, the factors of magnetic field strength and geometry, which relate to the magnet system, are extremely important for designing the MTDDS. Designing magnetic DDSs requires consideration of many factors, including magnetic properties and size of particles, strength of the magnetic field, drug loading capacity, accessibility of target tissue, and the rate of blood flow. Magnetically targeted DDSs aim to deliver the drug at a rate directed by the needs of the body during the treatment period and target the activity entity to the action site [14].

Magnetic Microcareers:

Magnetic microcarriers have the advantage of being site-specific, enabling them to be localized in the target area, while overcoming the issue of their rapid clearance by the RES. The linear blood velocity in capillaries is significantly less than in arteries, approximately 300 times less, at a rate of 0.05cm/sec. Therefore, a much smaller magnetic field, approximately 6-8 Koe, is sufficient to retain them in the capillary network of the target area [15]. This makes magnetic carrier technology a significant alternative for addressing bimolecular malformation, such as composition, inactivation, or deformation. There are several types of magnetic microcarriers, including

A. Magnetic Nanoparticles,
B. Magnetic Microspheres,
C. Magnetic Liposomes,
D. Magnetic Resealed erythrocytes,
E. Magnetic Emulsion,
F. Biomodulators,
G. Magnetic Neutrophils.

A. Magnetic Nanoparticles:

One of the most promising areas of research in MDDS is the use of magnetic nanoparticles. These nanoparticles are typically made of iron oxide and range in size from 1 to 100 nanometers [16]. They can be coated with a drug and then guided to a specific target within the body using an external magnetic field. Once the nanoparticles reach their target, the drug can be released from the nanoparticles to provide a highly targeted therapy. The use of magnetic nanoparticles in drug delivery has been studied extensively in cancer treatment. For example, a recent study found that magnetic nanoparticles could be used to deliver chemotherapy drugs directly to tumors, while minimizing the risk of side effects in healthy tissues. The magnetic nanoparticles were injected directly into the bloodstream, and an external magnetic field was used to guide the nanoparticles to

the tumor site. The results of the study showed that the use of magnetic nanoparticles led to a significant reduction in tumor growth. One of the advantages of using magnetic nanoparticles in drug delivery is their ability to penetrate deep into tissues. Magnetic nanoparticles can penetrate tissues much deeper than conventional drug delivery methods, allowing for more efficient drug delivery to deep-seated tumors. Magnetic nanoparticles can also be designed to release their drugs in a controlled manner, providing a sustained release of the drug over time. This sustained release can lead to improved drug efficacy and reduced toxicity.

B. Magnetic Microspheres:

Magnetic microspheres are tiny supramolecular particles, with a size less than 4μm, that can travel through capillaries without causing embolic occlusion, but they are sensitive to ferromagnetic forces, making them useful for being captured in microvessels and dragged into adjacent tissues by magnetic fields ranging from 0.5-0.8 Tesla (T). Two primary methods for preparing magnetic microspheres are phase separation emulsion polymerization (PSEP) and continuous solvent evaporation (CSE). By adjusting the size of microspheres, drug content, magnetite content, hydration state, and drug release characteristics of the carrier, the amount and rate of drug delivery via magnetic responsive microspheres can be controlled. A balance must be struck between the amount of drug and magnetite content of microspheres to create an efficient therapeutic system. The properties of magnetic microspheres, such as particle size analysis including size distribution, surface topography, texture, drug entrapment efficiency, percent magnetite content, in vitro magnetic responsiveness, and drug release are measured using techniques like scanning electron microscopy (SEM) [17].

One way to target magnetic microspheres is by incorporating magnetic particles into drug carriers (polymers) and using an externally applied magnetic field to direct the magnetic drug carriers to the desired site. The use of magnetic albumin microspheres was first reported by Widder [18].

In embolization therapy, magnetic microspheres are used to block blood vessels in tumors, preventing the tumors from receiving nutrients and oxygen. This can lead to tumor shrinkage and cell death. Magnetic microspheres have also been used in cancer treatment to deliver drugs directly to tumors, while minimizing the risk of side effects in healthy tissues. The use of magnetic microspheres allows for highly targeted therapy and reduces the risk of systemic side effects.

