

# Recent Applications of Magnetic Nanoparticles in Food Analysis

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## *Abstract:*

Nanotechnology has become a topic of interest due to the outstanding advantages that the use of nanomaterials offers in many fields. Among them, magnetic nanoparticles (m-NPs) have been one of the most widely applied in recent years. In addition to the unique features of nanomaterials in general, which exclusively appear at nanoscale, these present magnetic or paramagnetic properties that result of great interest in many applications. In particular, in the area of food analysis, the use of these nanomaterials has undergone a considerable increase since they can be easily separated from the matrix in sorbent-based extractions, providing a considerable simplification of the procedures. This allows reducing cost and giving fast responses, which is essential in the food trade to guarantee consumer safety. These materials can also be easily tunable, providing higher selectivity. Moreover, their particular electrical, thermal and optical characteristics allow enhancing sensor signals, increasing the sensitivity of the approaches based on this type of device. The aim of this review article is to summarise the most remarkable applications of m-NPs in food analysis in the last five years (2016-2020) showing a general view of the use of such materials in the field.

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Review

# Recent Applications of Magnetic Nanoparticles in Food Analysis

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**Abstract:** Nanotechnology has become a topic of interest due to the outstanding advantages that the use of nanomaterials offers in many fields. Among them, magnetic nanoparticles (m-NPs) have been one of the most widely applied in recent years. In addition to the unique features of nanomaterials in general, which exclusively appear at nanoscale, these present magnetic or paramagnetic properties that result of great interest in many applications. In particular, in the area of food analysis, the use of these nanomaterials has undergone a considerable increase since they can be easily separated from the matrix in sorbent-based extractions, providing a considerable simplification of the procedures. This allows reducing cost and giving fast responses, which is essential in the food trade to guarantee consumer safety. These materials can also be easily tunable, providing higher selectivity. Moreover, their particular electrical, thermal and optical characteristics allow enhancing sensor signals, increasing the sensitivity of the approaches based on this type of device. The aim of this review article is to summarise the most remarkable applications of m-NPs in food analysis in the last five years (2016–2020) showing a general view of the use of such materials in the field.

**Keywords:** food analysis; magnetic nanoparticles; nanomaterials; sample preparation; sensors; sorbent-based extraction

## 1. Introduction

The increasing concern of the global population about food products, their quality, composition and effect on health, as well as the globalisation of the food trade, make necessary the development of reliable strategies that allow food companies to ensure accurate knowledge about their products. This aspect not only involves the evaluation of ingredients and main components, but also those that are present at very low concentration levels and still have a negative effect on consumers such as organic pollutants and microorganisms that endanger food safety [1–3]. Therefore, the evaluation of novel analytical methods that lead to these requirements has become an issue of remarkable importance for the scientific community.

The assessment of food products is a complex challenge due to the complexity of these kinds of matrices and the low concentrations at which contaminants can be harmful for consumers. In this

regard, the development of very sensitive, rapid and selective methodologies results essential and the use of nanomaterials is a cornerstone to achieve these goals [4]. In recent years, nanotechnology has played an important role in many areas, including food analysis as it has been shown in many reports in the literature [1,4–7]. Particular attention has been paid to the use of nanoparticles (NPs) and, especially, in magnetic-NPs (m-NPs) [1,8].

These materials present a small size, from 1 to 100 nm, which gives them great surface area that is excellent for their use in analytical methods. Only a very low amount of material is required in microextractions to reach the same efficiency as in conventional procedures. This definitely constitutes an aspect of great relevance in the current trends based on the principles of sustainable and green chemistry [1]. Apart from that, m-NPs are characterised by other particular features such as high electrical conductivity, coercivity, high magnetic susceptibility and, especially, superparamagnetism that favour their separation from the samples, simplifying the procedures, shortening times and, consequently, reducing costs [1,9]. These characteristics make them ideal for the preparation of sorbents in microextraction techniques or for clean-up steps [8,10,11] and as materials for the preparation of sensors [1,10,12]. In this respect, their use in magnetic-micro-dispersive solid-phase extraction (m- $\mu$ -dSPE) has constituted their main application, while their utilisation in optical and electrochemical sensors has involved the main uses in these approaches, although other novel systems have also been described in the literature.

There are several types of m-NPs, including alloys and oxides involving both iron and cobalt, fundamentally (i.e., FePt, CoPt<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, Fe<sub>2</sub>O<sub>3</sub>, CoFe<sub>2</sub>O<sub>4</sub>, etc.). However, the most widely applied so far have been magnetite (Fe<sub>3</sub>O<sub>4</sub>) based NPs [9,12]. For their preparation, a great variety of procedures, such as co-precipitation, thermal decomposition, micro-emulsion, or hydrothermal synthesis, has been applied. Moreover, diverse techniques have been used to confirm their structures and assure their suitability for the required applications, including transmission electron microscopy (TEM), X-ray powder diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR) and infrared spectroscopy (IR), vibrating-sample magnetometry (VSM), scanning electron microscopy (SEM) or thermal gravimetric analysis (TGA), among others [8,9].

