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Biomedical Application of Magnetic Nanoparticles: A Review

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Abstract

The medical treatment technologies in healthcare industries are modernized by using nanoparticles. The effect of nanoparticles and its interaction on human cells show many significant results. In this paper I have studied the experimental and theoretical background of some biomedical applications of nanoparticles. It is found that gold (Au), silver (Ag), iron (Fe), silica (SiO2) and some polymeric nanoparticles are extensively used in the treatment of various deadly diseases. The nanoparticles of gold, silver, zinc oxide, silica, cerium oxide are studied mostly to investigate the suitable distribution methodology for medical diagnosis and treatment.

Keywords Magnetic nanoparticles, drug delivery, hyperthermia, superparamagnetism

1. Introduction

Nano-particles are particles having size lies between 1 to 100 nanometer (Gubin, 2009). They are undetectable by the human eyes. They have small particle size, large specific surface area with super paramagnetic behavior (Yarer, 2016).Nanoparticles can exhibit significantly different properties in comparison to their larger counterparts. The special feature of nanoparticles creates many significances in larger material to increase surface to volume ratio including magnetic properties. The study and application of using nanoparticles is growing day by day. Among them hyperthermia, targeted drug delivery, photo ablation, biosensors are biomedical potential applications using MNPs. The extraordinary features of magnetic nanoparticles (MNPs) are observed in biomedicine. They are very sensitive in external magnetic field. They can be manipulated under external magnetic field on various applications like cell separation, drug delivery and also as nano-heaters to destroy tumors. The special clinical purposes for using magnetic nanoparticles are a) stability in biological environment ii) low toxicity iii) appropriate magnetic properties under the activation of soft magnetic fields . The iron nanoparticles (Fe_30_4, Fe_2O_3) and magnetic ferrites in spinel structures doped with manganese, cobalt, Nickel or zinc are largely used magnetic nanoparticles in clinical treatment. The nanoparticles are coated with organic or inorganic compounds to increase their biocompatibility. They can be functionalized with several ligands stabilizing them in biological conditions**.** It is observed that the heating of Nano particles in tumor site can effective damage to the malignant tissue. The growth of cancer cell can be controlled by the action of nanoparticle around the temp 40 to 45 °C without affecting the normal tissues (Berry, 2003).

The commonly used nanoparticles for various treatment is shown below in Table 1.

Table 1: Application of Nanoparticles (McNamara, 2016)

Nanoparticles	**Treatments**		
TiO_2	Drug delivery	PTD (Photodynamic therapy)	
Ag	Drug delivery	Cancer Therapy	
Fe-Pt	Drug delivery	Bio imaging	Hyperthermia

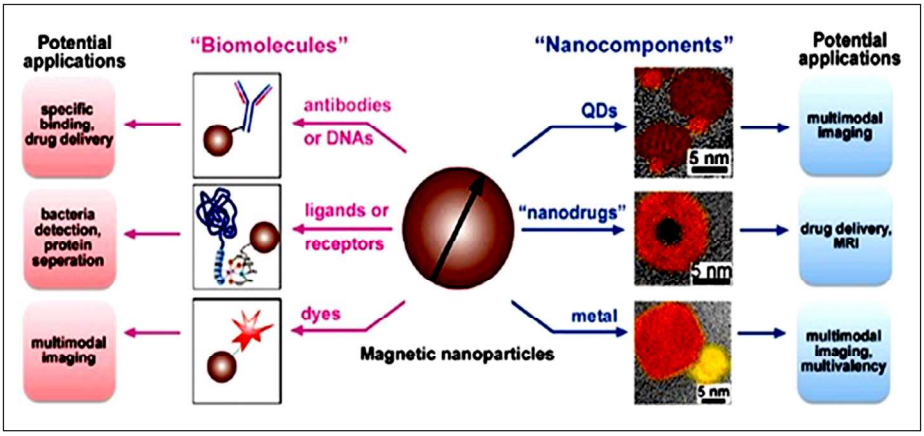

Fig. 1: Multifunctional application of Magnetic nanoparticles (Gao, Gu , Xu, B, 2009)

The diagram above explains the strategies to fabricate magnetic nanoparticles and their potential applications.

