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IRON OXIDE NANOPARTICLES AND THEIR PHOTOELECTROCHEMICAL AND MEDICAL APPLICATIONS A SHORT OVERVIEW

Marius Chirita, Ioan Grozescu

National Institute for Research and Development in Electrochemistry and Condensed Matter, Timisoara, Plautius Andronescu Str. 1, RO-300224, Timisoara, Romania

Abstract. In this article a short overview on iron oxide nanoparticles new developments is provided. Many novel approaches are described in the use of photoelectrochemistry such as solar energy conversion, water splitting, photocatalysts for the removal of organic and inorganic species from aqueous or gas phase. The nanocrystalline semiconductor thin films and core shell structures are shortly described and SPIO-Superparamagnetic Iron Oxide Core nanoparticles are also presented. Modern applications are to be discussed in cell separation, immunoassay, as contrast agents in magnetic resonance imaging, drug and gene delivery, radionuclide therapy and hyperthermia applications.
Keywords: photoelectrochemical, photocatalyst, magnetism, drug targeting, gene therapy, MRI, SPIO-Superparamagnetic Iron Oxide Core Structure

1. Introduction

The iron with his 26 protons in nucleus is a component of *transition elements* group. Isotopes like Fe54, Fe56, Fe57 and Fe58 are extremely stable. It is the last element produced in the nucleus of stars (only in the stars bigger than five solar mass) through nuclear fusion, so that the iron is the heaviest element created outside the cataclysmic supernova processes. In abundance, is the tenth in the Universe and the forth on the Earth (the second metal after aluminum). The Earth comprises 80% Iron in a 2160 miles radius sphere. Iron is widely spread in the nature in different chemical compounds. The interesting question about transition metals is that their valence electrons or the electrons they use to combine with other elements are to be found in more than one shell. This is the reason why, they often exhibit several common oxidation states. Normally, the iron has eight electrons on valence shield and due to oxygen's electronegativity it can form bivalent and trivalent combinations. There are three noteworthy elements in the transition metals family. These elements are iron, cobalt, and nickel, and they are the only elements known to produce a magnetic field. The Iron oxide (Fe_2O_3), the most common oxide of iron has the important magnetically properties too. From the viewpoint of the basic research, iron (III) oxide is a convenient compound for the general

study of polymorphism and the magnetic and structural phase transitions of nanoparticles. The existence of amorphous Fe_2O_3 and four polymorphs (alpha, beta, gamma and epsilon) is well established [1]. The most frequent polymorphs structure "alpha" (hematite) having a rhombohedral-hexagonal, prototype corundum structures and cubic spinel structure "gamma" (maghemite) have been found in nature. At a temperature of 650 ^oC, hematite turns into Fe_3O_4 with a high energy loss. Hematite has strongly antiferromagnetic properties. Gamma Fe_2O_3 (maghemite) is the ferrimagnetic cubic form of Fe(III) oxide and it differs from the inverse spinel structure of magnetite through vacancies on the cation sublattice. However, both compositions possess similar lattice parameters at 8.396 °A and 8.346 °A for magnetite and maghemite, respectively. In time, at room-temperature, the maghemite turns into hematite crystalline structure. The magnetic moment of bulk gamma type Fe2O3 is ~430emu/cc at room temperature while the magnetic moment of alpha type Fe2O3 is very small (~1emu/cc) [3] as compared to the gamma phase. Maghemite has the same crystalline structure like Fe_3O_4 (magnetite). Main distinct features of maghemite is the presence of vacancies in Fe position with symmetry reduction. This loss of symmetry is corresponding with a few diffraction spots in RX analyses. The other polymorphs, the cubic bixbyite structure "beta" and orthorhombic structure "epsilon", as well as nanoparticles of all forms, have been synthesized and extensively investigated in recent years [1,2]. Epsilon is a transition phase between hematite and maghemite. The first scientific reports about epsilon Fe_2O_3 was published in 1934 (Frestier and Guillain). The detailed structural characterization of epsilon phase was published by Tranc in 1998 and by Klemm and Mader later. Until now, the way to produce epsilon Fe_2O_3 is gamma–>epsilon->alpha Fe_2O_3. Beta Fe_2O_3 with his cubic bixbyite structure has paramagnetic properties. Gamma and epsilon type Fe2O3 are ferromagnetic; alpha Fe2O3 is a canted antiferromagnetic while beta type Fe2O3 is a paramagnetic material. The semiconductor properties of the hematite are extremely useful in solar energy conversion, photocatalyse, water splitting. The magnetic properties of maghemite play an important role in different applications of health care. Maghemite Fe_2O_3 is biocompatible and therefore is one of the most extensively used biomaterials for different applications like cell separation, drug delivery in cancer therapy, magnetic induced hyperthermia, MRI contrast agent, immunomagnetic separation IMC and others. For this purpose, a large number of magnetic materials in bulk as well as in the form of nanoparticles have been created for a variety of medical applications.

