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IRON OXIDE NANOPARTICLES - A BOON FOR THERAPEUTIC APPLICATIONS

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ABSTRACT

Over the years, many different iron oxide nanoparticles have been evaluated for a wide range of biomedical applications. The synthesis and characterization of iron oxide nanoparticles and their therapeutic applications are summarized here. The first section of this review focuses on Iron Oxide Nanoparticles (IONPs) chemical synthesis methods such as co-precipitation, thermal decomposition, microemulsion, and sol-gel. Green IONPs are synthesized using a variety of living organisms such as bacteria, plants, fungi, yeast, virus, and algae. Most studies claim that bio-synthesized IONPs are biocompatible and do not cause cytotoxicity in healthy cells. Many different analytical techniques, such as TEM, XRD, and FTIR, are used to evaluate the physicochemical properties of iron oxide nanoparticles. Second, this review discusses the importance of iron oxide nanoparticles in biomedical science, specifically for cell labelling, tissue repair, cancer treatment, immunotherapy, and stem cell therapy. More research in biomedicine should be conducted using the aspects of IONPs.

KEYWORDS: Cell labelling, cytotoxicity,iron oxide, stem cell therapy, therapeutic application.

1. INTRODUCTION

Nanotechnologies have developed as new powerful instruments in various technical applications throughout the last few decades. Due to these applications, scientists have made exceptional accomplishments in developing numerous nanodevices and nanomaterials (metal, oxide, and semiconductor). (Thomas Vangijzegam et al., 2018).

Nanomaterials have been used for medical reasons because they have a lot of good qualities. For one thing, nanomaterials are similar in size to biological materials like enzymes, proteins, and lipids, which has led to research in different types of nanomaterials. Magnetic iron oxide nanoparticles (IONs) have been used to help them interact with the nanomaterials, and they are larger than most individual molecules used as standard drugs, making them more effective (Edouard Alphandery et al., 2019).

Because of their intrinsic magnetic properties, magnetic iron oxide nanoparticles (IONPs) have been extensively studied among the many types of nanomaterials (i.e., superparamagnetic), allowing them to be used in a wide range of scientific fields such as electronics and environmental science. In addition to their exceptional magnetic capabilities, IONP's biocompatibility, stability, and environmental friendliness have made them the ideal platform for biomedical applications. (Thomas Vangijzegem et al., 2018).

Magnetic iron oxide nanoparticles are used in many biomedical and bioengineering applications, as well as in a lot of other uses. Magnetite (Fe_2O_3), maghemite (-Fe_2O_3), and mixed ferrites (MFe_2O_4 where M is Co, Mn, Ni, or Zn) are some of the iron oxide nanoparticles that can be synthesized. (Seyed Mohammadai Dadfar et al., 2019).

Iron oxide nanoparticles (IONPs) are synthesized through various physical and chemical processes, using toxic and reactive chemical reducing agents such as hydrazine hydrate and sodium borohydride, which affect adverse environmental and animal life. (Ashraf et al., 2019)

To overcome this barrier, it has recently been proposed to bio-synthesize IONPs using natural manufacturing methods such as bacteria, plants, yeast, fungi, and seaweeds, which employ some of their enzymes or proteins essential in the reduction of ferrous/ferric iron ions into crystallized nano-particulate iron. The biosynthesis of IONPs is a bottom-up approach that generates NPs via an oxidation/reduction reaction. (Alphandery.E et al., 2020, Noreen Ashraf et al 2019).

Magnetic nanoparticles (MNPs) have been various applications that have increased in recent years, and their tentacles are far and wide, such as material sciences and biomedical, agricultural, food, engineering, and environmental sciences. (Ashraf Noreen et al., 2019).

Iron oxide nanoparticles, for example, are well-known in the medical imaging industry for their use as contrast agents (CAs) in magnetic resonance imaging (MRI). They can cause local heat augmentation when exposed to an alternate magnetic field, a process known as magnetic hyperthermia. This property effectively eradicates cancer cells, which cannot survive at temperatures ranging from 42 to 49°C without affecting the healthy cells. (Thomas Vangijzegam., 2018).

