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PREPARATION TECHNIQUES, FUNCTIONALIZATION, AND CYTOTOXICITY OF MAGNETIC NANOPARTICLES: A REVIEW

Humaira Sultana[1]*, Afifa Shafiq[1], Muhammad Akram Choohan[2], Khalil Ahmad[2], Ume Habiba[2]

[1]Department of Pharmaceutics, Faculty of Pharmacy, The Islamia University of Bahawalpur, Bahawalpur, Punjab 63100, Pakistan.

[2]University College of Conventional Medicine, Faculty of Medicine and Allied Health Sciences, The Islamia University of Bahawalpur, Pakistan

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ABSTRACT

In the relatively new but fast-evolving field of nanomedicine and nanotransport systems, different nanoscale molecules are used to deliver therapeutic agents to precisely targeted sites or potentially function as diagnostic tools. In present review provides up-to-date accurate information on the latest advancements in nanomedicine and nanotechnology DDS through a complete review of nanomaterials discoveries. The potential and difficulties of using nanomedicine to deliver medications from synthetic or natural sources to their intended clinical purposes are also covered. Additionally, we have exclusive data on perspectives and trends in nanomedicine.

Keywords: Nanotechnology, Magnetic nanoparticle, Targeted drug delivery, Functionalization, Cytotoxicity

***Corresponding Author.** E-mail: madni3570@gmail.com

INTRODUCTION

Nanotechnology-based drug delivery structures have significantly increased drug delivery due to drug pharmacokinetic modifications, increased drug duration in the bloodstream, reduced toxicity, and increased drug half-life [**1**]. Magnetic nanoparticles, which constitute a large element of nanomaterials, can revolutionize prognosis and clinical treatment due to their special properties, superparamagnetic momentum, magnetic resonance, and tremendous natural interactions at the molecular and cellular levels [**2**]. MNPs, an integral product of nanotechnology, have facilitated a considerable range of prognostic and therapeutic properties in diseases that are unstable to human life, such as cancer and neurological and coronary heart diseases. MNPs, which are often used in the centric delivery of therapeutics, are basically entirely based on a targeted magnetic drug that acts through magnetic absorption of specific problems or has a strong ligand-receptor interaction. MNPs have a very critical feature due to the reality of the possibility of far-reaching manipulation of therapeutic agents when moving particles into the target tissue, and therefore they are recognized as magnetically focused carriers. The first-class magnetic houses, supersaturation and magnetic susceptibilities of magnetic nanoparticles, resulting from their herbal magnetic properties, represent the only risk for use. On the other hand, attractive and long-lasting medicinal residences can be created for these particles due to the potential of using a number of base coatings and the pharmacokinetic results and toxicity of magnetic nanoparticles delivered through human interactions with cells or organic proteins. can be avoided, leading to accelerated biocompatibility of magnetic nanoparticles. Magnetic nanoparticles have been seen in biomedical and industrial purposes due to their biocompatibility, easy soil modification, and magnetic properties. Magnetic nanoparticles can be used in extraordinary methods. The tendency to magnetic fields through magnetic nanoparticles is an attribute that leads to new achievements, so tablets associated with these particles in physics are focused on the use of magnetic discipline. Therefore, magnetic nanoparticles are the answer to transport drugs to preferred areas of the body [**3**].

MAGNETIC PARTICLES (MNP)

Magnetic particles that correspond to their unique magnetism exist in the structure of individual nanoparticles or clusters of micro-nanoparticles. Their use in different areas depends on the type of each individual nanoparticle. The composition, size, and synthesis process of MNPs vary in their applications, however, superparamagnetic, Ferro, and free particles can be used for a variety of targeted drug delivery functions. MNPs are strongly affected by the application of an external magnetic object due to the magnetic second of the neighborhood unit and the nature of the fields, so that when the external magnetic discipline disappears, they behave as inactive particles. Single-domain and superparamagnetic are factors of magnetic nanoparticles that underlie many of their positive factors [**4, 5**].

COMPONENTS

Magnetic nanoparticle consists of the following parts: 1) A magnetic core 2) Protective coating 3) Organic linker 4) Active molecule

Magnetic Core

At the center is the magnetic core, usually, properties of these particles depend upon the magnetic core. For medical applications, we use ferromagnetic materials because they are strongly attracted by a magnet as well as it shows superparamagnetism at room temperature.