In this paper, we summarize the main features of clinical applications, where magnetic biomaterials are used.

2. Physical properties

2.1 AlfaFe_2O_3-Hematite, physical properties

Hematite has the same crystallographic structure like (6:4) alpha Al_2O_3 - corundum. The anions have a hexagonal closed packed structure (characterized by the regular alternation of two layers; the atoms in each layer lie at the vertices of a series of equilateral triangles, and the atoms in one layer lie directly above the centers of the triangles in neighboring layers) and the cations occupy 2/3 of the octaedric sites [3]. In other words the oxygen ions occupy hexagonal sites and the iron ions are situated only in the surrounding octahedral sites**.**

As distances between atoms are rising with temperature, hematite magnetization depends strongly on this parameter. Therefore antiferromagnetic hematite nanoparticle deserves a special attention, due to the fact that is not a typical ferromagnet [4].

Below 260 K the magnetic arrangement has Fe^{3+} spins directed along the [111] axis and paired across the shared octahedral 260 K, the spins become essentially localized in (111) sheets face. However, the spins have canted slightly out of the plane, generating a weak ferromagnetic moment along the [111] axis. In addition to the antiferromagnetism below 260 K the hematite exhibits weak ferromagnetism above 260 K. This low temperature transition is called the Morin transition-T_M. The Morin temperature has been found to be strongly dependent on the size of the particles, generally decreasing with it and tending to disappear below a diameter of ~8nm for spherical particles [7]**.** Under 8nm, the hematite nanoparticle has superparamagnetic properties but these dimensions are strongly dependent of the synthesis methods. Superparamagnetic hematites with 20 nm radius have been reported.

The hematite photoelectrochemical properties were intensively studied in the last years, especially in water splitting, photovoltaic effects, photocatalitic effects. The biggest challenge is to produce cheap semiconductors with a low band gap and large absorption capacity from solar spectrum. Hematite has an absorption spectrum in visible between 600 and 295 nm [4]. Undopped nFe_2O_3 was intensively studied [4] and the efficiency in water electrolyze was 2%. In [4] an efficient coupling between n and p-hematite is presented. Type p-hematite was obtained by spray–pirolise method. In literature, the magnesium is the most studied p-dopant for hematite, as well as Ca and Ti which can be used for p-doping hematite obtaining. New dopants like Cu, Ca, Mg, Ni, Zr, Zn, are described in the literature lately. Photocurrent generation in nanostructured thin films was presented by many [5, 6, 9, 10].

Nanocrystalline semiconductor thin films prepared from colloidal suspensions are of great interest. Such thin film electrodes are named ‘nanostructured electrodes’. In the literature, alfa-Fe_2O_3 electrode has been reported to be thermodynamically stable towards