The delivery of medicinal substances using IONPs as carriers is a subject of research that has gotten much attention recently. IONPs can be employed as individual nanoparticles or as magnetic nano assemblies, which are nanoparticles enclosed in macromolecular matrices in the field of medication delivery. (Noreen Ashraf et al., 2018).

IONPs have recently been used as pigments and catalysts in a variety of industrial processes, in addition to biological sciences. Thus this review details various methods of IONP's synthesis and their application. (Noreen Ashraf et al., 2018).

2. METHODS OF SYNTHESIS

Nanoparticles made of iron oxide have different magnetic properties because different synthesis methods produce different nanoparticles. A careful choice is needed to ensure that the particles are in the right shape, size, distribution, and crystallinity when they are made. Many different ways can make superparamagnetic iron oxide nanoparticles(SPION). These include chemical, physical, and biosynthetic methods (S. Laurent et al., 2008 S. Hasany et al., 2012, C.Jiang et al., 2015, B.K. Sodipo et al., 2016). Almost all of the time, chemical techniques are used.

Biological techniques rely on reduction-oxidation processes, in which microbial enzymes or plant phytochemicals reduce salts to SPION. Such biosynthetic methods are widely regarded as environmentally friendly (green chemistry), and their products are biocompatible. Such approaches, however, have a low yield and a wide size distribution. Physical and biosynthesis protocols make up less than 10% of all SPION synthesis methods (C.Jiang et al., 2015). We will only discuss chemical synthesis approaches commonly used below.

2.1 Co-precipitation

The co-precipitation method is when both Fe^{2+} and Fe^{3+} aqueous salt solutions are precipitated at the same time with a weak or strong base. It is one of the most efficient and straightforward ways to make new things. This method commericially makes the majority of SPlON.The size, shape, and composition of the iron oxide nanoparticles can be affected by many factors, including the Fe^{2+} Fe^{3+} ratio, temperature, pH, the type of salt used, and the type of base used (NaOH, NH_4OH, Na_2CO_3). While the co-precipitation process is one of the most cost-effective ways to make high-yield SPION with the correct magnetic properties, the nanoparticles made by this method often have a low level of crystallinity. To get rid of – at least in part this co-precipitation has many problems, but many different ways have been used to fix them. Examples of these methods are co-precipitation of $FeCl_3.6H_2O$ with Fe_3O_4 nanoparticles in the presence of a magnetic field) or ultrasound. Co-precipitation of $FeCl_3.6H_2O$ with Fe_3O_4 nanoparticles (Y. Liu and S. Wu, 2011 S.K. Suh and C. Pereria, 2013 E. Roy et al., 2016, Seyed Mohammadali Dadfar et al., 2019).

2.2 Thermal decomposition

This method uses the heating of iron precursors can make SPION in high-boiling organic solvents and stabilizing surfactants produces SPlON method produces. This SPION with good crystallinity and size control. Amphiphilic surfactants like oleic acid, oleylamine, fatty acids, and hexadecylamine can be used to control the synthesis of nanoparticles. IONP's produced by this method are made at high temperatures, so they have good size dispersion and crystallinity because of the surfactant in the mixture. On the other hand, this method is not very good for the environment because dangerous chemicals like chloroform, hexane, and iron pentacarbonyl are used in the process. Furthermore, because the surfaces of magnetic nanoparticles are hydrophobic, an extra surface modification process is needed to make them water-soluble and biocompatible for use in medicine. Controlling the shape and size of nanoparticles when making SPION through thermal decomposition is dependent on the length of the reaction, the temperature of the reaction, and the ratio of precursor to surfactant (Park et al., 2004, R. Hufschmid et al. 2015, Seyed Mohammadali Dadfar., 2019).

2.3 Microemulsion

Microemulsion systems are thermodynamically stable, isotropic dispersions of two liquids that do not mix. In general, there are two types of microemulsions: regular micelles and reversed micelles. The regular micelles are made of oil and water. The dispersed phase is often used as a nano/micro-reactor because it provides a limited environment for the growth of nano- and microparticles. They use amphiphilic surfactants like cetyltrimethylammonium bromide (CTAB), sodiumdodecylsulfate (SDS), and polyethoxylates to make micelles in micelles (e.g., Tween-20 and -80) (N.Remya et al., 2016).

