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FUNCTIONALIZED Fe_3O_4 NANOCOMPOSITES AS PLATFORMS FOR BIOACTIVE MOLECULE IMMOBILIZATION AND TARGETED DRUG DELIVERY

N. V. Kusiak[1], K. P. Svyrydiuk[2]

This review summarises various modern approaches to the synthesis and functionalisation of magnetite (Fe_3O_4) magnetic nanoparticles and analyses their application as platforms for the immobilisation of biologically active molecules and pharmaceutical compounds. The main methods for producing Fe_3O_4 nanoparticles are discussed, in particular coprecipitation, hydrothermal, solvothermal and sol-gel synthesis, with an emphasis on their influence on the morphology, size and magnetic properties of the materials. Particular attention is paid to the surface functionalisation of nanoparticles via silanisation using APTES, MPTES and TEOS, which promotes the formation of active functional groups ($–NH_2$, –SH, Si–OH) and determines the mechanisms of interaction with drug molecules. The main types of interactions are analysed, in particular electrostatic, hydrogen, covalent and coordination bonds, which determine the efficiency of immobilisation and the kinetics of drug release. Examples are given of the immobilisation of proteins, enzymes, immunoglobulins and anticancer drugs (doxorubicin, cisplatin) on the surface of magnetic nanocomposites. It is shown that the chemical nature of the surface determines not only the adsorption properties but also the biocompatibility, stability and therapeutic efficacy of the systems. The application of Fe_3O_4 nanoparticles in targeted drug delivery, magnetically controlled systems, hyperthermia and biosensors is considered separately. It is concluded that there is great potential for the creation of multifunctional nanocomposites with controllable surface properties for modern applications in nanomedicine.

Key words: *magnetite, nanocomposites, surface functionalisation, drug immobilisation, targeted delivery.*

[1] Ph.D. in Chemistry,
Associate Professor of the Department of Chemistry
(Zhytomyr Ivan Franko State University, Zhytomyr);
(Chuiko Institute of Surface Chemistry National Academy of Science of Ukraine, Kyiv)
e-mail: nkusyak@ukr.net
ORCID: 0000-0002-0143-3399
[2] Master's degree,
Assistant at the Department of Chemistry
(Zhytomyr Ivan Franko State University, Zhytomyr)
e-mail: sviridyukk-97@ukr.net
ORCID: 0009-0000-1258-7644

ФУНКЦІОНАЛІЗОВАНІ НАНОКОМПОЗИТИ Fe_3O_4 ЯК ПЛАТФОРМИ ДЛЯ ІММОБІЛІЗАЦІЇ БІОАКТИВНИХ МОЛЕКУЛ ТА ЦІЛЬОВОЇ ДОСТАВКИ ЛІКАРСЬКИХ ПРЕПАРАТІВ

Н. В. Кусяк, К. П. Свиридюк

У цьому огляді узагальнено окремі сучасні підходи до синтезу та функціоналізації магнітних наночастинок магнетиту (Fe_3O_4) та проаналізовано їхнє застосування як платформ для іммобілізації біологічно активних молекул і фармацевтичних сполук. Обговорено основні методи отримання наночастинок Fe_3O_4, зокрема копреципітаційний, гідротермальний, сольвотермальний та золь-гель-синтез, з акцентом на їхньому впливі на морфологію, розмір та магнітні властивості матеріалів. Особлива увага приділяється поверхневій функціоналізації наночастинок шляхом силанізації з використанням APTES, MPTES та TEOS, що сприяє утворенню активних функціональних груп ($–NH_2$, –SH, Si–OH) та визначає механізми взаємодії з молекулами лікарських препаратів. Проаналізовано основні типи взаємодій, зокрема електростатичні, водневі, ковалентні та координаційні зв'язки, які визначають ефективність іммобілізації та кінетику вивільнення лікарського препарату. Наведено приклади іммобілізації білків, ферментів, імуноглобулінів та протипухлинних препаратів (доксорубіцину, цисплатину) на поверхні магнітних нанокомпозитів. Продемонстровано, що хімічна природа поверхні визначає не лише адсорбційні властивості, а й біосумісність, стабільність та терапевтичну ефективність систем. Окремо розглядається застосування наночастинок Fe_3O_4 цільовій доставці лікарських засобів, магнітно керованих системах, гіпертермії та біосенсорах. Зроблено висновок про великий потенціал створення багатофункціональних нанокомпозитів з керованими поверхневими властивостями для сучасних застосувань у наномедицині.

