Review Article

Magnetite (Fe₃O₄) - Synthesis, Functionalization and its Application

Aneela Hameed*, Hafiza Mehvish Mushtaq, Majid Hussain

Institute of Food Science and Nutrition, BahauddinZakariya University, Multan

Abstract

Nanoparticles are smaller than 100nm. Size of particle depends upon the method that is used for synthesis of nanoparticles. Magnetic nanoparticles consist of iron, cobalt and nickel and their chemical compounds. Their safety or toxicity is major concern for use in food. Magnetite, hematite and meghemite are types of magnetic nanoparticles. Magnetite (Fe₃O₄) common among the magnetic iron oxide nanoparticle that is used in food industry. Magnetite is getting popular due to its super paramagnetic properties and lack of toxicity to humans. Different methods are used to synthesize magnetic nanoparticles. Upon contact with air these particles loses magnetism and mono-dispersibility. To overcome this problem these nanoparticles are coated with natural or synthetic polymers, metals, organic and inorganic substances to create stable and hydrophilic nanostructures. Due to easy separation with magnet these magnetic nanoparticles are used as an affinity probe to remove bacteria from different food samples and have food related applications e.g, protein purification, enzyme immobilization and food analysis. These magnetic nanoparticles also used for removal of heavy metals and used in medical field.

1. Nanoparticles and Nanotechnology

The branch of science deals with Nano sized structures is known as nanotechnology and it has great position in agriculture, biomedical, pharmaceutical and many others divisions of science. It is a branch of science where nanoparticles are used in biological and biomedical application. It describes all sides of biological study (Sapsford et al., 2013).

Nanoparticles are smaller than 100 nm. Size of particles depends upon the method that is used in the production of nanoparticles and the raw materials. Nanoparticle size affects the physiochemical stability and biological activity. They have high surface area to volume ratio, resulting into a surface with very high free energy content. These particles have positive, negative or neutral charges that depend on the material used for the synthesis. During the synthesis polar particles dissolved in aqueous media but non-polar particles combine to form aggregates (Joye, Davidov-Pardo, & McClements, 2014).

2. Benefits in Food Sectors

Nanotechnologies offer benefits to food divisions. The applications of nanotechnologies seem to be related to needs in food divisions. Comparison of its applications and food sector needs is listed in Table 1.

Nanoparticles are capable to bind with bacterial cell wall. Lipopolysaccharides, Phospholipid, proteins and lipoteichoic acid are important component of bacterial membrane and exist on the surface of bacteria. The functional group of these biomolecules help bacteria adheres to various surfaces and in proliferation (Jiang, Yang, Vachet, & Xing, 2010).
Magnetite is getting popular due to its super paramagnetic properties and lack of toxicity to humans. These nanoparticles loses magnetism and mono-dispersibility upon contact with air (Mahdavi et al., 2013).

Table 1: Applications of nanoparticles in food sector

Sr. No.	Food sector needs	Nanotechnology applications
1.	To decrease in the use of agrochemicals	Safe food production
2.	To reduction in the occurrence of food-borne diseases	Hygienic food processing, packaging and storage
3.	To decrease in the use of artificial colors, flavors, preservatives	Maintenance of freshness and purity
4.	To reduce in salt, fat and sugar intake	Healthy, nutritionist and safe food
5.	To produce new and improved products	Improved taste and flavors
6.	To increase uptake and bioavailability of nutrients/supplements	Functional food for different lifestyles and consumers group
7.	To reduce food spoilage	Improved shelf life products
8.	To decrease in the cost of transportation of food products in the supply chain	Advanced functional packaging

Source: (H. Chen & Yada, 2011)

To overcome this problem, these are coated with natural or synthetic polymers to make stable and hydrophilic nanostructures that provide large number of surface functional group which are used for further modifications (Honary, Ebrahimi, Rad, & Asgari, 2013). Nanoparticles are coated with stabilizers such as polymers and surfactant to prevent aggregation and to stabilize them (T.-Y. Liu, Hu, Liu, Liu, & Chen, 2008). Coating type and its arrangement on magnetic core determine size and biological fate of particles (Chastellain, Petri, Gupta, Rao, & Hofmann, 2004).

3. Types of Magnetic Iron Oxide Nanoparticles

Three types of iron oxides are most common; hematite (α-Fe_2O_3), magnetite (Fe_3O_4), and meghemite (γFe_2O_3). These iron oxides have definite magnetic, catalytic and biomedical properties (Cornell, 2003).

3.1 Hematite (α-Fe_2O_3)

It is most stable n-type semiconductor under ubiquitous conditions and used as a starting material for the synthesis of magnetite (Fe_3O_4) and meghemite (γ-Fe_2O_3) (Wu et al., 2010). Hematite, due to coupling between Fe_3 ions across crystallographic plane, is weakly ferromagnetic (Xu, Habib, Gee, Hong, & McHenry, 2015).

3.2 Magnetite (Fe_3O_4)

Fe_3O_4 has a cubic inverse spinel structure. It can be both an n- and p-type semiconductor. Due to its small band gap (0.1eV) it has the lowest resistivity among iron oxides (Boxall, Kelsall, & Zhang, 1996). Magnetite is ferromagnetic because alternating Fe_2 and Fe_3 lattice separated by oxygen atoms that allow for electronic coupling (Dobson, 2001; S. Sun & Zeng, 2002).

3.3 Maghemite (γ-Fe_2O_3)

The structure of γ-Fe_2O_3 is cubic. It can be considered as fully oxidized magnetite, and it is an n-type semiconductor with a band gap of 2.0eV. It is ferromagnetic and have inverse spinal structure (Y.-k. Sun, Ma, Zhang, & Gu, 2004).