The main benefit of making SPION with microemulsion technology is that the size of the micelles can be changed to control the size of the nanoparticles. As a result, the particles' polydispersity improves because the micelles

are not significantly different in size. Microemulsion synthesis has a lot of problems, one of which is that it takes a long time to make because the temperature is low. This results in low crystallinity and low yields in SPION. High reaction temperature or heating synthetic iron oxide can improve the crystallinity of the particles (Y. Lee et al 2005, P. Tartaj et al., 2011).

There are also problems with scaling and how residual surfactants affect the properties of iron oxide particles when the microemulsion method is used, which are two more downsides (Seyed Mohammadali Dadfar et al., 2019).

2.4 Sol-gel

In the sol-gel method, tetraethyl orthosilicate (TEOS) is reduced in ethanol and 30 percent aqueous H_2O_2 with Fe^{3+} solutions to make colloidal sols. This makes silica-coated SPION more durable and easier to work with. This happens by making the sol harden through a chemical reaction or taking the solvent out. This makes a 3D network of iron oxide. After the gel has dried and the solvent has been removed, it must be crushed again to get iron oxide nanoparticles. The free energy can be reduced by adding a surfactant before it gels. This allows the formation of nano-sized iron oxides in high yields while avoiding the formation of 3D nanoparticles at room temperature. Because the sol-gel process is done at room temperature, more heat treatment is needed to get the crystalline forms.

The structure and properties of the SPION gel change the temperature, pH, the solvent used, and the concentration of salt precursors are different. The concentrations of TEOS and ammonia used to control the thickness of the silica shell (Seyed Mohammadali Dadfar., 2019).

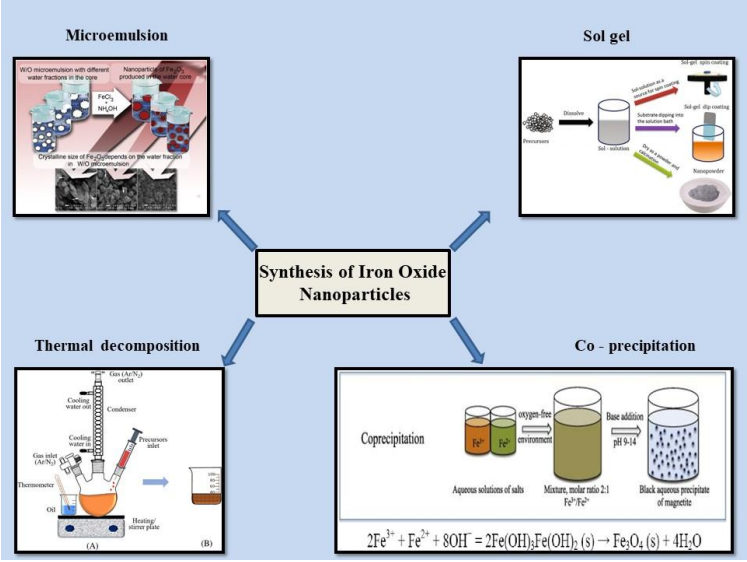

Fig.1 Methods available for the **synthesis of Iron Oxide Nanoparticles.**

3. IONP's green synthesis

Biomedicine and the environment safely, IONPs must have better biocompatibility and less toxicity. It may be best to make nanoparticles with suitable physicochemical properties by making them in a way that is based on nature. The NPs made using the plant's biological roots are safe and less harmful. This is because there may still be residual harmful compounds that have not been removed from the surface of physiochemically made NPs, making them less biocompatible and dangerous.

There are many advantages of using biologically made IONPs over chemically made IONPs, like better biocompatibility, environmental friendliness, time and money efficiency, and no need for stabilizing agents. Biologically active chemicals are more likely to be absorbed by FeONP metallic core when it comes into contact with the cell's molecular structure. This makes the core of the NPs look like a capsule.

