CHAPTER 2

BIOMEDICAL APPLICATIONS OF MNPs
2.1. Introduction

The development of new nanomaterials (NMs) especially magnetic nanoparticles (MNPs) have been studied extensively for the diagnosis and/or treatment of different diseases in biomedical research field. Some of the important field of applications are magnetic resonance imaging (contrast agents), biosensors (immunosensors, enzyme sensors), targeted drug delivery (drug nanocarrier), magnetic particle hyperthermia (heating mediators), cell tracking and separation (labels) and magnetically guided gene transfection etc. [1–6]

Decorated with special functionalities, MNPs allow the application of different molecular imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), single-photon emission tomography (SPECT), positron emission tomography (PET), ultrasound imaging, and optical imaging methods. [7] Their fascinating and unique properties are also exploitable across a range of therapies, including chemotherapy, photodynamic therapy, neutron capture therapy, thermal therapy, and magneto-therapy. NPs may be engineered that permit a combination of these therapies to be used, leading to synergetic medical effectiveness. The properties which define in vivo fate of NPs include size; shape, composition, hydrophilic-lipophilic balance, biodistribution, biocompatibility and surface charge of the NPs. [8-10] some of the important biomedical applications of MNPs are summarized in this chapter.

2.2. Biomedical applications of MNPs

The biomedical applications of magnetic particles can be traced back to the 1950s, when Gilchrist and co-workers treated lymphatic nodes and metastases by injecting metallic particles, which were heated using a magnetic field [11]. Analysing complex networks in animals using electrical or optical methods is challenging, because electrical fields are strongly attenuated by tissues. Therefore magnetic fields are promising for truly remote stimulation as they interact weakly with biological molecules and can penetrate deep into the body [12]. Indeed, there is a common assumption that the small size of NPs allows them to easily enter and traverse tissues, cells, and organelles since the actual
size of engineered NPs is similar to that of many biological molecules (e.g. proteins) and structures (e.g. viruses).

However, as pointed out recently [13], NPs may not freely or indiscriminately cross all biological barriers but these processes may instead be governed by the specific physico-chemical properties of the NPs themselves as well as the identity of the functional molecules added to their surfaces. Clearly, then, an increased understanding of the mechanisms that dictate the behavior and fate (biodistribution) of NPs upon introduction into the body is instrumental for the prediction of the potential toxicological responses to such nanomaterials (biocompatibility). Several of their characteristics, such as size uniformity, surface area, adsorption kinetics, biocompatibility, superparamagnetism and magnetic moment, can be finely tuned during the production process for specific purposes. Aside from the diverse functionalities conferred by the particle size itself (for instance, colloidal dispersion), magnetism offers additional properties that are of great biomedical interest. In particular, the ability to distally control the position of particles in a given media to induce their accumulation or separation from similar structures has found a spectrum of powerful applications in innovative medicines [14, 15]. For biomedical applications, biocompatible surfactants such as dextran, starch, chitosan, cationic liposomes, polyethylene-amine, poly (ethylene oxide) (PEO), folic acid, and polyethylene glycol have been used to coat magnetic NPs [16-21].

In spite of tremendous advancement in the field of medical science, cancer remains one of the leading causes of death worldwide. Cancer can be treated by various treatments such as chemotherapy, radiotherapy, immunotherapy, hyperthermia therapy etc. Though the treatments chemotherapy and radiotherapy were promising cancer modalities, complete cure of cancer without pronounced side effects and without damaging the normal cells is prime challenge in this field. In recent years development in the field of nanobiotechnology brought us new tools to treat diseases like cancer. One such an important tool is magnetic nanoparticles. Magnetic hyperthermia therapy with magnetic nanoparticles has currently gaining lot of attention in cancer treatment. Hyperthermia is not new to
mankind, as first hyperthermia treatment can be traced back to more than 3 centuries ago. On the other hand, the use of magnetic nanoparticles to treating the cancer is new.

In last two decades tremendous efforts have been taken all over the world to establish magnetic hyperthermia therapy as a major cancer modality. In spite of such effects, still there are no promising outputs except few clinical trials. However it has been found that hyperthermia therapy when used in conjunction with other existing cancer therapies such as chemotherapy and radiotherapy becomes more useful in treating the cancer. Selective heating and remote controlling the heating agents make it suitable for cancer non-invasive technique. Therefore in the present thesis, an attempt has been taken to prepare magnetic heating agents coated with biocompatible polymers and elaborated their effectiveness in magnetic particle hyperthermia treatment for cancer. Therefore the MNPs provide a synergetic effort of diagnosis (Magnetic resonance imaging) and treatment (Drug delivery and magnetic particle hyperthermia) for treating cancer. The principles and role of MNPS involved in these applications are discussed below.