3.4 Magnetic properties

Ferro and ferrimagnetic material nanoparticles shows distinctive form of magnetism below certain size 10-

Table 2: Properties of iron oxides nanoparticles

Sr. No.	1	2	3	4	6
Types	**Molecular formula**	**Density(g/cm^3)**	**Melting point^{0}C**	**Structure**	**Magnetism**
Magnetite	Fe_3O_4	5.18	1538	Inverse spinal	Ferromagnetism
Hematite	αFe_2O_3	5.26	1350	Corundum	Weakly ferromagnetism
Meghemite	$\gamma\, Fe_2O_3$	4.87	-	Inverse spinal	Ferrimagnetism

Source: (Teja & Koh, 2009)

20nm known as super-paramagnetic (Mikhaylova et al., 2004). In Ferro-magnetic materials domains are formed in the absence of external magnetic field. The size of each domain depends upon material (J. H. Lee et al., 2010). The walls of these magnetic domains moved by applying magnetic field and the movements of these domain walls give rise to hysteresis loop of ferromagnetic materials. Magnetization curve show saturation magnetization Ms, remanence magnetization Mr (residual magnetization at zero applied field strength) and the coercivity Hc. Coercivity, "intensity of magnetic field that is required to reduce magnetization from saturation to zero. (Livingston, 1981).

4. Synthesis of Magnetic Iron Oxide Nanoparticles

Nano materials formed during volcanic eruption by weathering of mineral (Hough et al., 2008). Bottom up approach in literature is wet chemical process (Wang & Xia, 2004). John Turkevich familiarized simple method to synthesized mono dispersed and stable colloidal gold nanoparticles in solution (Turkevich, Stevenson, & Hillier, 1951). Metal ion (Au^{3+}) reduced in solution, metal atoms adding to the surface of a growing nanoparticle (Schmid, 2011).

To prevent cluster formation of these nanoparticles these are stabilized by long chain molecules or ionic ligands. Nanoparticles synthesized by wet chemical process referred as colloids, small particles dispersed in solution evenly. The most common method that is used in industry is vapor phase synthesis. Bulk material is vaporized and condensed, nanoparticles form from nucleation and growth processes. Principle in this method is that gaseous phase become supersaturated to a point where it is thermodynamically suitable for nucleation of particles followed by condensation of remaining vapors.

By this method large quantity of material produced. In comparison to wet chemical process, vapor phase method has poor defined size and shape of particles. Researchers favor biological synthesis of nanoparticles. Species of bacteria and fungi and plants possess metabolic tool for synthesis of metals nanoparticles from metal ion precursors by both intra and extra catalysis (Narayanan & Sakthivel, 2010; Rai, Yadav, & Gade, 2008). Almost 50 species of bacteria known as nanoparticle producers including *Bacillus subtilis* (Beveridge & Murray, 1980), *Escherichia coli* (Du, Jiang, Liu, & Wang, 2007) and *Pseudomonas aeruginosa* (Husseiny, El-Aziz, Badr, & Mahmoud, 2007).

Various methods are used for preparation of magnetic nanoparticles:

- ✓ Co-precipitation
- ✓ Thermal decomposition
- ✓ Hydro- or solvothermal method
- ✓ Sol-gel polyol method
- ✓ Micro emulsion
- ✓ Sonolysis
- ✓ Microwave assisted synthesis
- ✓ Biosynthesis
- ✓ Electrochemical method
- ✓ Aerosol/vapor method

Table 3: Comparisons of different processes used to produce magnetic iron oxides nanoparticles

Technique	Reaction and condition	Temperature (^{o}C)	Duration	Mass distribution	Nature	Output
Co- precipitation	Easy, ubiquitous	20-150	Minutes	Comparatively excellent	Good	High
Thermal decomposition	Complicated, still atmosphere	100-350	Hours- days	Outstanding	Superb	High
Hydro-or solvothermal synthesis	Easy, high pressure	150-220	Hours-days	Outstanding	Superb	High
Sol-gel polyol method	Complicated, ubiquitous	25-200	Hours	excellent	Acceptable	Medium
Micro emulsion	Complicated, ubiquitous	20-80	Hours	excellent	Acceptable	Low
Sonolysis	Easy, ubiquitous	20-50	Minutes	excellent	Bad	Medium
Microwave assisted synthesis	Easy, ubiquitous	100-200	Minutes	standard	Acceptable	Medium
Biosynthesis	Complicated, ubiquitous	Room temperature	Hours-days	Approximate	Bad	Low
Electrochemical method	Complicated, ubiquitous	Room temperature	Hours-days	Standard	Standard	Medium
Aerosol/vapor method	Complicated, still atmosphere	›100	Minutes-hours	comparatively excellent	Standard	High

(Wu, Wu, Yu, Jiang, & Kim, 2015)

4.1 Co-precipitation

The co-precipitation process is simplest and efficient chemical pathway to produce super-paramagnetic iron oxide nanoparticles (SPIONs). (López-López, Durán, Delgado, & González-Caballero, 2005). Transformation of mono dispersed magnetite from ferromagnetism to para-magnetism when diameter of particles lower than 20nm is known as super-paramagnetism (Woo et al., 2004). Magnetite magnetized in magnetic field and not retains magnetism when magnetic field is removed. Chemical co-precipitation involves co-precipitation of ferric and ferrous by adding base usually NaOH (D. K. Kim, Mikhaylova, Zhang, & Muhammed, 2003) or NH$_3$ (T. Liu, Cheng, & Yang, 2005). 16.25 FeCl$_3$ and 6.35 g of FeCl$_2$ dissolved in 200 mL deoxygenated distilled water. 2M NaOH added and stirring for 60 minutes and pH of solution ± 12. Completed precipitation of Fe$_3$O$_4$ at pH between 8 and 14 (Laurent et al., 2008). Cooled to room temperature, and precipitates separated by magnet, washed with deoxygenated distilled water till pH neutral. Finally Fe$_3$O$_4$ washed with acetone and dried in oven at 60-700C.