3.1 Bacterial synthesis of IONPs

Bacterial synthesis is green, cost-effective, and energy-efficient to make nanostructures. It takes advantage of microorganisms' hidden biomineralization power. Bacterial synthesis is linked to how microbes remove harmful metals from their bodies and how metallic nanostructures are made. Membrane proteins, like ATPase, that act as protein anti-transporters are also crucial for ionic efflux.

The production of an enzyme called iron reductase by *Actinobacter* produces IONP when there is iron salt in the water. It has also been shown that *Actinobacter* extracellular reductase reduces Fe^{3+} to Fe^{2+}. When FeO-OH was used as a precursor for iron metal, *Thermoanaerobacter sp.,* an anaerobic thermophilic bacteria, made magnetite($Fe_2O_{4)}$ NP mono distributed extracellularly. The NPs had an average size of 13.1 nm (Bharde et al., 2008, Moon et al. 2010).

Bacillus subtilis are commonly used for the synthesis of bacteria-based IONPs. The size of these IONPs ranged from 60 to 80 nm. There are also a few reports about bacteria making IONP, (Sundaram et al., 2012, Noreen Ashraf et al., 2018).

3.2 IONP production aided by fungi

Verticillium sp. and *Fusarium oxysporum*,when mixed with ferric and ferrous salts like other microbes, make IONPs outside of their bodies. In this process, many different biomolecules, like proteins, are released outside the body to help reduce anionic iron ions. The next step is to make crystallized magnetite (Fe_3O_4) with a ferromagnetic transition and spontaneous magnetization properties at low temperatures. When the cell-free extract was mixed with iron (III) chloride solution, it was found that *Alternaria alternata* caused the extracellular stable maghemite (c-Fe_2O_3) nanoparticles to be made. *A. fumigates, C. globosum, P. chlamydosporium, A. wentii, and C.lunata* few other fungal species that can make iron microcrystalline structures. *Aspergillus oryzaeTFR9*-produced FeNPs are very stable and homogeneous when mixed with $FeCl_3$. Another group of scientists looked into using *Alternaria alternatae fungi* to make IONPs from Fe_3O ions. They did this by growing the fungi in the dark. According to their characterization, the made IONPs were also cube-shaped, with an average diameter of 93 nm. The nanoparticles made by scientists were able to kill both Gram-positive (*Bacillus subtilis, Staphylococcus aureus) and* gram-negative pathogens *(Escherichia coli, pseudomonas aeruginosa*) (Kaul et al.,2012, Raliya 2013, Mohamed et al., 2015, Sarkar et al., 2017)

3.3 IONPs synthesized from yeast

Yeast Saccharomyces cerevisiae to learn more about making micro rods made of the mineral goethite (a-FeO(OH). This study reports in this study about how rod-shaped anisotropic a-FeO(OH) particles turned into isotropic nanoparticles with sizes less than 10 nm, and the results were confirmed by transmission electron microscopy (TEM). There may be a place where (proteins and Fe_3O ions interact) (If proteins have a water group at the a-FeO(OH) site). It happens because the Fe^{3+} ions interact with the protein lattice complex, making smaller NPs with more protein inside the lattice. When IONPs are made, they use a natural glycolipid from the yeast part of the sophorolipid family. In Dynamic Light Scattering -DLS, and UV–Visible measurements, sophorolipids made a complex with the surface of NPs with diameters between 10 and 30 nm, which caused the complex to form. Bacteriophage (M_{13}) is a long *E. coli* virus wrapped in a cap made of five different proteins. In order to make zerovalent iron nanoparticles, a protein called pIII was made that had five copies on one end of the phage. This made it more specific to Fe^{2+}. Compared to protein pIII, the protein pVIII in viral capsid had the most crucial role in metal binding. In order to make 4ED-pVIII-M_{13}, a protein called pVIII was made that had one more negatively charged residue than normal pVIII. This extra negatively charged residue was called AAEEEDPAK (AEGDDPAK). The iron nanoparticles that were made had a face-centred cubic shape. Used asymmetrical T4 bacteriophage capsid to make gold-coated iron ternary core/shell nanostructures at room temperature. The Tobacco Mosaic Virus was used to make film-shaped iron oxide nanoparticles with a diameter of 2 nm (Shenton et al., 1999, Xu et al.,2012, Sharan et al., 2015, Noreen Ashraf et al., 2019).