Ключові слова: *магнетит, нанокомпозити, функціоналізація поверхні, іммобілізація лікарських засобів, цільова доставка.*

Introduction

The vast majority of biological processes begin and take place at the molecular level. Consequently, the search for diagnostic and therapeutic solutions is conducted at the nanoscale. The application of nanoparticles (NPs) in medicine is determined by processes occurring at the biointerface. In this context, manipulating surface properties is of crucial importance, as this can determine the fate and functionality of the nanosystem, and this can be achieved using various surface functionalisation methods (Kohale et al., 2026). Among the matrices whose surfaces are subject to functionalisation and which have been actively investigated in recent years are magnetically controlled oxide materials, particularly those based on iron. Potential applications for these nanoparticles include fields such as catalysis, biomedicine, environmental remediation and electronics (Fig. 1).

Magnetite, haematite, and maghemite are various forms of iron oxide nanoparticles (IONPs) (Fig. 2), with Fe_3O_4 NPs being widely used in clinical practice due to their superparamagnetic properties and biocompatibility (Chatterjee et al., 2025; Das et al., 2025).

IONPs exhibit properties such as superparamagnetic, diamagnetic and ferromagnetic behaviour, and their manipulation in a magnetic field opens up numerous possibilities in biomedicine. Ferromagnetic materials retain a stable net magnetic moment after exposure to a magnetic field, whereas paramagnetic materials exhibit a weaker net moment during exposure, which is not retained after the field is removed. Diamagnetic materials lack unpaired electrons, resulting in a net magnetic moment of zero. Consequently, these materials exhibit minimal response to applied magnetic fields due to the rearrangement of electron orbitals. Paramagnetic iron oxide with particle sizes < 20 nm is known as superparamagnetic iron oxide nanoparticles (SPIONs). NPs with superparamagnetic properties are of particular interest due to their ability to exhibit high magnetic interaction under the influence of an applied magnetic field, and this interaction disappears in the absence of a magnetic stimulus. The two main parts of coated nanoparticles are the core and the shell. The core consists of magnetic elements such as Fe, Co or Ni, and associated oxides. It plays a significant role in the quantum effect and magnetic properties. The role of the shell is to stabilise the core and protect it from external environmental influences.

This review is devoted to an analysis of some methods for the synthesis and surface functionalisation of one of the iron oxides

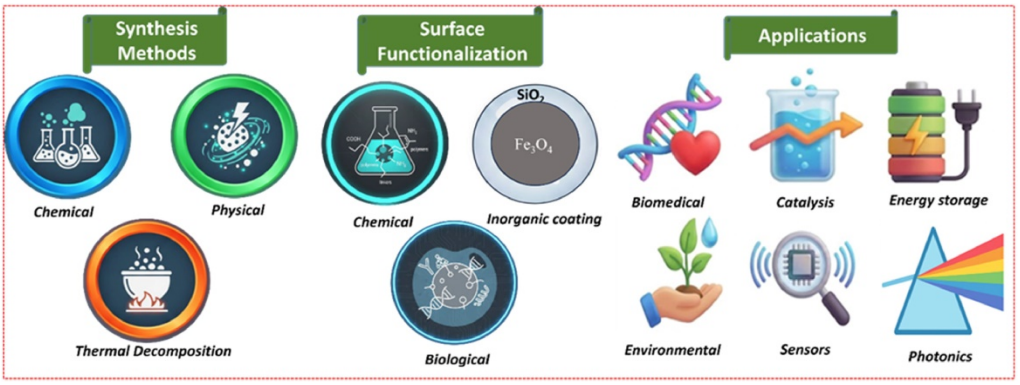


Fig. 1. Schematic overview of Fe_3O_4 NPs: synthesis routes, structure–property relationships, multifunctional applications (Kohale et al., 2026)