2. Methodology

This review article is prepared under the basis of articles published in different journals, books review papers and open accesses articles. Some results are presented from Ph.D. thesis done by researcher's .The fundamental methodology and mechanism used in biomedical applications are discussed. In this paper the different procedures of nanoparticles applications on biomedicine are discussed and compared on the basic of researches carried out by different scientist. The nanoparticle can be manipulated or controlled by external magnetic field under different technique are explained.

The methodology used for treatment using Magnetic nanoparticles in biomedical applications is one of the best technology in this era.

2.1 Drug delivery procedure

The term drug delivery refers to the transfer of a pharmaceutical compound into the body. The preferred methods are non-invasive oral (through the mouth), nasal, pneumonia (inhalation), and rectal routes. Magnetic nanoparticles has become very popular in drug delivery procedure**.** The delivery with minimum side effects is the best feature of magnetic nanoparticles as therapeutic drugs **(**Nikam , 2014).

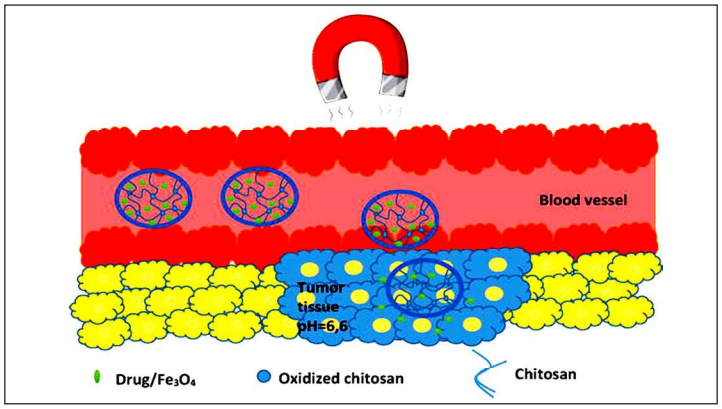

Fig. 2: Magnetic drug delivery system under external magnetic field (Fouad, 2020)

The nanoparticlesc carrier anti cancer drugs release the medicince at the tumor site either by enzymatic activity with suitable physiological conditions like PH and temeprature (Dobson , 2006).

The non toxic and biocompatibility including superparamagentism natute of nano particles at room temperatute makes them suitable candidates in vivo application .This is significant for the nanoparticles having size less than 200 mm(Ito, 2005).

If the nanoparticles having saturation magnetisation M_s about 70 emu/gm , they are guided towards the site through external magnetic field . Due to superparamagnetism, they do not agglomerate if applied magnetic filed has been removed (Berry , 2003).

2.2 Magnetic hyperthermia

The phenomenon of generation of heat by MNPs by variable magnetic field simply called magnetic hyperthermia. The heating is achieved by low frequency EM waves through the power absorption by magnetic nanoparticles. This technique is one of the most important approaches to induce heat by electromagnetic radiation in soft frequency order. There are some precautions on energy production, selectivity and localization to minimize the damage in healthy tissues (Williams, 2017).

Researches on magnetic behavior of nanoparticles on biomedicine is increasing day by day. There are so many clinical trials involving the use of nanomaterial. And new options and possibilities are increased in magnetic hyperthermia approaches and its implementation in the department of oncology medicine and beyond.

The MHT measurements can be done by using a heat station as shown in figure (3). The heating device coupled with a solenoid having N turn as shown in figure below. The alternating magnetic field having suitable amplitude and frequency is applied as a result the temperature of ferrofluid raised significantly. The heat exchange between the ferrofluid and surroundings is maintained by using insulation cover around the fluid (as in fig 3). The SAR of the ferrofluid is calculated by measuring slope of the graph plotted between the temperature and time is recorded (fig 4) by the device provided. The current gives the estimation of magnetic strength. The frequency of AC is measured from the values of L (inductance) and capacitance C (Laha , 2015).