3.4 IONPs production aided by algae

Experiments on the use of macroalgae brown seaweed extract called *Sargassum muticum* can make magnetite Fe_3O_4 NPs. The presence of sulfated polysaccharides in the extract makes ferric chloride ($FeCl_3$) solution break down. Transmission Electron Microscope (TEM) and X-Ray Diffraction (XRD) tests showed that the Fe_3O_4 NPs made crystallized, with an average particle diameter of 18.4 nm. *Chlorococcum sp.* is a microalga that grows in the soil, used to synthesize IONP's. The size of the synthesized IONP's ranged from 20 to 50 nm.

FTIR analysis showed that biomolecules like amine and carbonyl were found in the glycoproteins and polysaccharides made by algal cells, even though the exact production method is unknown. Previous research has reported that algae play a significant role in making IONPs (Mahdavi et al., 2013, Subramaniyam et al., 2015 Asharf et al., 2019).

4. Iron oxide nanoparticles characterization

Analytical methods look at iron oxide nanoparticles' physical and chemical properties. Inductively coupled plasma mass spectrometry (ICP-MS) and the 1,10-phenanthroline assay are two common ways to measure iron concentrations. The flame atomic absorption spectrometry (FAAS) method can also be used.

The composition and crystallographic phase of crysta llized SPION can be found using a high-resolution TEM, SAED pattern (HRTEM). They are treated as waves instead of particles when they pass through TEM specimens, usually 100 nm thick. Many nanometers are in the range of high-energy electrons, but the distance between atoms in the sample is nearly a hundred times greater. To make things even more specified, the electrons are scattered at different angles by some of the atoms in the sample. Others flow through the sample unhindered.

So, it is evident that it is made up of many small spots, each of which corresponds to one that meets the diffraction criterion for a crystal structure in the sample. Using Scherrer's equation, XRD is also used to figure out crystal structure and determine the size of SPION'S crystals. According to the equation, the size of crystallites in a solid is linked to the spread of a peak in a diffraction pattern. Hydrodynamic techniques can be used to determine the hydrodynamic diameter of

nanoparticles in a solution and the colloidal stability and aggregation. (K. Woo et al., 2004, S. Mahajan et al., 2012).

Dynamic Light Scattering (DLS) is a powerful and easy-to-use tool. The flaws in DLS are very alert to the presence of large particles. To use nanoparticle tracking analysis (NTA) can be sized particles from 30 nm to 1000 nm. Another thing is that NTA has a lower detection limit than DLS does (V. Filipe et al. 2010).

NMR spectroscopy, FTIR spectroscopy, and x-ray photoelectron spectroscopy (XPS) analyses are used to determine iron oxide nanoparticles' surface features and make sure the presence of functional groups is present. A technique called small-angle x-ray scattering (SAXS) or ultra small-angle x-ray scattering (USAXS) can be used to figure out the shape and size of iron oxide nanoparticles (USAXS).

As X-rays move through the material at minimal angles, the elastic scattering behaviour of X-rays is recorded. This information is used to determine how dense material is at the nanoscale. Superconducting quantum interference measuring devices are used to discern the magnetic properties of nanoparticles. DLS and NTA are used to determine the space occupied by the iron oxide nanoparticles. (T.Li et al., 2016, A. Ali et al 2016., Seyed Mohammadali et al., 2019).

5. Applications in medicine

IONPs with magnetic and superparamagnetic properties can be used for photothermal therapy (PTT), photodynamic therapy (PDT), magnetic hyperthermia therapy (MHT), immunotherapy, and more. IONPs (photo absorbers) help PTT turn laser energy into heat, killing cancer cells. PDT is a three-step clinical treatment method that activates light sensitizers, activates and releases reactive oxygen species (ROS), and kills specific cells in the body. (Zhou et al., 2014).

