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Author	Family Name	**Omoruyi**
	Particle	
	Given Name	**Inono C.**
	Prefix	
	Suffix	
	Role	
	Division	Department of Chemistry
	Organization	University of Benin
	Address	Benin City, Edo State, Nigeria
	Email	
Author	Family Name	**Omoruyi**
	Particle	
	Given Name	**Jeffery I.**
	Prefix	
	Suffix	
	Role	
	Division	Department of Crop Improvement and Management
	Organization	Rubber Research Institute of Nigeria
	Address	PMB 1049, Iyanomo, Benin City, Edo State, Nigeria
	Email	
Author	Family Name	**Aghedo**
	Particle	
	Given Name	**Oscar N.**
	Prefix	
	Suffix	
	Role	
	Division	Department of Science Laboratory Technology
	Organization	University of Benin
	Address	Benin City, Edo State, Nigeria
	Email	
Author	Family Name	**Archibong**
	Particle	
	Given Name	**Ukeme D.**
	Prefix	
	Suffix	

	Role	
	Division	Department of Science Laboratory Technology, Faculty of Life Science
	Organization	University of Benin
	Address	Benin City, Nigeria
	Email	
Corresponding Author	Family Name	**Ifijen**
	Particle	
	Given Name	**Ikhazuagbe H.**
	Prefix	
	Suffix	
	Role	
	Division	Department of Research Operations
	Organization	Rubber Research Institute of Nigeria
	Address	PMB 1049, Iyanomo, Benin City, Edo State, Nigeria
	Email	larylans4u@yahoo.com
		ifijen.hilary@rrin.gov.ng

Abstract	Magnetic iron oxide nanoparticles (IONs) stand out among a plethora of drug nanocarriers as sturdy nanoplatforms due to exceptional magnetic and biological properties, which allow them to achieve significant drug loading as well as targeting capabilities. These applications necessitate accurate nanoparticle design in terms of numerous characteristics that must be evaluated in tandem to achieve maximum therapeutic efficacy. This concise overview summarizes recent advances in the roles of untreated and modified iron oxide nanoparticles for drug delivery. These modifications included chitosan, poly(vinylpyrrolidone), poly(vinyl alcohol), poly(lactic-co-glycolic acid), and poly(ethylene glycol). One of the key areas of research in the targeted drug delivery domain is the invention of nanocarriers that allow for the efficient delivery of therapeutic chemicals to specific sites. Drugs loaded onto iron oxide nanoparticles can be efficiently guided and selectively delivered to selected sites by precisely altering the structural features of the nanoparticles.

Keywords (separated by '-')	Iron oxide - Nanostructures - Drug delivery - Magnetic

Application of Magnetic Iron Oxide Nanostructures in Drug Delivery: A Compact Review

Inono C. Omoruyi, Jeffery I. Omoruyi, Oscar N. Aghedo, Ukeme D. Archibong, and Ikhazuagbe H. Ifijen

Abstract Magnetic iron oxide nanoparticles (IONs) stand out among a plethora of drug nanocarriers as sturdy nanoplatforms due to exceptional magnetic and biological properties, which allow them to achieve significant drug loading as well as targeting capabilities. These applications necessitate accurate nanoparticle design in terms of numerous characteristics that must be evaluated in tandem to achieve maximum therapeutic efficacy. This concise overview summarizes recent advances in the roles of untreated and modified iron oxide nanoparticles for drug delivery. These modifications included chitosan, poly(vinylpyrrolidone), poly(vinyl alcohol), poly(lactic-co-glycolic acid), and poly(ethylene glycol). One of the key areas of research in the targeted drug delivery domain is the invention of nanocarriers that allow for the efficient delivery of therapeutic chemicals to specific sites. Drugs loaded onto iron oxide nanoparticles can be efficiently guided and selectively delivered to selected sites by precisely altering the structural features of the nanoparticles.

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I. C. Omoruyi
Department of Chemistry, University of Benin, Benin City, Edo State, Nigeria

J. I. Omoruyi
Department of Crop Improvement and Management, Rubber Research Institute of Nigeria, PMB 1049, Iyanomo, Benin City, Edo State, Nigeria

O. N. Aghedo
Department of Science Laboratory Technology, University of Benin, Benin City, Edo State, Nigeria

U. D. Archibong
Department of Science Laboratory Technology, Faculty of Life Science, University of Benin, Benin City, Nigeria

I. H. Ifijen (✉)
Department of Research Operations, Rubber Research Institute of Nigeria, PMB 1049, Iyanomo, Benin City, Edo State, Nigeria
e-mail: ifijen.hilary@rrin.gov.ng