Despite the unique features of m-NPs that favour their application in the area of food analysis, they have hardly been used without further modifications [13,14]. Their combination with other materials has been carried out in most of cases in order to overcome the ease with which they can be oxidised and their trend to aggregation [15]. In fact, to the best of our knowledge, modified m-NPs have been used in all works published in the last five years in sample preparation, and the use of non-modified m-NPs only has been reported for the preparation of sensors used for the evaluation of inorganic compounds [16]. Besides, such combinations also allow increasing their selectivity of the sorbents and the number of active points on the surface or enhancing electrical and optical properties in sensors [1,4,5]. In this respect, they have been combined with polymers or specific molecularly imprinted polymers (MIPs), with different types of aptamers (Apts) and antibodies (Abs), especially in sensor applications, or even with one or more nanomaterials including metal-organic frameworks (MOFs), carbon based nanomaterials and other types of NPs.

The aim of this review article is to compile the most widespread applications of m-NPs in the field of food analysis over the last five years (2016–2020), describing the most relevant uses as sorbents for miniaturised extraction techniques, as well as their use for the preparation and application of sensors. A critical discussion of the main advantages and disadvantages of their use will be presented and the most promising approaches and current trends in the area will be pointed out in order to give the reader a general overview of this issue.

## 2. Recent Applications in Food Analysis

### 2.1. Recent Applications in Sample Preparation

#### 2.1.1. Combined with Carbonaceous Nanomaterials

Carbonaceous nanomaterials have been one of the most widely applied sorbent materials in analytical chemistry due to their unique properties provided by the particular arrangement of carbon atoms disposed in planar sheets. A great number of frameworks based on this basic structure exists, including fullerenes, carbon nanotubes (CNTs), graphene, nanodiamonds (NDs), nanofibers (NFs), nanohorns (NHs), etc. All of them present good chemical and thermal stability, as well as mechanical strength, variable electrical conductivity, larger specific surface area and a great capacity to establish  $\pi$ - $\pi$  interactions [5,6,17]. For these reasons the combination of the advantages brought by these materials with those associated with m-NPs, constitutes a good strategy widely used in sample preparation in the area of food analysis as can be seen in Table 1, in which some of the most recent applications in this field have been compiled [18–27].

Most of the works reported are focused on the combination of iron oxide NPs together with CNTs and their different versions and functionalised forms [19,21–23,28], as well as graphene and modified graphene [20,24,27]. However, graphitized carbon black (GCB) has also been applied [26], along with ternary composites using NDs [18], and other non-carbonaceous nanomaterials. They have been used for the analysis of organic compounds in milk [18,19,26,27], fruit [18,29], oil [24], meat [18] or cereal based products [20,22], among others such as beverages, eggs, cacao, honey and coffee.

Although in most cases these sorbents are used as extraction materials, their application as clean-up sorbents has also been carried out showing a clear reduction of the matrix effect. As an example, Ma et al. [22] used a combination of  $\text{Fe}_3\text{O}_4$  and multi-walled CNTs (MWCNTs) for the clean-up step of the QuEChERS (quick, easy, cheap, effective, rugged, safe) renowned method applied for the extraction of 20 mycotoxins from rice, millet, wheat, corn and coix seed prior to determination by ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Apart from reducing the pre-treatment time as a consequence of using a magnetic sorbent easily removed by an external magnet, the whole methodology showed very good sensitivity with limits of detection (LODs) in the range 0.0006–1.6337  $\mu\text{g}/\text{kg}$  and an extraction efficiency similar or even better than for other sorbents commonly used in this technique such as octadecylsilane ( $\text{C}_{18}$ ), primary-secondary amine (PSA) and GCB, with recovery values between 70% and 113%.

Despite the fact that the introduction of carbonaceous materials already increases the possibility of establishing interactions with the target analytes, favouring the extraction efficiency; in some cases, further functionalisation with specific groups could considerably improve the selectivity of the procedure as was demonstrated by Fu et al. [19]. In this work, authors compared the extraction rate of 13 sulfonamides from milk samples using MWCNTs and those modified with  $\text{C}_{18}$  and p-Tolyl isocyanates (Tol). Results showed that the inclusion of those moieties on the surface of the sorbent clearly improved the extraction efficiency of the applied vortex assisted-magnetic-micro-dispersive solid-phase extraction (VA-m- $\mu$ -dSPE) method. Moreover, as the absorption percentage was slightly higher with Tol-MWCNTs for most of the target analytes, this modified sorbent was used for the validation of the methodology using high-performance liquid chromatography-mass spectrometry (HPLC-MS) as the determination technique. Results showed good sensitivity with LODs of 2–10  $\text{ng}/\text{L}$  and adequate recovery values in the range 81–109%. However, authors noticed that the hydrophobic interactions established by Tol moieties hindered the correct removal of some interferences with similar nature as the target analytes.