photoanodic decomposition over the entire pH range. Photocurrent quantum efficiency is only 0.8% at the maximum of the photocurrent spectrum [6]. Trapping of electrons by oxygen-deficient iron site, low mobility of holes, recombination of electrons and holes, are responsible for the poor photocurrent efficiency. Moreover, in the nanocrystalline alfa-Fe_2O_3 semiconductor thin film/electrolyte system, the mechanism of photo-induced charge separation and transportation are still unknown and the topics are open to further studies. Compared to the bulk semiconductor electrode, the mechanism of photocurrent generation in nanostructured thin film is quite different. In a conventional photoelectrochemical cell employing single-crystal or polycrystalline materials, the charge separation was facilitated by the space charge layer at the electrode/electrolyte interface [7]. The potential gradient of the space charge layer region promotes the flow of electrons and holes in the opposite direction. In this nanostructured system, the electrolyte can penetrate the whole colloidal porous film up to the surface of the back contact. The semiconductor/electrolyte junction occurs at each nanoparticles, much like a normal colloidal system. Under illumination, the light absorption in any individual colloidal particles will generate an electron–hole pair [8]. If the kinetics of whole transfer to the electrolyte is much faster than the recombination process, electrons can create a gradient in the electrochemical potential between the particle and the back-contact. This may be one of the reasons why nowadays the semiconductor and optical properties of alfa-Fe_2O_3 are under close investigation.

In photocatalytic process, like in photoelectric process, photons need certain energy to penetrate the band gap to generate the electron dislocation towards conduction level. After recombination, the electrons can react with donors or acceptors situated on the photocatalyst surface in two directions:

a) The holes react with water or OH group for radical-hydroxyl production responsible for organic substances degradation
b) The electrons react with dissolved oxygen to form superoxid ions with strongly effects. Much more, the superoxid ions can react furthermore evolving into hidroxyl ions.

The core-shell structures and nanocomposites structures are particularly interesting architectures in photocatalysts. Charge separation mechanism in core-shell, involve the electrons photogeneration in the first (shell) and their injections in conduction level of the second (core) in n-p structures and vice versa in p-n structures. Development of these semiconductor systems is very promising and has the potential to contribute significantly to the area of photocatalysis. By changing parameters, such as the thickness of the shell or the

particle radius of the core, we can improve the photocatalitic, optical and magnetic properties of the photocatalyst. It is the d orbital of the Fe (III) ions which is very important for photocatalysis applications. The carrier mobility in maghemite and magnetite are relatively low because of the narrowness of the d bands. This has been explained by Wait et all [11], who suggested that narrow bands arise from orbitals which do not appreciably overlap, therefore electrons or holes do not move as freely, that is, they have lower mobility. The band structure of hematite has been reported to involve a conduction band composed of empty Fe (III) orbitals. The valence band edge is made up of mixture of Fe^{3d} orbital and O^{2p} orbital [12]. The reported optical absorption of 2.2 eV is the result of weak transitions between d-d orbitals. The band gap which is important in photocatalytic applications has a value of 3 eV, and involves a strong charge transition between O^{2p} and the empty Fe^{3d} orbitals [12]. Others have reported that the direct transitions from O^{2p} valence band orbitals to the conduction band orbitals occur within the 3-4.7eV range [13].

An examination of the orbital arrangement of maghemite crystals has not been carried out. One of the best methods for photocatalytic process improvement is the hematite deposition on the SiO_2 surface microsphere, making a nanocomposite structure. They are special because SiO_2 granules have a low reactivity and a very good optical transmission.

2.2 Gamma Fe_2O3-maghemite, physical properties

Maghemite has a similar crystalline structure to magnetite and the same chemical composition as hematite being a metastabile phase between magnetite and hematite. In the crystalline structure of magnetite and maghemite, oxygen ions are cubic close packed with both octahedral and tetrahedral sites occupied by iron, whereas in hematite, oxygen ions are hexagonally close packed, and iron is present only in octahedral sites. The main differences between magnetite and maghemite are the presence of Fe II in magnetite and the presence of cation vacancies in maghemite [14]. The ionic radius of Fe (II) is larger than of Fe(III) so that the Fe(II)-O bond is longer and weaker than Fe(III)-O bond. Since the acid dissolution involves the breakdown of the Fe-O bond, the dissolution of magnetite is faster than the maghemite one [14]. Gama Fe_2O_3 has ten percent lower magnetic properties than magnetite Fe_3O_4 and a lower density than hematite. Cherepy [13] carried out ultra fast studies of photoexcited electron dynamics in both maghemite and hematite semiconductor nanoparticles. They found that hematite had an absorption spectra with 200, 230, 285 and 340, extending to 560 nm corresponding to 6.2; 5.4; 4.4; 3.6 and 2.2 eV respectively [5].

