Gels Horizons: From Science to Smart Materials

K. S. Joshy
Thomas Sabu
Vijay Kumar Thakur *Editors*

Magnetic Nanoparticles

A New Platform for Drug Delivery

Springer

Gels Horizons: From Science to Smart Materials

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Preface

Targeted delivery of anticancer drugs is regarded as one of the supports of cancer treatment as it could allocate for improved treatment competence and less adverse effects. A promising drug delivery advance is magnetic drug targeting which can be recognized if a drug delivery vehicle holds a strong magnetic moment. Here, in this book, we discuss the diverse types of magnetic nanomaterials which can be used as magnetic drug delivery vehicles, approaches to magnetic targeted delivery as well as promising strategies for the enhancement of the image-guided delivery and the therapeutic action. The evolution in the progress of magnetic nanoparticle-based therapies for different biomedical applications is described here in this book. Most appreciably, magnetic nanoparticles have been extensively applied in drug delivery and hyperthermia treatment for cancer. However, current applications of magnetic nanoparticles reveal their promise toward decreasing implant infection and increasing tissue growth. To build the most efficient magnetic nanoparticle systems for diverse biomedical applications, numerous new applications of magnetic nanoparticles in the medical arena as well as remaining confronts for such clinical use are discussed in this book.

The book is divided into seven chapters that cover the synthesis, characterization and property of magnetic nanoparticles and their advancement in biomedical fields. The book also deals with the significant applications of magnetic nanoparticles for the treatment of cancer.

Chapter 1 “Magnetic Nanoparticles and Its Biomedical Applications” by Jeena Varghese discusses the development of nanoscience and nanotechnology for the advancement in the research and technologies based on magnetic nanoparticles. The possibility of tailoring its physicochemical properties including biocompatibility for the application of magnetic nanoparticles as a promising candidate in pharmaceutical and biomedical fields was also discussed. The applications such as disease therapy—extensively chemotherapy, drug delivery, MRI and tissue engineering —make use of MNPs in a wider range.

Chapter 2 titled “Surface Chemistry and Properties of Magnetic Nanoparticles” prepared by Anshida Mayeen et al. explains the surface chemistry and diversified applications of magnetic nanoparticles. Surface chemistry of magnetic nanoparticles possesses a huge role in controlling different physical and chemical properties of magnetic nanoparticles. These nanostructures were applicable in diversified fields such as ultrahigh density data storage, nanomedicine, magneto-electric memory devices, in biosensing, magnetic resonance imaging, hyperthermia, gene and drug delivery.

Chapter 3 entitled "Magnetic Nanoparticles for Image-Guided Drug Delivery" by Ruby Varghese et al. summarizes physiochemical properties and pharmacokinetics of magnetic iron oxide nanoparticle as well as an attempt to provide an overview of hierarchical advances describing theranostic system which includes approaches and strategies utilized by magnetic iron oxide nanoparticle-based nanoplatform as well as enhancement in the application of image-guided drug delivery technique.

Chapter 4 "Magnetic and Fluorescent Nanogels for Nanomedicine" prepared by Vineeth M. Vijayan et al. summarizes some of the important fundamental fields related to this topic and how nanogels intersect with other important areas specifically targeting healthcare applications.

Chapter 5 entitled "Magnetic Glyconanoparticles for Biomedical Applications" prepared by Prajitha V. et al. presents the glyconanotechnology and application of magnetic glyconanoparticles in various fields such as drug delivery, bio-imaging, lectin binding, materials for controlled cell culture, surface modifiers, artificial tissues and artificial organic substrates due to their hydrophilic character and the ability of compatibility with bio-molecules.

Chapter 6, prepared by Sandhya Gopalakrishnan, entitled "Magnetic Nanoparticles for Hyperthermia a New Revolution in Cancer Treatment," reviews the latest advances in the field of magnetic nanoparticles, describing the important types with examples and major applications.

Chapter 7 "Magnetic Nanoparticles for Cancer Treatment," prepared by Subin Balachandran, gives a brief outlook of different approaches that are available for recognizing and curing cancer with the help of incorporation of magnetic nanoparticles. We have also discussed about the recent multimodal theranostic approaches which effectively reflects the application of nanotechnology in cancer therapy.

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About the Editors

K. S. Joshy is a post-doctoral researcher at the International and Inter University Center for Nanoscience and Nanotechnology, Mahatma Gandhi University, Kerala, India. His research interests include synthesis and characterization of nanoparticles with application for drug delivery. He has authored 10 research articles in high-impact journals, 1 book chapter and has been a co-editor on 1 book.