**Table 1.** Recent applications of magnetic carbonaceous nanomaterials as extraction sorbents in food analysis.

Analytes	Matrix	Nanomaterial	Extraction Technique	Determination Technique	Recovery %	LOD	Reference
Vitamin B <sub>12</sub>	Milk-based infant formula, orange and peach juice, meat, salami, powder milk (2 mL extract)	Fe <sub>3</sub> O <sub>4</sub> @MWCNTs@NDs (50 mg)	m-μ-dSPE	HPLC-DAD	>98	2.85 μg/L	[18]
13 Sulfonamides	Milk (30 mL)	Fe <sub>3</sub> O <sub>4</sub> @MWCNTs-p-tolyl (40 mg)	VA-m-μ-dSPE	HPLC-(Q-OrbiTrap)-MS	81–109	2–10 ng/L	[19]
4 Aflatoxins	White and moldy bread (20 mg)	Fe <sub>3</sub> O <sub>4</sub> @3Dgraphene (20 mg)	In-syringe-m-μ-dSPE	HPLC-FD	59–69	0.06–0.1 μg/kg	[20]
6 PAEs	Carbonated soft drinks (-)	MWCNT-Fe <sub>3</sub> O <sub>4</sub> /AgNPs (10 mg)	m-μ-dSPE	GC-(Q)-MS	97–109	10.8–22.5 ng/L	[21]
20 Mycotoxins	Rice, millet, wheat, corn, coix seed (5 g)	Fe <sub>3</sub> O <sub>4</sub> @MWCNT (20 mg)	QuEChERS	UHPLC-(QqQ)-MS/MS	74–113	0.0006–1.6337 μg/kg	[22]
6 Sudan dye, Para Red	Chili powder, chili tomato sauce, ketchup (10 g)	Fe <sub>2</sub> O <sub>3</sub> @COOH-MWCNT (20 mg)	m-μ-dSPE	HPLC-DAD	-	0.13–0.84 μg/L	[23]
Sesamol, sesamin, sesamolol	Sesame oil (0.1 g)	Fe <sub>3</sub> O <sub>4</sub> @GO (1.4 mg)	VA-m-μ-dSPE	HPLC-UV	85–87	0.02–0.05 mg/kg	[24]
7 Multiclass pesticides	Raisin product (5 g)	Fe <sub>3</sub> O <sub>4</sub> @r-GO (10 mg)	m-μ-dSPE	GC-(Q)-MS	93–119	14–40 μg/kg	[25]
6 Mycoestrogens	Cow milk (8 mL)	Fe <sub>3</sub> O <sub>4</sub> @GCB (100 mg)	VA-m-μ-dSPE	UHPLC-(QqQ)-MS/MS	70–91	3–9 ng/L	[26]
4 Sulfonamides	Milk (1.5 mL)	Fe <sub>3</sub> O <sub>4</sub> @graphene (15 mg)	VA-m-μ-dSPE	CE-DAD	3–105	0.89–2.31 μg/L	[27]

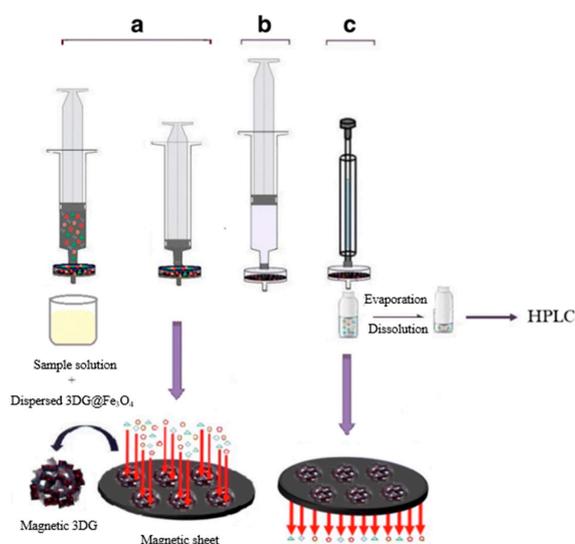
CE: capillary electrophoresis; COOH-MWCNT: carboxylated multi-walled carbon nanotubes; DAD: diode array detector; FD: fluorescence detection; GC: gas chromatography; GCB: graphitized carbon black; GO: graphene oxide; HPLC: high performance liquid chromatography; LOD: limit of detection; m-μ-dSPE: magnetic-micro-dispersive solid-phase extraction; MS: mass spectrometry; MS/MS: tandem mass spectrometry; MWCNT: multi-walled carbon nanotube; ND: nanodiamond; NP: nanoparticle; PAE: phthalate ester; Q: single quadrupole; QqQ: triple quadrupole; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, Safe; r-GO: reduced-graphene oxide; UHPLC: ultra-high performance liquid chromatography; UV: ultraviolet; VA: vortex assisted.