Ferromagnetic Materials

These materials are strongly attracted by the magnet e.g. Iron, cobalt, and nickel further reduced, particles become superparamagnetic means they become magnetic in the presence of an external magnet but revert to a nonmagnetic state when the external magnet is removed giving magnetic nanoparticles unique advantage of working in biological environments [**6**].

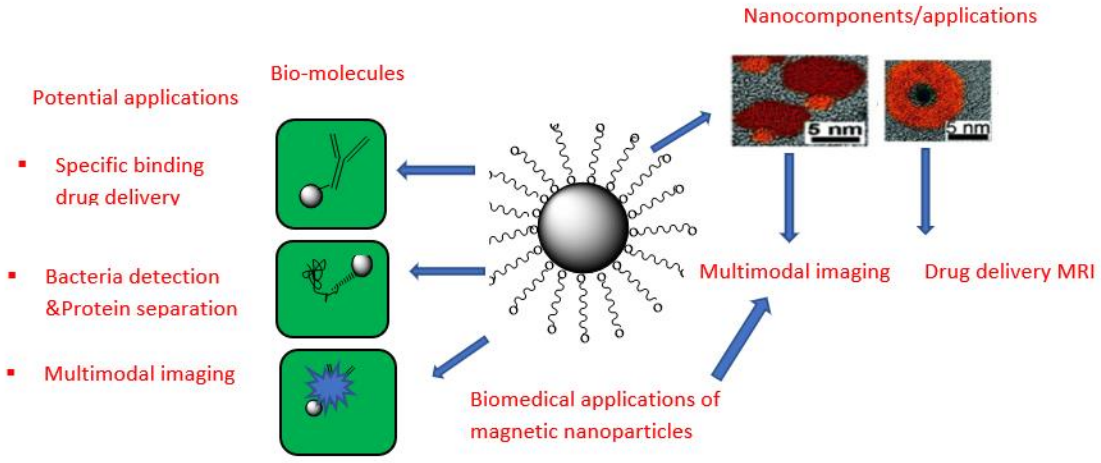

Figure 1. schematic presentation of different biomedical applications of magnetic nanoparticles.

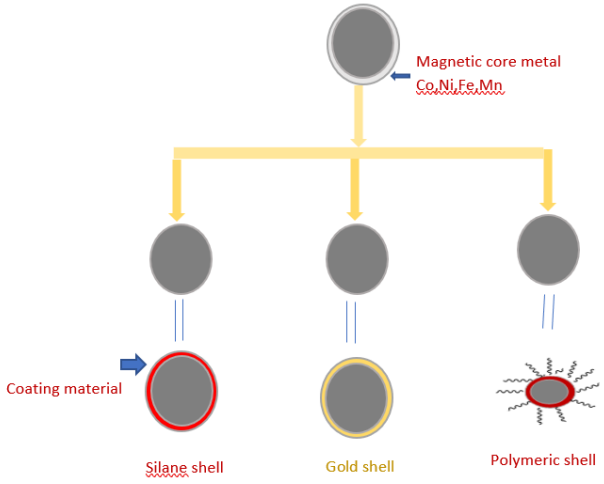

Figure 2. Components of magnetic nanoparticles

PREPARATION TECHNIQUES OF MAGNETIC NANOPARTICLES

The process to be optimized early in the synthesis, as even a small version of the entire method can raise a radical change in the desired result. Therefore, the chemical and bodily homes of synthesized nanoparticles prefer to be tightly controlled to be positively and profitably utilized in biomedical applications. There are special methods of synthesis of magnetic nanoparticles [**7-9**].

