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EFFECT OF COATING SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES WITH OLEIC ACID AND PEG ON THEIR PROPERTIES FOR MAGNETIC TARGETING APPLICATIONS: A REVIEW

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ABSTRACT

Superparamagnetic iron oxide nanoparticles (SPIONs) with all their unique properties have great potential in biomedical applications, including cancer treatment using targeted drug delivery systems and magnetic hyperthermia therapy. However, the stability of nanoparticles and their biocompatibility are major challenges in the success of these applications. Coating nanoparticles with oleic acid and polyethylene glycol (PEG) is often used to improve their dispersion stability and biocompatibility. In this review, we will discuss how the properties of SPION such as colloidal stability, magnetic properties, hyperthermia properties, drug loading, and drug release capabilities are improved when SPION is coated with oleic acid and PEG. It was found that in general, coating using oleic acid and PEG would improve the properties of SPION, such as increasing the hydrodynamic diameter and zeta potential values, and decreasing the polydispersity index and coercive filed values, making it more suitable for biomedical applications. This review aims to provide a thorough understanding of coating strategies to optimize SPION performance in magnetic targeting applications, and identify challenges and opportunities for future development.

Keywords: SPION; oleic acid; PEG; targeted drug delivery; magnetic hyperthermia

INTRODUCTION

Nanoparticles have many unique characteristics such as large surface area to volume ratio, certain magnetic properties, and novel optical properties. Therefore, nanoparticles are often used for biomedical applications, such as cancer treatment by targeted drug delivery method and magnetic hyperthermia using magnetic nanoparticles.

According to World Health Organization, cancer is the leading cause of 10 million deaths all around the world in 2020 [2]. Unfortunately, most cancer treatments today are non-specific, where drug are given intravenously so that drugs are distributed generally. This general distribution then causes side effects where the drug also damages healthy cells [3]. The main objective of using magnetic nanoparticles is to deliver drugs directly to cancer cells and minimize the side effects [4].

Magnetic nanoparticles are usually made from iron oxide which in its bulk state has ferromagnetic or ferrimagnetic properties. Ferromagnetic and ferrimagnetic materials will be divided into small areas of aligned magnetic moments called domains. The domain itself is only observed in crystal whose size is above 100 nm [5]. When this iron oxide particles reduced its size to nano scale, the iron oxide will form a single domain state and new magnetic property

will appear which are called superparamagnetism [6]. We call them superparamagnetic iron oxides nanoparticles (SPIONs).

Superparamagnetism is a magnetic property where the magnetization can change direction constantly due to temperature fluctuations [6]. In targeted drug delivery and magnetic hyperthermia applications, this superparamagnetic property is required for two reasons: (i) Superparamagnetic nanoparticles do not have residual magnetization when external magnetic field is no longer applied, therefore avoiding potential blood flow blockage caused by magnetic aggregation. (ii) Nanoparticles that only have one single domain will behave like a giant magnetic moment which is composed of individual magnetic moments of all the atoms that formed the nanoparticles, so that they have a high susceptibility value [7]. Therefore, for this biomedical application, SPIONs are needed.

Not only do they required to have superparamagnetic properties, for biomedical applications, magnetic nanoparticles also required to fullfill certain parameters such as size, charge, biocompatibility, stability, zeta potential, and magnetic targeting ability [8]. To help achieve the desired properties, magnetic nanoparticles are also always coated with polymers such as chitosan, dextran, polyethyleneimnine (PEI), polyvinylalcohol (PVA), polyvinylpyrolidone (PVP), polyethylene glycol (PEG), and oleic acid (OA) [7 – 9].

Most review articles that have been published only briefly discuss magnetic nanoparticles and their various coating polymers. A critical gap in the literature is the lack of comprehensive reviews that analyze in detail the changes in the properties of these nanoparticles following their surface modification with specific polymers [8, 10, 11]. Specifically, no review articles have exhaustively addressed the specific impact of surface modification with oleic acid and PEG on superparamagnetic iron oxide nanoparticles.

Therefore, this review article uniquely aims to fill this knowledge gap by thoroughly investigating how crucial properties such as colloidal stability, magnetic properties, hyperthermia efficiency, drug loading, and drug release change when SPIONs surface are modified with oleic acid and PEG. We anticipate that this specific foucs on the mechanisms of modification with oleic acid and PEG will provide clear guidance and valuable perspectives on strategies for optimizing the functional properties of SPIONs for biomedical applications.