The absorption spectra for maghemite has been identified at 200 and 285 nm, corresponding to 6.2 and 5.4eV respectively. The optic value of maghemite band gap is 2.3 eV [6]. The photodisolvation process of maghemite, constitutes a powerful limit in use of this material in photoelectrochemichal applications.

The main distinct feature of maghemite is the presence of vacancies in Fe sites paralleled with crystal symmetry loss confirmed by RX diffraction. At room temperature, the magnetic moment of bulk gamma type Fe2O3 is ~430emu/cc and the magnetic moment of alpha type Fe2O3 is very small (~1emu/cc) [3]. Under 15nm [15], gamma Fe_2O_3 nanoparticles become superparamagnetic. Due to special magnetic properties, maghemite can be used with success for a variety of medical purposes: cell separation, drug delivery in cancer therapy, magnetic induced hyperthermia, MRI contrast agent, imunomagnetic separation IMC as well as other applications.

3. Iron in biology

Iron is an extremely important metal in living systems, especially for oxygen transport responsibility and electron transport linking the oxidation of substrates to the reduction of O_2. Generally, iron can link any kind of biomolecules, therefore the iron can adhere to membranes, proteins, nucleic acids. While "free" iron (which binds non-specifically to many cellular components) can catalyze production of toxic free radicals, in cells iron is generally stored in the centre of metalloproteins. The healthy human adults possess some 3 to 4 g of iron in their body. Less than 1% of iron makes a stable bound with various enzymes and redox proteins or is being transported through the blood by transferrin. In Nature, many redox reactions are dependent on iron-containing enzymes whereby electron transport is facilitated by changes in the metal oxidation state. Nitrogen fixation and photosynthesis are examples of processes in which iron-containing enzymes play vital roles. From this point of view, especially for their magnetic properties and for their biocompatibility, the ferromagnetic and superparamagnetic nanoparticles gamma Fe_2O_3 is involved in many interesting applications in biology and medicine. The size of nanoparticles involved, is a key element for the reason that very tiny particles (below one micrometer) can penetrate the tissue at cellular and subcellular level. For this purpose nanoparticles need to be coated by biopolymers [15]. The optimal magnetic core of functionalized nanoparticle is 20-50% from the total weight. Typically, magnetic nanoparticle probes for biomedical applications are comprised of nanoscale superparamagnetic iron oxide (SPIO) cores of magnetite and/or maghemite encased in

polysaccharide, synthetic polymer, or monomer coatings. Due to the Si-OH group on the silica surface, silica coated nanoparticles have a great potential for biomedical applications.

3.1 SPIO-Superparamagnetic Iron Oxide Core Structure

SPIO typically consists of two components: an iron oxide core and a hydrophilic coating. The SPIO core can be composed of magnetite (Fe_3O_4) and/or maghemite (γ Fe_2O_3). The main differences between maghemite and magnetite physical properties were presented in the first paragraph. A very good classification of the SPIO sizes in literature is presented by Andrew Tsourkas and coworkers in [16]. SPIO sizes range greatly from 2 to 3 nm for citrate inhibited growth SPIO, tens of nanometers for polymer coated polycrystalline iron oxide nanoparticles through to micrometers can be use for orally ingestible contrast agents. Larger diameters are available and are useful in such enterprises as cell tracking and separation, cell rheology and membrane deformation, and as contrast agents for the gastrointestinal tract, but have limited functionality in molecular imaging applications due to their limited accessibility to the neo- and microvasculature. Categories of SPIO, based on their overall diameter (including iron oxide core and hydrated coating), are noted in the literature [17] as oral-SPIO at between 300 nm and 3.5 μm; standard SPIO (SSPIO) at approximately 60–150 nm; ultra small SPIO (USPIO) of approximately 10–40 nm [18]; and nanocrystalline iron oxide nanoparticles (MION—a subset of USPIO) of approximately 10–30 nm [20]. MION nanoparticles are so named to underline the single crystal nature of their core. This is in contrast to SPIO greater than 50 nm that are comprised of multiple iron oxide crystals. Agents of all types excluding the MION category SPIO have either completed or are currently undergoing clinical testing. Generally speaking, all SPIO agents with less than a 50 nm diameter have been used for similar molecular imaging applications *in vivo*.