5. Surface Coating

For practical use of magnetic nanoparticles (MNP's), excluding the selection of suitable magnetic core, well modification of surface coating material is a main task. Surface modification changes the magnetic properties of magnetic materials so the performance of MNP's depends upon the type of material that is used for coating and how this material link with the magnetic core surface (Umut, 2013).Surface coating of MNP's plays an important role in biomedical applications. Organic and inorganic surface coating is important to reduce the agglomeration of MNP's, provides good biocompatibility and serve as a base for further modification (Umut, 2013).

5.1 Surface coating materials

Organic, inorganic substances and polymers are used for coating. Some organic molecules oleic acid, sodium oleate and dodecylamine used for coating. These molecules enhance water solubility of magnetic nanoparticles. Silica is most common inorganic materials used for this purpose due to their biocompatibility.

Polymers that are commonly used for coating are polyethyleneimine, polyvinyl alcohol, polyethylene glycol, dextran and chitosan (Umut, 2013).

5.1.1 Silica (SiO₂)

Silica is inorganic material that is commonly used for coating. The advantages of silica coating are, silanol groups are present on the surface which react with coupling reagent and provides strong attachment of surface ligand on magnetic nanoparticles (Ulman, 1996). Silica coating provides good stabilization to magnetic nanoparticles in liquid dispersion. Stober method used for the formation of silica coated magnetic nanoparticles, where hydrolysis of tetra-ethylorthosilicate (TEOS) in alcohol media under catalysis by ammonia (Stöber, Fink, & Bohn, 1968).

5.1.2 Chitosan

Different types of polymers used for coating of magnetic nanoparticles (MNP's) because these polymers are inexpensive and non-immunogenic and non-antigenic. They attached through carboxylate group to MNP's surface. Chitosan is natural polysaccharide and cationic polymer. This polymer is nontoxic, hydrophilic and biodegradable. Y. Chang and D. Chen prepared chitosan coated magnetic particles, chitosan first carboxy-methylated then bound covalently on the surface of magnetite nanoparticles through carbodiimide activation (Chang & Chen, 2005). J. Zhi et al. suggested another method for in situ synthesis of chitosan-magnetite nano-composites by water-in-oil micro emulsion (Zhi, Wang, Lu, Ma, & Luo, 2006). By this method spherical chitosan

nanoparticles varying in size from 10 nm to 80 nm with cubic shaped magnetite core were synthesized.

5.1.3 Dextran

Dextran is branched polysaccharide composed of glucose subunits and commonly used due to high biocompatibility. Studies have shown that dextran resistant to enzymatic degradation and most stable in tissue environment (Crepon, Jozefonvicz, Chytry, Rihova, & Kopecek, 1991).

Iron oxides nanoparticles functionalized with organic material provide nanoparticles with good biocompatibility and biodegradeability.

5.1.4 Polyethyleneimine PEI

Polyethyleneimine is cationic, synthetic polymer and has linear or branched forms. It is toxic and non-biodegredable. It binds to DNA, used for gene delivery (Kircheis, Wightman, & Wagner, 2001).

5.1.5 Surfactant and small molecules

Choice of solvent is very important for obtaining sufficient repulsive interaction to prevent agglomeration and stable colloidal solution. Surfactant and small molecules functionalized iron oxides NP are divided into three types according to the surface properties of modified iron oxides NP's

- Oil soluble
- Water soluble
- Amphiphilic

Oil soluble functionalization used to prevent agglomeration and increase stability give rise to mono-dispersity.

Oleic acid is C18 compound and has cis double bond in middle creating a twist. Such twists provide the stability to NP's. Stearic acid is also C18 compound but not has double bond so it not stabilizes the NP's. Oleic acid

forms thick protective monolayer, produce mono-disperse particles. To obtain thermodynamically stable dispersions of magnetic NP's Alkyl phosphonates and phosphates are used (Sahoo et al., 2005).

5.1.6 Biological molecules

Antibody targeted nanoparticles used as probe for different application in detecting specific bacteria (Bhattacharya et al., 2011). These biomolecules improve the biocompatibility of particles.

5.1.7 Metal and nonmetal

By controlled oxidation of single pure metal/ nonmetal shell such as carbon, iron, silver, gold, palladium and platinum nanoparticles are protected. There are two ways to synthesize metal coated nanoparticles:

- Metal ions direct reduction on the surface of nanoparticles.

- Reduction of metal ion on the surface of small molecules, polymer or SiO_2 functionalized nanoparticles.

Fe_3O_4 nanoparticles functionalized with Nobel metals by reducing the Ag+ and Au+ ions (Mandal et al., 2005). This gives stability to magnetic nanoparticles for long time. Particles prepared have size range in between 18-30 nm. Gold coating provides stability and also aid in binding of biological molecules that have –SH grouped for various biomedical applications. Recently gold coated nanoparticles are prepared by sonolysis of gold ions and amino-modified Fe_3O_4 nanoparticles solution, reducing agent added drop wise (Wu, He, Chen, Tang, & Nie, 2007). Size of prepared nanoparticles is 30 nm.

6. Magnetic Iron Oxides Food Applications

Due to easy separation with magnetic, magnetic iron oxides nanoparticles are used in various fields. Magnetic nanoparticles consist of iron, cobalt, nickel and their chemical compounds. Their safety or toxicity is prime important concern for use in food. Magnetite

(Fe_3O_4) common among the magnetic iron oxide nanoparticles and it is used in food industry (Cao et al., 2012). The reason behind application of magnetite in food industry is that, they are non-toxic, have good biocompatibility, when external magnetic field removed they cannot retain residual magnetism. Magnetic nanoparticles functionalized by special group (NH_2, COOH, OH) and this is suitable for additional modification by bioactive compounds attachment (Berry & Curtis, 2003). Some food linked applications of magnetic iron oxide are:

- Protein purification

- Enzyme immobilization

- Food analysis

6.1 Protein purification

Chromatography, ultra sonication, precipitation, centrifugation and dialysis are mostly used for protein purification. Disadvantages of these techniques are time consuming, pretreatments, expensive instrumentation and skilled operators. Magnetic separation has advantages and old but emerging technique. Magnetic nanoparticles immobilized with ligands have affinity for target protein (Franzreb, Siemann-Herzberg, Hobley, & Thomas, 2006).