As previously indicated, the combination of m-NPs with more than one type of carbonaceous nanomaterial has also been tested for the evaluation of organic compounds from food matrices in order to improve the extraction performance. In this regard, Ulusoy et al. [18] took advantage of the simultaneous application of two different carbonaceous nanomaterials (MWCNTs and NDs) to prepare a magnetic composite with  $\text{Fe}_3\text{O}_4$  for the extraction of vitamin  $\text{B}_{12}$  from milk-based infant formula and cereals prior to its analysis by high performance liquid chromatography-diode array detector (HPLC-DAD). In this case, apart from the advantages related to the combination of MWCNTs with the m-NPs due to the strong van der Waals interactions points provided by this carbon-based nanomaterial, the addition of NDs to the prepared composite also improves its quality. NDs avoid the  $\pi$ - $\pi$  interactions between the graphene sheets that constitute the MWCNTs, decreasing the trend to aggregation of this material, which commonly diminishes its surface area and the number of active points that can interact with target analytes. Authors remarked that the particular characteristics of the prepared magnetic nanomaterial lead to a clear improvement in the extraction efficiency of the procedure highlighting the benefits of this new-generation material. This fact allowed the validation of a wide variety of complex food matrices of different nature with very good results, giving rise to a LOD of 2.85  $\mu\text{g/L}$  and recovery values higher than 98%.

Another carbon-based material most commonly combined with m-NPs for the evaluation of food commodities has been graphene [20,27] and its varieties including graphene oxide (GO) [24] or reduced-GO (r-GO) [25]. These materials involve an easier synthesis with lower residues production than CNTs, which has increased their use in this and other related areas [17]. Nevertheless, as with CNTs, the  $\pi$ - $\pi$  stacking, hydrophobic interactions and van der Waals forces between sheets lead to the formation of agglomerates that decrease the nanomaterial surface area. In this respect, the combination with NPs, and particularly m-NPs, seems to be a good strategy to avoid these problems [27,30]. Additionally, the use of oxide forms also favours such an aspect, increasing the polarity and hydrophilicity of the material with the introduction of hydroxyl, carboxy and epoxy groups on its surface, although the ultra-lightness of GO and r-GO forms also makes very useful their combination with NPs and m-NPs to hinder their aggregation tendency [27]. An interesting application was that developed by Wu et al. [24] who only needed 1.4 mg of  $\text{Fe}_3\text{O}_4$ @GO as sorbent to carry out the VA-m- $\mu$ -dSPE of sesamol, sesamin and sesamolins from 0.1 g of sesame oil prior to their separation and analysis by HPLC-ultraviolet (UV) detection. Although the authors used 5.7 mL of dichloromethane (DCM) for sample solubilisation and matrix clean-up, which reduces the sustainable and green character of the methodology, solvent consumption and sample requirements were demonstrated to be lower than other compared procedures. For example, saponification or solid-phase extraction (SPE) using alumina as sorbent could need up to 160 mL and 300 mL of organic solvent and 0.5 g and 5 g of sample, respectively. Apart from that, it is worth mentioning that thanks to the use of m-NPs and the ease of removing them from the matrix with the assistance of an external magnet, the pre-treatment step could be time reduced when VA-m- $\mu$ -dSPE was employed, obtaining recovery values in the same order or even higher than in the other cases (85–87%) and very good sensitivity, with LODs in the range 0.02–0.05 mg/kg.

Another strategy also applied in the area of food analysis for m-NPs@graphene sorbents has been the preparation of three-dimensional graphene (3Dgraphene). This approach consists of reassembly the two-dimensional graphene structure in aerogels, sponges or foams in order to favour the separation between sheets, avoiding agglomeration and active surface restrictions. In addition, such modification also leads to lower density, faster mass and electron transport kinetics, as well as to enhanced mechanical strength, as a consequence of the framework and unique properties of graphene [30]. Moreover, the addition of m-NPs to the structure also improves the characteristics of the material favouring the performance of the extraction process and decreasing the complexity as well as time consumption, which also involves a reduction of costs, aspect of great importance for routine procedures in food industry. Another interesting application of 3Dgraphene was carried out by Sereshti et al. [20], who made use of the advantages of m-NPs in a different way than usual in this kind of extraction