3.2 Biomedical applications

Magnetic separation of cells and bio molecule

This techniques are based on the contrast of magnetic susceptibility between medium (containing other nonmagnetic) and separand (magnetic). The process is described shortly and very clear by D Bahadur and Jyotsnendu Giri [21].

In living systems exists a few cells or biomolecules which have intrinsic magnetic properties. We can classify magnetic bio-separation into two modes. For the first case, the separand may have sufficient intrinsic magnetic moment (e.g. red blood cells and magnetotactic bacteria) and can be directly separated by applying magnetic fields. In the second case we can

manipulate the cells or biomolecules which are nonmagnetic in nature by attachment of magnetic responsive entity. The separation of cells or compounds may be done by direct and indirect procedures. In the first, ligands are immobilized on magnetic particles, and incubated with the medium (cells or compounds) for some time. The target cells bind with these ligands and the complex formed can be separated by a magnetic field. Second, in the indirect procedure, the target cell initially interacts with the ligand (primary antibody). The secondary antibody is then immobilized on magnetic particles and added to the medium containing the cells. The separand may be removed form the immunomagnetic particles after separation is done.

The superparamagnetic materials exhibit magnetic properties only in the presence of magnetic field and these can be used in very effectively magnetic separation of cells or bio molecules. The isolation of various macro molecules such as enzymes, enzyme inhibitors, DNA, RNA, antibodies and antigens etc. from different sources including nutrient media, fermentation broth, tissues extracts and body fluids, has been done by using magnetic absorbents. In case of enzyme separation, the appropriate affinity ligands are immobilized on polymer coated magnetic carrier or magnetizable particles. Immobilized protein A or protein G on silanized magnetite [22] and fine magnetotactic bacteria [23] can be used for isolation and purification of IgG [24]. Monosized superparamagnetic particles, Dynabeads, have been used in isolation of mRNA, genomic DNA and proteins. Isolation and separation of cells (prokaryotic, eukaryotic) or antigen have been done by immobilization of specific antibodies against the target (cells or antigen) i.e. by immunomagnetic separation [25, 26,27]

Removal of cancer cells from bone marrow is one of the most important applications of magnetic separation. Tumour cell separation from peripheral blood has been performed by immobilization of antibody on silica coated with superparamagnetic iron oxide [28].

Drug Delivery

The activity of most pharmaceuticals or drugs against certain diseases or disease sites suffers from their inability to gather selectively in the pathological organ or cells. Any kind of drug intravenously administrated is distributed in the entire body. This problem may be solved by selectively and quantitatively accumulating the drug to the target site (organ). Targeted drug delivery by external physical force (magnetic field) is an innovative new approach, capable to improve drug targeting. Magnetic drug transport technique is based on the fact that the drug can be either encapsulated in to a magnetic micro-sphere (or nano-sphere) or conjugated on the surface of the micro/nano sphere. When the magnetic carrier is

intravenously administered, the accumulation can take place within the area to which the magnetic field is applied and often augmented by magnetic agglomeration [29]. Efficiency of accumulation of magnetic carrier depends on physiological parameters [30] e.g. particle size, surface characteristics, field strength and blood flow rate etc. The magnetic field assists to movement of the magnetic carrier into a specific tissue. It has been observed that immobilization of MTC (magnetic target carriers) occurs within the tumor area when magnetic field is removed [31].

Site-directed drug targeting is one way of local or regional antitumor treatment. The efficiency of chemotherapy treatment may be enhanced to a great extent by magnetically assisted delivery of cytotoxic agent to the specific site. There are a large number of magnetic carrier systems which demonstrate increasing drug concentration efficiency at the tumor site [32,33]. In case of brain tumors, the therapeutic ineffectiveness of chemotherapy is mainly due to the impervious nature of the blood-brain barrier (BBB), presence of drug resistance and lack of tumor selectivity. Various novel biodegradable magnetic drug carriers are synthesized and their targeting to brain tumor is evaluated *in vitro* and in animal models. New cationic magnetic aminodextran micro spheres (MADM) have been synthesized. Its potentiality for drug targeting to brain tumor is under investigation [34]. The blood-brain barrier (BBB) is a separation of circulating blood and maintained by the choroid plexus in the central nervous system (CNS). Endothelial cells restrict the diffusion of microscopic objects (e.g. bacteria) and large or hydrophilic molecules into the CSF, while allowing the diffusion of small hydrophobic molecules (O2, hormones, CO2). Cells of the barrier actively transport metabolic products such as glucose across the barrier with specific proteins.