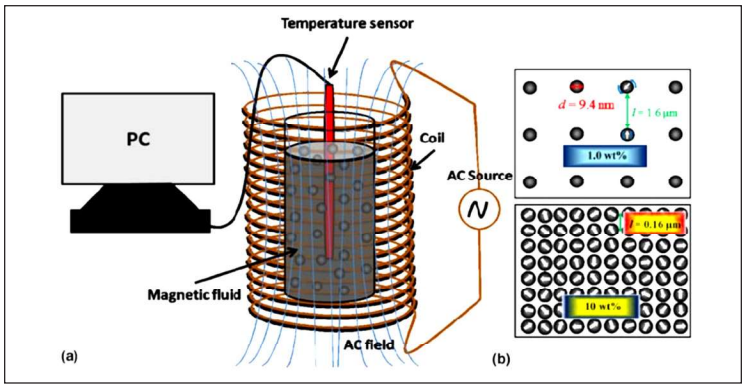

Fig. 3: Experimental set up for MHT measurement (Laha, 2015)

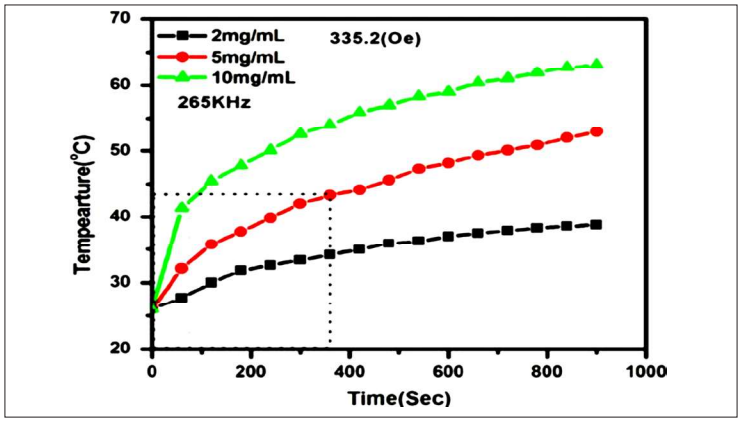

Fig. 4: Variation of temperature and time for different ferrofluid under magnetic field Oe (Nikam, 2014)

The nature of heating curves for the different concentrations of ferrofluids under magnetic field of frequency 265 KHz is shown by figure 4 above. The sample were heated from room temperature to 70°C .The origin of heat generation from nanoparticles in a ferrofuids subjected to alternating magnetic field could be due to hysteresis or relaxation of magnetism .It is also studied that for super paramagnetic nanoparticles, there is no hysteresis loss but energy loss arises due to Neel and Brownian relaxation .

Mechanism

In hyperthermia measurement procedure, a colloidal suspension of ferrofluids are used which is subjected to alternating magnetic field (B). Under this action the heat energy is dissipated in the medium which is produced by hysteresis loss. The additional heat energy is also produced due to the activation of magnetic nanoparticles through" Neel and Brownian" relaxation. Neel relaxation is the rotation of magnetic moment inside a stationary magnetic nanoparticles. While Brownian relaxation is the rotation of entire magnetic nanoparticles along with the magnetic moment. (Deissler, 2014)

In Neel approximation, the magnetic spin of the particle simply rotates .But in Brownian relaxation the entire rotation of particles take place (Guardia, 2012). The rotation procedure is shown below in fig 5.