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Introduction

Nanostructures have developed over the past few years into new, potent tools in a variety of technical applications [1–10]. Researchers have become increasingly interested in these applications, which has led to excellent developments in the creation of many types of nanomaterials and nanodevices [11–17]. Due to their inherent magnetic properties (superparamagnetism), magnetic iron oxide nanoparticles (IOMNPs) have received the most attention among the various types of nanomaterials studied [18, 19]. These properties allow them to be used in a variety of scientific fields like electronics or the environment. Ions are the perfect platform for biological applications because of their exceptional magnetic characteristics as well as their biocompatibility, stability, and environmental friendliness [20]. Co-precipitation, sol–gel, hydrothermal, and other techniques are used to create magnetic nanoparticles, among others [18]. The co-precipitation approach may be used to create magnetite nanoparticles with a narrow size distribution and a particle size range from 5 to 100 nm, and the magnetism of the nanoparticles can be improved by clustering them [18, 19].

Targeted nanomedicine using magnetic nanoparticles has emerged as one of the most potent methods for diagnosis and therapy [21]. One more benefit is the ability to employ an external magnet to deliver medications to target organs utilizing the core magnetic nanoparticle. This could solve a number of issues, including off-target adverse effects, poor drug solubility, brief life cycle, etc. [22]. Due to changes in the drug's pharmacokinetics, an extension of the drug cycle's half-life, a consistent release of the medication, and a decrease in the toxicity associated with the drug, drug delivery systems based on nanotechnology have significantly improved therapeutic outcomes [23, 24]. Cell separation, immunoassay, tissue regeneration, hyperthermia, tumor targeting, and drug administration are just a few of the uses for inorganic magnetic iron oxide nanoparticles (MNPs), which have the generic chemical formula Fe_3O_4. Due to their particular characteristics, which include small particle size, superparamagnetic and specific magnetic features, low toxicity, high half-life, and catalytic activities, MNPs have come to be the focus of innovative materials science [25–27].

Magnetic iron oxide nanostructures with a variety of capabilities could acquire desirable characteristics by adding functional groups to their surfaces [25]. For instance, magnetic iron oxide nanoparticles can be coated with many active medications as well as other active ingredients, opening up a wide range of possible uses in nanomedicine, such as targeted drug delivery. These nanoparticles, which can migrate toward magnets, are being researched as potential medication delivery vehicles. In this work, the roles of untreated and modified iron oxide nanoparticles for drug delivery were investigated. These modifications included chitosan, poly(vinylpyrrolidone), poly(vinyl alcohol), poly(lactic-co-glycolic acid), and poly(ethylene glycol).

Drug Delivery

As new materials and technologies were developed, there was a surge in the study and development of therapeutic drug delivery systems. More sophisticated pharmaceutical systems were made possible by the advancement of biotechnology and our understanding of physiological mechanisms. As a result, there has been an increase in drug delivery system development strategies that exhibit improved abilities to alter and regulate the administration of active substances [28, 29]. Nanotechnology is one of the most often used methods in this area for regulating drug distribution and improving the effectiveness, safety, and caliber of the systems. In addition, patient therapy is enhanced. Iron oxide nanoparticles (IOMNPs) are useful for regulating drug distribution and for enabling drug targeting, one of the most crucial tactics [29]. These nanoparticles and/or implantable magnets can be used in magnetic drug targeting, which involves delivering the particles to the desired place, fixing them there while the active substance is released, and acting locally [29]. This method can lower dosage requirements and get rid of unwanted effects. IOMNPs are undergoing trials to look into the possibility that they could be used as drug carriers in this situation. The focus of Turrina et al. (2021) is on the binding patterns of the bee venom peptide lasioglossin III on bare IOMNPs [32]. Due to its cationic characteristics and strong binding potential, lasioglossin has a strong antibacterial behavior. The maximum drug loading of 22.7% is reached in phosphate-buffered saline when the effects of pH, buffer type, particle concentration, and time are taken into account. Temperature and salt content were shown to be sensitive desorption conditions after analysis. Using dynamic light scattering, zeta potential, and infrared spectroscopy, the nanoparticles and peptide-ion complexes are examined. Furthermore, cytotoxicity tests done on *Escherichia coli* reveal that bound lasioglossin has greater antibacterial action than free peptide. For the development of cationic peptide drug delivery carriers, bare IOMNPs are a promising platform material. The biocompatibility of Fe_3O_4 NPs was examined by Kansara et al. [33] using cytotoxicity assays and cell cycle analysis in the human breast adenocarcinoma cell line (MCF-7) as part of another study. Fe_3O_4 NPs were produced using the co-precipitation method. After 24 h of exposure to the two higher concentrations, flow cytometric analysis showed a significant ($P = 0.05$) increase in the internalization of Fe_3O_4 NPs in MCF-7 cells, as shown by an increase in the side scatter intensity. Fe_3O_4 NPs were shown to be biocompatible in the cytotoxicity experiments, NRU and MTT, since there was no significantly higher NRU (88% at concentration 150 M/mL) and a reduction in mitochondrial succinate dehydrogenase activity (96%) was detected at the maximum concentration after 24 h of exposure (Fig 2a, b). After a 24 h exposure, Fe_3O_4 NPs-treated MCF-7 cells showed no change in cell cycle progression. The results of the study showed that, despite being significantly internalized, Fe_3O_4 NPs synthesized using the safe-by-design method had no negative effects on cells as determined by cytotoxicity assays and cell cycle analysis in MCF-7 cells. As a result, these NPs may be used as a vehicle for the delivery of specific medications.