Von Tappeiner et al idea on photodynamic therapy can be used to treat melanoma, bladder, and esophageal cancer. Hyperthermia is a simple treatment for tumour cells denoted by heating them from 41℃ to 45℃. Living cells have their self-healing systems by nature, so they can repair themselves when they get hurt, making hyperthermia procedure useful conventionally (Triesscheijn et al. 2006, Espinosa et al. 2016, Saeedi et al., 2017).

Furthermore, when the IONPs are homogeneous and small in size, which extend their use in magnetic hyperthermia to eliminate the cancer cells. Immunotherapy utilizes the help from cells like dendritic and T cells, or macrophages, to kill cancer cells instead of the whole tumour. This is different from partial thromboplastin time (PTT), photodynamic therapy(PDT), and maintenance hemodialysis (MHD). IONPs play an essential role in delivering tumour-specific antigens to dendritic and T cells. (Goldberg 2015).

There are many ways IONPs can help with Magnetic Resonance Imaging (MRI) in the central nervous system(CNS). They can be used as contrast agents to look at areas of the blood-brain barrier. They can also be used to track cells in the CNS that have been injured or damaged, and they can be used to look at cerebrovascular perfusion. (Ashraf and other people., 2018).

Cells are marked with different colours todifferentation. Cells can be labelled with ferro-paramagnetic nanoparticles to make it easier to look at them during using MRI to look at them. There are two ways to tag cells. One is by attaching magnetic nanoparticles to a cell surface and the other is by encasing magnetic nanoparticles in a fluid phase endocytosis process.. The best way to do this is to coat the surface of magnetic NPs with a biocompatible ligand like insulin, lactoferrin, transferrin, or albumin, without affecting the nature of NPs'(Yeh et al., 1993, Schoepf et al., 1998, Lobel et al., 2000, Mahmoudi et al,. 2011).

Encasing superparamagnetic NPs (20 nm size) in ceruloplasmin, lactoferrin, and transferrin showed that they had a strong affinity for receptors on human fibroblasts. (Gupta et al.,2004).

The effects of these NPs on the morphology and adhesion abilities of fibroblast cells in the skin were then studied with SEM and TEM. The size of the protein-encased NPs made a difference on how well they could interact with fibroblast cells. In addition, the interactions between NPs that were encased and those that were not were very different. IONPs could be used to label brain stem cells, Which has recently caught the scientific community's attention.

The nano-neurotoxicity of different protein-encased NPs, have been studied choosing suitable model cells. Researchers have already found a lot of different types of cells that could be used in nanosafety tests when it comes to labelling neural cells. They found that dimercapto succinic acid (DMSA) coated IONPs are a better choice for six different neural cell types than progressive muscular atrophy(PMA) coated IONPs. This includes neural stem cells, immortalized cell lines and cancer cell lines from murine and human sources (Joriset al., 2017).

5.1 Tissue regeneration

Previous studies have used biomolecules or drug-encased IONPs that contain ligands recognized by a receptor on the target cell or tissue that has to be repaired. It has been long since IONPs have been used in medical applications. These NPs were made of morphological cube superparamagnetic magnetite Fe_3O_4 NPs linked to different proteins for tissue repair. These particles affects human dermal fibroblasts in cell viability, cytoskeleton

organization, adhesion. For morphological analysis SEM, TEM, fluorescence, and light microscopy were also used to analyse how fibroblasts and NPs interact. This study found that underivatized IONPs were taken by the fibroblasts, possibly through endocytosis, which caused damage to the cytoskeleton and broke up the cell membrane. Ceruloplasmin or lactoferrin-coated nanoparticles, on the other hand, did not get inside the cells and stayed on the surface. This study showed how customized IONPs can help cells or tissues repair themselves through cellular response. (Joris et al., 2008; Veiseh et al., 2010 Ashraf Noreen et al., 2019).

5.2 Oncology treatment

Magnetic properties of elemental iron particles have made them cytotoxic, and coating them with gold has made them more resistant to oxidation. The oxidation of iron particles increases reactive oxygen species (ROS), starting the cell death process. Thereby decreasing the ROS scavengers. Iron nanoparticles might slow the growth of the mitochondrial membranes. This could be because iron is susceptible to redox changes. Cell death caused by Fe@AuNPs can be reversed in normal cells, but it cannot be reversed in cancer cells. Studies have reported that IONP's activate the MTOR pathway, which did not cause autophagy in normal cells (IMR-90) but reverse uses the phenoma in the cancer cells (A549), (Khan et al., 2012).