Thomas Sabu is currently Professor and Pro-Vice Chancellor in Mahatma Gandhi University, Kerala, India, in addition to being the founder director of the International and Inter University Centre for Nanoscience and Nanotechnology. After his B.Tech. in polymer science and rubber technology from University of Cochin, he went on to do his Ph.D. from Indian Institute of Technology, Kharagpur. Prof. Thomas is the Chief Editor of Nano-Structures and Nano-Objects and has received many national and international awards, including Fellowship of the Royal Society of Chemistry, MRSI award, SESR award, the Dr. A. P. J. Abdul Kalam Award for Scientific Excellence, an honorary degree by Université de Lorraine, and multiple fellowships by prestigious societies and universities. Prof. Thomas' research has spanned many areas of nanocomposite and polymer science and engineering, and he has edited more than 70 books, holds 5 patents and has authored over 750 research publications.

Dr. Vijay Kumar Thakur is currently a faculty member in the School of Aerospace, Transport and Manufacturing at Cranfield University. Prior to this, Dr. Thakur worked as a Staff Scientist in the School of Mechanical and Materials Engineering at Washington State University, US. Some of his other prior significant appointments include being a Research Scientist in Temasek Laboratories at Nanyang Technological University, Singapore and a Visiting Research Fellow in the Department of Chemical and Materials Engineering at LHU–Taiwan. He did his post-doctoral study in Materials Science and Engineering at Iowa State University and received Ph.D. in Polymer Chemistry (2009). He received his B.Sc. (Chemistry, Physics and Mathematics), B.Ed. and M.Sc. degree in Organic Chemistry from Himachal Pradesh University, Shimla, India. Dr. Thakur is an editorial board member of several SCI peer reviewed international journals as well as member of scientific bodies around the globe.

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Chapter 1
Magnetic Nanoparticles and Its Biomedical Applications

Jeena Varghese, I. S. Vidyalakshmi, and Riju K. Thomas

1 Nanoscience, Nanotechnology and Nanoparticles

Nanotechnology offers a broad spectrum of applications in almost all fields of science. The daily lives of humans changed after the development of nanoscience. As an example, the replacement of bulky electronic devices to tiny ones made our lives easier and more advanced. Nanoscience and technology follow a symbiotic relationship with each other. The technologies like scanning tunneling and scanning force microscopy enhanced the development of nanoscience. They provide images and operate objects on surfaces with adequate precision even in ambient surroundings or in liquids [1].

The word "nano" means "*dwarf.*" Nanotechnology deals with both single nano-objects and materials, and devices based on them, and with processes that occur in the nanometer range [1, 2]. An illustration of the nanometer scale in comparison with the known systems is shown in Fig. 1. Typically, nanoparticles have dimension between 1 and 100 nm and possess significant differences in properties from the corresponding bulk material. Nanoparticle's research is one of the highly demanding areas of scientific research owing to its potential applications in biomedical, optical and electronic fields. Nanoparticles act as a bridge between bulk and atomic or molecular structures. The physical properties of bulk materials are constant irrespective of its size; however, when it comes to the nano-scale, the picture is different. For example, the quantum confinement in semiconductor particles, surface plasmon resonance in metallic nanoparticles and superparamagnetism

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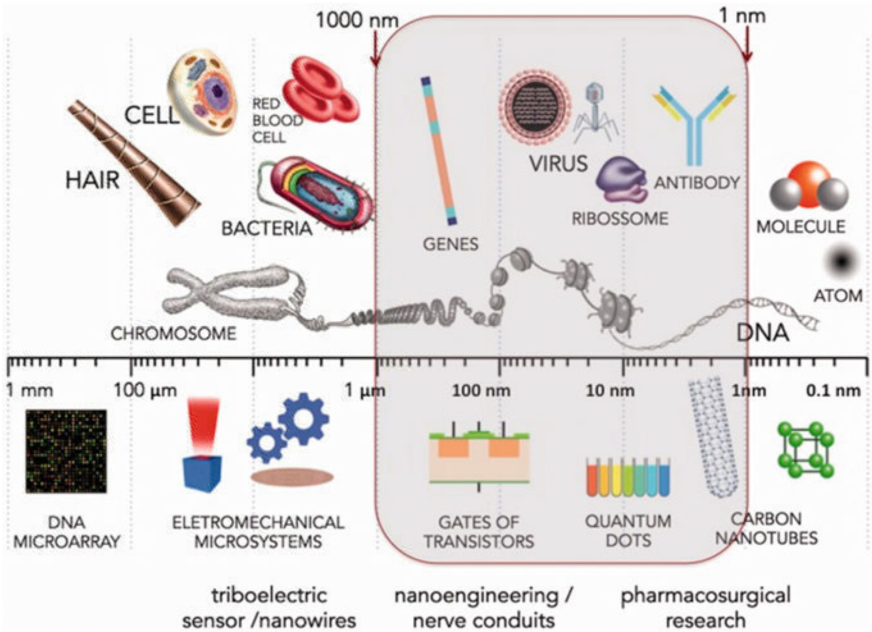

Fig. 1 Illustration of nano-scale range in comparison with the known systems. Adapted from Ref. [1]. Copyright obtained from Taylor & Francis 2017

in magnetic materials have size-dependent properties. When the size reduces to nano-scale, the properties of materials will also change. The percentage of atoms at the surface of a material becomes significant at this stage. One of the most size-dependent characteristic is their magnetic property. Hence, scientists prefer nanoparticles having sizes that are comparable with that of magnetic domains in the corresponding bulk materials [2].