technique for the determination of aflatoxins in bread samples. In this work, the authors placed 20 mg of  $\text{Fe}_3\text{O}_4@3\text{Dgraphene}$  on a magnet sheet located in a filter holder, as shown in Figure 1. After conditioning the nanomaterial using methanol (MeOH) and water, 50 mL of an aqueous-organic extract, obtained after ultrasound assisted-solid-liquid extraction of 3 g of dried bread matrix, were loaded in a syringe and passed through the material magnet filter. By pulling back the plunger, the adsorbent particles were removed from the magnetic sheet and dispersed into the syringe. Then, the plunger was pushed to pass the sample solution through the filter and the analytes were eluted using 700  $\mu\text{L}$  of MeOH and subsequently analysed by HPLC-fluorescence detection (FD). Validation of the methodology led to intermediate recovery values (59–69%) and good sensitivity with LODs in the range 0.06–0.1  $\mu\text{g}/\text{kg}$ .



**Figure 1.** Scheme of an in-syringe-magnetic-micro-dispersive solid-phase extraction ( $m\text{-}\mu\text{-dSPE}$ ) using  $\text{Fe}_3\text{O}_4@3\text{Dgraphene}$  as sorbent for the evaluation of aflatoxins in bread samples. (a) Sample loading, (b) washing by distilled water, (c) desorption using MeOH. Reprinted from [20], with permission from Springer, 2020.

Apart from that, the combinations with other materials that provide complementary properties to the magnetic carbonaceous composites have also been evaluated. Among them, combinations of magnetic CNTs, graphene or GO with other non-magnetic NPs, polymers or MOFs have also been carried out. The main objectives in all these studies were to increase the reproducibility, stability and above all, the extraction efficiency and the selectivity of the sorbent. An interesting example is the combination with non-magnetic NPs as carried out Moazzen et al. [21] for the extraction of six phthalic acid esters (PAEs). The authors prepared a sorbent composite constituted of  $\text{Fe}_3\text{O}_4$  NPs, MWCNTs and Ag NPs since this last component provides considerable mechanical and thermal strength, catalytic enhancement and increase of the surface area, which enlarge the possibility of interaction with target compounds, accelerating the absorption and desorption processes. The good performance of the extraction process based on the developed MWCNT- $\text{Fe}_3\text{O}_4/\text{AgNPs}$  sorbent allows its application in complex carbonated soft drinks using only 10 mg, obtaining recovery values in the range 97–109% and LODs of the method between 10.8 ng/L and 22.5 ng/L.

As can be seen in all these examples, the combination of m-NPs with carbonaceous nanomaterials not only improves the active interaction sites of the magnetic material, increasing the selectivity and efficiency of the extraction procedure, but also improves the performance of the methodology because of the synergic effect of the advantages provided by both nanostructures. Moreover, in addition to the benefits already described, the possibility of reusing these sorbents should also be highlighted as has been demonstrated in most of the articles compiled in Table 1. This aspect reinforces the valorisation

of the new sorbents developed, as well as the methodologies carried out based on their application, especially in the field of food analysis, in which the use of simple, cheap and low cost procedures that allow the producers to guarantee the safety of consumers, is essential for the correct development of market and food industry.

### 2.1.2. Combined with Metal-Organic Frameworks

MOFs are in general composed by a metal ion or a metal cluster centre, self-assembled with a 3D organic ligands framework. They have been extensively used in food analysis in the last decades due to their pore design and functionalisation flexibility and high surface area, as shown in different reviews dealing with the topic [31,32]. Their combination with m-NPs to form the so-called magnetic MOFs (m-MOFs) or magnetic frameworks composites (m-FCs) provides them in general with a better stability than MOFs alone, as well as superparamagnetism, rapid and easy adsorption/desorption steps and high recycling rates. Table 2 shows a selection of recent applications of m-MOFs to the food analysis field [33–42]. The works reported describe the extraction of both organic [33,34,36–38,41–43] and inorganic [39,40] compounds in a wide variety of matrices.