2.2.1. Magnetic resonance imaging

Imaging of human internal organs with high spatial resolution is very important for medical diagnosis, treatments and follow-up. In this respect, magnetic resonance imaging (MRI) marks a very important breakthrough as it offers the ability to achieve extraordinarily high temporal and spatial resolution in addition to its non-invasive feature in comparison with X-ray-based imaging techniques. MRI was invented in the early 1970s [15]. The first commercial set up capable of human scanning appeared about 10 years later [16]. Now it has become one of the most important and powerful clinical diagnostic tools [22].

The fundamental working principle of MRI is based on computer-assisted imaging of relaxation signals of proton spins within the human body excited by radiofrequency waves in a strong magnetic field. Although MRI itself gives
detailed images, making a diagnosis based purely on the resulting images may not be accurate, since normal tissues and lesions often show only small differences in relaxation time. MRI contrast agents can help to clarify images which allow better interpretation. The most successful type which has widely been investigated consists of gadolinium-based small molecular complexes, e.g. Ga-DTPA (diethylenetriaminepentaacetic acid) [19-21]. Its main clinical applications are focused on detecting the breakage of the blood brain barrier (BBB) and on changes in vascularity, flow dynamics, and perfusion.

Superparamagnetic iron oxide (SPIO) is a different class of contrast agents, and it has received great attention since its development as a liver contrasting agent 20 years ago [22]. It was the first nanoparticulate MRI contrast agent, and is still used clinically. Gd-based contrast agents enhance the signal in $T_1$-weighted images [23]. On the other hand, SPIO provides a strong contrast effect in $T_2$-weighted images, due to its different contrasting mechanism [21]. Furthermore, its nanoparticulate properties represented by the nanosized dimension and shape allow different biodistribution and opportunities beyond the conventional imaging of chemical agents. The recent development of cellular and molecular imaging enables visualization of the disease-specific biomarkers at the molecular and cellular levels, which has led to increased recognition of NPs as MRI contrast agents in which iron oxide NPs has been the prevailing and only clinically used nanoparticulate agent.

**Basic principles of contrast agents**

‘Contrast’ refers to the signal differences between adjacent regions, which could be ‘tissue and tissue’, ‘tissue and vessel’, and ‘tissue and bone’. Contrast agents for X-ray and CT show contrasting effects according to the electron-density difference, and they produce direct contrast effects on their positions. However, the contrast mechanism is more complicated for MRI, where the contrast enhancement occurs as a result of the interaction between the contrast agents and neighbouring water protons. This can be affected by many intrinsic and extrinsic factors such as proton density and MRI pulse sequences. The basic
principle of MRI is based on nuclear magnetic resonance (NMR) together with the relaxation of proton spins in a magnetic field [23, 24a].

When the nuclei of protons are exposed to a strong magnetic field, their spins align either antiparallel or parallel to the magnetic field. During their alignment, the spins precess under a specified frequency, known as the Larmor frequency \(w_0\), see Fig. 2.1a). When a ‘resonance’ frequency in the radio-frequency (RF) range is introduced to the nuclei, the protons absorb energy and excited to the antiparallel state. After the disappearance of the RF pulse, these excited nuclei relax to their initial, lower-energy state (Fig. 2.1b). There are two different relaxation pathways. First, known as longitudinal or \(T_1\) relaxation which involves the decreased net magnetization \(M_n\) recovering to the initial state (Fig. 2.1c). The second, called transverse or \(T_2\) relaxation, involves the induced magnetization on the perpendicular plane \(M_{xy}\) disappearing by the dephasing of the spins (Fig. 2.1d). Based on their relaxation processes, the contrast agents are classified as \(T_1\) and \(T_2\) contrast agents. Usually commercially available \(T_1\) contrast agents are paramagnetic complexes, while \(T_2\) contrast agents are based on iron oxide NPs, which are the most representative nanoparticulate agents. When a RF pulse is applied to spins, transverse magnetization on the xy-plane \(M_{xy}\) perpendicular to the direction of the static magnetic field is generated (Fig. 2.1 b). Net magnetization \(M\) as a vector has the components of \(M_z\) and \(M_{xy}\), which produce the interrelated process of spins. The change in \(M_z\) is due to energy transfer, whereas that in \(M_{xy}\) is due to the process of spin dephasing, that is, the randomization of the magnetization of excited spins with the same phase coherence immediately after the application of an RF pulse.
Their phase coherence in xy-plane disappears due to the difference of magnetic field experienced by the protons. The magnetic-field difference is produced by the system performance in shimming and the magnetic properties of imaging objects. Although the inhomogeneity of the static magnetic field by the system imperfection can be reduced by a variety of tools, including shimming coils and shimming algorithms and the usage of the spin echo sequence to reverse this effect, it affects the decay of transverse magnetization. As another source of field inhomogeneity, the magnetic properties of imaging objects can cause phase incoherence. The spin–spin interaction between the hydrogen nuclei or electrons causes a loss of transverse coherence, which produces the true and characteristic T2 relaxation of tissues. For example, the proton interaction of macromolecules in tissue can induce a local magnetic field, as well as a change in the actual magnetic field in their vicinity. Furthermore, local magnetic field
gradients can be induced from the differences in the magnetic susceptibility between the adjacent and different tissues or by contrast agents [24b].