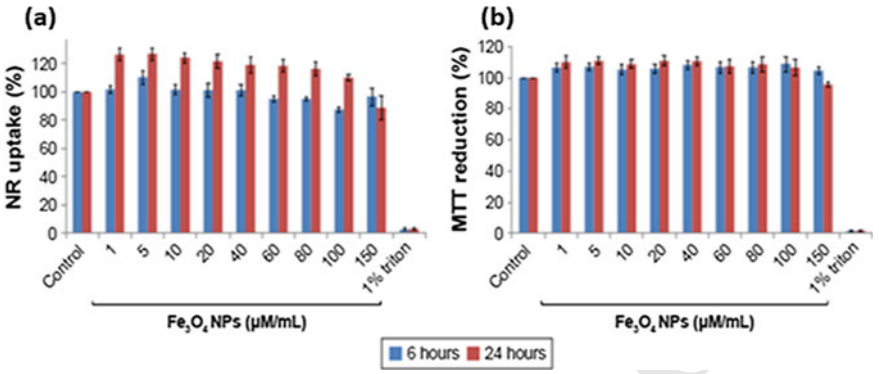

Fig. 1 Cytotoxicity of Fe_3O_4 NPs in MCF-7 cells. **a** NR uptake (%); **b** MTT reduction (%). Notes: The viability of the control cells was considered as 100%. Data are expressed as mean ± standard error of the mean from three independent experiments. Abbreviations: NPs, nanoparticles; MCF-7, human breast adenocarcinoma cell line; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NR, neutral red [33]

Polymeric layers, capsules, particles, or vesicles were suggested since the composition of the exterior coating has a significant impact on the characteristics of these nanoparticles and their ability to successfully carry active compounds [28]. In order to make these particles biocompatible and appropriate for further functionalization through the attachment of various bioactive molecules, the surfaces of these particles are often modified utilizing organic polymers and inorganic metals or oxides [34]. However, in order for the drug delivery system incorporating IOMNPs to be successful, a number of crucial factors must be taken into account.

The delivery system must have functional groups that can be further changed to control drug release or bind targeted units, as well as the ability to easily disperse in aqueous solutions [28] (Fig. 1).

To attach various medications to IOMNPs, nanostructured devices with a core–shell architecture are frequently used. The shell is the surface coating for nanoparticle functionalization, and the core is made up of nanoparticles. With this approach, the system's biodistribution, biocompatibility, and pharmacokinetics can all be enhanced [35]. As a result of their ability to shield nanoparticles from oxidation and give them stability, synthetic and natural polymers are the most often employed surface coatings in IOMNPs.

The following substances are used: poly(vinylpyrrolidone), polyvinyl alcohol, poly(lactic-co-glycolic acid), and chitosan [28]. Due to its non-fouling qualities and decreased opsonization of blood proteins, PEG—which is hydrophilic, uncharged, and biocompatible—was used to coat the IOMNPs. Due to their ability to avoid