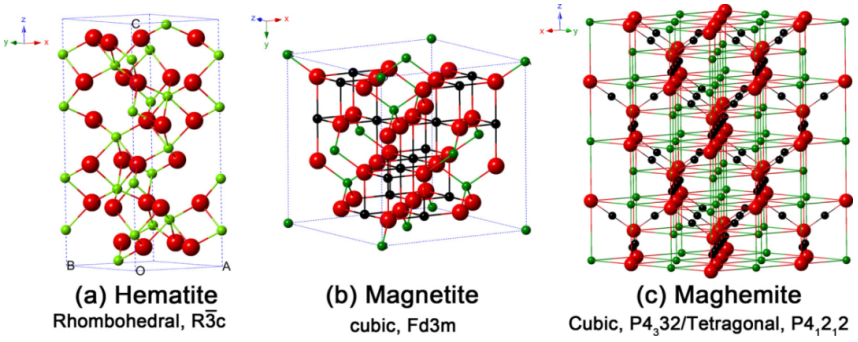


Fig. 2. Crystal structure and crystallographic data of the hematite, magnetite and maghemite (the black ball is Fe^{2+}, the green ball is Fe^{3+} and the red ball is O^{2-}) (Wu et al., 2015)

magnetite, an analysis of some recent studies on the development of new composite materials based on it, as well as an investigation of the characteristics of the immobilisation of biologically active molecules and pharmaceutical compounds.

Materials and Methods

This review is based on a comprehensive analysis of the latest scientific literature on magnetite (Fe_3O_4) nanoparticles and their functionalised nanocomposites. The literature search was conducted using leading scientific databases, including Scopus, Web of Science, ScienceDirect, Taylor & Francis, PubMed, the American Chemical Society (ACS), the Royal Society of Chemistry (RSC), Wiley Online Library, ResearchGate and Google Scholar. The following keywords were used: "Fe_3O_4 nanoparticles", "surface functionalization", "drug immobilization", "magnetic nanocomposites" and "targeted drug delivery".

Particular attention was paid to publications from the last decade, although early fundamental studies were also considered to provide a broader scientific context. The selected studies were analysed in terms of synthesis methods, surface modification strategies, types of interaction with bioactive molecules, and biomedical applications. To ensure the reliability and scientific validity of the analysis, only peer-reviewed articles relevant to this topic were included.

Results

A review of the literature indicates the existence of a wide range of approaches to the synthesis and functionalisation strategies for Fe_3O_4 nanoparticles, each of which results in different physicochemical and biomedical properties. The following sections summarise the main conclusions regarding the methods of synthesis, surface modification and practical application of magnetite-based nanocomposites.

Methods for producing magnetite based nanocomposite systems.

Various methods have been developed for the synthesis of magnetite (Fe_3O_4) nanoparticles, allowing precise control over their size, morphology, and magnetic properties (Rezaei et al., 2024). The most widely used approach

is co-precipitation, which involves the reaction of Fe^{2+} and Fe^{3+} salts in alkaline media and is valued for its simplicity and scalability. However, this method often results in broad particle size distribution and limited control over morphology. Hydrothermal and solvothermal methods provide improved crystallinity and uniformity by conducting reactions under high temperature and pressure conditions (Fig. 3 a) (Ahmad et al., 2025; Izaz et al., 2025). Thermal decomposition is another widely used technique that produces highly monodisperse nanoparticles with excellent control over size, although it requires organic solvents and elevated temperatures.

The sol–gel method allows the formation of homogeneous oxide networks and is suitable for coating applications, particularly in the fabrication of core–shell structures (Fig. 3 b,c) (Kusiak et al., 2021). Reverse micelle techniques enable the synthesis of ultra-small nanoparticles by confining reactions within nanoscale droplets. Microwave-assisted synthesis offers rapid heating and reduced reaction times, leading to uniform particle formation. Additionally, sonochemical methods utilize ultrasonic energy to enhance nucleation and particle dispersion. Recently, green synthesis approaches using plant extracts or biocompatible agents have gained attention due to their environmental friendliness. Each synthesis method significantly influences the surface chemistry and functionalization potential of Fe_3O_4 nanoparticles. Therefore, the choice of synthesis route plays a crucial role in determining their suitability for biomedical applications.

The functionalisation of the magnetite surface.

The functionalisation of the magnetite (Fe_3O_4) surface is a key step in the creation of stable and effective nanocomposites for the immobilisation of drugs. In an aqueous environment, the Fe_3O_4 surface is characterised by the presence of hydroxyl groups (≡Fe–OH), which are formed as a result of the hydration of the oxide surface. These groups act as active sites for subsequent chemical transformations, in particular silylation reactions. (Popescu et al., 2019; Rarokar et al., 2024). Surface hydroxyl groups can be protonated or deprotonated depending on the pH of the medium:

$$\equiv Fe–OH + H^+ \leftrightarrows \equiv Fe–OH_2^+$$

$$\equiv Fe–OH \leftrightarrows \equiv Fe–O^- + H^+$$

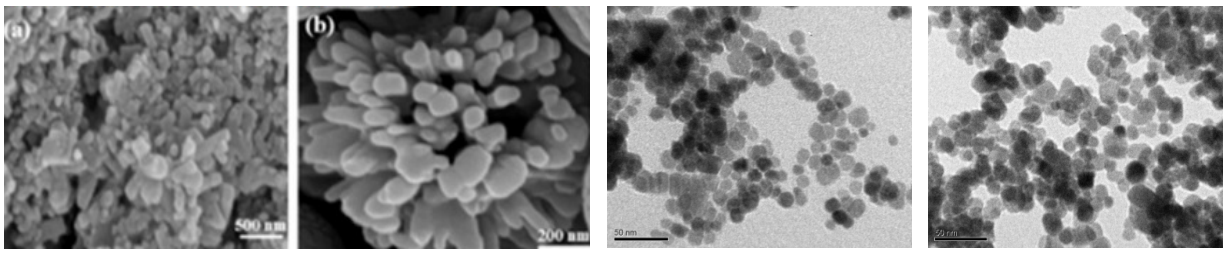
This determines the surface charge and the surface's ability to interact electrostatically with drug molecules. One of the most common modification methods is silylation, which is based on the hydrolysis and condensation of alkoxysilanes. The general reaction of silane coupling can be described as follows:

$$\equiv Fe–OH + (RO)_3–Si–R' \rightarrow \equiv Fe–O–Si–R' + 3ROH$$

This leads to the formation of a strong Fe–O–Si covalent bond, which ensures the stability of the functional layer.

$$\equiv Fe–OH+(RO)_3Si–R' \rightarrow \equiv Fe–O–Si–R' + 3ROH$$

Among silanes, (3-aminopropyl)triethoxysilane (APTES) is of particular importance, as it introduces amino groups ($–NH_2$) onto the surface of nanoparticles. Structurally, this can be represented as $Fe_3O_4–O–Si–(CH_2)_3–NH_2$. Aminofunctionalisation significantly expands immobilisation possibilities, as $–NH_2$ groups can participate in electrostatic interactions, hydrogen bonds and covalent bonds. When the pH decreases, the amino groups are protonated:



a **b** **c**

Fig. 3. SEM morphology of FeONPs produced by a microemulsion-hydrothermal technique (Ahmad et al., 2025) (a) and TEM images of Fe_3O_4 (b) and Fe_3O_4 /SiO_2 NPs (c) produced by a sol–gel method (Kusiak et al., 2021)

$$–NH_2 + H^+ – NH_3^+$$

which facilitates the binding of anionic drug molecules. Furthermore, amino groups can react with aldehyde agents, such as glutaraldehyde, to form imine bonds (Schiff bases):

$$–NH_2 + OHC–R–CHO \rightarrow –C=N^- + H_2O$$

$$-NH_2 + OHC–R–CHO \rightarrow -C=N^- + H_2O$$

Another important type of functionalisation is the introduction of thiol groups (*–SH*) using agents such as MPTES or DMSA. Thiol groups are weak donor centres and are capable of forming coordination bonds with metal ions. In particular, in the case of platinum-containing compounds, the formation of a *Pt–S* bond is possible:

$$Pt– Cl + R – SH \rightarrow Pt–S–R + HCl$$

$$Pt-Cl+R-SH\rightarrow Pt-S-R+HCl$$

This mechanism is key to the immobilisation of cisplatin and similar compounds. Thiol functionalisation ensures high selectivity and bond strength, which directly influences the release kinetics. Silylation using tetraethoxysilane (TEOS) leads to the formation of an SiO_2 shell containing a large number of silanol groups (*Si–OH*). Such surfaces are characterised by high hydrophilicity and the ability to form hydrogen bonds with drug molecules. Furthermore, the SiO_2 shell performs a protective function, preventing particle aggregation and ensuring stability in biological environments.

Thus, the type of functional groups determines the nature of the interaction between the surface of the nanocomposite and the drug molecules. Amino functionalisation provides universal binding mechanisms; thiol groups are responsible for the specific coordination of metal-containing compounds, whilst silane surfaces promote physical adsorption and the formation of hydrogen bonds. The choice of an appropriate functionalisation method allows for the targeted regulation of the efficiency of drug immobilisation and subsequent release, which is of crucial importance for the development of modern nanomedicine systems.