Therefore, transverse relaxation is affected by inhomogeneous magnetic fields produced from tissue-inherent factors or external sources, and the total relaxation time, $T_2^*$ is described by:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma B_s,$$

where $\gamma B_s$ represents the relaxation by the field inhomogeneities and is called susceptibility effect. The magnetization of paramagnetic materials such as gadolinium complexes is directly dependent on the number of ions and they have no net magnetization in the absence of an external magnetic field. However, ferromagnetic iron oxides have very large magnetic susceptibility which can persist even upon removal of the external magnetic field. Nanosized iron oxide particles are superparamagnetic, losing their magnetization in the absence of an external magnetic field. When an external magnetic field is applied, they exhibit strong magnetization, which can cause microscopic field inhomogeneity and activate the dephasing of protons. Therefore, iron oxide NPs shorten $T_2$ and $T_2^*$ relaxation times of the neighbouring regions, and produce a decreased signal intensity in $T_2$- and $T_2^*$-weighted MR images.

### 2.2.2. Drug delivery

Drug delivery is an intriguing field of research that has captured the interest of researchers because delivering a medicine to its site of therapeutic action is one of the main limitations of pharmaceutical and biotechnology industries. The field of drug delivery has also attracted the attention of the pharmaceutical industry because it offers a strategic tool to expand current drug markets; new delivery technologies could repackage classic drugs, thus offering a competitive edge after the expiration of patents and preclude competition from generics. Targeted drug-delivery systems can convey drugs more effectively and conveniently than those of the past, increase patient compliance, extend the product life cycle, provide product differentiation and reduce healthcare costs.
A drug delivery system (DDS) is defined as a system in which the bioactive agent (drug) is integrated with a non-active agent (carrier) in such a way that the drug is released from the carrier in a predetermined manner, at a constant rate in what is known as zero-order release, in a cyclic manner, or in response to an external trigger such as a change in pH, ionic strength or temperature of the medium [25-27]. Ideally the carrier system, whether it is synthetic or natural, should be able to provide a nontoxic support system that can be manufactured on an industrial scale and can be translated into a cost-effective, clinically practical medicine. In addition to controlling the rate and duration of the drug release, the DDS should be able to target the drugs to specific organs and tissues, as well as individual organelles within the individual cells (i.e. tumors, bacterial cells of definite species) or respond to a biofeedback mechanism such as glucose levels in hyperglycemia patients.

Thus, although efficient drug delivery is one of the most prominent problems faced by the biotechnological and pharmaceutical industries, nanotechnology can promote the innovative utilization of the myriad existing drugs produced by these industries. Nanotechnology focuses on formulating therapeutic agents in biocompatible nanocarriers, such as NPs, nanocapsules, micellar systems and dendrimers. Moreover, one of the major advantages that nanotechnology offers is targeted drug delivery to the site of disease. This can be achieved either through passive targeting of drugs to the site of action or by active targeting of the drug (Figure 2.2) [27-31]. The application of nanobiotechnology to drug delivery has benefited all streams of medical science with oncology being the foremost.