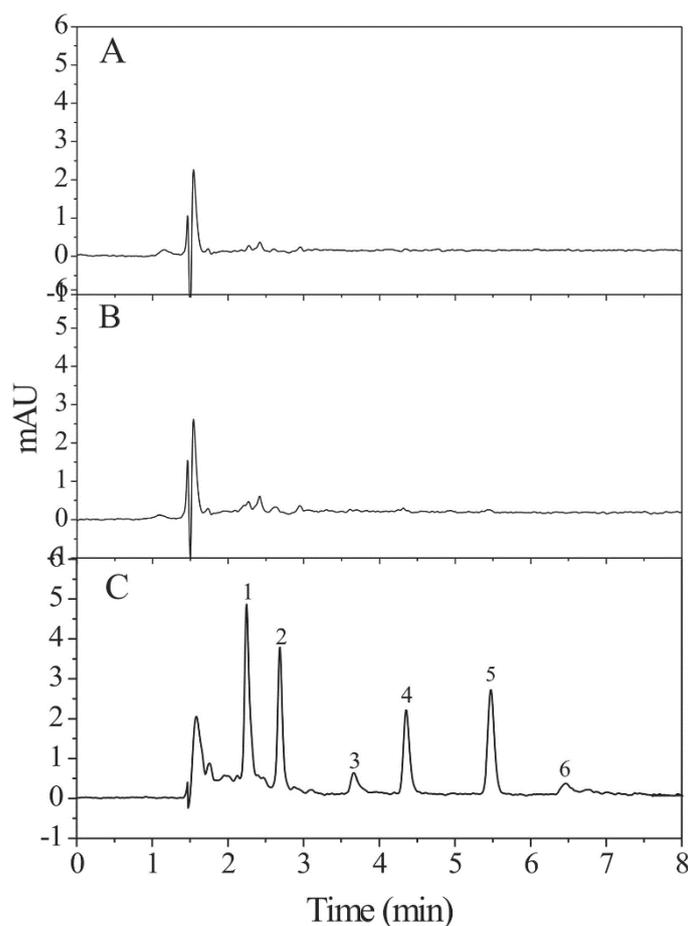
There are different techniques to synthesise m-MOFs, i.e., mixing, seeding and surface modification, which gives mixed, embedded and core-shell structures. Each of them shows different advantages and disadvantages already discussed in the literature [44].

The mixing technique is the easiest way to synthesise m-MOFs, since it consists on mixing MOFs with a m-NP precursor. However, co-precipitation makes difficult the control of the structure, and elution is normally difficult. Some examples of m-MOFs synthesised in this way can be found in the food analysis field [33,34]. Durmus et al. [33] proposed a multi-component  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{MIL-53}(\text{Al})$  composite synthesised by co-precipitation of MIL-53(Al) with core-shell  $\text{Fe}_3\text{O}_4@\text{SiO}_2$  m-NPs.  $\text{Fe}_3\text{O}_4$  NPs were first prepared by precipitation using Fe(II) and Fe(III), the  $\text{Fe}_3\text{O}_4@\text{SiO}_2$  core-shell NPs were synthesised using the Stöber biphasic method [45] and MIL-53(Al) was commercially purchased. Authors structurally and morphologically characterized  $\text{Fe}_3\text{O}_4$ ,  $\text{Fe}_3\text{O}_4@\text{SiO}_2$  and  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{MIL-53}(\text{Al})$ . Regarding surface characteristics,  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{MIL-53}(\text{Al})$  exhibited higher surface area and total pore volume than the others, as expected. Ten mg of this composite was successfully applied to extract aflatoxin B<sub>1</sub> from 2 mL of 11 different species extracts using m- $\mu$ -dSPE, with a LOD of 0.5  $\mu\text{g/L}$  and good recovery values (71–97%). A mixture of acetone/acetonitrile (ACN)/DCM (1:1:2, *v/v/v*) was used as elution solvent and fluorescence spectrophotometry as detection technique. Shi et al. [34] also employed a simple mixing method for the synthesis of  $\text{Fe}_3\text{O}_4\text{-NH}_2@\text{MIL-101}$ . In this case, amine-functionalised  $\text{Fe}_3\text{O}_4$  particles ( $\text{Fe}_3\text{O}_4\text{-NH}_2$ ) were prepared by mixing 1,6-hexanediamine with  $\text{FeCl}_3$ , ethylene glycol (EG) and anhydrous sodium acetate, while MIL-101 was hydrothermally synthesised by mixing  $\text{Cr}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$  with terephthalic acid (BDC). They were later mixed to obtain  $\text{Fe}_3\text{O}_4\text{-NH}_2@\text{MIL-101}$ . A simple experiment was used to check the adsorption capacity of  $\text{Fe}_3\text{O}_4\text{-NH}_2@\text{MIL-101}$  against  $\text{Fe}_3\text{O}_4\text{-NH}_2$ , which consisted in dispersing the same amount of each in a Sudan Red 7B solution, showing that, with the help of an external magnet, the  $\text{Fe}_3\text{O}_4\text{-NH}_2@\text{MIL-101}$  supernatant became clear while the other did not change colour. This demonstrated the excellent extraction capacity of porous MIL-101. Three mg of this composite was used for the m- $\mu$ -dSPE of 6 Sudan dyes in tomato sauce. The analytes were extracted with  $2 \times 5$  mL ACN from 4 g sample and the extracts were dried and redissolved in 1 mL of MeOH/water which was the liquid phase in the extraction procedure. Ethyl acetate ( $2 \times 1$  mL) was used as elution solvent, obtaining recovery values in the range 70–93% and LODs of 0.5–2.5  $\mu\text{g/g}$ . Figure 2 shows the typical HPLC-DAD chromatograms of a tomato sauce sample (A), a spiked tomato sauce sample (B) and a spiked tomato sauce sample submitted to the  $\text{Fe}_3\text{O}_4\text{-NH}_2@\text{MIL-101}$  m- $\mu$ -dSPE procedure. The authors also compared the synthesised composite with other commercial sorbents- $\text{C}_{18}$ , hydrophilic-lipophilic balance (HLB) and alumina- showing higher extraction efficiencies than HLB and alumina and comparable to  $\text{C}_{18}$ . Furthermore, the sorbent demonstrated good performance when reused up to 10 times using a simple reconditioning protocol.