6.2 Enzyme immobilization

Enzymes are biological catalyst. Enzymes are used in food are Carbohydrase, proteases, lipases and lysozymes have outstanding catalytic activity. Enzymes in Free State show less stability towards pH, heat and other factors. Enzymes immobilization is most common method that is used to improve the stability and reusability of an enzyme. Protein engineering, enzyme modification and medium engineering are other techniques those are being used to improve the reusability of enzymes. (Mateo, Palomo, Fernandez-Lorente, Guisan, & Fernandez-Lafuente, 2007). Different inorganic and organic supports used to immobilize enzymes (Y. Li, Xu, Deng, Yang, & Zhang, 2007; C. Oh et al., 2006). Magnetic nanoparticles used as alternatives for enzyme immobilization. They have some advantages:

- They have large surface area due to which they have high enzyme loading capacity.

- Enzymes are collected from mixture by applying external magnetic field (X. Liu et al., 2011).

Covalent bonding and physical adsorption are two methods that are commonly used for enzyme immobilization. In covalent bonding chemical groups that are present on magnetic nanoparticles are linked by covalent bonding to chemical groups of an enzyme. Disadvantage of this method is, activity of an enzyme reduced. Due to the presence of weak forces, hydrogen forces between enzymes and magnetic particles, physical adsorption applied. This method is simple but at minor change in pH, temperature and ionic strength adsorbed enzyme fall off.

6.3 Food analysis

In food division, analysis of food is of major importance to ensure food safety. The techniques that basically used for food analysis are culturing and colony counting. But these techniques are time consuming and laborious. Magnetic nanoparticles used for food analysis because they have large surface area, easy separation from complex mixture. Magnetic nanoparticles integrated with detection techniques such as PCR, immunoassay, HPLC and biosensor for food analysis. PCR mostly used for pathogen detection in food samples. Magnetic nanoparticles showed advances in pre-concentration process. Submicron super paramagnetic anion exchanger used to concentrate target bacteria for multiplex PCR (K. Yang, Jenkins, & Su, 2011).

7. Heavy Metal Removals from Water

Heavy metals are carcinogenic, these metal introduced into environment and contaminate water supplies (Fu & Wang, 2011). Various methods are used for removal of these heavy metals. The methods includes sedimentation, oxidation/reduction, carbon adsorption, chemical precipitation, filtration and ion exchange (Shin & Jang, 2007). Study showed that functionalized super paramagnetic iron oxides used for removal of heavy metals from water. 99% removals of arsenic from contaminated water by reduced magnetite grapheme oxide have proven (Chandra et al., 2010). In another study, poly(3,4-ethylenedioxythiophene) magnetite nanoparticles showed conjugate heavy metal ions spread within an aqueous solution (Shin & Jang, 2007).

8. Biomedical Applications

Biomedical uses of magnetic nanoparticles are;

- MRI (Magnetic Resonance Imaging)

- Drug delivery and Hyperthermia (Teja & Koh, 2009).

MRI used in clinical medicine and powerful imaging technique. After injection super-paramagnetic iron oxide nanoparticles coated with hydrophilic polymer(poly-oligo-ethylene oxide mono-methyl ether methacrylate POEOMA) accumulated in tissue and result in proton improvement compared to neighboring tissue (J. K. Oh & Park, 2011).

In vivo MRI, super-paramagnetic iron oxide nanoparticles allow determination of diseased tissue among healthy ones. Small sized particles with hydrophilic surface have longer plasma half-life and lead to easier elimination of the super-paramagnetic iron oxide nanoparticles in blood circulation (Mornet, Vasseur, Grasset, & Duguet, 2004). The basic requirements for drug delivery methods are: stability for prolonged circulation, controllable release of therapeutics, non-toxicity to cells and high loading efficiency (Lutz et al., 2006). Recently F. M. Kievit et al. established a magnetic nanoparticles system made of super paramagnetic iron oxide nanoparticle (IONP's), coated with polyethylenimine (PEI) and poly(ethylene glycol) (PEG) for magnetic resonance imaging(Kievit et al., 2009). D. Kim et al. synthesized chitosan and starch coated iron oxide nanoparticles to treat carcinoma cells by magnetic hyperthermia (D. H. Kim, Kim, Kim, & Lee, 2009).

9. Traditional Techniques for Detection of Bacteria

Traditional techniques to detect food borne pathogen have time consuming steps such as isolation, enrichment and counting.

9.1 Traditional fast detection techniques

Rapid techniques developed in last two decades. These includes small biochemical kits, antibody and nuclear acid based analysis and modified conventional tests (Kayal & Charbit, 2006). Swaminathan and Feng provide an outstanding review of fast detection techniques (Feng, 2001; Swaminathan & Feng, 1994).

9.1.1 Biochemical kits

By this method bacteria identified on the basis of their biochemical characteristics with accuracy of 90-99% (Panchal et al., 2005). Many species of Gram bacteria identified by this method. These kits require single isolate of bacteria and 24 hours incubation time period.

9.1.2 Antibody based assays

Bacteria identified by this method on the basis of antigen-antibody reaction. Western blot analysis, (ELISA)enzyme linked immuno-sorbent assay and immune-fluorescent assay are types of immunoassay (Schwartz & Wormser, 2002). Antibodies are labeled to target specific bacteria. To improve specificity and strength of these methods, there is complete understanding of micro-organism, reaction to antibodies, antigen expression and food matrix (Banada & Bhunia, 2008).