The important physical characteristics of nanomaterials are prescribed by the nano-objects they contain. The two main classifications of nanomaterials are compact materials and nanodispersions. Nanostructured materials come under the category of compact materials. These materials are isotropic in the macroscopic composition, and they consist of contacting nanometer-sized units as repeating structural elements. In the second category, nanodispersions comprise a homogeneous dispersion medium like a vacuum, gas, liquid or solid and nano-sized inclusions diffused in this medium and secluded from each other. In these dispersions, the distance between the nanoparticles can be varied from fractions of a nanometer to tens of nanometers. The latter case deals with nanopowders whose grains are separated by thin layers of light atoms and thus prevent the agglomeration or cluster formation of these materials. The most interesting materials for magnetic investigations are the materials containing magnetic nanoparticles and isolated in non-magnetic matrices at the distances longer than their diameters.

2 Magnetic Nanoparticles

Nanomaterials having magnetic elements like iron, nickel, chromium, cobalt, manganese and their chemical compounds are commonly known as magnetic nanoparticles (MNPs). They are superparamagnetic in nature. These particles can be used both in their bare form or coated with a surface coating and functional groups chosen for specific uses. Among them, the most quested nanoparticles are the ferrite nanoparticles. These particles can be grown by clustering of a number of individual superparamagnetic nanoparticles. The cluster of these particles will form magnetic beads.

Under the action of an external magnetic field from an electromagnet or a permanent magnet, these magnetic nanoparticles can attach to a functional molecule, and thus, they allow the transportation to a targeted location. The surface coating helps to prevent the aggregation and reduces the interaction of the particles with the system environment. Their stability in the solution can be improved by using surfactants, silica, silicones or phosphoric acid derivatives. Overall, functionalized MNPs have been broadly used in quite a lot of medical applications, for instance, immunoassay, diagnostic testing, cell isolation and drug delivery [2–4].

2.1 Physical Properties of MNPs

The movement of particles having mass and electric charges such as electrons, protons, positive and negative ions in the material is responsible for magnetic effects. The magnetic dipole formed due to the spinning motion of the electrically charged particle is called a magneton. These magnetons can be seen as clusters in ferromagnetic materials. Some exchange forces make all these magnetons to align in the same direction in a ferromagnetic material, and this refers to the ferromagnetic domains. A ferromagnetic material can be distinguished from paramagnetic material due to these domains. A ferromagnetic material can be made into a single domain by decreasing its size below a critical value. The smallest free-energy state of ferromagnetic particles possesses uniform magnetization only when the size of the particle is smaller than a certain critical size, and all others will have a nonuniform magnetization. These are usually referred to as single-domain particles and multidomain particles, respectively. The hysteresis loop characterized by remanence and coercivity explains the nature of ferromagnetic materials in an applied magnetic field, in which the coercivity corresponds to the thickness of the curve. The coercivity is a size-dependent parameter. The size of a particle and coercivity has a Gaussian relationship. This means when the size of the particle decreases, coercivity increases to the maximum and then reduces to zero (Fig. 2).

Superparamagnetism will occur when the coercivity becomes zero. This will happen as the size of the single-domain particle further reduces below a critical diameter. Thermal effects are responsible for superparamagnetism. The thermal

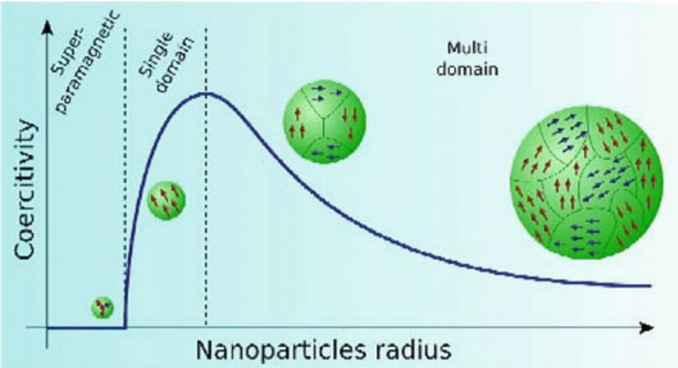

Fig. 2 Illustration of coercivity-size relation in MNPs. Adapted from Ref. [3]. Copyright obtained from Springer 2012

fluctuations in superparamagnetic particles are much stronger to spontaneously demagnetize a formerly saturated congregation. Thus, the coercivity of these particle will become zero and shows no hysteresis. Nanoparticles show magnetic behavior only in the presence of an external magnetic field, and all other times, they are in a non-magnetic state. This gives them an exceptional benefit of functioning in biological environments [3, 5, 6].