METHOD

This review article will explain how surface modification of SPIONs with oleic acid and PEG will change their properties. A literature search was carried out on three different databases, namely Taylor & Francis, Scopus, and Springer using the keywords: (“Magnetite” OR “Fe3O4”) and “Superparamagnetic” AND “Core-shell” AND (“Drug Delivery” AND “Cancer Therapy”) AND (“PEG” AND “Oleic Acid”). We limited the search so that the articles reviewed were only articles published by international English-language journals, resulting in a total of 632 research articles. Figure 1 shows the PRISMA guidelines for the procedure of sorting research articles.

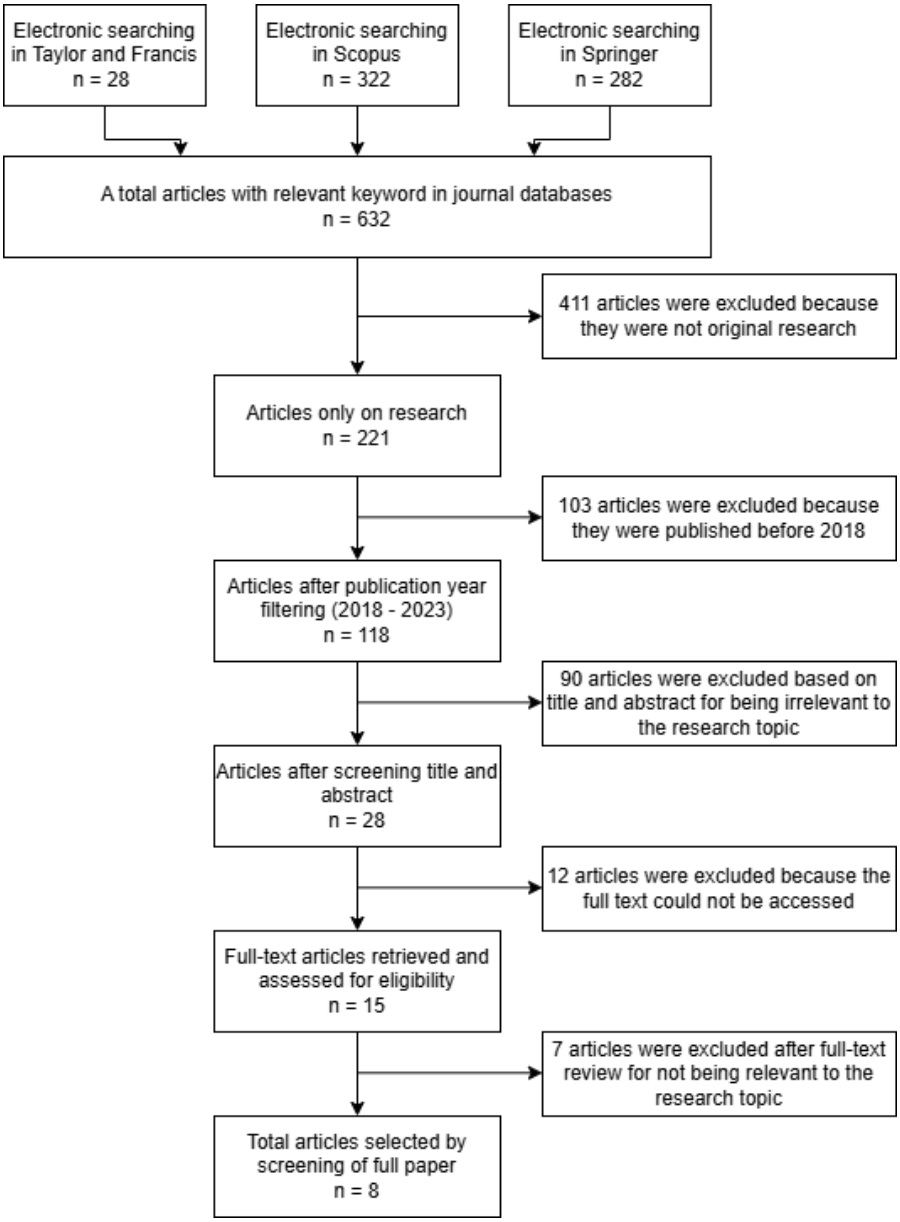

Figure 1. The PRISMA guidelines in selection procedures

The types of articles were limited to research articles, resulting in 221 articles. The publication year of the articles was the limited to 2018-2023, resulting in 118 articles. The articles were then selected by their titles and abstract, and the 28 most relevant articles were selected. However, only 15 articles can be fully accessed. The fifteen articles were then read thoroughly and 8 articles were selected to be reviewed. The articles reviewed are in Table 1 below.