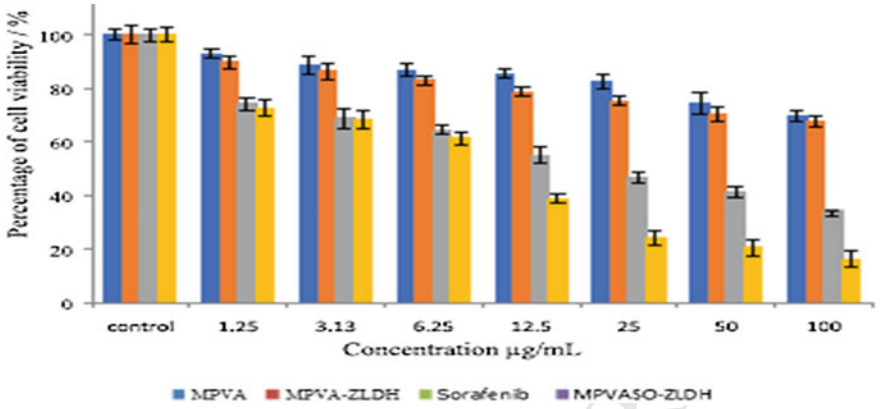

Fig. 2 Cytotoxicity assay of MPVA, MPVA-ZLDH (the nanocarriers), sorafenib, and MPVASO-ZLDH (the nanoparticles) against HepG2 cells at 72 h of incubation [25]

immune system detection, nanoparticles can prolong their duration in the bloodstream and accumulate in target cells and tissues [28]. Yallapu et al. (2010) investigated the potential of polyethylene glycol (PEG) functionalized magnetic nanoparticles (MNPs) as a drug delivery system, as an MRI agent, and as an antibody conjugate [36]. A water-dispersible MNP formulation is created by coating an iron oxide core first with oleic acid (OA), then with OA-PEG. For prolonged drug delivery, hydrophobic doxorubicin partitions into the OA layer. The circulation of the MNPs was assessed in mouse carotid arteries, and the T1 and T2 MRI contrast qualities were established in vitro. The amine functional group on antibodies was coupled to an N-hydroxysuccinimide group (NHS) on the OA-PEG-80 for active targeting of the human MCF-7 breast cancer cell line. Results The optimized formulation comprised an iron-oxide core that was around 8 nm thick and a mean hydrodynamic diameter of 184 nm. The MNPs prolong the circulation period in vivo and reach a 30% relative concentration 50 min after injection. They also improve the T2 MRI contrast. In vitro, doxorubicin-loaded MNPs exhibited sustained drug release and dose-dependent antiproliferative effects; the drug effect was boosted by transferrin antibody-conjugated MNPs. The authors came to the conclusion that targeted medication delivery systems and MRI contrast agents could be created using PEG-functionalized MNPs. Mohanta et al. (2018) created almost spherical Fe_3O_4 nanoparticles with sizes in the 8–20 nm range using a sonication assisted co-precipitation approach to address the growing interest in magnetic nanoparticles for drug delivery applications [37]. The produced nanoparticles were further stabilized by coating with PEG-400, a hydrophilic and biocompatible polymer, to improve surface functioning. To assess their feasibility for drug delivery applications, various approaches were used to characterize both uncoated and PEG-400 coated iron oxide particles. The water-soluble anticancer medication daunorubicin hydrochloride was loaded onto the PEG-400 coated iron oxide nanoparticle for this purpose. Specifically, they changed the PEG/iron oxide ratio to optimize the PEG coating, which improved drug

loading and stability by effectively functionalizing the surface. In physiological and acidic pH circumstances, the drug release study has been seen. A higher amount of drug release at low pH indicated the functionalized particles' potential utility as drug delivery vehicles. The functionalized particles also displayed pH-responsive drug release.

Additionally, water-soluble synthetic polymers, polyvinylpyrrolidone (PVP) and poly(vinyl alcohol) (PVA), are frequently employed in medicinal applications. The preparation of hydrogel structures is made possible by their emulsifying and adhesive characteristics. IOMNPs may participate in hydrogen bonding between polymer chains, which prevents nanoparticle aggregation [30]. For instance, magnetic drug nanoparticles made using (PVA) polymer, layered double hydroxide (LDHs), and drug as the coating agent and magnetic iron oxide nanoparticles (MNPs) as the core [25] were the subject of an investigation by Ebadi et al. in 2020. First, the Fe_3O_4 nanoparticles were created using the co-precipitation process. After that, Zn/Al-LDH, sorafenib, and polyvinyl alcohol were applied to the surface (SO). Studies using XRD and FTIR show that the iron oxide crystal structure is present in the core. The TGA findings confirmed the existence of the core and shell. When the Fe_3O_4 nanoparticles were coated with polyvinyl alcohol, Zn/Al-LDH, and the medication sorafenib, the saturation magnetization was observed to be decreased from 80 to 57 emu/g. According to HRTEM photographs, the average size of naked Fe_3O_4 nanoparticles is about 30 nm. Additional structural analyses revealed that the addition of the shell produced homogeneous particles with a particle size distribution of roughly 95 nm. It was discovered that the pseudo-second-order equation controlled the kinetics of drug release from the nanoparticles. The results of cell viability assays clearly demonstrated that the magnetic iron oxide nanoparticles coated with polyvinyl alcohol-sorafenib-Zn/Al-layered double hydroxide were more effective than sorafenib alone against HepG2 liver cancer cells (Fig. 2), while they showed no cytotoxicity toward 3T3 fibroblasts (Fig. 3). These findings demonstrate the potential of the coated Fe_3O_4 magnetite nanoparticles as a drug delivery vehicle for biomedical applications.