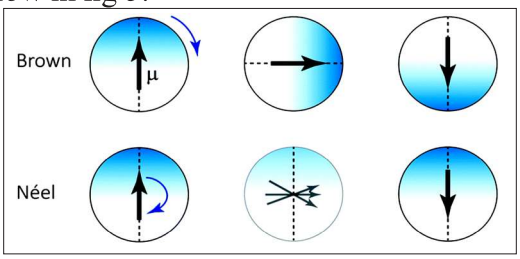

Fig. 5: Brown and Neel relaxation in a particle core with rotation of magnetic moment μ (Ilg, 2020).

Measurement

The important parameter to study hyperthermia is SAR. It indicates the specific absorption rate in W/g. It measures the heat energy absorbed per unit mass by magnetic nanoparticles in alternate magnetic field B having frequency f (Guradia, 2012)**.**

$$SAR = \frac{C}{m}\frac{\Delta T}{\Delta t}$$

Where C =specific heat/volume of water. The density of magnetic nanoparticles is m and $\frac{\Delta T}{\Delta t}$ is the temperature gradient with respect to time.

For effective cancer hyperthermia treatment, the product of amplitude and frequency should be in threshold value of order $5x10^9$ A/m.s otherwise there may be some clinical complications (Guradia, 2012**).** Hence we have to use efficient nanoparticle with optimized SAR value play major challenges in magnetic hyperthermia (MHT) research in treatment procedure for Cancer.

2.3 MRI and contrast agent

It is a special kind of imaging technology which is non-invasive in nature. It is used in many forms starting from detection of diseases .It is used in both diagnosis with treatment monitoring. It is specially designed to produce strong magnetic field.

Mechanism

The relaxation rates of hydrogen nuclei in water is measured by MRI. In local magnetic field, the nuclei are affected. The nature of effect is different on different tissues. As we know, the hydrogen nuclei align along the direction of applied magnetic field. As a result the protons are excited by the pulses of suitable frequency and relax to their original position when the pulses are off. The emission of characteristic electromagnetic signatures take place. These emissions are used to read the morphology of the human body by suitable imaging. If the natural and diseased tissues cannot be diagnosed by signals emitted then the spectrum made more distinct by further using magnetic nanoparticles as contrast agent. They can be conjugated to their antibodies to identify which one is disorder tissues (Pankhurst, 2003)

The contrast agents work in

a. Spin-lattice or longitudinal relaxation i.e T_1

b. Spin-spin or transverse relaxation i.e T_2

The relaxation process for the tissues can be controlled or manipulated by using the magnetic contrast agents around the targeted tissues. Due to super-paramagnetic, biodegradability, and surface properties. It is found that iron oxide nanoparticles are largely used in magnetic resonance imaging as a contrast (Hee, 2005)

3. Discussions

The biomedical applications by using different nanoparticles and their compounds are tabulated below.

Table 3: Biomedical applications of nanoparticles and their compound (Hoshyar, 2016)

Area	Nanoparticle Application of nanoparticles in Vivo	Special feature
For Optical imaging	The Site specific imaging using quantum dots through optical imaging.	1. Lymph nodes, lung blood vessels, and tumors imaging 2. Target specification through surface functionalization and subcutaneous imaging without cutting in surgery.
For MRI	Cancer identification through Super paramagnetic (iron oxide)	1. Sharp imaging of lymph node, bone marrow and liver as contrast . 2. Easy alternation of magnetic resonance relaxation rate of target fluids.
Drug delivery and genetic purposes	a) Cancer therapy through nanoparticle based on polymer and lysosome	1. Delivery through surface functionalization. 2. Strategies for solubilizing water-insoluble drugs.
	b) Neurodegenerative disease therapy	1. Transport across blood–brain barrier 2. Gene therapy
	c) HIV therapy	1. Emulsification. 2. DNA incorporation
	d) Ocular therapy	1. Drug prolongation with in ocular mucus.
	e) Respiratory therapy	1. Mitigation of inflammatory responses in respiratory tract

In modern anticancer therapy the silver nanoparticles play vital role. They are very popularly used nanoparticles for detection as well as diagnosis of malignant tumors. The special features are given below. The drug delivery system is controlled and triggered by using silver (Ag) nanoparticles in naomedicine. Their antimicrobial activity and efficiency against cancer cells require the cellular uptake through diffusion, phagocytosis, pinocytosis and receptor-mediated endocytosis (Joshi, 2017).