Co-precipitation

The phrase "co-precipitating" ability is a technique in which one or more surrounding fabrics—generally soluble under those conditions—precipitate through nucleation. Nanomaterials for precipitation are commonly used for more than a few organic functions due to the reality of the basic practical method, much less dangerous (pre-cursors) required. With the aid of a precipitating agent, co-precipitation is typically conducted with preferred salts and a base, typically in an aqueous media, with or without the goal of producing insoluble stable particles. This technique allows for the production of magnetic nanoparticles at either room temperature or at room temperature. high temperature resulting in an unbalanced yield, amount, and shape [**10**]. The kind of salts employed, the pH of the solution, the ion ratio, the ionic strength of the medium, the reaction temperature, and numerous reaction circumstances, such as the rate of addition of the primary solution and the rate of mixing, all affect the size and form of the synthesized nanoparticles. For profitable precipitation, the pH must be in the range of 8 to 14. [**11**]

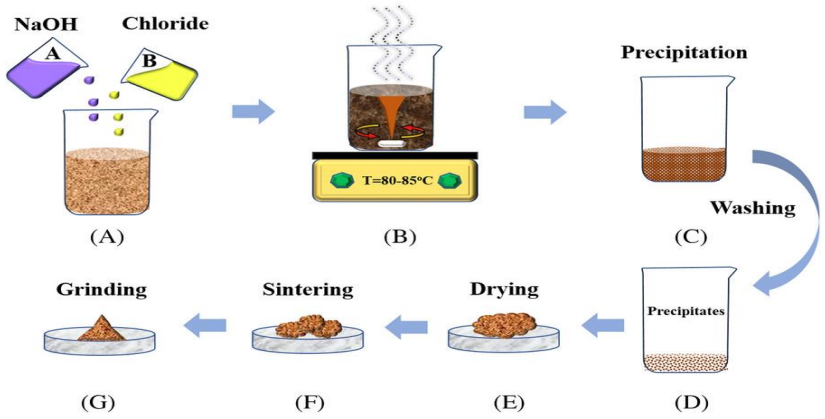

Figure 3. The following are the procedures for making ferrite nanoparticles by coprecipitation: Precipitation, precipitates after washing, drying at 80 °C, sintering at 1100 °C, and grinding of the finished product are shown in (A), (B), (C), and (D), respectively.

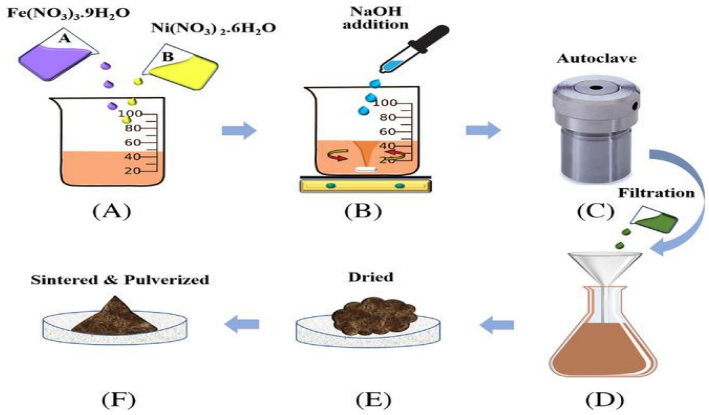

Figure 4. Illustration of ($NiFe_2O_4/Fe_2O_3$) nanocomposite synthesis via hydrothermal method: (A) addition of precursors(B) magnetic stirring while adding NaOH (C) autoclaving the mixture for 20 hours at 180 °C, (D) filtering, (E) drying at 100 °C, and (F) annealing in air for two hours at 400–800 °C, followed by comminution.

Hydro-thermal

Hydrothermal is considered the most popular strategy to produce inorganic nanoparticles, especially metals and oxides. Typically, wet-chemical techniques for crystallisation in a sealed vessel make up the hydrothermal method. The aqueous solution is kept in the vessel at a high stress level and high temperature (130–250 °C) (0.3–4 MPa). Large-diameter NPs are frequently produced using the hydrothermal method [**12,13**] Nanomaterial tuning from a few nanometers to hundreds of nanometers is possible using the hydrothermal technique. In general, the awareness of the precursors, along with the reaction time and response temperature, lead to the dominance of the synthesised nanoparticle's size and dispersion [**14,15,16**].