9.1.3 Nuclear acid-based assays

These methods based on PCR (Polymerase chain reaction). Nuclear-acid based assays are very sensitive and selective (Kaittanis, Santra, & Perez, 2010).

10. Magnetic Nanoparticle Sensors

Nanoparticles are very small particles in between 1-100 nanometers. Kaittanis et al provided a review on use of nanoparticles in clinics to detect microbial pathogens (Kaittanis et al., 2010). These particles are attached with ligands. Detection methods are color based, fluorescence based (Qin, He, Wang, & Tan, 2008), immunology based and PCR based . Electronic, conducive, spectroscopic and light scattering properties of nanoparticles modified by changing structural parameters to change response patterns distinctive to specific type of interaction of nanoparticle with pathogen (Kaittanis et al., 2010). For magnetic resonance imaging (MRI) super-paramagnetic nanoparticles used as contrast agent (Weinstein et al., 2010; J. Yang et al., 2008).

These particles are used in protein purification, enzyme immobilization and food analysis (Cao et al., 2012). When attached to antibodies these are used for immunogenic separation of bacteria, viruses, proteins and nucleic acid. Li and his co-workers used antibody conjugated nanoparticles to isolate *Escherichia.coli O157:H7* from ground beef (Varshney, Yang, Su, & Li, 2005). Magnetic nanoparticles conjugates with proteins and microbes are used in detoxification of bio fluids, tissue repair, immuno-assay cell separation, and hyperthermia and drug delivery.

Magnetic nanoparticles conjugates and bacteria are also used to quantify DNA, mRNA and pathogenic microbes. Nanoparticles added in pathogenic matrix and signal are detected by (SQUID)superconducting quantum interference device, magnetic-relaxometer and magnetic resonance imaging (H. Lee, Sun, Ham, & Weissleder, 2008). Li and his co-workers used magnetic nanoparticles conjugated with streptavidin as "mass enhancers" to intensify frequency change in *Escherichia coli O157:H7* and signals detected by a quartz crystal microbalance (QCM) DNA sensor (F. Liu et al., 2007).

11. Capture Bacteria with Functionalized Nanoparticles

Identification is most important in microbiology and environmental biology. For extraction of micro-organisms nanoparticles are used as affinity probe (C.-T. Chen, Reddy, Ma, & Ho, 2012). Modified magnetic nanoparticles used as affinity probe for selective

concentrating of target species (Chen g-Tai Chen et al., 2006). Kell et al described synthesis of vancomycin-modified silica-encapsulated iron oxide nanoparticles (Kell et al., 2008). Lo, Chen, Chen & Chen coated iron oxide nanoparticles with Titania and used these nanoparticles as affinity probe under microwave heating and also measure capturing efficiency of these nanoparticles towards eight bacterial strain (Lo, Chen, Chen, & Chen, 2007). They concluded that Titania coated magnetic nanoparticles has higher affinity for bacteria containing lipopolysaccharides. Interaction of nanoparticles with Gram-Positive bacteria is due to lack of lipopolysaccharides structure. S. Li, Guo, Liu, Yang, & Hui, separate bacteria from water by anion-exchange/cation-exchange magnetic nanoparticles. They spiked bacteria in tap water. This water analyzed by (MALDI-MS) matrix assisted laser desorption ionization ass spectroscopy. After 2 hours they detected 1×10^3 CFU/mL. At neutral pH separation functions well (S. Li, Guo, Liu, Yang, & Hui, 2009).

Conclusion

Literature showed that magnetite is getting popular due to its super paramagnetic properties and lack of toxicity to humans. These nanoparticles lose magnetism and mono-dispersibility upon contact with air. So different organic and inorganic compounds are used to stable these nanoparticles. It was concluded that there are different methods used for its synthesis but co-precipitation is most efficient method. Due to easy separation with magnet these magnetic nanoparticles are used as an affinity probe to remove bacteria from different food samples and have food related applications e.g, protein purification, enzyme immobilization and food analysis. These magnetic nanoparticles also used for removal of heavy metals and used in medical field. More effort still required to explore the use of functionalized magnetite in food industry.

References

Banada, P. P., & Bhunia, A. K. (2008). Antibodies and immunoassays for detection of bacterial pathogens *Principles of bacterial detection: biosensors, recognition receptors and microsystems* (pp. 567-602): Springer.

Berry, C. C., & Curtis, A. S. (2003). Functionalisation of magnetic nanoparticles for applications in biomedicine. *Journal of physics D: Applied physics, 36*(13), R198.

Beveridge, T., & Murray, R. (1980). Sites of metal deposition in the cell wall of Bacillus subtilis. *Journal of bacteriology, 141*(2), 876-887.

Bhattacharya, D., Chakraborty, S. P., Pramanik, A., Baksi, A., Roy, S., Maiti, T. K., . . . Pramanik, P. (2011). Detection of total count of Staphylococcus aureus using anti-toxin antibody labelled gold magnetite nanocomposites: a novel tool for capture, detection and bacterial separation. *Journal of Materials Chemistry, 21*(43), 17273-17282.

Boxall, C., Kelsall, G., & Zhang, Z. (1996). Photoelectrophoresis of colloidal iron oxides. Part 2.—Magnetite (Fe 3 O 4). *Journal of the Chemical Society, Faraday Transactions, 92*(5), 791-802.

Cao, M., Li, Z., Wang, J., Ge, W., Yue, T., Li, R., . . . William, W. Y. (2012). Food related applications of magnetic iron oxide nanoparticles: enzyme immobilization, protein purification, and food analysis. *Trends in Food Science & Technology, 27*(1), 47-56.

Chandra, V., Park, J., Chun, Y., Lee, J. W., Hwang, I.-C., & Kim, K. S. (2010). Water-dispersible magnetite-reduced graphene oxide composites for arsenic removal. *ACS nano, 4*(7), 3979-3986.