C. Magnetic Liposomes:

Liposomes are tiny vesicles made up of a lipid bilayer that encloses an aqueous volume. They contain several components, such as phospholipids and cholesterol, that make up their structure. However, in magneto liposomes, magnetite is also incorporated into the liposome's composition. These are magnetic carriers that can be created by trapping Ferro fluid within the core of the liposomes. Alternatively, magneto liposomes can be produced by attaching ligands to the surface of the vehicles or incorporating target lipids into the structural phospholipid matrix [19]. Another method of preparing magnetoliposomes involves using the phospholipid vesicle as a nanoreactor for in situ precipitation of magnetic nanoparticles. Some magnetoliposomes also contain didodecyl methyl ammonium bromide and an ionic magnetic fluid. Magnetoliposomes have been successfully used for site-specific targeting, cell sorting, and as a magnetic resonance contrast enhancing agent. Thermo-sensitive magnetoliposomes can release entrapped drugs after selective heating caused by electromagnetic fields. Additionally, magneto-fluorescent liposomes have been used to increase the sensitivity of immune fluorescence. Magneto liposomes undergo various characterizations to determine their physical attributes such as size, shape, size distribution, surface charge, percent capture, percent magnetite content, entrapped volume lamellarity through freeze fracture microscopy and P-NMR, phase behavior drug release, quantitative determination of phospholipids, and cholesterol analysis. These characterizations are crucial in ensuring that magneto liposomes are efficient drug carriers and are suitable for targeted drug delivery [20].

D. Magnetic Released Erythrocytes:

Resealed erythrocytes offer several advantages as drug carriers, including their biodegradability, biocompatibility, ability to encapsulate a variety of materials in a small volume, and potential for organ targeting. Magnetic resealed erythrocytes containing ferrofluids and loaded drugs have been developed to further improve their functionality. In vitro studies have been conducted on erythrocytes loaded with

ibuprofen and magnetite using the preswell technique, with various process variables analyzed, such as drug and magnetite concentration, and sonication of ferrofluids [21]. The loaded erythrocytes effectively responded to an external magnetic field and were characterized in vitro for drug efflux, hemoglobin release, morphology, osmotic fragility, magnetic responsiveness, and percent cell recovery. Diclofenac sodium-bearing erythrocytes have also been prepared and characterized for various in vitro parameters [22]. In animal studies, local thrombosis in arteries was prevented by magnetic targeting of aspirin-loaded red cells, which exerted a thrombolytic effect. Thrombosis was induced in dogs and rabbits, with a completely occluding red thrombus developing in 80% of cases after 4 to 5 hours. A SmCo5 magnet was externally secured to one of the arteries, but it had no influence on clot formation. Autologous red cells loaded with ferromagnetic colloid compound and aspirin were intravenously administered, and arteriothrombosis on the magnet application side was completely aborted, with no detrimental effect on clot formation in the control artery [23].

Overall, magnetic released erythrocytes have shown potential as a targeted drug delivery system with the ability to improve drug efficacy while minimizing adverse effects. Further research is needed to optimize the loading and targeting process and to determine the safety and efficacy of this approach in human studies.

E. Magnetic Emulsion:

In addition to magnetic modulated systems such as microcapsules and microspheres, magnetic emulsion has also been explored as a drug carrier for chemotherapeutic agents. This emulsion is an oil-in-water type emulsion that is magnetically responsive and carries a chemotherapeutic agent that can be specifically localized to a target site by applying an external magnetic field [24]. Akimoto and Morimoto prepared magnetic emulsion by using ethyl oleate-based magnetic fluid as the dispersed phase, casein solution as the continuous phase, and an anticancer agent called methyl CCNU trapped in the oily dispersed phase as an active chemotherapeutic agent. Magnetic emulsion has the potential to provide site specificity for certain chemotherapeutic agents [25].

One of the main applications of magnetic emulsions is in biomedical engineering, where they can be used as drug delivery systems or contrast agents for magnetic resonance imaging (MRI). By applying a magnetic field, the magnetic nanoparticles in the emulsion can be directed to a specific site within the body, allowing for targeted drug delivery or imaging. In addition to their biomedical applications, magnetic emulsions also have potential uses in areas such as environmental remediation and industrial processes. For example, they could be used to separate oil and water in wastewater treatment, or to improve the efficiency of catalytic reactions in chemical production. Overall, magnetic emulsions are a promising area of research with many potential applications in various fields. However, further studies are needed to optimize their properties and explore their full range of uses.