CHARACTERIZATION

Following are some most commonly used analytical techniques for characterization:

Transmission Electron Microscopy

Magnetic nanoparticles are characterized for its size by TEM. Transmission electron microscopy (TEM) is used in the determination of particle core size. It reports the total particle size of the core. It provides details on the size distribution and the shape. However, this technique needs an analysis by image treatment, and must be performed on a statistically significant large number of particles. High-resolution transmission electron microscopy (HRTEM) gives access to the atomic setting [**18,19**]. On a Formvar-coated copper TEM grid (300 mesh size), a drop of an aqueous dispersion of (magnetic nanoparticles) is applied, and the grid is then left to air-dry. After that electron beam is passed through it and the image of the particles can be seen on fluorescent screen.

Scanning Electron Microscopy

Scanning electron microscopy (SEM) used for the determination of morphology and size distribution of particles in the scales of micro to Nano range [**20**].

FUNCTIONALIZATION OF MNPs

Surface change or functionalization is a fundamental aspect of magnetic nanoparticle (MNP) synthesis and application. Functionalized MNPs have been the center of attention in biomedical applications. The major purposes of surface change of MNPs are (1) to stop agglomeration, (2) to enhance floor catalytic activity, (3) to improve physicochemical and mechanical properties, and four to expand solubility and biocompatibility [**21**]. The functionalization process that gives MNPs their typical morphology can be one of the 4 kinds of core-shell structure, matrix dispersed structure, Janus structure, or shell-core-shell structure [**22, 23**]. Three mechanisms used for functionalization are ligand addition, exchange, and encapsulation [**24, 25**]. Encapsulation, it is an excellent method in terms of available coating materials - when you consider that every natural fabric (polymers, surfactants) and inorganic material (silica, carbon, metal, steel oxides) can be used for encapsulation [**26, 27**]. PVA, Dextran, chitosan, alginate, polyethylene glycol (PEG), commonly used for functionalization method [**28**].