The utilization of a polyglycolic acid and polylactic acid copolymer (PGA) in drug delivery systems showed considerable promise [38]. This polymer may be formed into many forms and sizes and is soluble in the majority of common solvents, making it possible to encapsulate a variety of molecules [30]. As one method of maintaining the particles in the joint cavity by an external magnetic field, and managing the drug release for the treatment of arthritis and osteoarthritis, PLGA microparticles comprising co-encapsulated dexamethasone acetate and IOMNPs were devised [39]. The ability of the DU145 prostate carcinoma cell line to proliferate in monolayer culture was examined by Hajikarimi et al. (2014) for the uptake and cytotoxic effects of magnetic poly lactic-co-glycolic acid (PLGA)-coated iron oxide nanoparticles as a carrier of 5-fluorouracil (5-FU) and X-ray [40]. Following monolayer cultivation, DU 145 cells were exposed to 2 Gy X-rays (6 Megavolts (MV)) and various doses of 5-FU or 5-FU-loaded nanoparticles for 24 h. Atomic adsorption spectroscopy was then used to determine the rate of nanoparticle penetration (AAS). Using a colony

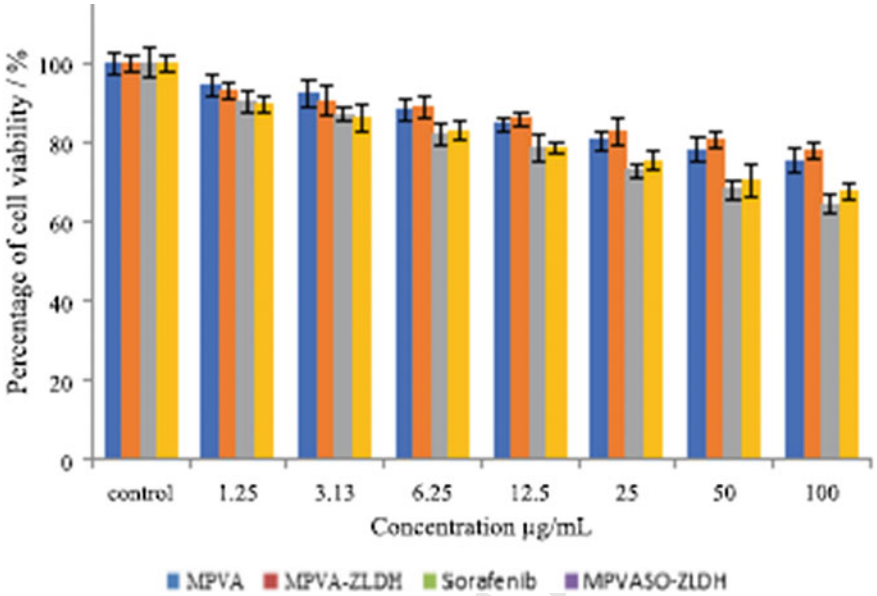

Fig. 3 Cytotoxicity assay of MPVA, MPVA-ZLDH (the nanocarriers), sorafenib, and MPVASO-ZLDH (the nanoparticles) against normal 3T3 cells at 72 h [25]

formation experiment, the cytotoxicity effect of these nanoparticles with/without X-ray radiation was assessed. Results from spectroscopy revealed that when nanoparticle concentrations increased, the iron content and thus the cellular absorption of 5-FU-loaded nanoparticles increased. Additionally, as the quantities of 5-FU and 5-FU-loaded nanoparticles increased in combination with X-ray radiation, the ability of the cells to proliferate diminished. However, compared to free 5-FU, the amount of colony number reduction after treatment with 5-FU-loaded nanoparticles and 2 Gy of megavoltage X-ray radiation was much greater. Drug-loaded nanoparticles could therefore transport 5-FU into cells more effectively. Therefore, PLGA-coated iron oxide nanoparticles are efficient 5-FU drug delivery systems. The PLGA coating on iron oxide nanoparticles makes them biocompatible and provides a suitable surface for cell penetration.