Table 1. List of research articles that will be reviewed along with their surface modifications and properties to be analyzed.

Ref.	Surface Modification	Properties to be Analyzed			
		Colloidal Stability	Magnetic Properties	Hyperthermia	Drug Loading and Drug Release
Ioncica, et al [12]	PEG	✓	✓	✓	-
Kovrigina, et al [13]	Oleic Acid	✓	-	-	✓
Kovrigina, et al [14]	Oleic Acid and PEG	✓	-	-	✓
Namikuchi, et al [15]	PEG	✓	-	-	-
Heydaryan, et al [16]	Oleic Acid	✓	✓	✓	-
Andhare, et al [17]	PEG	✓	✓	✓	-
Dabbagh, et al [18]	PEG	✓	✓	✓	✓
Hemben, et al [19]	PEG	✓	-	-	-

In this review, there are 2 articles that discuss surface modification with oleic acid, 5 articles that discuss surface modification with PEG, and 1 article that discuss surface modification with oleic acid and PEG. Then, we will discuss how this surface modification will affect colloidal stability, magnetic properties, hyperthermia properties, drug loading, and drug release capabilities.

RESULTS AND DISCUSSION

Oleic Acid

Oleic acid is a fatty acid composed of a carboxylic acid group and an unsaturated aliphatic chain. The alipathic chain is composed of 18 carbon atoms and has a C=C double bond at a certain position in the chain. So, the overall chemical structure can be written as $(CH_3(CH_2)_7CH=CH(CH_2)_7COOH)$ [20].

Oleic acid has amphiphilic properties. Carboxylic acids containing the -COOH carboxylic group will be polar and can interact with water, so they are hydrophilic, while the aliphatic chain with its double bond shows a lack of hydrogen which makes it hydrophobic.

Magnetic nanoparticles tend to aggregate due to magnetic attraction and Van der Waals forces between nanoparticles. Therefore, chemical stabilization is needed [21]. Coating nanoparticles with oleic acid can reduce the tendency of nanoparticles to aggregate because oleic acid will provide steric repulsion which prevents agglomeration [22]. Apart from that, oleic acid is also able to control particle size, increase lipophilicity, and disperse nanoparticles in organic solutions [22 - 24].

Through FTIR characterization, it was known that oleic acid was absorbed via the carboxyl group onto the surface of SPIONs. Furthermore, there is ligand exchange between the hydroxyl group of SPIONs and the carboxylate groups of oleic acid on the surface of the nanoparticles

[24 - 25]. The interaction between the carboxyl group and the metal atom of SPIONs is divided into four types depending on the separation of wavenumber value between symmetric and asymmetric bands of the carboxylic group, these bonds are called monodentate, bridging bidentate, chelating bidentate, and ionic interactions [25]. In monodentate, the negatively charged oxygen of the carboxylate group will bind covalently to the metal ion. In the chelating bidentate, the charge of the carboxylate group is divided into two oxygen atoms and both bind covalently to one metal ion. In bridging bidentate, the two oxygen atoms will bind covalently with two different metal ions [26]. FTIR results will also show the presence of CH_2 groups which indicates that the tail of oleic acid which is composed of hydrocarbon chains will make the nanoparticles coated by oleic acid hydrophobic.

Oleic acid can form single, double, or multilayer layers in nanoparticles structures [25]. In the first layer, oleic acid will coat the nanoparticles through chemical bonds between carboxylic groups and metal atoms. Then in the second coating, the hydrophobic tail of the first layer will interact with the oleic acid in the second coating through hydrophobic interactions [23]. Coating SPIONs with oleic acid will make them hydrophobic, which means they cannot be dispersed in aqueous medium. To overcome this, hydrophobic ligands can be exchange for ligands that can dissolve in water, such as PEG. Non-polar solvents can also be used, or by ionizing the carboxyl group [23]. The ionized carboxyl group will produce the more hydrophilic COO- ion.