2.2 Magnetic Behavior of MNPs

There are five types of magnetism. The orbital motion of electrons in an atom produces atomic current loops, and they try to oppose the applied magnetic field. Most of the materials show this kind of repulsive behavior, and this is known as diamagnetism. Since the diamagnetism is very weak and other magnetic properties possessed by the material thus overpowers the effects of the current loops. Generally, the materials with filled electronic subshells whose magnetic moments are paired will show diamagnetic behavior. Since all the magnetic moments are paired, there will be zero magnetic moments. They also have a negative susceptibility ($\chi < 0$), and they are weakly repelled by a magnetic field. All these effects can be overcome only if there will be a net magnetic moment. Paramagnetic behavior can be seen in materials which possess uncoupled magnetic moments. Hence, here they have a small positive magnetic susceptibility ($\chi \sim 0$). Ferromagnetic materials have aligned atomic magnetic moments of equal magnitude. The crystalline structures of these ferromagnetic materials permit direct coupling interactions between the moments that cause an increase in the flux density. Since the magnetic moments are aligned in a ferromagnetic material, they show spontaneous magnetization in the absence of an external magnetic field (Fig. 3). Materials that retain permanent magnetization even after the removal of an external field are called hard

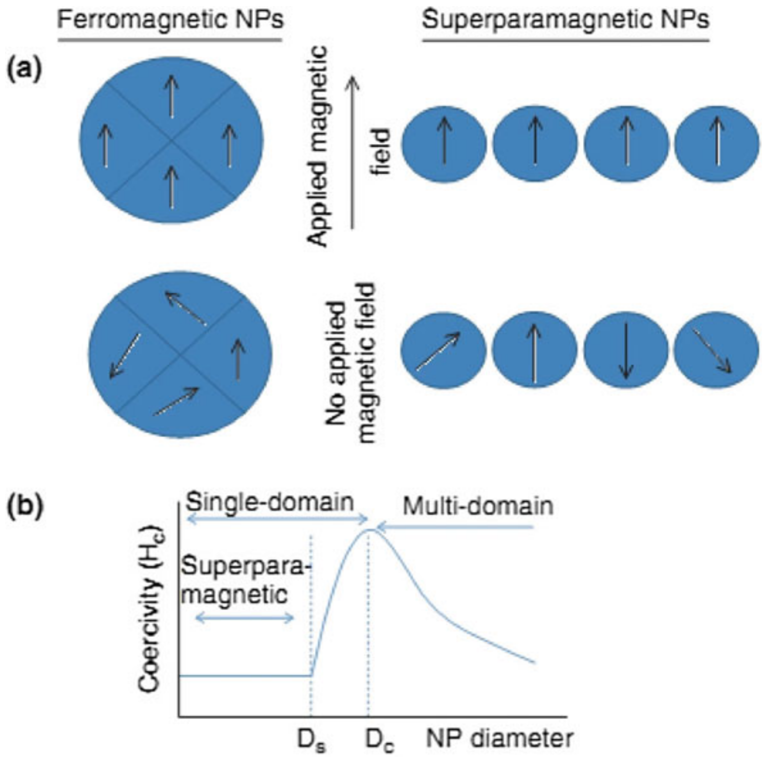

Fig. 3 **a** Ferromagnetic and superparamagnetic NPs; nature of magnetization under applied magnetic field. **b** Relationship of magnetic domain structures with particle diameter; D_s and D_c are the superparamagnetic and critical size thresholds. Adapted from ref. [3]. Copyright obtained from Springer 2012

magnets. Antiferromagnetism can be seen in materials having atomic magnetic moments of equal magnitude that are arranged in an antiparallel way. They also have a zero net magnetization. Above Neel temperature, the random fluctuation of equal and oppositely aligned atomic moments of materials exhibit paramagnetic behavior. As a consequence, their long-range order disappears. An ordered but nonparallel arrangement of atoms of some materials in a zero applied field below a certain characteristic temperature shows ferrimagnetic behavior. Commonly speaking, the antiparallel alignment of neighboring non-equivalent sublattices within a magnetic domain results in a substantial net magnetization [3, 5, 6].

2.2.1 Magnetocaloric Effect

The heating up of some magnetic materials in the presence of a magnetic field and cooling down after removing it is known as the magnetocaloric effect (MCE) [7].