2.2.2.1. Passive targeting

Passive targeting exploits the anatomical differences between normal and diseased tissues to deliver the drugs to the required site because the physiology of diseased tissues may be altered in a variety of physiological conditions through the enhanced permeability and retention (EPR) effect. This occurs because tumor vasculature is leaky; hence circulating NPs can accumulate more
in the tumor tissues than in normal tissues. Besides exploiting the structural framework of cancerous tissues, the EPR effect is also observed at the site of inflammation. The only difference between infection-induced EPR effect and that of cancer is duration of retention period; the retention in normal tissue, where inflammation occurs, is shorter than with cancer because the lymphatic drainage system is still operative; thus swelling may dissipate in a matter of a few days. The EPR effect has been greatly exploited for delivering various therapeutics at the site of action and many studies potentially support this mechanism of passive targeting. A number of passively targeting nanocarriers were developed in the 1980s and 1990s. One of the examples is Doxil (or Caelyx), a sterically stabilized PEGylated liposome that encapsulates doxorubicin. Doxil has shown good drug retention in the liposomal formulation with enhanced circulation time and is up to 6 times more effective in comparison with free doxorubicin. It was approved for the treatment of metastatic breast cancer, advanced ovarian cancer and AIDS-related Kaposi's sarcoma. Both in animal models and in patients, such systems have been shown to result in significant improvements in reduction of tumor size, working through the EPR mechanism [32].

**Figure 2.2.** Schematic representation of different drug-targeting approaches
2.2.2.2. Localized delivery

Another approach is the direct intratumor delivery of anticancer agents using NPs which can be used in the treatment of local cancers such as prostate, head and neck cancers. NPs not only act as an effective carrier for such drugs; protecting them from undesirable physiological conditions but also allow selective and controlled release of drugs at their target sites [33].

2.2.2.3. Active targeting

Active targeting, on the other hand requires the conjugation of receptor specific ligands that can promote site specific targeting [34, 35]. The success of drug targeting depends on the selection of the targeting moiety, which should be abundant, have high affinity and specificity of binding to cell surface receptors and should be well suited to chemical modification by conjugation. The active targeting can be achieved by molecular recognition of the diseased cells by various signature molecules overexpressed at the diseased site either via the antigen-antibody interactions, ligand-receptor or by targeting through aptamers.

The therapeutic agent can be actively targeted by conjugating the carrier with a cell or tissue-specific ligands thereby allowing a preferential accumulation of the drug at the diseased site. Thus, the submicron size range of nanosystems as well as the ability to couple/conjugate different targeting ligands offers excellent opportunities to breach the physiological barriers and access different tissues followed by an efficient cellular uptake and intracellular internalization; various nanosystems can be accumulated at higher concentrations than normal drugs.

2.2.3. Magnetic particle hyperthermia (MPH)

Targeted delivery and therapies for cancer are more than “hot” topics for scientists and clinicians. This concept has been introduced and discussed by the popular press and is now sought by cancer patients. Several cancer-specific molecules can be used to bind to cancer cells to deliver NPs to malignant cells [36]. Recently, hyperthermia using magnetic NPs has emerged as a promising
cancer modality either alone or in combination with existing modalities like radiotherapy and chemotherapy.

The concept of using heat to treat cancer is not new. In the late 1800, physicians were using heat as treatment method for cancer. Clearly, there were no randomized controlled trials to describe hyperthermic treatment of cancer, but many reports described patients “cured” of their disease after undergoing febrile illness or external heating of superficial tumors [36]. Whereas hyperthermia once referred to whole body hyperthermia, depending on a specific location (hyperthermic peritoneal perfusion), or an entire body region (isolated limb hyperthermia), now we can describe hyperthermia in terms of cellular, tissue (i.e. portions of organ), or any of the above combination.

Temperatures above 42 °C will induce cell death in some tissues. Cancerous cells heated to temperatures in the range of 41 °C to 47 °C begin to show signs of apoptosis [33–37], while increasing temperatures above 50 °C is associated with less apoptosis and more frank necrosis. Various types of pharmacologic or biologic agents “death-inducing signalling complexes” [37] activate caspase-8 and cause apoptotic cell death in an orderly fashion. Heat or cold like noxious stimuli can induce proapoptotic proteins to induce caspase-9. Caspase-8 or -9 expression causes a cascade effect that eventually leads to cell death. Apoptosis requires protein creation mechanisms to be intact. Necrosis, however, is a much quicker/sudden cell death. The extreme example involves heating cells to boiling temperatures where the proteins instantly denature and the cells literally fall apart as lipid bilayers “melt.” Cell necrosis, however, is fundamentally based on protein denaturing. Apart from thermal extremes, cell exposure to strong acids and bases can cause necrosis as well. Use of magnetic NPs (ferro- or ferri-magnetic or superparamagnetic) as a heating mediator in hyperthermia was first introduced by Jordan et al [13] in 1993. With rapid development in the field of bionanotechnology in recent years, various attempts have been made to synthesize ferrimagnetic/superparamagnetic NPs for effective hyperthermia. Hyperthermia can then be induced by AMF exposure. Thus,
magnetic NPs can be used for cancer therapy at the same time as diagnosis. (Fig. 2.3.)