Chang, Y.-C., & Chen, D.-H. (2005). Preparation and adsorption properties of monodisperse chitosan-bound Fe 3 O 4 magnetic nanoparticles for removal of Cu (II) ions. *Journal of Colloid and Interface Science, 283*(2), 446-451.

Chastellain, M., Petri, A., Gupta, A., Rao, K. V., & Hofmann, H. (2004). Superparamagnetic Silica-Iron Oxide Nanocomposites for Application in Hyperthermia. *Advanced Engineering Materials, 6*(4), 235-241.

Chen, C.-T., Reddy, P. M., Ma, Y.-R., & Ho, Y.-P. (2012). Mass spectrometric identification of pathogens in foods using a zirconium hydroxide immobilization approach. *International Journal of Mass Spectrometry, 312*, 45-52.

Chen g-Tai Chen, Chen, W.-Y., Tsai, P.-J., Chien, K.-Y., Yu, J.-S., & Chen, Y.-C. (2006). Rapid enrichment of phosphopeptides and phosphoproteins from complex samples using magnetic particles coated with alumina as the concentrating probes for MALDI MS analysis. *Journal of proteome research, 6*(1), 316-325.

Chen, H., & Yada, R. (2011). Nanotechnologies in agriculture: new tools for sustainable development. *Trends in Food Science & Technology, 22*(11), 585-594.

Cornell, R. (2003). Schwertmann, The Iron Oxides: Structure, Properties, Occurences and Uses: Wiley-VCH, Weinhein.

Crepon, B., Jozefonvicz, J., Chytry, V., Rihova, B., & Kopecek, J. (1991). Enzymatic degradation and immunogenic properties of derivatized dextrans. *Biomaterials, 12*(6), 550-554.

Dobson, J. (2001). Nanoscale biogenic iron oxides and neurodegenerative disease. *FEBS letters, 496*(1), 1-5.

Du, L., Jiang, H., Liu, X., & Wang, E. (2007). Biosynthesis of gold nanoparticles assisted by Escherichia coli DH5α and its application on direct electrochemistry of hemoglobin. *Electrochemistry Communications, 9*(5), 1165-1170.

Feng, P. (2001). Rapid methods for detecting foodborne pathogens. *FDA, editor. Bacteriological Analytical Manual Online.*

Franzreb, M., Siemann-Herzberg, M., Hobley, T. J., & Thomas, O. R. (2006). Protein purification using magnetic adsorbent particles. *Applied microbiology and biotechnology, 70*(5), 505-516.

Fu, F., & Wang, Q. (2011). Removal of heavy metal ions from wastewaters: a review. *Journal of environmental management, 92*(3), 407-418.

Honary, S., Ebrahimi, P., Rad, H. A., & Asgari, M. (2013). Optimization of preparation of chitosan-coated iron oxide nanoparticles for biomedical applications by chemometrics approaches. *International Nano Letters, 3*(1), 1-5.

Hough, R., Noble, R., Hitchen, G., Hart, R., Reddy, S., Saunders, M., . . . Gray, D. (2008). Naturally occurring gold nanoparticles and nanoplates. *Geology, 36*(7), 571-574.

Husseiny, M., El-Aziz, M. A., Badr, Y., & Mahmoud, M. (2007). Biosynthesis of gold nanoparticles using Pseudomonas aeruginosa. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 67*(3), 1003-1006.

Jiang, W., Yang, K., Vachet, R. W., & Xing, B. (2010). Interaction between oxide nanoparticles and biomolecules of the bacterial cell envelope as examined by infrared spectroscopy. *Langmuir, 26*(23), 18071-18077.

Joye, I. J., Davidov-Pardo, G., & McClements, D. J. (2014). Nanotechnology for increased micronutrient bioavailability. *Trends in Food Science & Technology, 40*(2), 168-182.

Kaittanis, C., Santra, S., & Perez, J. M. (2010). Emerging nanotechnology-based strategies for the identification of microbial pathogenesis. *Advanced Drug Delivery Reviews, 62*(4), 408-423.

Kayal, S., & Charbit, A. (2006). Listeriolysin O: a key protein of Listeria monocytogenes with multiple functions. *FEMS microbiology reviews, 30*(4), 514-529.

Kell, A. J., Stewart, G., Ryan, S., Peytavi, R., Boissinot, M., Huletsky, A., . . . Simard, B. (2008). Vancomycin-modified nanoparticles for efficient targeting and preconcentration of Gram-positive and Gram-negative bacteria. *Acs Nano, 2*(9), 1777-1788.

Kievit, F. M., Veiseh, O., Bhattarai, N., Fang, C., Gunn, J. W., Lee, D., . . . Zhang, M. (2009). PEI–PEG–chitosan-copolymer-coated iron oxide nanoparticles for safe gene delivery: synthesis, complexation, and transfection. *Advanced functional materials, 19*(14), 2244-2251.

Kim, D. H., Kim, K. N., Kim, K. M., & Lee, Y. K. (2009). Targeting to carcinoma cells with chitosan-and starch-coated magnetic nanoparticles for magnetic hyperthermia. *Journal of Biomedical Materials Research Part A, 88*(1), 1-11.

Kim, D. K., Mikhaylova, M., Zhang, Y., & Muhammed, M. (2003). Protective coating of superparamagnetic iron oxide nanoparticles. *Chemistry of Materials, 15*(8), 1617-1627.

Kircheis, R., Wightman, L., & Wagner, E. (2001). Design and gene delivery activity of modified polyethylenimines. *Advanced Drug Delivery Reviews, 53*(3), 341-358.

Laurent, S., Forge, D., Port, M., Roch, A., Robic, C., Vander Elst, L., & Muller, R. N. (2008). Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications. *Chemical reviews, 108*(6), 2064-2110.