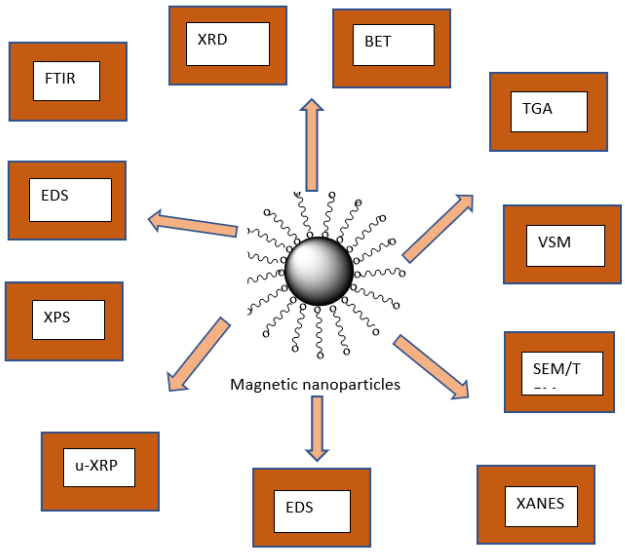

Figure 6. Various characterization parameters of magnetic nanoparticles

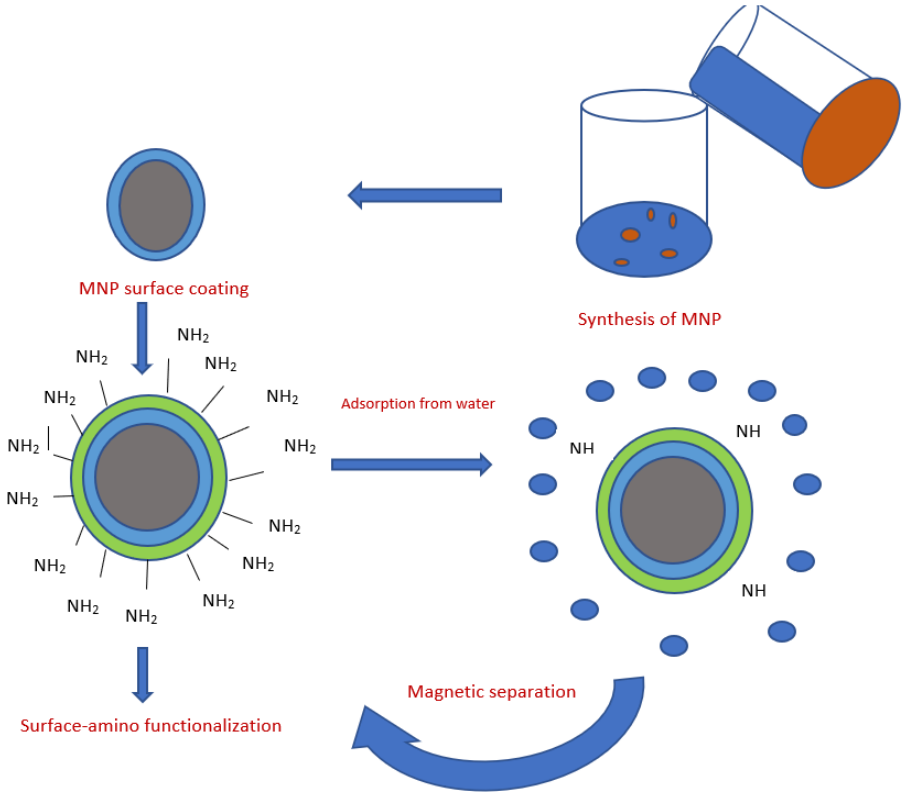

Figure 7. Functionalized magnetic nanoparticles.

EFFECTIVE PARAMETERS IN THE DESIGN OF MAGNETIC NANOPARTICLES

The design and synthesis of nanoparticles require knowledge of the principles of the nature of nanostructures [**29, 30**]. These particles are used as a drug that moves to a specific tissue and is not harmful to the patient or as a contrast agent in medical imaging [**31**]. In this section, we examine the physiological barriers that MNP face and the physical changes that are applied to improve the performance of MNPs in the body [**32**]. The important physical and physiological parameters in the design of nanoparticles with biological applications.

Extracellular Barriers

High ionic energy and solubility heterogeneity in nanoparticles cause them to collect in the blood as they enter the bloodstream, eventually changing their magnetic properties and arresting them. [**33, 34**]. In addition to the aforementioned, nanoparticles in the vascular environment are constrained by factors such the particle size to target tissue anatomy. When it affects organs like the brain and kidneys, the issue is worse. For instance, powerful cell-to-cell junctions found in the blood-brain barrier (BBB) restrict small-sized particles and appropriate physicochemical sites from passing past the blood-brain barrier in the brain, which limits the charge of pinocytosis [**35**].

Intra-cellular Barriers

Intracellular constraints act as a barrier to the entry of drug-carrying particles as well as extracellular barriers, which are not just restricted to the extracellular area [**36**]. When a nanoparticle is connected to the target membrane, it is often removed by ligand-dependent endocytosis and then disassociated from its function inside the cell by acidifying interactions in the endosome chamber, however most of these endosomes proceed towards the lysosome [**37**].

STAGES OF ACTIVITY OF MAGNETIC CARRIERS

Upload the Drug

Drug binding is by means of covalent approach with fission and reconnection capability-or by using physical strategies such as hydrophobic interactions that expand specificity in drug delivery [**38, 39**]. Proper design of nanoparticles when loaded with a precise drug can be used as a greatest drug delivery system; this reduces non-specific cellular interactions, controls the secretion of therapeutic agent, the capacity to take delivery of a range of loaded capsules or use, and makes nanoparticles feasible in cellphone imaging and tracking [**40, 41**].

BODY ENTERING AND APPROACHING THE TISSUE

The drug-carrier complex formed in the form of Ferro fluid enters the body with the aid of intravenous or arterial injection [42]. With the help of an exterior magnetic area (produced from everlasting magnets) and a gradient above the field, the drug can be guided and centred at the tumor site or different goal tissues are furnished [**43**].

Targeting

The focused on of these particles is not specific and is frequently completed via non-specific methods such as tissue-specific pore dimension or more suitable permeability and retention effect (EPR) in tumor tissues [**44, 45**].