Applications of Fe_3O_4 NPs

Fe_3O_4 NPs are widely used in biomedicine due to their superparamagnetic properties, biocompatibility and ease of surface functionalisation. They are actively employed for targeted drug delivery, where an external magnetic field facilitates the accumulation of therapeutic agents in specific areas. Furthermore, Fe_3O_4 NPs serve as contrast agents in magnetic resonance imaging (MRI) and as mediators in magnetic hyperthermia for cancer treatment (Roy & Roy, 2022; Kohale et al., 2026). Apart from biomedical applications, they are also used for environmental remediation, catalysis and biosensing, thanks to their large surface area and ability to modulate surface chemical properties (Fig. 4).

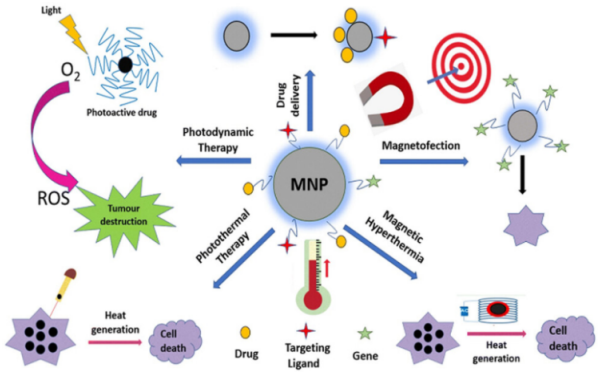


Fig. 4. The various therapeutic applications of MNPs (Azari et al. 2026)

Immobilisation of bioactive molecules and drugs on the surface of MNPs.

One of the most important steps in creating multifunctional nanocomposites is the immobilization of biologically active molecules, including immunoglobulins and drugs, on their surface (Popescu et al., 2019; Mishra & Yadav, 2024; Rarokar et al., 2024). Surface functionalization will facilitate the delivery of the drug exclusively to target cells in the body. Therefore, an important part of the research involves modeling the conditions and studying the mechanism of antibody immobilization on the surface of a magnetosensitive carrier (Gorbyk et al., 2026).

For example, the intensity of interactions between serum albumin and dendrimer-coated MNPs strongly depended on the composition of surface groups and the pH of the medium (Shao et al., 2009). The quenching of fluorescence of tryptophan residues in serum albumin following interaction with nanoparticles was investigated. A study of the interaction of Fe_3O_4 nanoparticles with human serum albumin showed (Huang et al., 2007) that the protein molecule exerts a stabilizing effect on the magnetite nanoparticles, preventing them from aggregating in an aqueous medium. It has been established that Fe_3O_4 nanoparticles functionalized with oleic acid and PEG have a high affinity for the albumin molecule ($K_{ass} > 10^5$/mol).

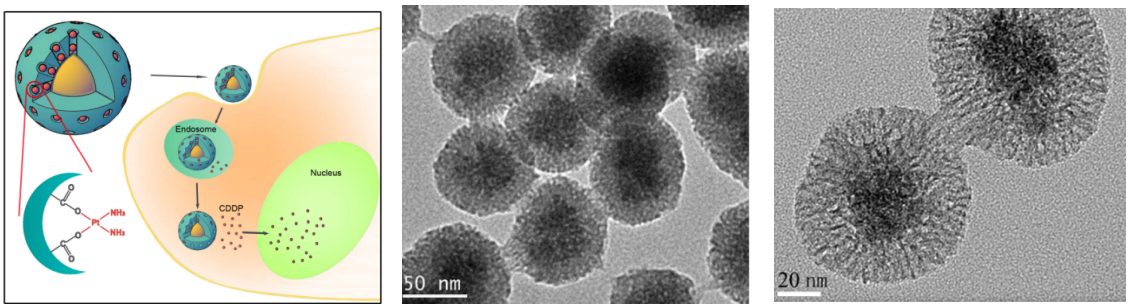
A 22-fold increase in the binding capacity of Fe_3O_4/SiO_2/PAA microspheres for lysozyme compared to Fe_3O_4/SiO_2 microspheres at the same pH values is discussed in (Qiu et al., 2010). The active amino groups of the magnetic carriers of zinc/tetraaminophthalocyanine/ Fe_3O_4 (ZnTAPc) nanocomposites with a diameter of about 15 nm were used to attach lactase via glutaraldehyde (Wu et al., 2009). The amino groups located on the surface of the composite are capable of covalently binding to glutaraldehyde, and the terminal aldehyde group of glutaraldehyde can covalently bind lactase. The optimal pH value for maintaining the activity of immobilized lactase, as for free lactase, is 3.0, and the optimal temperature for immobilization is 45 °C. The degree of immobilization and the Michaelis constant (K_m) of lactase were 25% and 20.1 μM, respectively. The im ed lactase exhibited high stability and can be used as a sensitive biocomponent for constructing a fiber-optic biosensor based on enzymatic catalysis.