Lee, H., Sun, E., Ham, D., & Weissleder, R. (2008). Chip–NMR biosensor for detection and molecular analysis of cells. *Nature medicine, 14*(8), 869-874.

Lee, J. H., Fang, L., Vlahos, E., Ke, X., Jung, Y. W., Kourkoutis, L. F., . . . Roeckerath, M. (2010). A strong ferroelectric ferromagnet created by means of spin–lattice coupling. *Nature, 466*(7309), 954.

Li, S., Guo, Z., Liu, Y., Yang, Z., & Hui, H. K. (2009). Integration of microfiltration and anion-exchange nanoparticles-based magnetic separation with MALDI mass spectrometry for bacterial analysis. *Talanta, 80*(1), 313-320.

Li, Y., Xu, X., Deng, C., Yang, P., & Zhang, X. (2007). Immobilization of trypsin on superparamagnetic nanoparticles for rapid and effective proteolysis. *Journal of proteome research, 6*(9), 3849-3855.

Liu, F., Li, Y., Su, X.-L., Slavik, M. F., Ying, Y., & Wang, J. (2007). QCM immunosensor with nanoparticle amplification for detection of Escherichia coli O157: H7. *Sensing and Instrumentation for Food Quality and Safety, 1*(4), 161-168.

Liu, T.-Y., Hu, S.-H., Liu, K.-H., Liu, D.-M., & Chen, S.-Y. (2008). Study on controlled drug permeation of magnetic-sensitive ferrogels: effect of Fe 3 O 4 and PVA. *Journal of Controlled Release, 126*(3), 228-236.

Liu, T., Cheng, Y., & Yang, Z. (2005). Design optimization of seal structure for sealing liquid by magnetic fluids. *Journal of Magnetism and Magnetic Materials, 289*, 411-414.

Liu, X., Lei, L., Li, Y., Zhu, H., Cui, Y., & Hu, H. (2011). Preparation of carriers based on magnetic nanoparticles grafted polymer and immobilization for lipase. *Biochemical Engineering Journal, 56*(3), 142-149.

Livingston, J. (1981). A review of coercivity mechanisms. *Journal of Applied Physics, 52*(3), 2544-2548.

Lo, C.-Y., Chen, W.-Y., Chen, C.-T., & Chen, Y.-C. (2007). Rapid enrichment of phosphopeptides from tryptic digests of proteins using iron oxide nanocomposites of magnetic particles coated with zirconia as the concentrating probes. *Journal of proteome research, 6*(2), 887-893.

López-López, M., Durán, J., Delgado, A., & González-Caballero, F. (2005). Stability and magnetic characterization of oleate-covered magnetite ferrofluids in different nonpolar carriers. *Journal of Colloid and Interface Science, 291*(1), 144-151.

Lutz, J.-F., Stiller, S., Hoth, A., Kaufner, L., Pison, U., & Cartier, R. (2006). One-pot synthesis of PEGylated ultrasmall iron-oxide nanoparticles and their in vivo evaluation as magnetic resonance imaging contrast agents. *Biomacromolecules, 7*(11), 3132-3138.

Mahdavi, M., Ahmad, M. B., Haron, M. J., Namvar, F., Nadi, B., Rahman, M. Z. A., & Amin, J. (2013). Synthesis, surface modification and characterisation of biocompatible magnetic iron oxide nanoparticles for biomedical applications. *Molecules, 18*(7), 7533-7548.

Mandal, M., Kundu, S., Ghosh, S. K., Panigrahi, S., Sau, T. K., Yusuf, S., & Pal, T. (2005). Magnetite nanoparticles with

tunable gold or silver shell. *Journal of Colloid and Interface Science, 286*(1), 187-194.

Mateo, C., Palomo, J. M., Fernandez-Lorente, G., Guisan, J. M., & Fernandez-Lafuente, R. (2007). Improvement of enzyme activity, stability and selectivity via immobilization techniques. *Enzyme and Microbial Technology, 40*(6), 1451-1463.

Mikhaylova, M., Kim, D. K., Bobrysheva, N., Osmolowsky, M., Semenov, V., Tsakalakos, T., & Muhammed, M. (2004). Superparamagnetism of magnetite nanoparticles: dependence on surface modification. *Langmuir, 20*(6), 2472-2477.

Mornet, S., Vasseur, S., Grasset, F., & Duguet, E. (2004). Magnetic nanoparticle design for medical diagnosis and therapy. *Journal of Materials Chemistry, 14*(14), 2161-2175.

Narayanan, K. B., & Sakthivel, N. (2010). Biological synthesis of metal nanoparticles by microbes. *Advances in colloid and interface science, 156*(1), 1-13.

Oh, C., Lee, J.-H., Lee, Y.-G., Lee, Y.-H., Kim, J.-W., Kang, H.-H., & Oh, S.-G. (2006). New approach to the immobilization of glucose oxidase on non-porous silica microspheres functionalized by (3-aminopropyl) trimethoxysilane (APTMS). *Colloids and Surfaces B: Biointerfaces, 53*(2), 225-232.

Oh, J. K., & Park, J. M. (2011). Iron oxide-based superparamagnetic polymeric nanomaterials: design, preparation, and biomedical application. *Progress in Polymer Science, 36*(1), 168-189.

Panchal, R. G., Halverson, K. M., Ribot, W., Lane, D., Kenny, T., Abshire, T. G., . . . Little, S. (2005). Purified Bacillus anthracis lethal toxin complex formed in vitro and during infection exhibits functional and biological activity. *Journal of Biological Chemistry, 280*(11), 10834-10839.

Qin, D., He, X., Wang, K., & Tan, W. (2008). Using fluorescent nanoparticles and SYBR Green I based two-color flow cytometry to determine Mycobacterium tuberculosis avoiding false positives. *Biosensors and Bioelectronics, 24*(4), 626-631.