Due to surface properties including size and morphology, silver (Ag) nanoparticles are suitable materials for cellular internalization mechanism. The cancer cells can be minimized by silver ions and oxidative stress through apoptosis. The structural and functional impairment occurs due to interaction of cancel cells with silver nanoparticles and ions. (Gherasim, 2010**).**

Some of the therapeutic applications of silver nanoparticles (AgNPs) in modern medicine are tabulated below.

Table 4: Applications silver nanoparticles (Jasni et al., 2021)

Name	Application I	Application II
Anti-bacterial therapy	Antibiotic formulation	Surface coating
Antiviral therapy	Antiviral formulation	Surface coating
Cancer therapy	Antitumor formulations	Chemo/radio therapy
Tissue engineering	Surface coating	Membrane Scaffold /Hydo-gel therapy
Wound care	Surface coating	Film/mat/scaffold dressings

In Nano medicine, Gold (Au) are commonly used nanomaterial with large range of applications. Researchers have used gold nanoparticles to enhance plant plastids and DNA. They are also used in optical-electronics properties like sensory probes, electronic conductors, therapeutic agents, etc. In medical science, they are used in effective drug delivery including catalysis on medical treatment. Gold nanoparticles act as antibiotic and antifungal agent including anti-microbial. They are used in photodynamic therapy. It is a special type of treatment in which gold nanoparticles are placed on site and are excited using light. The particles rapidly heated that action kills unwanted cells. Since gold particles are quite dense, and hence they can be used in electron microscopy. They are used to identify biomarkers of cancers. In chemical reactions they act as a catalysis and infectious agents. (Dykman, 2011)

The graph below shows some results of using of nanoparticles in cancer treatment on various years.

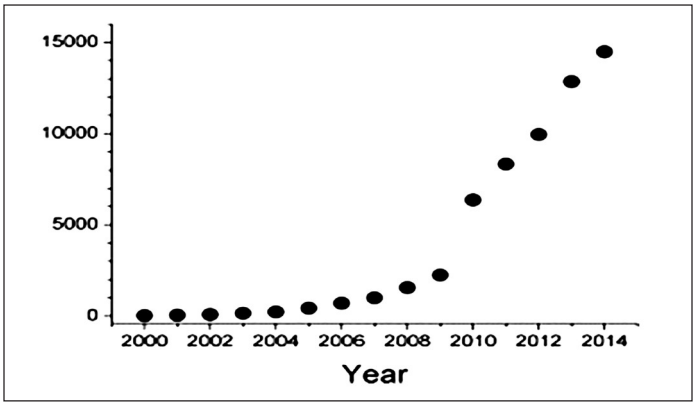

Fig. 6: Frequency of Research connecting nanoparticles with biomedicine applications (Juan, 2015)

4. Conclusions

The plant based natural medicine and technology are used widely against various diseases. In this era, people are interested to use medicines of natural origin specially taken from herbs by natural practices and traditions. Research shows that about 1/4th of medicines and their pharmacy compounds available today are obtained from natural resources. The delivery systems using nanoparticles or Nano-medicine are relatively new although rapidly growing methodology .The substances in Nano scale are used to predict and controlled through diagnostic tools on specific area. Through Nanotechnology or Nano medicine, the chronic and complex human diseases can be easily treated with precise medicines in specific site with less damage. The drug delivery and imaging process using nanoparticles are more effective now. Basically, the synthesized nano particles have been coated using coatings materials to acquire biocompatibility. The non-toxicity including safety, stability and bio-distribution are also major components during treatment procedure. The huge priority was given so as to acquire the early cancer detection through different approaches like MRI using magnetic nanoparticles.

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