Passive Targeting

This technique is quite effective at extending the blood half-life of MNPs and is applicable to a wide range of situations, including tumours, unusual structures, specific vascular damage, inflammation, and contamination. The phenomenon of greater penetration and retention impact serves as the foundation for passive targeting in its entirety (EPR). This process, on the one hand, facilitates the departure and accumulation of macromolecules and nanoparticles in the tissue by increasing their leakage from the arteries [**46**]. Factors including capillary insufficiency, blood pressure, and lymphatic drainage affect the stage of this aggregation. This targeting and aggregation of inactivated nanoparticles with sizes between 1 and 10 nm occurs. The spontaneous clearance of the reticuloendothelial machinery (RES), which is made up of bone marrow cells, blood monocytes, and tissue macrophages, presents another opportunity for passive targeting. Delivering contrast chemicals for imaging or drug delivery vectors to the target tissue is made possible by the removal of MNPs by phagocytic cells [**47**]

Active Targeting

Ligands with robust affinity on the surface of the particles to specific molecules on the surface of the patient's phone are used to obtain the particles in the target tissue. In malignant tissues like tumours, antigen-antibody or receptor-ligand interaction takes place after particle buildup caused by EPR [**48**]. Proteins, peptides, aptamers, and other tiny molecules can all function as ligands. In conditions like breast cancer, malignant melanoma, and squamous cell carcinoma, the substance is utilised to distribute MNPs to a wide range of neoplastic tissues, or the F3 peptide, which binds to tumour endothelium nuclei. Fast peptides and small compounds, as opposed to monoclonal antibodies, will boost the polyvalent binding pathway's affinity for binding [**49**].

CYTOTOXICITY OF MAGNETIC NANOPARTICLES

The ability of positive chemicals or mediator cells to damage living cells is referred to as telephone cytotoxicity. Cytotoxicity is a necessary issue, as the destruction of healthful living cells round the wound will adversely have an effect on the restoration process. Cytotoxicity is the universal excellent of being poisonous to cells and is no longer affected with the aid of chemical stimuli, physical/environmental conditions (exposure to temperature, excessive pressures, or radiation) or exposure to different cells (e.g., NK or T cells) [**51, 52**].

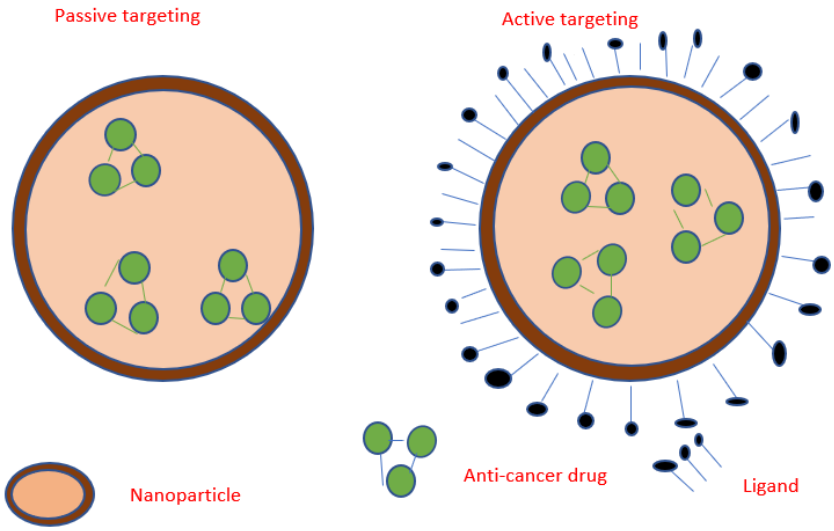

Figure 8. Passive targeting versus active targeting strategies for anticancer drug delivering system.

Chemical toxicity can occur in many ways; however, it has generally been thought to be divided into two main classes: disruption of specific biomolecular ambitions or pathways (eg, enzyme activation/inhibition and receptor agonist/antagonist effects) or damage to cellular machinery that can lead to cell phone stress and cytotoxicity [53,54]. By treating cells with a cytotoxic compound, it can motivate quite a number of telephone fates. Using a cytotoxic compound, healthy residing cells can be caused to bear both necrosis (accidental cellphone death) and apoptosis (programmed cell death) [**55, 56**]. By analyzing the extent of cancer cell cytotoxicity, anticancer drugs can inhibit the proliferation of target cells, either by scrambling their genetic material or by blocking the nutrients the cells want to live on [**57-60**]

CONCLUSION

Magnetic nanoparticles overcome the problem of drug delivery, by addressing the problems of toxicity, localization, and treatments for diseases such as (CF)cystic fibrosis, and tumors. But there are only a few clinical trials. This field is still emerging and has a long way to go.

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