**Table 2.** Recent applications of magnetic metal-organic frameworks as extraction sorbents in food analysis.

Analytes	Matrix	Nanomaterial	Extraction Technique	Determination Technique	Recovery %	LOD	Reference
Aflatoxin B <sub>1</sub>	Species (2 mL extract)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @MIL-53(Al) (100 mg)	m-μ-dSPE	FD	71–97	0.5 μg/L	[33]
6 Sudan dyes	Tomato sauce (1 mL extract)	Fe <sub>3</sub> O <sub>4</sub> -NH <sub>2</sub> @MIL-101 (3 mg)	m-μ-dSPE	HPLC-DAD	70–93	0.5–2.5 μg/kg	[34]
2 Pyrethroid pesticides	Fruit juice (100 mL, 1:3 v/v aqueous solution)	Fe <sub>3</sub> O <sub>4</sub> @MAA@TMU-21 (4 mg)	m-μ-dSPE	HPLC-UV	93–105	0.05–0.1 μg/L	[35]
3 Organophosphorus pesticides	Rice (25 mL extract)	Fe <sub>3</sub> O <sub>4</sub> @ThGA@TMU-6 (2 mg)	m-μ-dSPE	HPLC-UV	88–107	0.5–1.0 μg/L	[36]
8 Sedative drugs	Pork meat (10 mL tert-butyl methyl ether extract)	Fe <sub>3</sub> O <sub>4</sub> @TbBd@ZIF-8 (7 mg)	VA-m-μ-dSPE	HPLC-MS/MS	73–93	0.04–0.2 μg/kg	[37]
6 Benzoylurea insecticides	Tea infusion (8 mL)	Fe <sub>3</sub> O <sub>4</sub> @ATP@ZIF-8 (30 mg)	VA-m-μ-dSPE	HPLC-DAD	79–114	0.7–3.2 μg/L	[38]
Hg(II)	Fish and canned tuna (100 mL diluted extract)	Fe <sub>3</sub> O <sub>4</sub> @DTIM@MOF-199 (24 mg)	m-μ-dSPE	FAAS	95–102	10 ng/L	[39]
Sn(II), Sn(IV)	Canned tuna fish, canned cherry, tomato paste (250 mL diluted extract)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @PAN@MIL-101(Cr) (21 mg)	UA-m-μ-dSPE	ET-AAS	87–96	5.0 ng/L	[40]
4 Triazole fungicides	Honey, fruit juices (30 mL diluted extract)	Fe <sub>3</sub> O <sub>4</sub> @APTES-GO@ZIF-8 (16 mg)	m-μ-dSPE	HPLC-DAD	72–111	0.014–0.109 μg/L	[41]
4 Tetracycline antibiotics	Milk, egg, chicken muscle, kidney (10 mL extract)	Fe <sub>3</sub> O <sub>4</sub> @MOF-199/(EHA/DVB/MMA) polyHIPE (1.2 cm diameter, 6.0 mm thickness)	m-SCSE	HPLC-FD	87–111	1.9–13.9 μg/L (milk and egg); 1.8–13.0 μg/kg (chicken muscle and kidney)	[42]

APTES: (3-aminopropyl) triethoxysilane; ATP: attapulgite; Bd: bencidine; DAD: diode array detector; DTIM: 4-(5)-imidazoledithiocarboxylic acid; DVB: divinylbenzene; EHA: 2-ethylhexylacrylate; ET-AAS: electrothermal atomic absorption spectroscopy; FAA: flame atomic absorption spectroscopy; FD: fluorescence detection; GO: graphene oxide; HPLC: high performance liquid chromatography; LOD: limit of detection; MAA: methylacrylic acid; m-μ-dSPE: magnetic-micro-dispersive solid-phase extraction; MMA: methyl methacrylate; m-SCSE: magnetic-stir cake sorptive extraction; MS/MS: tandem mass spectrometry; PAN: 1-(2-Pyridylazo)-2-naphthol; polyHIPE: polymerised high internal phase emulsion; Tb: 1,3,5-triformylbenzene; ThGA: thioglycolic acid; UA: ultrasound assisted; UV: ultraviolet; VA: vortex assisted.