F. Biomodulators:

Biological response modifiers (BMRs) have the ability to modify the host, tumor, and microbial responses in four ways [26]. The first way is through the augmentation of host effector mechanisms directed against tumor cells or microorganisms. The second way is through the decrease of host response that interferes with tumor resistance by a quantitative increase in endogenous effector resistance or by redirecting their sites and duration of action. The third way is through the augmentation of tumor sensitivity to host cells by dedifferentiating tumor cells. Lastly, the fourth way is through the increase in host tolerance of conventional cancer treatment. There are two types of BMRs: indirect and direct agents. Indirect agents include white cell chemoattractant/activator peptides, interleukins (1 to 4), and immunomodulators such as interferon (α, β, γ). Direct acting BMRs are the final lymphocyte effector molecules, which include antibodies, lymphotoxin, and tumor necrosis factor (TNF, also called Cachetin).

G. Magnetic Neutrophils:

In some medical conditions, traditional methods of targeting white blood cells through chemotaxis do not work due to the presence of chemotactic factors and inhibitors of neutrophil-directed chemotaxis in the patient's serum. This is observed in conditions such as chronic lymphocytic leukemia, alcoholic cirrhosis, Crohn's disease, haemodialysis, sarcoidosis, and Hodgkin's disease. Even though not all patients show a failure of chemotaxis, these conditions are life-threatening. To address this issue, a method of making neutrophils ingest a system based on magnetite should

be developed so that severe infection sites can be selectively approached for therapy [27].

APPLICATION:

Magnetically loaded drug delivery systems have a wide range of applications in the field of medicine. Some of the key applications of magnetically loaded drug delivery systems are:

Site-specific Drug Delivery System:

Magnetic delivery of cancer treatment involves the use of magnetic nanoparticles to selectively deliver chemotherapy agents to tumor sites. These magnetic nanoparticles can be coated with chemotherapeutic agents and then targeted to the tumor site using an external magnetic field. One advantage of this approach is that it can reduce the negative side effects of systemic chemotherapy by delivering the drugs directly to the tumor site, thus sparing healthy tissues. Magnetic drug targeting can also overcome the problem of drug resistance by delivering the drugs directly to the cancer cells. Regional chemotherapy via a regional artery is another approach that delivers a more concentrated dose of the chemotherapy agent directly into the tumor while limiting systemic drug concentration. Drug-carrying MPs can achieve wide dispersion throughout the tumor through the action of magnetic force on the particles. In addition, magnetic guidance can be applied to loco-regional cancer treatment, where chemotherapy is delivered to a specific region of the body, such as the esophagus, to avoid the first-pass effect and permit a higher local concentration of the chemotherapeutic agent in the tumor. Overall, magnetic drug delivery is a promising approach for cancer treatment and ongoing research aims to optimize its efficacy and minimize its side effects.

Magnetic Delivery Chemotherapy Drugs to Liver Tumors:

The first clinical cancer therapy trial using Magnetic microspheres (MMS) was conducted by Lübbe in Germany for the treatment of advanced solid cancer in 14 patients was. The Magnetic microspheres used were small, approximately 100 nm in diameter, and contained 4_-epidoxorubicin. The phase I study revealed that the method was minimally toxic and that the Magnetic microspheres accumulated in the target area. However, MRI measurements showed that more than 50% of the Magnetic microspheres ended up in the liver, likely due to their small size and low magnetic susceptibility, which limited their ability to remain at the target organ. FeRx, a startup company in San Diego, developed carbon-coated iron particles of irregular shape, measuring between 0.5-5nm in diameter, with very high magnetic susceptibility. These were used in a phase I clinical trial for the treatment of inoperable liver cancer, in which 32 patients were treated without experiencing any treatment-related toxicity. Up to 60 mg of doxorubicin in 600 mg Magnetic microspheres could be super-selectively infused. The company has recently launched a large phase I/II trial for the treatment of hepatocellular carcinoma in China, Korea, and the US. Preclinical research is currently underway to explore the use of magnetic particles loaded with different chemotherapeutic drugs, including mitoxantrone, mitomycin C, etoposide, paclitaxel, or oxaliplate. For brain tumors, the effectiveness of chemotherapy is hindered by the impermeability of the blood-brain barrier (BBB), drug resistance, and lack of tumor selectivity. Novel biodegradable magnetic drug carriers are being synthesized and evaluated for their targeting ability to brain tumors in vitro and in animal models. Magnetic amino dextran microspheres (MADM) with cationic properties have been synthesized and studied for their potential in targeting drug delivery to brain tumors, showing longer retention in brain tissue.