Fe_3O_4/Au core-shell nanocomposite particles, attached to the surface of a magnetic glassy carbon electrode, were used to immobilize myoglobin (Mb) during the preparation of an Mb/Fe_3O_4/Au biofilm (Qiu et al., 2010). The properties of the nanocomposite were characterized using transmission electron microscopy, ultraviolet and visible spectroscopy, and cyclic voltammetry. The Fe_3O_4/Au nanoparticles exhibited magnetic properties, high electrical conductivity, and biocompatibility (due to the Au layer), which allowed for the maintenance of biological activity and facilitated the electrochemical attachment of Mb in the biofilm. The proposed method indicates the potential for use in the development of new biosensors and bioelectronic devices.

A new and relatively simple method for the preparation of Fe_3O_4/chitosan (CS) magnetic nanocomposites (Семко та ін., 2010) was proposed, which were used for the immobilization of lipase. The effects of reaction conditions, reaction temperature, and the CS/$Fe(OH)_2$ ratio were investigated. Transmission electron microscopy revealed that the diameter of the nanocomposites was approximately 80 nm, and Fe_3O_4 magnetic nanoparticles with a diameter of 20 nm were uniformly distributed in chitosan. The adsorption capacity for lipase was 129 mg/g. Protein A was immobilized on the surface of Fe_3O_4/SnO_2 nanoparticles. It was shown that the resulting magnetic nanosorbent can be used for the selective extraction of immunoglobulins from biological media (Gu et al., 2010). The composition of air-dried samples of activated Fe_3O_4/SnO_2 nanocomposites ranged from 88–92% Fe3O4 and 3–5% SnO_2 (the tin content is expressed as oxide, although the tin-containing shell consisted of tin (IV) hydroxides and tin acids of various structures (Thanh et al., 2019; Mu et al., 2015). By immobilizing *Staphylococcus aureus* protein A onto activated magnetic nanoparticles, a coating selective for immunoglobulin fragments was formed, which allowed for the preparation of an IgG-binding sorbent. The ability to isolate immunoglobulins from biological media using the sorbent prepared by the method has been demonstrated. By replacing *Staphylococcus aureus* protein A with a receptor center of a different type, the proposed method can be used for the adsorption of other biological and biochemical entities.

In (Zhu et al., 2014) magnetic mesoporous nanocomposites based on silicon dioxide with a «core-shell» structure were synthesised, containing a high concentration of Fe_3O_4@nSiO_2@ mSiO_2-COOH in the form of suspended carboxyl groups for the conjugation and release of cisplatin (CDDP) for the treatment of cancer. Water-soluble sodium carboxyethylsilanetriol was condensed with TEOS to form mesoporous shells modified with carboxyl groups (Fig. 5). The carboxyl groups inherent in the resulting nanocomposites serve as effective anchors for coordination with Pt atoms in the anticancer drug cisplatin, leading to an increase in the amount of loaded drug and its sustained release. The resulting nanocomposites demonstrate excellent dispersibility in water with a well-defined size distribution (approximately 85 nm), ordered mesoporosity, superparamagnetism and high magnetic susceptibility (37.0 emu/g^{-1}). They can be used for magnetically guided delivery and controlled release of CDDP, which exhibits higher cytotoxicity than free CDDP against MCF-7 and A549 cancer cell lines. The nanocomposites can not only effectively transport the encapsulated cisplatin into cancer cells, but also mediate its delayed release in endosomes or lysosomes, leading to enhanced antitumour efficacy.

A new plasma technology was used to synthesize carbon-iron magnetic nanoparticles (CMNPs) from benzene or acetonitrile at room temperature and atmospheric pressure structures (Ma et al., 2009). Scanning electron microscopy revealed that the nanoparticles are spherical in shape and have a diameter of 40–50 nm. Free doxorubicin (DOX) mol-



a **b**

Fig. 5. Schematic illustration of the preparation of Fe_3O_4@nSiO_2@mSiO_2-COOH, and the complexation process for CDDP with carboxyl groups suspended in the channels of mesoporus shells (a) and TEM image of Fe_3O_4@nSiO_2 @mSiO_2-COOH (b) (Zhu et al., 2014)

ecules were then immobilized on activated CMNP surfaces via to obtain CMNP/DOX conjugates. The antitumor activity of CMNP/DOX conjugates was confirmed in studies of their cytotoxicity against tumor cells.