Polyethylene Glycol (PEG)

Polyethylene glycol or PEG is a neutral synthetic polymer that is hydrophilic. PEG can be prepared with various terminal functional groups. By varying these functional groups, PEG can be attached to various surfaces [9]. The designation of PEG is determined by a number indicating its average molecular weight, which is in the range of 200 – 300,000 [27].

PEG has hydrophilic properties and very high surface mobility. Therefore, surface modification of SPIONs with PEG is able to increase solubility and make nanoparticles nonimmunogenic, nonantigenic, biocompatible, and resistant to proteins, thereby increasing circulation time and delivery efficiency of nanoparticles in the blood [27 - 29].

The PEG surface can be further functionalized and can be derivatized with other molecules for special purposes, including oleic acid. When modifying the surface of SPIONs with PEG and oleic acid, the oleic acid will bind to the nanoparticles and act as reservoir to accommodate the drug, and the PEG layer is used for conjugation to antibodies or target cells [30]. PEG can bind to oleic acid through the esterification process, which is the reaction between the carboxylic acid group and the hydroxyl group. This esterification process can take place with the help of a homogeneous catalyst in the form of an inorganic acid such as HCl [31].

Colloidal Stability

Reviewing the colloidal stability of a nanoparticles can be evaluated from parameters such as: nanoparticle diameter, hydrodynamic diameter, zeta potential, and polydispersity index (PDI).

Nanoparticle diameter refers to the measured diameter of the nanoparticle. A nanoparticle diameter with a size range of 10 – 200 nm is desired, because if the size is less than 10 nm it can be quickly excreted by the kidney clearance system, whereas if the size is above 200 nm the nanoparticles will be collected in the spleen and reduce plasma concentration [32]. The hydrodynamic diameter is the diameter of a hard sphere that will experience the same drag force as the particle when moving in a liquid, but in practice, these dissolved particles can be of any shape [33]. Zeta potential refers to the electrical potential difference between fluid adjacent to the surface of nanoparticle and the fluid around the nanoparticle [34], to achieve

colloidal stability, a value above +30 mV or – 30 mV is required [13]. Polydispersity index (PDI) is a dimensionless parameter that describes the degree of non-uniformity of the particle size distribution [15]. If PDI < 0.05 the nanoparticles have uniform size or monodisperse, whereas if PDI > 0.7 then the nanopaticles have very diverse sizes [15].

Kovrigina, et al, in two different studies [13 - 14], have succeeded in synthesizing Fe_3O_4 nanoparticles, then reviewed their colloidal stability before and after being coated with oleic acid, the results are shown in Table 2. It can be seen that the zeta potential value changes from positive to negative after coating, this is due to the negatively charged carboxyl group of oleic acid. Coating with oleic acid also increase zeta potential values and decreasing PDI values. This means that the electrostatic stability is better and the size distribution is smaller after being coated with oleic acid.

Table 2. Changes in colloidal stability parameter values after nanoparticles were coated with oleic acid.

Ref.	Diameter measured by TEM (nm)		Hydrodynamic Diameter (nm)		Zeta Potential (nm)		PDI	
	Uncoated	Coated	Uncoated	Coated	Uncoated	Coated	Uncoated	Coated
[13]	-	-	123 ± 7	112 ± 18	23 ± 8	-43 ± 0.9	0.205 ± 0.005	0.172 ± 0.010
[14]	10 ± 2.5	100 ± 40	15.6 ± 2.2	112 ± 19	36.0 ± 0.9	-43 + 0.8	0.296 ± 0.003	0.172 ± 0.009

Hedayran, et al [16], also studied the effect of oleic acid concentration on the colloidal stability of $CoFe_2O_4$ nanoparticles. The concentration of oleic acid given was varied from 1 mmol to 20 mmol. The results showed that increasing the concentration of oleic acid would prevent agglomeration, maintain the shape of the nanoparticles, and reduce the size distribution of the nanoparticles. This is because the oleic acid molecules that are absorbed on the surface of the nanoparticles will reduce the surface tension and growth rate of the nanoparticles. However, this advantage is only obtained up to a concentration of 7.5 mmol, because after that the particle size becomes non-uniform and the size distribution widens. Too much oleic acid will cause the hydrocarbon chains between oleic acid to bond together creating a bridge-like structure and making the coating imperfect [25].