One example of a successful study involved magnetic doxorubicin in liposome, which showed significant anticancer effects in nude mice with colon cancer [28].

Topical Magnetic delivery:

Topical Magnetic Delivery refers to a method of delivering drugs or other therapeutic agents to specific areas of the body using magnetic fields. This approach involves the use of magnetic particles or microspheres that are applied topically to the skin or other tissues. The particles are then activated using an external magnetic field, which causes them to migrate towards the targeted area. This approach has the potential to improve drug delivery to specific tissues and organs, while minimizing systemic exposure and reducing side effects. Topical Magnetic Delivery is still an area of active research and development, and there is ongoing work to optimize the effectiveness and safety of this approach.

Magnetic Bioseparation:

Bioseparation is crucial for the success of many biological processes, and new techniques are constantly being developed to improve it. Magnetic separation is the most promising technique among the different bioseparation techniques. The development of magnetically responsive microspheres has allowed for the removal of cells and molecules by applying magnetic fields and for the concentration of drugs in anatomical sites with restricted access. These applications have established biomedical uses in protein and cell separation. The addition of monoclonal antibodies, lectins, peptides, or hormones to the magnetic particles has increased the efficiency and specificity of these applications. Magnetic absorbents have been used to isolate various macromolecules, including enzymes, enzyme inhibitors, DNA, RNA, antibodies, and antigens from different sources such as nutrient media, fermentation broth, tissue extracts, and body fluids. Affinity ligands are immobilized on polymer-coated magnetic carriers or magnetizable particles for enzyme separation. Silanized magnetite and fine magneto tactic bacteria with immobilized protein A or protein G have been used for the isolation and purification of Ig G. Mono-sized superparamagnetic particles, Dyna beads, have been utilized in the isolation of mRNA, genomic DNA, and proteins [29].

Magnetic Delivery System in MRI:

Nuclear magnetic resonance (NMR) is commonly used in medical applications to obtain detailed images of internal structures in the body such as organs, tissues, and bones. This technique uses magnetic field gradients generated by superconducting magnets and is a useful replacement for other diagnostic techniques such as positron emission tomography, computed tomography, and angiography. MRI can be used to examine soft tissues like the brain, liver, and kidneys and can also be used for high-magnetic-field evaluations such as chemical biopsy. It can also detect the magnetic field of paramagnetic deoxyhemoglobin, making it useful for detecting future events like stroke. However, the sensitivity of magnetic resonance devices is reduced when molecular and cellular imaging is used [30]. To obtain magnetic scans at a scale of 100 μm using targeted biomarkers, a device equipped with superconducting magnets that generate a strong magnetic field and frequencies below 500 MHz is needed. High-temperature superconductors (HTS) have been used to create radiofrequency receiving coils used in experimental MRI. However, HTS has several disadvantages, including cryogenic systems and higher expenses. HTS materials lack manipulability due to their geometry and length and have suboptimal operation. Therefore, more research is needed to create a feasible HTS MRI to replace standard materials. To improve magnetic resonance by taking maximum advantage of HTS, magnetic compounds capable of improving the quality, contrast, and amplification of the signal have been investigated. Clinically approved compounds include Gd3+ and Mn2+ compounds due to their strong effect on T1 shortening. However, their toxicity and biocompatibility have not yet been adequately studied [31]. In contrast, magnetic nanoparticles (MNPs) are more effective as MRI contrast agents because they are better promoters of T2 relaxation and can be modified by core size and coating [32]. MNPs have shown their ability as contrast agents to generate soft-tissue images with high resolution and outstanding contrast, showing anatomical details, tissue morphology, and providing therapy against various ailments when loaded or functionalized with therapeutic agents, such as antibodies, peptides, and sugars. MNPs also stand out for their null or lack of appreciable toxicity and present longer blood retention times in most cases [33], increasing their capacity for diagnosis and therapy against diseased cells. For example, MNPs functionalized with epithelial growth factors and peptides of the Arg-Gly-Asp type, among others, have been widely proposed as diagnostic agents in different types of cancer [34]. Functionalizing MNPs not only provides the mentioned advantages but also acts as a coating to improve their operative in vivo. PEG coating is commonly used in iron oxide MNPs [35], which without a coating tend to form aggregates that considerably decrease their magnetic properties in addition to rapid capture by the cells of the reticular endothelial system. MNPs targeted for MRI were synthesized from Fe3O4 cores and subsequently functionalized, thus improving their properties in vivo. For example, Sun et al. synthesized MNPs coated initially with PEG followed by chlorotoxin and Cy5.5 molecules. MRI and fluorescence microscopy results showed that MNPs could bind effectively to glioma cells, acting as an imaging contrast and as part of the diagnosis [36,37]. Similarly, Anbarasu et al. functionalized Fe3O4 NPs with monoclonal