Fe_3O_4 nanoparticles were pre-stabilized with polysaccharides (chitosan, O-carboxymethylchitosan, and N-succinyl-O-carboxymethylchitosan), and the adsorption of the antitumor drug camptothecin (CPT) onto the nanoparticles was investigated (Zhu et al., 2009). It has been shown that the size of magnetite/polysaccharide/CPT nanocomposites, as well as the efficiency of binding and release of the antitumor drug and the ability for nonspecific binding to protein molecules (bovine serum albumin), depend on the structure of the polysaccharide.

Colloidally stable, surface-modified poly(N,N-dimethylacrylamide-CO-acrylic acid) iron oxide-based nanoparticles were characterized using SEM, elemental analysis, and dynamic light scattering (DLS), and their zeta potential was measured (Macková et al., 2015). The efficacy of superparamagnetic nanoparticles was determined during the oxidation of blood lipids and serum proteins using 2-thiobarbituric acid and ThioGlo fluorofluor. A comparative study of the activity of the synthesized composite and cisplatin against Lewis carcinoma in male C57BL/6 mice was conducted. Tumor size was measured, and the number of metastases in the lungs was determined. The potential for using the obtained nanocomposites as effective antitumor agents was established.

Core-shell Fe_3O_4/SiO_2 nanoparticles, functionalised with 3-aminopropyltrimethoxysilane (NH_2) and folic acid (FA), were developed as a dual-targeting system for the delivery of doxorubicin (Dox) in work (Azari et al., 2026). SPIONs were synthesised as the core, coated with silicon dioxide and conjugated with FA to ensure binding to the folate receptor. Structural characterisation confirmed a cubic spinel structure of Fe_3O_4 (XRD) with an average particle size of 11 nm (HRTEM) and a hydrodynamic diameter of 14 nm (DLS). Magnetic measurements demonstrated strong superparamagnetic properties, confirming the possibility of external control. Cytotoxicity was assessed using MTT assays on A549 (lung cancer) and 5637 (bladder cancer) cell lines, demonstrating selective activity against malignant cells. Drug release studies revealed a pH-dependence: at pH 5.4, 50% of DOX was released within 4 hours and 68.09% within 93 hours, compared to 42% and 52.89% at pH 7.4. Kinetic modelling indicated first-order release kinetics. Taken together, these results indicate that Fe_3O_4/SiO_2 core nanoparticles represent a promising platform for the targeted and sustained delivery of doxorubicin, thereby reducing side effects and expanding the therapeutic potential of the treatment.

A series of studies (Lee & Yeo, 2015; Wani et al., 2016) is devoted to a review of the current literature on the synthesis of magnetosensitive nanocomposites for biomedical applications, nanorobots for oncological and neutron-capturing therapy, and the immobilization of cisplatin, as well as to investigating their effects on various types of cancer cells. With the aim of creating new forms of magnetically controlled drug delivery systems for oncology, a series of experimental samples of new types of magnetosensitive nanocomposites, as well as magnetic fluids based on them, for biomedical applications; their physical, chemical, and

biological properties were studied and systematized (Горбик та ін., 2013; Petranovska et al., 2018; Petranovska et al., 2019).

Theoretical assessments of the conditions for transport and fixation of magnetosensitive nanocomposites using an external magnetic field were performed. It has been shown that with an optimal selection of magnetic systems, it is possible to retain drug-loaded nanocontainers even in large main blood vessels. The calculations indicate a realistic possibility of targeted delivery and retention of magnetic carriers in target organs (Кусяк та ін., 2025a; Кусяк та ін., 2025b; Gorbyk et al., 2026).

The cytotoxic effect of magnetosensitive nanocomposites with an adsorbed cytostatic agent, conjugated with a monoclonal antibody, on the viability of the human breast cancer cell line MCF-7 was studied. The use of magnetic nanocomposites containing an antitumor drug and the monoclonal antibody CD-95 was accompanied by a significant synergistic effect of cytotoxic action. Their efficacy exceeded the combined effect of the corresponding control doses of cisplatin and the antibody by 20–200 %.