Figure 2.3. Schematic illustration of the therapeutic strategy using magnetic particles.

The complete cure of cancer cells without damaging the surrounding healthy cells/tissues is still not achieved with magnetic hyperthermia therapy. The magnetic hyperthermia found more advantageous when used in conjunct with other cancer treatments like radiotherapy and chemotherapy. Hyperthermia is categorized into three parts:

1. Whole body hyperthermia
2. Regional or localized hyperthermia
3. Interstitial hyperthermia

Local hyperthermia may be applied externally to treat tumors near the skin’s surface or with probes to reach deep-seated cancerous tissues. For multiple tumor locations or larger tumors; regional hyperthermia focuses laser, microwave or ultrasound energy on diseased tissues. Whole-body hyperthermia treats cancers that have spread to several regions by using thermal chambers to elevate a patient’s body temperature to just below 42°C (National Cancer Institute). The particles used in hyperthermia exhibit ferro- or ferrimagnetic properties. Ferro- and ferrimagnetic particles display magnetism even in the
absence of an applied magnetic field [39]. An applied alternating magnetic field can provide the energy necessary to reorient the particles’ magnetic moments. This magnetic energy, when dissipated, is converted to thermal energy [40]. In addition to causing changes in the magnetic moments, this energy can force the NPs to physically rotate. Hyperthermia cancer treatment uses the heat generated by this conversion to destroy cancerous tissues. The friction created as NP rotate through viscous fluid to return to their original position also generated the heat. Frictional heating, however, contributes much less than magnetic heating to the particles’ total heat generation.

**Figure 2.4.** Antitumor immune response induced by hyperthermia using magnetite NPs. (A) Rats photographed on the 28th day after the MCL injection. Rat glioma T-9 cells (1×10^7 cells) were transplanted subcutaneously into the left femoral region of F344 rats. On the 9th day after transplantation into the left side, another aliquot of the T-9 cell suspension (1×10^7 cells) was transplanted subcutaneously into the right femoral region. The MCLs were injected into the left tumor only, on the 11th day after the first transplantation. When hyperthermic treatment was repeated three times at 24-h intervals, both tumors had disappeared by the 28th day after the MCL injection. (B) The hypothesis for the mechanism of immune response after hyperthermic treatment using magnetite NPs. [38]
Fig. 2.4 shows the destruction of tumor by means of magnetic hyperthermia therapy [38]. The use of magnetic NPs can improve hyperthermia cancer treatment. Cancerous cells typically have diameters of 10 to 100 micrometers and have been shown to absorb magnetic particles. This increases the effectiveness of hyperthermia by delivering therapeutic heat directly to cancerous cells. NPs can also effectively cross the blood-brain barrier, an essential step in treating brain tumors [39-41].

Many studies have confirmed the feasibility of MPH cancer treatment. Hergt et al [40] performed in vitro experiments to evaluate the heating effects of commercially available magnetite (Fe₃O₄) particles. Study samples consisted of a sphere of compressed magnetite particles embedded in a large volume of KCl/Carrageenan-gel. The samples were exposed to an alternating magnetic field (H = 18 kA/m, frequency = 300 kHz) and the surface temperatures of the particle spheres were recorded. The heat generated depended heavily on particle size, size distribution and microstructure. The results proved that even small amounts of particles with suitable properties can generate the heat required for magnetic particle hyperthermia.