MRI contrast agents

Magnetic resonance imaging is considered to be one of the most powerful techniques in diagnostic, clinical medicine and biomedical research. This is an innovative technique that can provide information on the physical and chemical states of the tissues. The magnetic resonance images are obtained by placing the area of interest within a powerful, highly uniform static magnetic field. Since hydrogen nucleus (single proton) is abundant in the body due to the high water content of the biological tissue, the static magnetic field will make most of the protons to align with the field. These protons (nuclear spins) then move out of their alignment by the application of an alternating magnetic filed, which in turn is produced by the radio frequency coil near the specimen (static magnetic field). The resonant frequency of the alternating magnetic field should be in the radio frequency range (15–60 MHz). The nuclei

absorb energy from the oscillating magnetic field and undergo transition from the lower energy state to the higher energy state. When the alternating magnetic field is switched off, the nuclei return to the equilibrium state thereby emitting energy at the same frequency as previously absorbed. Further, this induces a signal in the coil, which is the source of alternating magnetic field. This nuclear magnetization can be transformed to diagnostic images through a series of algorithms. In an MRI image, contrast is due to different signal intensities form each tissue, produced in the presence of RF pulses. This response depends on proton concentration (water content), chemical and molecular structure of the tissues [35]. By varying the number and sequence of the pulsed radio frequency, images based on different tissues characteristics are possible.

MRI can provide information that differs from other imaging modalities. Its major technological advantage is that it can characterize and discriminate among deferent tissues using their physical and biochemical properties. The ability of MRI techniques to get images in multiple planes offers special advantages for radiation or surgical treatment.

Though MRI can provide definite noninvasive diagnoses, the sensitivity or the specificity of such processes can be improved by the addition of contrasting agents. These may be paramagnetic macromolecular compounds, superparamagnetic iron oxide or rare earth metal ion (Gd) complexes. Paramagnetic metal ions reduce the T1 relaxation of water protons and enhance the signal intensity, hence images are brighter. Superparamagnetic iron particles (SPIO) are more effective than monomolecular [36] or macromolecular Gd contrast agents for this purpose.

The most commonly used superparamagnetic material is Fe_3O_4 with different coatings such as dextrans[37], polymers[38], and silicone [39]. SPIO causes marked shortening of T2 relaxation and hence reduction of signal intensity occurs in MR images. So far it has been mainly used as a liver-specific contrast agent for intravenous application. It may be used for detection of metastases in non-enlarged lymph nodes. When contrast agent is interstitially applied, none of it is accumulated in the lesion since metastases do not have an intact phagocytosing system. Thus, a contrast agent induces a signal effect in normal tisue, but not in metastases and therefore contrast is enhanced [40].

Hyperthermia for treatment of cancer

Heat treatment of organs or tissues, through increasing the temperature up to 42–46^{0}C is known as hyperthermia [41,42,43]. In hyperthermia it is essential to establish a heat delivery system, such that the tumor cells are heated up or inactivated while the surrounding tissues

(normal) are unaffected. Though different hyperthermia techniques depend upon the heating methods used, each one has certain limitations. Boundary effects limit microwave, ultrasound, and RF hyperthermia. High frequency microwave beams have poor depth penetration and low frequency microwaves are difficult to focus on target areas. Though ultrasound has high penetration and focusing abilities, applications are limited by strong absorption by bone and high reflection by air cavities (lung etc.) [44]. By this technique it is difficult to heat up targets of high perfusion area to the desired temperature due to continuous dissipation of heat [45]. Interstitial technique device is implanted into the tumor, which acts as a heat source if connected with external power sources.