For PEG coated nanoparticles, the results of research by Ioncica, et al. [12], Kovrigina, et al. [14], and Dabbagh, et al. [18], show that coating with PEG will increase the hydrodynamic diameter value so that stability is better. For the results by Ioncica, et al. [12], coating with PEG will increase the zeta potential value, while the research results by Kovrigina, et al. [14], and Dabbagh, et al. [18], the zeta potential value decreases, giving rise to a tendency to agglomerate. Complete results can be seen in Table 3.

To avoid this agglomeration, Hemben, et al. [19], proposed a new PEG-coated nanoparticles synthesis method. Where the nanoparticles are shot by a magnetron which transmits energy so that metallic vapor is produced. This metallic vapor is then condensed and deposited onto the silicon wafer which has been coated with PEG [19]. Then PEG-coated nanoparticles were obtained with minimal agglomeration with an average diameter of 47 nm.

Table 3. Changes in colloidal stability parameter values after nanoparticles were coated with PEG.

Ref.	Diameter measured by TEM (nm)		Hydrodynamic Diameter (nm)		Zeta Potential (nm)		PDI	
	Uncoated	Coated	Uncoated	Coated	Uncoated	Coated	Uncoated	Coated
[12]	10 ± 1.2	-	19.8 ± 0.4	135 ± 38.8	-14	-26.9	0.14	-
[12]	15.6 ± 1.6	-	24.7 ± 5.7	132.6 ± 36.9	-23.9	-28.3	0.11	-
[14]	10 ± 2.5	200 ± 50	15.6 ± 2.2	196 ± 15	36.0 ± 0.9	27 ± 3	0.296 ± 0.003	0.5 ± 0.03
[18]	175 ± 72	179 ± 90	-	-	-25.8 ± 1.4	-5.5 ± 0.9	-	-

Namikuchi, et al. [15], have successfully synthesized Fe3O4 nanoparticles coated with PEG with molecular weights of 4000 g/mol, 8000 g/mol, and 20000 g/mol. Dissolution of the precursor was also carried out at two different temperatures, namely 85 °C and 140 °C. Table 4 below shows the average size of the PEG coated nanoparticles obtained.

Table 4. Average size of PEG-coated nanoparticles with variations in dissolution temperature and PEG molecular weight

Dissolution Temperature (°C)	Diameter of PEG Coated Nanoparticles (nm)		
	4000 g/mol	8000 g/mol	20000 g/mol
85	603 ± 120	562 ± 139	658 ± 108
140	129 ± 34	148 ± 34	153 ± 18

The measurement results show that nanoparticles with a dissolution temperature of 85 °C have a much larger size than nanoparticles with a dissolution temperature of 140 °C. For a dissolution temperature of 140 °C, the molecular weight of PEG will be directly proportional to the average nanoparticle size and shorten the size distribution. This shows that there is a relationship between PEG molecular weight and size at high temperatures. If applied carefully, the size and size distribution of the nanoparticles can be well controlled [15].

Magnetic Properties

The superparamagnetic properties of nanoparticles can be viewed from the following parameters: saturation magnetization (M_S), remanent magnetization (M_R), coercive field (HC), and blocking temperature (T_B).

Saturation magnetization is the maximum magnetization value of a material. This is achieved when the material is completely magnetized and all magnetic moments have the same direction as the direction of the external magnetic field. For magnetic targeting and hyperthermia applications, a high MS value is desired because this means the nanoparticles will be responsive to the influence of external fields. Remanent magnetization is the value of magnetization that remains in a material when the effects of an external field are removed. Meanwhile, the coercive field is the external magnetic field value needed so that the magnetization value of the material can return to zero. For magnetic targeting and hyperthermia applications, zero M_R and H_C are desired, because this means that the nanoparticles will not remain magnetized when the external field is removed, thus avoiding blockage of blood flow due to agglomeration. The blocking temperature is the transition temperature between superparamagnetic state and the blocked state (a state where the magnetic properties of the nanoparticles are the same as the

bulk state) [35]. If the temperature is above T_B the nanoparticles are superparamagnetic. A low TB value is desired, so that application can be carried out at room temperature.

Hedayran, et al. [16], who reviewed the effect of oleic acid concentration on magnetic properties, found that as the concentration increases, the saturation magnetization value and coercive field appear to decrease. This decreases occurs because as the surfactant concentration increases, more and more of the magnetic layer becomes inactive on the surface of the nanoparticles. However, just like the colloidal stability results, this only applies up to a concentration of 7.5 mmol, as seen in Table 5.