Hilger et al [29] used magnetic particle hyperthermia to treat breast cancer in mice. Fluid containing iron oxide particles was injected into tumors grown from human breast adenocarcinoma cells. Tumor and healthy tissue temperatures were monitored throughout the 4-minute application of the alternating magnetic field (H = 6.5 kA/m, frequency = 400 kHz). Therapeutic temperatures were obtained, but regions of insufficient heating were also observed. Cool spots were consistent with lower concentrations of magnetic fluid, emphasizing the importance of fitting the magnetic particle distribution to the tumor’s shape [41a]. Jordan and others also explored the effects of magnetic particle hyperthermia on mammary carcinoma in mice. Magnetic fluid containing magnetite (Fe₂O₃/Fe₃O₄) particles was delivered by intratumoral injection (0.015 mg magnetite/mm³). Post-injection examination of the cancerous tissues showed deep fluid penetration. An alternating magnetic field (H =6-12.5 kA/m, frequency = 520 kHz) was applied for 20-30 minutes. Widespread death of
cancerous cells was observed after MPH treatment. This study also tracked tumor growth in the 50 days following treatment. MPH treatment halted growth in some tumors, but did not impede growth in others. These differences were attributed to the inconsistent distribution of the magnetic fluid in the tumors. [41b]

2.3. Biocompatibility issue

By virtue of their unique physical and structural properties, engineered nanomaterials have the potential to dramatically improve the treatment and diagnosis of disease. However, the inability to control their pharmacokinetics and biodistribution has hindered widespread realization of this potential [41a]. Most nanomaterial formulations are rapidly sequestered by cells of the mononuclear phagocyte system (MPS) following intravenous administration. The MPS consists of dendritic cells, blood monocytes, and tissue-resident macrophages in the liver, spleen, and lymph nodes that are responsible for clearing, processing, and degrading foreign materials from circulation [42, 43]. On top of lowering the dose available for accumulation at a therapeutic site, MPS uptake can lead to inflammation [13], compromised host defense [44], release of toxic byproducts and redistribution of nanomaterials to sensitive areas in the body. Moreover, uncertainty regarding the eventual fate of nanomaterials after they accumulate in MPS organs raises the possibility of delayed or chronic toxicity. Uncontrolled and often unpredictable localization, along with concerns regarding the toxicity have created a barrier to the clinical translation of many engineered nanomaterials. Tailoring the interaction of nanomaterials with physiological systems has become a major focus of nanomedicine research.

Physiological environments, such as blood, interstitial fluid, and cellular cytoplasm contain complex mixtures of proteins. When a nanomaterial enters a physiological environment, these proteins rapidly adsorb to its surface and form what is known as the protein ‘corona’. The protein corona alters the composition of the nanomaterial along with its aggregation state, giving it a ‘biological
identity’ that is distinct from its ‘synthetic identity’ – the surface chemistry, size, and shape of a nanomaterial after synthesis.

The biological identity is the form of a nanomaterial ‘seen’ by biomolecules, cells, and biological interfaces, and is responsible for the kinetics, transport, and reactivity of a nanomaterial in a physiological system. Adsorption of blood proteins is most relevant and most studied since nanomaterials are typically administered intravenously. Blood contains thousands of different proteins, each of which may potentially interact with a nanomaterial. The blood protein corona is complex, consisting of dozens of proteins including apolipoproteins, adhesion mediators, signalling and transport proteins, complement components, and coagulation factors. Many of these proteins act as opsonins that mark a nanomaterial for efficient uptake by MPS phagocytes either in their native state or after undergoing a conformational change. In addition, adsorbed proteins can modulate the activation of enzymatic cascades, leading to thrombosis or anaphylaxis. Recent study has shown that the synthetic identity of a nanomaterial plays an important role in determining the composition of the protein corona and the subsequent cellular interactions. However, relationships linking the size, shape, and surface chemistry of a nanomaterial to protein adsorption and phagocytic cell uptake are poorly developed [45].

The most widely-applied strategy to prevent nonspecific protein adsorption and phagocyte uptake is to graft nanomaterials with linear chains of biocompatible polymers such as dextran, polyvinyl alcohol, polyethylene glycol etc. Out of which PEG was preferably used not only to block nonspecific protein adsorption but also to increase the blood circulation time. The grafting of PEG chain molecules to nanomaterial surfaces is often known as PEGylation. Grafting nanomaterials with PEG is effective at slowing the rate of MPS uptake and prolonging blood residence time [14, 44, 45]. In essence, a fundamental understanding of nanomaterial toxicology (nanotoxicology) is highly desirable both from the material’s stand point as well as from the biological system’s point of view.
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References:


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[41] (a) S. Nie, Nanomedicine 55 (2010) 52351.