antibodies, presenting possible active targeting and showing excellent efficacy in MRI [38]. Other MNPs were doped with elements such as Mn and Zn, improving their magnetic properties and increasing the T2 relaxation time, improving MRI contrast [39]. Chee et al. [40] designed iron oxide MNPs functionalized with bisphospholytic peptides, providing high biocompatibility and cell adhesion and showing an improvement in MRI compared with commercial contrast agents.

Magnetic Hyperthermia in Cancer Therapy:

Magnetic hyperthermia is a promising cancer therapy that combines the use of magnetic nanoparticles with an alternating magnetic field to generate localized heating and selectively destroy cancer cells. The concept behind magnetic hyperthermia is based on the fact that cancer cells are more susceptible to heat compared to normal cells due to their higher metabolic rates [41]. By selectively heating the tumor tissue, it is possible to destroy cancer cells while minimizing damage to healthy tissues. The magnetic nanoparticles used in magnetic hyperthermia are typically composed of iron oxide, which has magnetic properties and can generate heat when exposed to an alternating magnetic field. These particles are designed to be biocompatible and can be functionalized with specific molecules, such as antibodies, peptides, or proteins, to target them to the tumor site. Once the magnetic nanoparticles are delivered to the tumor, an alternating magnetic field is applied, causing the particles to heat up and selectively destroy the cancer cells [42].

The heating effect generated by the magnetic nanoparticles can be precisely controlled by adjusting the parameters of the alternating magnetic field, such as frequency, amplitude, and duration. This allows for precise heating of the tumor tissue while minimizing damage to surrounding healthy tissues.

In addition to its direct effect on cancer cells, magnetic hyperthermia can also improve the efficacy of other cancer therapies, such as chemotherapy and radiation therapy. By increasing the temperature of the tumor tissue, the permeability of the blood vessels can be increased, allowing for better drug delivery to the tumor site. This can improve the effectiveness of chemotherapy and reduce the dosage needed to achieve a therapeutic effect, minimizing side effects associated with systemic drug delivery [43].

Magnetic hyperthermia has been shown to be effective in treating various types of cancers, including breast cancer, prostate cancer, and brain tumors. In preclinical studies, magnetic hyperthermia has been shown to induce complete tumor regression in some cases, leading to improved survival rates.

Despite its promising results, there are still some challenges that need to be addressed before magnetic hyperthermia can be widely used in the clinic. One of the main challenges is the need for better targeting of the magnetic nanoparticles to the tumor site, as well as the need for more precise and efficient heating of the tumor tissue. Additionally, there is a need for more clinical trials to evaluate the safety and efficacy of magnetic hyperthermia in humans [44].

Magnetic System for Diagnosis of Disease:

Magnetic systems have been widely used in the diagnosis of various diseases. One example is magnetic resonance imaging (MRI), which uses powerful magnets and radio waves to create detailed images of the inside of the body. MRI is commonly used to diagnose conditions such as tumors, neurological disorders, and joint problems.

Another example is magnetic particle imaging (MPI), which uses magnetic nanoparticles to create images of the body's blood vessels and organs. MPI is a relatively new imaging technique that has the potential to provide highly sensitive and accurate images, particularly for the early detection of diseases such as cancer [45]. Magnetic systems have also been used in the development of magnetic biosensors, which can detect biological molecules such as proteins and DNA. These biosensors have applications in medical diagnosis, environmental monitoring, and food safety. Overall, magnetic systems have proven to be valuable tools in the diagnosis of diseases and have the potential for further advances in the field of medicine.