Magnetic nanomaterials exhibiting high specificity and biocompatibility have been synthesised to detect molecular interactions *in vitro* and *in vivo* and are used as biosensors for effective diagnosis. Magnetic anisotropy is used to regulate the critical magnetic field required to switch the magnetisation of the element between two stable states, thereby creating a binary barcode. Currently, magnetic biosensors for diagnostics are based not only on the properties of magnetic nanoparticles, but also on functionalised coated materials. Magnetic sphere-based biosensors are functionalised MNPs through the conjugation of target ligands, which gives magnetic sphere-based biosensors new specificity. At the same time, MNPs, together with target receptors and functionalised spheres/materials, act as a signal generator or detector, determining the sensitivity of the biosensors (Fig. 6).

Discussion

A comparative analysis of published studies clearly shows that no single synthesis or functionalisation strategy can be considered universally optimal. Each approach has its own advantages depending on the intended biomedical application. For example, the co-precipitation method offers scalability, whilst thermal decomposition provides excellent size control and monodispersity. Surface functionalisation plays a decisive role in determining not only the efficiency of immobilisation but also the biological characteristics of nanocomposites. The introduction of amino, thiol or silanol groups allows for the precise tuning of intermolecular interactions, which directly influences drug loading capacity and release kinetics. Importantly, the interaction between

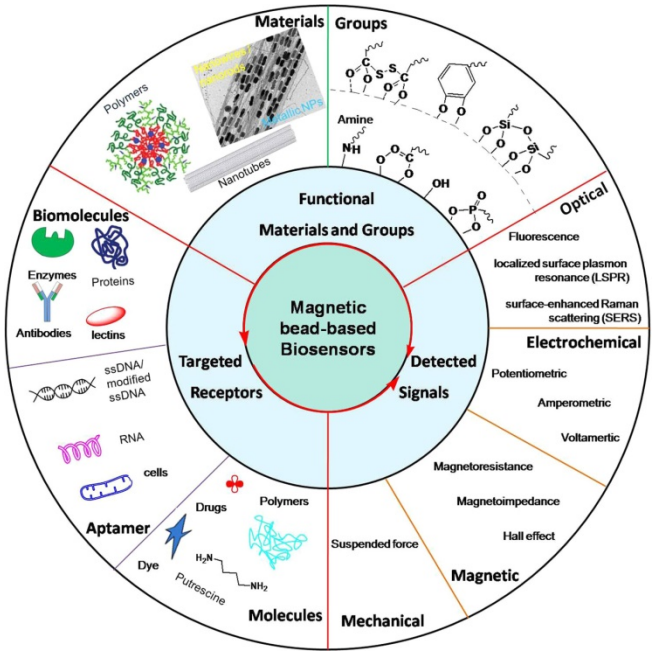


Fig. 6. Schematic representation of a magnetic biosensor (Wu et al., 2015)

synthesis conditions and surface chemistry remains a critical factor affecting reproducibility and stability. In many cases, minor changes in experimental parameters lead to significant differences in nanoparticle behaviour, complicating standardisation. Overall, current research trends are shifting towards the development of multifunctional and stimulus-responsive systems capable of controlled drug delivery, improved targeting efficiency and reduced side effects.

Conclusions

This review summarises current approaches to the synthesis, functionalisation and application of magnetite nanoparticles as versatile platforms for the creation of biomedical nanocomposites. It is shown that the synthesis method determines the size, morphology and magnetic properties of Fe_3O_4 nanoparticles, which directly influences their subsequent functionalisation and performance in applied systems. It has been established that surface modification using silanes (APTES, MPTES, TEOS) is a key tool for controlling interfacial interactions, as it allows the introduction of various types of functional groups and the regulation of the types of bonds with biomolecules. It has been established that the type of functional groups determines not only the binding efficiency but also the kinetics of drug release. Examples of the immobilisation of proteins, enzymes, immunoglobulins and anticancer drugs are provided, demonstrating the high efficiency of magnetic nanocomposites in biomedical applications. The potential for using Fe_3O_4 nanoparticles in targeted delivery systems, magnetically controlled therapies and biosensors has been demonstrated. The results obtained indicate that the rational selection of synthesis and functionalisation methods opens up broad possibilities for the creation of multifunctional nanomaterials with specified properties. Prospects for further research relate to the development of multi-stimulating systems, the improvement of biocompatibility and a deeper understanding of the mechanisms of interaction between nanoparticles and biological objects. Furthermore, future research should focus on integrating several functional components into a single nanoplatform, thereby achieving a synergistic effect in treatment and diagnosis. The development of such advanced systems requires not only the refinement of synthesis strategies, but also a deeper understanding of nanobiological interactions at the molecular level.

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