IONP's have been used in stem cell therapy by having them inside the cells, where they can be found with MRI and activated with magnetic actuation. Using IONPs after oligodendrocyte precursor cells (OPCs) have been transplanted may help regenerate the central nervous system by increasing myelin formation and thus restoring the protective sheath around the nerve fibres (Connell et al., 2015, Zhao et al 2018).

5.3 Immunotherapy

IONPs can affect the immune system in the following ways: They influence macrophage polarisation (i.e., causing a shift from anti-inflammatory and pro-tumor M2-type macrophages to anti-inflammatory and pro-tumor M1-type macrophages), as evidenced by the fact that the THP-1 monocy test shifted from an M2-like phenotype before IONP exposure to an M1-like phenotype after IONP exposure. They increase the efficacy of immune-suppressive drugs used in organ transplantation, as evidenced by the fact that myco phenolic acid (MPA) combined with IONPs effectively inhibited the secretion of the cytokines interleukin (IL)-2 and tumour necrosis factor (TNF) at a concentration of microscopic polyangiitis(MPA) lower than the required amount to achieve a similar effect in the absence of IONPs. IONPs reduce the harmful effects seen at high MPA concentrations. (Laskar et al., 2013, Zanganeh et al., 2016).

5.4 Treatment of wastewater

The hydro Ianthanum oxide encased magnetite (Fe_3O_4) core magnetic NPs (Fe3O4@SiO2) have been synthesized water phosphate removal, (Lai et al., 2016).

Another study looked at the ability of IONPs to remove total ammonia, nitrogen, phosphates, and chemical oxygen demand from household wastewater. Recently, IONPs and multi-wall carbon nanotubes (MWCNTs) have been investigated to treat industrial wastewater generated during the anaerobic digestion of beet sugar. (Ashraf Noreen et al., 2019).

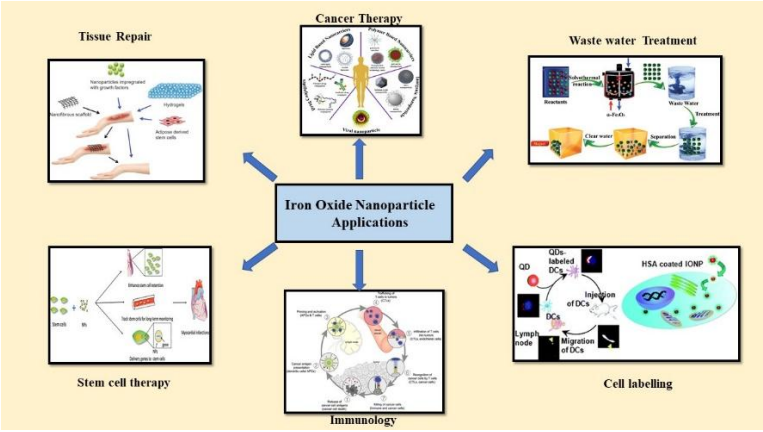

Fig.2 Iron Oxide Nanoparticles Application.

6. CONCLUSION

Iron oxide nanoparticles have a lot of interesting properties, which is why they are used so often in biological research. They can be made in various ways, each with advantages and disadvantages. Co-precipitation, thermal decomposition, microemulsion, and sol-gel have made iron oxide nanoparticles. IONPs are made using many living organisms, including bacteria, plants, animals, and by-products. They are made in an environmentally friendly way. Nanoparticle properties must be changed to meet the needs of biomedical applications, such as the core size, size distribution, crystallinity, shape, and saturation magnetization. These methods of making NP's does not need to use dangerous chemicals. Iron oxide nanoparticles have unique properties that make them

perfect magnetic drug delivery devices, especially cancer treatment. Thorough research into the therapeutic applications of magnetic nanocarriers is needed before they can be used in commercial human medicines.

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