The biodegradable polymer poly (lactic-co-glycolic acid, or PLGA), which exhibits appealing properties and provides opportunities to tailor the physicochemical properties, drug release properties, and biological behavior of the PLGA-based nanospheres, is widely used to create polymeric biodegradable carriers [29]. When it comes to encapsulating highly hydrophilic medications like doxorubicin, double emulsion solvent evaporation techniques fall short (Dox). Before the PLGA nanospheres solidified, the drug diffused quickly into the exterior aqueous phase, which is the cause of this problem. Superparamagnetic iron oxide nanoparticles (SPIONs) and Dox were co-encapsulated with the PLGA polymer in a study by

Mosafer et al. (2018), with a focus on the double emulsion solvent evaporation-based methodologies to achieve the effective method in terms of nanoparticle size, particle size distribution, and drug loading [41]. The low affinity of Dox for the PLGA polymer could lead to limited entrapment efficiency because Dox has a high solubility in water. The chloroform solution was used to extract Dox into this organic phase with TEA to neutralize Dox in favor of Dox lipophilicity, improving the entrapment efficiency and LC. To improve the antiproliferation action of Dox inside cellular organelles like lysosomes (pH is approximately 5.5), faster Dox release of NPs at low pHs might be advantageous while restricting its release in blood circulation. In vitro Dox release from NPs in pH 7.4 PBS and pH 5.5 acetate buffers at 37 °C is depicted in Fig. 4. At pH 5.5, compared to pH 7.4, the cumulative Dox emission increased by almost 2.5 times. There was an early burst release for both the acetate and PBS media within the first two hours following incubation, followed by a gradual release throughout the following 12 h (13 and 36% for pH 7.4 and pH 5.5, respectively) (Fig. 4). Then, within 20 days, a constant release was seen in both buffers (20.2 ± 0.5% in pH 7.4 and 50.1 ± 0.5% in pH 5.5). The cumulative drug release phase for NPs over the course of 36 days reached 27.4 ± 0.3% and 60.1 ± 0.6% at pH 7.4 and pH 5.5, respectively. Overall, the cumulative Dox release was found to be about three times larger at pH 5.5 than at pH 7.4 (Fig. 4), which may have been caused by the protonated Dox's enhanced solubility at lower pH. In conclusion, the NPs seem to be suitable for reaching the lowest possible release in blood and the highest possible release in lysosome, which depends on the pH of media, drug diffusion, and matrix-erosion mechanisms.

By deacetylating chitin, chitosan is a naturally occurring, biocompatible, biodegradable, and low-toxic substance. Its lengthy chain, produced by the fusion of glycosidic linkages and 2-amino-2-deoxy-d-glucan, results in a positive charge that pulls the systems toward the negatively charged cell membrane [42]. As a result, IOMNPs coated with chitosan can exhibit mucoadhesive qualities and improve nanoparticle retention in the target regions [30]. Since chitosan coating does not alter the thermal or magnetic properties of IOMNPs, numerous systems were created

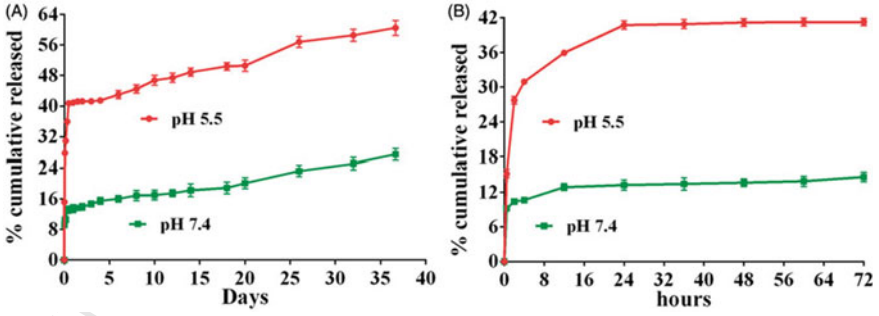

Fig. 4 In vitro release profile of Dox from NPs in pH 7.4 PBS and pH 5.5 acetate buffers. **a** For 36 days and **b** for 72 h (n = 3) [41]