Table 5. Effect of oleic acid concentration on the saturation magnetization and coercive field of nanoparticles.

Oleic Acid Concentration (mmol)	Saturation Magnetization M_S (emu/g)	Coercive Field H_C (Oe)
1	73.6	420
2	57	254
3.5	49	97.3
5	43.5	78.4
6.25	40.2	75.2
7.5	48.3	67.2
10	51.1	131.5
15	41.9	125.2
20	44.5	89.5

Ioncica, et al. [12], Andhare, et al. [17], and Dabbagh, et al. [18], have succeeded in reviewing the effect of PEG coating on the magnetic properties of iron oxide nanoparticles as shown in Table 6.

Table 6. Changes in magnetic properties parameter values after nanoparticles were coated with PEG.

Ref.	Saturation Magnetization M_S (emu/g)		Remanent Magnetization M_R (emu/g)		Coercive Field H_C (Oe)		Blocking Temperature (°C)
	Uncoated	Coated	Uncoated	Coated	Uncoated	Coated	
[12]	-	34	-	0	-	-	-
[12]	-	78	-	1.1	-	-	-
[17]	46.82	42.49	7.62	4.54	190.89	57.6	-45

It seems that all the magnetic parameters values were reduced after coating by PEG. This can happen because the surfactant makes the magnetic surface of the nanoparticle dead and the interaction between the (A)-[B] sites in the spinel structure of the nanoparticle is reduced because it was replaced by PEG which coated the nanoparticle. In research by Andhare, et al. [17], it was also found that the blocking temperature of these nanoparticles was 228 K or around – 45 °C. This means that the nanoparticles are superparamagnetic if the temperature is above – 45 °C, so they can be applied at room temperature.

Hyperthermia Properties

In the application of magnetic hyperthermia, SPIONs when given an alternating magnetic field (AMF) are able to produce heat due to the vibration of the nanoparticles. This heat can then directly kill cancer cells or can also be used to destroy the encapsulation layer and release the drug stored inside [8].

The heat produced by nanoparticles occurs due to two things, relaxation and hysteresis loss. Relaxation is divided into two, namely Neel Relaxation and Brownian Relaxation. The heat generated by Neel Relaxation is caused by changes in the direction of magnetic moments that occur continuously relative to the crystal lattice (internal dynamics), while the heat generated by Brownian Relaxation is caused by the physical rotation of the particles themselves relative to the dispersing medium (external dynamics) [8].

There are two general parameters that can be used to review the ability of nanoparticles to produce heat. The first parameter is specific loss power (SLP) which provides the efficiency of nanoparticles in generating heat when exposed to AMF [16]. The higher the SLP, the more efficient it will be in converting magnetic energy into heat. The second parameter is the specific absorption rate (SAR) which provides an overview of the amount of electromagnetic energy absorbed by a unit mass of biological tissue in a certain time interval [8].

The research results of Hedayran, et al. [16], show that increasing the concentration of oleic acid will increase the SLP value up to a concentration of 7.5 mmol according to the results shown in Table 7. The increase in the SLP value from a concentration of 1 mmol to 7.5 mmol can be caused by a decrease in the average diameter and size distribution of nanoparticles [16]. Looking at the coercive field and saturation magnetization values, it also appears that the SLP behavior almost follows the HC/MS ratio, where a decrease in this ratio will increase SLP and vice versa [16]. The increase in SLP values due to variations in magnetic properties and morphology can be caused by increasing Neel and Brownian relaxation mechanism [36].

Table 7. Effect of oleic acid concentration on maximum temperature differences and SLP values.

Oleic Acid Concentration (mmol)	Maximum Temperature Difference After 300 s (°C)	Specific Loss Power (W/g)
1	1.9	33.5
3.5	6.2	100
7.5	17.5	268.5
20	5.7	85

In this research, Hedayran, et al. [16], also analyzed the influence of the dispersing medium and the intensity of the magnetic field provided on the resulting SLP value. It was found that, at all concentrations, the SLP value in the hexane dispersion medium would have a higher SLP value compared to that dispersed with DI-Water. This is due to the reduced contribution of Brownian Relaxation because the viscosity of DI-Water is higher than hexane so that rotation is limited. For its effect on magnetic field intensity, it was tested in the range 100 – 400 Oe. The results show an increase in the SLP value as the intensity increases, this indicates an increase in hysteresis loss.

