Magnetic nanoparticles: coating and applications

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Magnetic nanoparticles (MNPs) have great potential in material science, drug delivery, magnetic resonance imaging, and therapeutic applications. Indeed, a number of iron oxide nanoparticles have been withdrawn due to their poor clinical performance and/or toxicity issues. MNPs have successfully been converted into water-soluble, stable, bio-accessible systems using the proprietary various coating strategy. Herein, we summarize the data of applications and coating strategies of MNPs.

iron oxide nanoparticles | functionalization | coating | nanomedicine | applications

1. Introduction

Magnetic nanoparticles (MNPs) represent a significant doorway for various biomedical applications.[1][2][3][4][5][6][7] MNPs have become vital for drug delivery,[1][2] magnetic resonance imaging (MRI),[8][9][10][11] hyperthermia therapy,[4][12] biosensing,[13] and biocatalysis.[13] MNPs are particularly promising tags due to their high physical and chemical stability, cost-effectivity, and optimal surface-to-volume ratio.[14] Iron oxide NPs are promising nanomaterials among magnetic materials due to their excellent biocompatibility, easy synthesis, and price. MNPs can be easily manipulated using an external magnetic field for tumor targeting. The most promising Fe_3O_4 magnetite MNPs are due to their ferrimagnetism characteristics. Numerous works about the synthesis, functionalization, and applications of Fe_3O_4 MNPs have been reported.[15][16][17] The synthesis method plays a key role in determining the morphology, particle sizes, and shape. However, MNPs may not be stable upon oxidation and possess high surface energy, leading to aggregation.[18] Therefore, it is essential to consider the coating of such MNPs. The wrong coating leads to instability in an aqueous solution and biological liquids, toxicity, and high reactive oxygen species formation.[18][19][20]

2. MNPs Coating

MNPs have become materials with great potential. Due to the high surface energy MNPs have some limitations in use because of the ability to form aggregates spontaneously. Therefore, some coating procedures are required for better stability in an aqueous solution. MNPs with a hydrophobic surface are easily absorbed in the protein surface and have low circulation time. Moreover, non-functionalized iron nanoparticles can form reactive oxygen species, which are highly toxic for organisms. The magnetite core can be coated with organic or inorganic compounds, surfactants (oleic acid, lauric acid, etc.), and artificial or natural polymers that lead to stabilization (Figure 1).[20][21]

Biocompatible organic polymers such as polyethylene glycol (PEG), chitosan, dextran are among them. Other coating options are liposomes, silica, silica oxide, and ceramics surface. One advantage of coatings is surface protein absorbance, which can increase circulation time, protect from blood components, and «decrease the toxicity to zero.»[22][23][24] Protein immobilization may facilitate targeted delivery or the formation of a protein-ligand complex. The ligands, for example, can be drug systems for cancer treatment. One protein that can be used for such a procedure is human serum albumin (HSA).[25][26][27] HSA is the most abundant protein in plasma. It is a monomeric multidomain biomolecule, representing the main determinant of plasma oncotic pressure, and displays an extraordinary ligand binding capacity. HSA is a wide platform for drug discovery, suitable transport for therapy, and diagnostics. According to its properties, HSA can lead the transport to cancer tissue due to passive transport (Enhanced permeability and retention effect, EPR-effect) or cancer cells receptors binding (gp60, FcRn, SPARC, etc.).[28]

Figure 1. Schematic representation of possible surface coating of MNPs.

3. Applications

Various applications of MNPs can be attributed to the difference in the behavior of particles in nanoscale compared to their bulk counterparts. High magnetic properties can be used for manipulation by an external magnetic field which leads to possible targeted delivery, magnetic separation, MRI, and hyperthermia effect (Table 1).[1][2][3][4][5][6][7][29][30][31][32] The high surface capacity of MNPs makes it possible to form MNPs-drug or gene complexes that can solve cancer immune resistance and hereditary diseases. Furthermore, drug targeting is promising for avoiding the side effects of conventional chemotherapy by reducing the distribution of drugs, increasing tissue selectivity, and lowering the doses of cytotoxic compounds. Possible surface functionalization can be a primary factor in producing various smart systems for therapy and diagnostics. Furthermore, incorporating a drug or gene can be achieved by coating with agents that provide coupling points for conjugation, complexation, or encapsulation. The use of MNPs in the drug delivery area is a specific, sensitive, and cost-effective strategy with excellent efficiency potential.

Table 1. Various applications of MNPs.

1	contrast agents for MRI[8][9][10][11][30]
2	carriers for target-specific drug delivery[1][2][33]

3	carriers for gene therapy[1][2][29][33]
4	hyperthermia based cancer treatments[4][12]
5	carriers for vaccine and antibody production
6	nanoplatforms for therapy (the nucleus of smart constructions)[6]
7	magnetic separation with further preparation of pure compound or detection of compounds, metabolites, etc.
8	magnetic sensing probes for in vitro or i*n vivo* diagnostics[13][33]

Further applications include an enhanced separation and detection of low concentration targets. These MMPs can also help isolate nucleic acids, proteins, hormones, pathogens, and small molecules in a complex biological matrix. Certain molecules presented in low amounts can predict the diseases, and their detection is appropriate for saving the lives of patients. For example, nucleic acid diagnostics plays a vital role in many fields, such as biology and medicine. The use of MNPs to discriminate wild-type and mutant DNA is vital for cancer diagnostics. Short RNA detection helps to identify the deregulation of various biological pathways, such as cell proliferation, differentiation, and apoptosis. Like nucleic acids, proteins are key biological molecules in organisms. Numerous examples of proteins are dispersed through an organism, including hormones, antibodies, enzymes, etc. Abnormal protein quantities or the appearance of antibodies can lead to disease or be a predictor of disease. Therefore, sensitive and specific diagnosis techniques are necessary.

MRI is a great non-invasive diagnostic tool in various research fields and medical diagnostics. Usually, MNPs generate local magnetic fields that interfere with the transverse relaxation time (T_2) of protons, resulting in a darker signal in tissue. Furthermore, producing MNPs with targeting moieties leads to the possible detection of targeted molecules or diseases on the organism level. The possible use of MNPs for imaging and hyperthermia therapy opens the area of theranostics production.

4. Conclusion

MNPs demonstrate high potential for various areas that combine the synergistic effects of magnetic and multifunctional nanomaterial parts. MNPs can be efficiently used in various systems to detect molecules or targets or be a biocompatible nucleus for smart construction. An ideal nanoparticle for biological application should have the following features: easy administration, excellent *in vivo* stability and biocompatibility, and selectivity. The ability to observe the accumulation of the MNPs in real-time, disease progression, and simultaneous hyperthermia and chemotherapeutic therapy can solve the problem of drug-resistance cancer. However, multifunctional smart MNPs exhibiting all these features are extremely rare. The next-generation MNPs may solve many problems in different areas of research and medicine.

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