[30]. Due to the electrostatic attraction between the positively charged nanoparticles, chitosan with low molecular weight can prevent these nanoparticles from aggregating [43]. Due to the partial protonation of its amino groups in water at physiological pH, which decreases chitosan solubility, this polymer exhibits some limits as a coating material. These issues can be resolved chemically, increasing the water solubility of chitosan derivatives [44]. For the pH-responsive release of 5-FLU delivery in A549 and HeLa S3 cell cultures and the ensuing synergistic cytotoxicity of 5-FLU and ROS, Ayyanaar et al. (2020) presented the synthesis, characterization, and evaluation of chitosan-coated magnetic iron oxide nanoparticles (Fe_3O_4@OA-CS-5-FLU-NPs) [45]. In this case, magnetic nanoparticles were created using the conventional co-precipitation method. It was simple and quick to create Fe_3O_4@OA-CS-5-FLU-NPs using in situ loading. The proposed Fe_3O_4@OA-CS-5-FLU-NPs were successfully synthesized and subjected to numerous spectroscopic and microscopic analyses to characterize them. The Fe_3O_4@OA-CS-5-FLU-NPs' targeted drug release profile was investigated in the presence of ROS, including H_2O_2, and pH induction. The magnetic characteristics of the Fe_3O_4@OA-CS-5-FLU-NPs showed promise and might be applied to magnetic targeted and pH-responsive drug delivery systems. The ROS-responsive polymeric nanocarriers are released from Fe_3O_4@OA-CS-5-FLU-NPs via pH-triggered drug release under slightly acidic conditions of pH 5.2 and pH 7.4. Fe_3O_4@OACS-5-FLU-NP, the product that was made available, revealed satisfactory levels of cytotoxicity, morphological alterations, and inhibition of colony formation for A549 and HeLa S3 cancer cells (Fig. 5). At 24 h, the IC50 values were 12.9 and 23 g/mL, respectively. The Fe_3O_4@OA-CS-5-FLU-NPs were active and safe for anticancer biomedical applications, according to the results of the MTT assay, fluorescence staining, and colony formation assays. The system for enhanced cancer theranostics presented by the current inquiry is strong and should be further studied.

A modified magnetic nanoparticle was created and produced by Hami (2020) to be employed as a targeted medicine delivery method [46]. On the surface of chitosan-modified iron magnetic nanoparticles, nanocurcumin loading was done twice. In the initial stage, chitosan was added as a coating polymer on the surface of iron magnetic nanoparticles. The final reaction was carried out in the next step by coating the surface of magnetic iron nanoparticles modified by chitosan with nanocurcumin. The structure, shape, physicochemical properties, and presence of nanocurcumin layers on chitosan in nanoparticles with a diameter of 20 nm were clearly seen in the results of transmission and scanning electron microscopy. The iron–oxygen peak in Fourier transform infrared spectroscopy showed magnetic iron nanoparticles, and the oxygen–hydrogen peak revealed nanocurcumin layers on chitosan. Additionally, X-ray spectroscopy demonstrated iron, carbon, oxygen, and nitrogen peaks, which supported the presence of these components in the final composition. By using a magnetic instrument called a vibration sample meter to analyze the magnetic properties of iron-chitosan magnetic nanoparticles loaded with nanocurcumin, it was discovered that the magnetic saturation of iron oxide nanoparticles at room temperature was 63.1 emu g^{-1} as determined by the magnetic curve. Due to the