Magnetic System for Contraceptive Drug:

Magnetic systems have been explored as a potential method for contraceptive drug delivery. One approach is to use magnetic nanoparticles loaded with contraceptive drugs that can be targeted to specific areas of the body using external magnetic fields.

For example, magnetic nanoparticles loaded with the contraceptive drug levonorgestrel have been developed and tested in vitro and in vivo. In one study, magnetic nanoparticles were targeted to the ovaries of rats using an external magnetic field, resulting in a

significant decrease in ovulation compared to control groups [46]. Another approach is to use magnetic microcapsules containing contraceptive drugs that can be delivered via injection or implanted subcutaneously. The microcapsules can then be targeted to specific areas of the body using magnetic fields [47]. These magnetic systems have the potential to provide targeted drug delivery with lower doses of the contraceptive drug, reducing side effects and increasing efficacy. However, further research is needed to optimize the delivery system and ensure safety and efficacy in human subjects.

FUTURE PERSPECTIVES:

The future perspective of magnetically driven drug delivery systems (MDDS) is promising, as they have the potential to improve drug delivery, reduce side effects, and increase treatment efficacy in a variety of applications. However, there are also some challenges which require further careful attention. First, the magnitude and shape of the magnetic force, determined by its field and field gradient, must be carefully tailored to suit the intended area. This can be a challenging task for in vivo applications, and seeking the expertise of electrical or biomedical engineers is highly recommended.

Second, Improving Targeting Efficiency: While magnetic nanoparticles can be engineered to target specific cells or tissues, achieving high targeting efficiency remains a challenge. Improving the targeting efficiency of MDDS is essential to achieve effective drug delivery while minimizing the risk of toxicity and side effects.

Third, it is crucial for the size of MMS to be sufficiently small, so as not to obstruct the blood vessels along which they are directed towards the target organ. Furthermore, if there is a preference for circulating the particles throughout the body, as opposed to injecting them near the treatment site, there are additional advantages to having smaller particles that minimize their entrapment in other organs like the lungs or liver.

Fourth, Biocompatibility is a critical factor for MDDS to be successful in clinical applications. The materials used for MDDS must be biocompatible, non-toxic, and able to be eliminated from the body without causing adverse reactions.

Fifth, the amount of drug that can be loaded onto magnetic particles is limited, which can limit the effectiveness of MDDS. Increasing drug loading capacity while maintaining magnetic properties is essential to improve drug efficacy. And also, Biological barriers, such as the blood-brain barrier, can limit the effectiveness of MDDS. Overcoming these barriers is crucial to deliver drugs to targeted sites, such as the brain, for the treatment of neurological disorders. Despite these challenges, the future perspective of MDDS is promising. Continued research and development in this field will likely lead to significant advances in the field of medicine, with the potential to revolutionize drug delivery and improve the treatment of a variety of diseases [48].

CONCLUSION:

In conclusion, MDDS represent a highly promising approach for targeted drug delivery, with the potential to significantly improve the efficacy and safety of drug therapies. The review has highlighted the numerous benefits of MDDS, including their ability to selectively deliver drugs to specific sites within the body, thereby minimizing off-target effects and reducing toxicity. However, the review has also emphasized the significant challenges that must be addressed in order to optimize the design and function of MDDS. These include issues such as toxicity, biodistribution, and immune response, as well as potential hurdles associated with scaling up production and conducting clinical trials. Addressing these challenges will be essential to ensuring the safety and efficacy of MDDS in clinical settings.

In spite of those drawbacks Magnetic nanocarriers play important role in targeted drug delivery system.

Looking to the future, the review has identified several important areas of research that could help to advance the field of MDDS. These include the development of novel materials and designs, the integration of imaging and diagnostic capabilities into MDDS, and the exploration of new therapeutic applications and targets. Additionally, the ethical and regulatory implications of MDDS must be carefully considered, including issues related to informed consent, data privacy, and access to healthcare.

In summary, while there are still significant challenges to overcome, the development of MDDS represents an exciting area of research with the potential to revolutionize drug delivery and improve

patient outcomes. By continuing to explore new approaches and address key challenges, we can maximize the potential of MDDS to advance the field of medicine and benefit patients worldwide.

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