Intracellular hyperthermia is a technique where fluids containing submicron-sized magnetic particles (typically 1–100nm) are injected, these particles are easily incorporated into the cells, since their diameters are in the nanometer range. These magnetic particles selectively heat up tissues by coupling AC magnetic field to targeted magnetic nano particles. As a result, the whole tumour can be heated up uniformly. This technique is based on the fact that tumor cells are more sensitive to temperature than normal cells, and they have a very good appetite for iron oxide (nine times more than normal cells).

Gene Delivery

Magnetic particles can be used as a new and effective method of enhancing and targeting nucleic acid delivery [46,47]. One of the primary reasons for the limited efficacy of nucleic acid delivery systems is insufficient contact with target cells. This can be overcome by physical methods of targeting. Nucleic acid vectors are associated with magnetic particles and magnetic fields which are used to mediate the rapid contact of these vectors with the target cells. This technique called magnetofection is applicable to viral as well as to non viral vectors. Other key advantages are that saturation level transfection which is achieved at low dozes, that it is fast and simple.

Immunomagnetic separation of cells, detection, immobilization and modification of biologically active compounds

In this application, a ligand is coupled to the magnetic nanoparticles and is applied directly to the sample cells. During incubation the magnetic particles are bound to the target cells and thus stable magnetic complexes are formed. Then they can be separated using an appropriate magnetic separator. Magnetic nanoparticles used to label the cells have no negative effect on the viability of the attached cells, and the isolated cells remain

phenotypically unaltered. Due to its small size, it is able to avoid mechanical stress for the cells. The particles form a stable colloidal suspension and do not sediment or aggregate in magnetic fields.

Magnetic modifications of standard immunoassays can be successfully used for the determination of various biologically active compounds. Specific antibodies or antigens are immobilized on the magnetic particles by chemical bounding. Magnetically based assays are faster than the standard micro titration plate based assays.

Recently, the invertase was immobilized by various methods: by immersion / dipping the support in enzymatic solution, by direct attachment via carbodiimide activation and by activation with sodium citrate to magnetic nanoparticles support [48]. The magnetic nanometric support was synthesized by thermal co/precipitation of ferric and ferrous chloride ions using different work conditions; there were obtained 4 support types. The supports were characterized by Fourier Transform Infrared (FTIR). It was calculated the efficiency of the enzyme immobilization on different supports. Biologically active compounds [48,49] immobilized on magnetic carriers can be removed from the system by using an external magnetic field or can be targeted to the desired place. They can be used to express their activities in the process or can be used as affinity ligands enabling the capture or modification of the targeted molecules or cells.

This technology can be used to modify antibodies. Magnetically-label d antibodies have been proposed for clinical applications as a therapeutic agent for the induction of hyperthermia.

Conclusions

This paper outlines the main properties of iron oxide nanoparticles and their various photoelectochemical and bio-medical applications. A short general presentation is provided. Many novel approaches are described in the use of photoelectrochemistry such as solar energy conversion, water splitting, photocatalysts for the removal of organic and inorganic species from aqueous or gas phase. SPIO-Superparamagnetic Iron Oxide Core nanoparticles are presented. Modern applications are to be discussed in cell separation, immunoassay, as contrast agents in magnetic resonance imaging, drug and gene delivery, radionuclide therapy and hyperthermia applications. Magnetic forces can be used *in vitro* to direct the particles so that bound cells and molecules can be moved and *in vivo* to target and hold the magnetic carriers at anatomical sites or within cells for applications such as hyperthermia. Sometimes surface modification of these magnetic carriers is necessary for *in vivo* drug delivery or making these biocompatible. The applications of nano materials to photoelectrochemistry and

biotechnology/biosciences (so-called nanobiotechnology), are gradually increasing, and is a challenging area for future research. The solutions of these future problems from this area are in connection with new technological advances in surface chemistry, physics, geochemistry, molecular biology and biophysics. Moreover, it is possible that further research will lead to the fantastic problems of the genetically coded biological growth of artificial inorganic materials.

Like a mini web-cams, this nanoparticles continues to demonstrate strongly capacities to investigate deep inside into our biological universe. The use of magnetic materials in these aria research fields is restricted only by the imagination of researchers who create and exploit them.

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