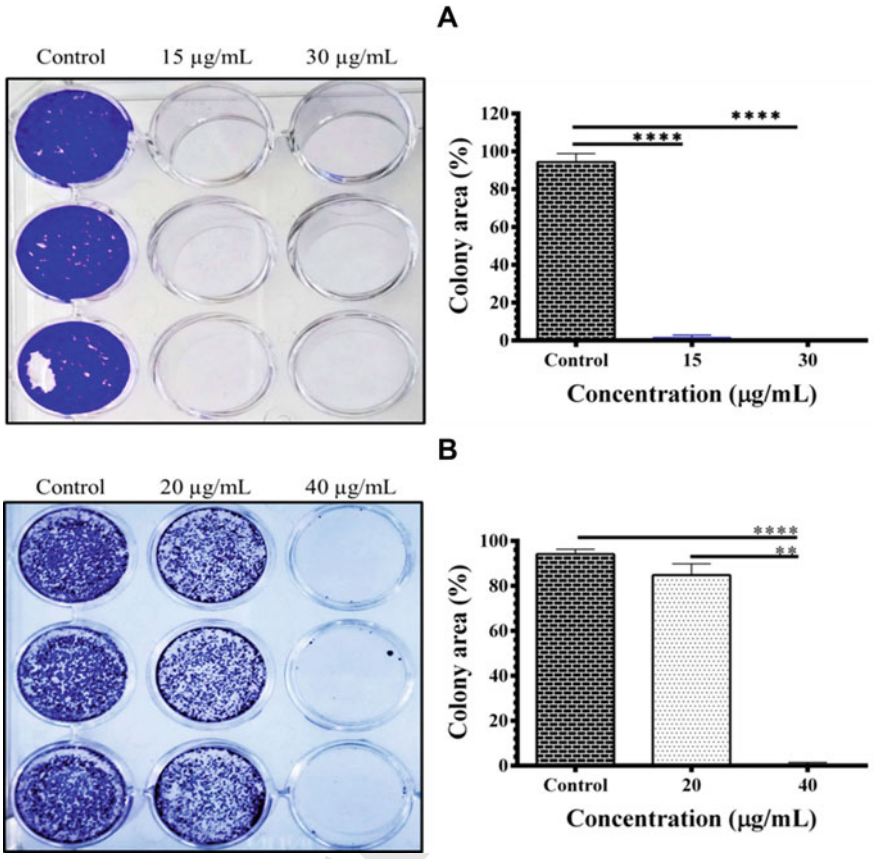

Fig. 5 Colony formation in the presence of Fe_3O_4@OA-CS-5-FLU-NP examined against A549 and HeLa S3 cells: **a** A549 and **b** HeLa S3 cells. The colony area was calculated by ImageJ software using colony area (mean ± SD). Significance of ****$p < 0.0001$ and **$p < 0.01$ as compared with the untreated control group [45]

stabilization of polymeric groups on the nanoparticle surface, the magnetic saturation (35.3 emu g^{-1}) of iron-chitosan magnetic nanoparticles loaded with nanocurcumin clearly decreased. This proof showed that iron magnetic nanoparticles modified with chitosan successfully loaded with nanocurcumin. The results of this study showed that nanocurcumin was successfully loaded on the surface of magnetic iron nanoparticles modified by chitosan.

Inorganic substances, bioactive chemicals, and organic surfactants can also be applied on the surface of IOMNPs. Specifically, when IOMNPs are generated in organic solutions, organic surfactants are used to functionalize them. Dimercaptosuccinic acid has the ability to produce nanoparticles with an anionic surface that resists opsonization and clearance by the reticuloendothelial system, hence lowering the toxicity to cells [30]. Additionally, oleic acid and trisodium citrate are able to

stabilize nanoparticles by generating repulsive forces (mostly steric repulsion) to counterbalance the magnetic and van der Waals attractive forces [47]. In order to achieve more effective coatings of the IOMNPs, with improved dispersion capacity in solutions and lower nanoparticle clustering, surfactants showing lower values of critical micelle concentrations were used [29]. This is because long hydrocarbon chains in surfactants can produce hydrophobic nanoparticles. When utilized in IOMNP systems, inorganic substances such as carbon, metals, silica, oxides (both metal and non-metal), and sulfides showed the benefit of enhancing the antioxidant properties of these nanoparticles [49]. SiO_2 can improve the dispersion of IOMNP in solutions, increasing their stability and protecting them in acidic media [29].

A barrier against IOMNP oxidation, carbon-based coatings exhibit chemical and thermal stability, high electrical conductivity, and solubility [30]. Additionally, the creation of a positively charged silver coating by the electron transfer between silver and IOMNPs in a nanosystem enables the conjugation of several antibiotics to the silver-decorated nanoparticles [29]. IOMNPs frequently contain oxides and sulfides to stabilize the nanosystem and promote desirable magnetic characteristics [30]. The application of metal coatings with modifications including substances like thiol can enable their coupling with a variety of biomolecules. ZnO was chosen as the best compound for an anticancer nanosystem due to both its intrinsic anticancer properties and biocompatibility because the choice of a coating for the IOMNPs must take into account both their intrinsic properties and the purpose of the system [29]. Examples of bioactive compounds that can be employed in IOMNP-based systems include peptides, lipids, and proteins. They ought to be able to preserve both the magnetic characteristics and the stability of the nanoparticles [30].

Concluding Remarks

This review summarizes the roles of untreated and modified iron oxide nanoparticles for drug delivery. The superior size, surface, mechanical, optical, and magnetic properties of iron oxide NPs make them ideal for drug delivery. The nanoparticles' tiny size and wide surface area boost their solubility and bioavailability, which in turn increases their capacity to penetrate the blood–brain barrier (BBB), enter the respiratory system, and be absorbed through the skin's tight connections. The majority of the studies under review functionalized the iron oxide NPs' surface with targeting ligands, imaging, and therapeutic moieties. This allowed for the protection of IOMNPs with biocompatible materials to stop biodegradation, changes, and aggregation as well as the entrapment of the bioactive agent on the particle via adsorption or covalent attachment. As a result of a stronger drug action at lower doses and a consequent improvement in therapy, IOMNPs exhibit significant promise for use in medication delivery. This will minimize toxicity and adverse effects. These results show that IOMNPs may be used in drug delivery applications, and that achieving adequate drug release control on the target tissues is beneficial in a variety of clinical

conditions, including infections, inflammations, and malignancies. However, given their therapeutic uses, further toxicological clinical studies on IOMNPs are required.

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Chapter 22

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