Rai, M., Yadav, A., & Gade, A. (2008). CRC 675—current trends in phytosynthesis of metal nanoparticles. *Critical reviews in biotechnology, 28*(4), 277-284.

Sahoo, Y., Goodarzi, A., Swihart, M. T., Ohulchanskyy, T. Y., Kaur, N., Furlani, E. P., & Prasad, P. N. (2005). Aqueous ferrofluid of magnetite nanoparticles: fluorescence labeling and magnetophoretic control. *The Journal of Physical Chemistry B, 109*(9), 3879-3885.

Sapsford, K. E., Algar, W. R., Berti, L., Gemmill, K. B., Casey, B. J., Oh, E., . . . Medintz, I. L. (2013). Functionalizing nanoparticles with biological molecules: developing chemistries that facilitate nanotechnology. *Chemical reviews, 113*(3), 1904-2074.

Schmid, G. (2011). *Nanoparticles: from theory to application*: John Wiley & Sons.

Schwartz, I., & Wormser, G. P. (2002). Bacterial Pathogenesis: A Molecular Approach. *Clinical Infectious Diseases, 35*(5), 638-639.

Shin, S., & Jang, J. (2007). Thiol containing polymer encapsulated magnetic nanoparticles as reusable and efficiently

separable adsorbent for heavy metal ions. *Chemical communications*(41), 4230-4232.

Stöber, W., Fink, A., & Bohn, E. (1968). Controlled growth of monodisperse silica spheres in the micron size range. *Journal of Colloid and Interface Science, 26*(1), 62-69.

Sun, S., & Zeng, H. (2002). Size-controlled synthesis of magnetite nanoparticles. *Journal of the American Chemical Society, 124*(28), 8204-8205.

Sun, Y.-k., Ma, M., Zhang, Y., & Gu, N. (2004). Synthesis of nanometer-size maghemite particles from magnetite. *Colloids and Surfaces A: Physicochemical and Engineering Aspects, 245*(1), 15-19.

Swaminathan, B., & Feng, P. (1994). Rapid detection of food-borne pathogenic bacteria. *Annual Reviews in Microbiology, 48*(1), 401-426.

Teja, A. S., & Koh, P.-Y. (2009). Synthesis, properties, and applications of magnetic iron oxide nanoparticles. *Progress in crystal growth and characterization of materials, 55*(1), 22-45.

Turkevich, J., Stevenson, P. C., & Hillier, J. (1951). A study of the nucleation and growth processes in the synthesis of colloidal gold. *Discussions of the Faraday Society, 11*, 55-75.

Ulman, A. (1996). Formation and structure of self-assembled monolayers. *Chemical reviews, 96*(4), 1533-1554.

Umut, E. (2013). Surface modification of nanoparticles used in biomedical applications. *Mod. Surf. Eng. Treat, 5*, 185-208.

Varshney, M., Yang, L., Su, X.-L., & Li, Y. (2005). Magnetic nanoparticle-antibody conjugates for the separation of Escherichia coli O157: H7 in ground beef. *Journal of Food Protection®, 68*(9), 1804-1811.

Wang, Y., & Xia, Y. (2004). Bottom-up and top-down approaches to the synthesis of monodispersed spherical colloids of low melting-point metals. *Nano letters, 4*(10), 2047-2050.

Weinstein, J. S., Varallyay, C. G., Dosa, E., Gahramanov, S., Hamilton, B., Rooney, W. D., . . . Neuwelt, E. A. (2010). Superparamagnetic iron oxide nanoparticles: diagnostic magnetic resonance imaging and potential therapeutic applications in neurooncology and central nervous system inflammatory pathologies, a review. *Journal of Cerebral Blood Flow & Metabolism, 30*(1), 15-35.

Woo, K., Hong, J., Choi, S., Lee, H.-W., Ahn, J.-P., Kim, C. S., & Lee, S. W. (2004). Easy synthesis and magnetic properties of iron oxide nanoparticles. *Chemistry of Materials, 16*(14), 2814-2818.

Wu, W., He, Q., Chen, H., Tang, J., & Nie, L. (2007). Sonochemical synthesis, structure and magnetic properties of air-stable Fe3O4/Au nanoparticles. *Nanotechnology, 18*(14), 145609.

Wu, W., Wu, Z., Yu, T., Jiang, C., & Kim, W.-S. (2015). Recent progress on magnetic iron oxide nanoparticles: synthesis, surface functional strategies and biomedical applications. *Science and Technology of Advanced Materials, 16*(2), 023501.

Wu, W., Xiao, X., Zhang, S., Zhou, J., Fan, L., Ren, F., & Jiang, C. (2010). Large-scale and controlled synthesis of iron oxide magnetic short nanotubes: shape evolution, growth

mechanism, and magnetic properties. *The Journal of Physical Chemistry C, 114*(39), 16092-16103.

Xu, S., Habib, A., Gee, S., Hong, Y., & McHenry, M. (2015). Spin orientation, structure, morphology, and magnetic properties of hematite nanoparticles. *Journal of Applied Physics, 117*(17), 17A315.

Yang, J., Gunn, J., Dave, S. R., Zhang, M., Wang, Y. A., & Gao, X. (2008). Ultrasensitive detection and molecular imaging with magnetic nanoparticles. *Analyst, 133*(2), 154-160.

Yang, K., Jenkins, D. M., & Su, W. W. (2011). Rapid concentration of bacteria using submicron magnetic anion exchangers for improving PCR-based multiplex pathogen detection. *Journal of Microbiological Methods, 86*(1), 69-77.

Zhi, J., Wang, Y., Lu, Y., Ma, J., & Luo, G. (2006). In situ preparation of magnetic chitosan/Fe 3 O 4 composite nanoparticles in tiny pools of water-in-oil microemulsion. *Reactive and Functional Polymers, 66*(12), 1552-1558.