Andhare, et al. [17], examined changes in the hyperthermia properties of $Co_{0.7}Zn_{0.3}Fe_2O_4$ (CZF) nanoparticles before and after being coated with PEG. Conditions were tested at various CZF

concentrations in the water dispersion medium, and the results obtained were shown in Table 8. Samples coated with PEG showed better SAR values compared to uncoated samples.

Table 8. SAR values for CZF and PEG-CZF at different concentrations.

Nanoparticles Concentration (mg/mL)	SAR (W/g)	
	CZF	PEG-CZF
2	108.15	141.46
4	134.98	170.93
6	141.54	176.65
8	165.79	217.12
10	166.89	246.09

Temperature analysis was also carried out where CZF and PEG-CZF nanoparticles were given the same AMF intensity and then the temperature increase as a function of time was examined. The results obtained are shown in Table 9. The PEG-coated sample showed a lower temperature increase than CZF for the same concentration. This can happen because the PEG layer reduces the active magnetic surface, thereby reducing its magnetic properties. For the same time interval, the rate of increase in temperature is directly proportional to the concentration. This means the higher the concentration of nanoparticles in the dispersion medium, the faster it will reach saturation conditions.

Table 9. Saturated temperature of CZF and PEG-CZF at different concentrations.

Nanoparticles Concentration (mg/mL)	Saturated Temperature (°C)	
	CZF	PEG-CZF
2	41	40
4	43	43
6	45	44
8	48	45
10	50	47

Dabbagh, et al. [18], have succeeded in synthesizing porous Fe_3O_4 nanoparticles encapsulated by PEG. To release the encapsulated drug, the nanoparticles must provide sufficient power from the AMF to produce heat capable of melting the PEG, namely at a temperature around 48 °C [18]. Tests were carried out on different AMF strengths, and the temperature rise and SAR values were shown in Table 10. It was found that the minimum required AMF strength was 47.2 kA/m.

Table 10. Saturated temperatures and SAR for various AMF strengths.

AMF Strenghts (kA/m)	Saturated Temperature (°C)		SAR (W/g)
	Measurements Time 15 minutes	Measurements Time 90 minutes	
31.5	40	42	120.4
47.2	43	48	172.0
63.0	50	56	206.3

Drug Loading and Drug Release Capabilities

In all research articles reviewed, all results related to drug loading and drug release were carried out using the drug Doxorubicin (DOX). For drug loading, the drug loading capacity and drug loading efficiency are analyzed. The results can be seen in Table 11.

Table 11. Comparison of drug load capacity and drug loading efficiency for nanoparticles before and after being coated with oleic acid and PEG.

Ref.	Surface Modification	Drug Loading Capacity DOX/MNP (ug/mg)		Drug Loading Efficiency (%)	
		Uncoated	Coated	Uncoated	Coated
[13]	Oleic Acid	2 ± 1	868 ± 37	0.4	86.8
[14]	Oleic Acid	n.d	868	n.d	87
[14]	PEG	n.d	590	n.d	59

*not determined, negligible amount of DOX. DOX loading efficiency = DOX in solution after after loading/initial amount of DOX.

The results in Table 11 show that nanoparticles coated with oleic acid and PEG will have much better drug loading capabilities compared to nanoparticles that are not coated with anything. Coating with oleic acid and PEG can increase the loading capacity due to the presence of a surfactant shell which can form a porous layer so that there is more interaction with the drug.

The results obtained regarding drug release were that its ability appeared to be influenced by pH. Under alkaline conditions, the drug release ability is low, and under acidic conditons, the release ability is high. This may occur due to the good stability and solubility in acidic medium compared to alkaline medium. Moreover, protonation of DOX at acidic pH increases its solubility resulting in even better release.

CONCLUSION

Coating SPIONs with oleic acid and PEG is generally able to improve the properties of nanoparticles for biomedical applications. In terms of colloidal stability, this coating will increase the stability of the nanoparticles thereby preventing them from agglomerating. In terms of magnetic properties, the saturation value decreases due to the reduction in magnetic surfaces, but the remanence and coercive values decrease drastically which is needed for superparamagnetic properties. In terms of hyperthermia, the results depend on the concentration and intensity of the AMF used. Meanwhile, in terms of drug loading and drug release, this coating process will make nanoparticles able to accommodate more drugs and release them well in acidic conditions. A more in-depth analysis of magnetic properties is still needed.

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