**Figure 2.** Typical high performance liquid chromatography-diode array detector (HPLC-DAD) chromatograms of a tomato sauce sample (A), a tomato sauce sample, (B) a spiked tomato sauce sample (C) a spiked tomato sauce sample submitted to the  $\text{Fe}_3\text{O}_4\text{-NH}_2\text{@MIL-101}$   $\text{m-}\mu\text{-dSPE}$  procedure. Reprinted from [34] with permission from Elsevier, 2020.

Another way to synthesise m-MOFs is by surface modification [35–37]. In this regard, Yamini et al. [35] employed a layer-by-layer strategy to prepare a TMU-21 based MFC capable of extracting 2 pyrethroid pesticides from fruit juice after a  $\text{m-}\mu\text{-SPE-HPLC-UV}$  method. First,  $\text{Fe}_3\text{O}_4$  NPs were synthesised from Fe(II) and Fe(III) by precipitation. Then, bis-pyridin-4-ylmethylene-naphthalene-1,5-diamine (4-nbpy), the principal ligand of TMU-21, was synthesised from 4-pyridinecarboxaldehyde in ethanol (EtOH) and 1,5-diaminonaphthalene after the addition of DCM. The MFCs were assembled by dispersing methylacrylic acid (MAA)-modified  $\text{Fe}_3\text{O}_4$  ( $\text{Fe}_3\text{O}_4\text{@MAA}$ ) with zinc nitrate dimethylformamide (DMF) solution, 4-nbpy and the acidic ligand 4,4'-oxybis(benzoic acid) ( $\text{H}_2\text{oba}$ ) DMF solution.  $\text{Fe}_3\text{O}_4\text{@TMU-21}$  sorbent showed excellent water, solvent and thermal stability and combined the magnetic properties of  $\text{Fe}_3\text{O}_4$  with the increase of the surface area provided by TMU-21. Four mg of this nanomaterial was used for the extraction of the analytes from a 1:3  $v/v$  aqueous juice solution, taking advantage of the  $\pi\text{-}\pi$  stacking, hydrophobic and hydrogen-bond interactions. 1-butanol was used as elution solvent (80  $\mu\text{L}$ ), providing good results in terms of recovery (93–105%) and LODs (0.05–0.1  $\mu\text{g/L}$ ). Shakoaurian et al. [36] used the same approach to synthesise a TMU-6 based MFC to determine 3 organophosphorus pesticides in rice. In this case,  $\text{Fe}_3\text{O}_4$  NPs functionalised with thioglycolic acid (ThGA) was mixed with zinc acetate, and the resulting product with the MOF principal ligand *N,N*-Bis[1-(pyridine-2-yl)ethylene]-benzene-1,4-diamine (4-bpmb) and  $\text{H}_2\text{oba}$  gave  $\text{Fe}_3\text{O}_4\text{@ThGA@TMU-6}$  superparamagnetic NPs. Rice samples (2 g) were powdered, ultrasound extracted with 3 mL EtOH and centrifuged. Two mL of the supernatant was diluted in 23 mL water and submitted to the  $\text{m-}\mu\text{-dSPE-HPLC-UV}$  method using 1-butanol (100  $\mu\text{L}$ )

as the elution solvent. The phenyl groups in the 4-bpmb ligand in  $\text{Fe}_3\text{O}_4@\text{ThGA}@\text{TMU-6}$  favour the adsorption of non-ionizable organophosphorus pesticides through  $\pi$ - $\pi$  stacking, hydrophobic and hydrogen bond formation, a fact that is demonstrated through the higher extraction efficiencies of the  $\text{Fe}_3\text{O}_4@\text{ThGA}@\text{TMU-6}$  composite with respect to that of  $\text{Fe}_3\text{O}_4@\text{ThGA}$ . This nanomaterial could be used up to 20 times giving LODs between 0.5–1.0  $\mu\text{g/L}$  and recovery values ranging from 88% to 107%. In another work [37],  $\text{Fe}_3\text{O}_4$  NPs were functionalised with 1,3,5-triformylbenzene (Tb) and bencidine (Bd) in dimethyl sulfoxide (DMSO) to give  $\text{Fe}_3\text{O}_4@\text{TbBd}$  microspheres. They were then made to react with  $\text{HAuCl}_4\cdot\text{H}_2\text{O}$  in MeOH and the so-formed  $\text{Fe}_3\text{O}_4@\text{TbBd-Au}$  particles were finally dispersed in a mercaptoacetic acid EtOH solution to give rise to  $\text{Fe}_3\text{O}_4@\text{TbBd-Au-COOH}$ . These particles were added to a mixture of  $\text{Zn}(\text{NO}_3)_2\cdot 6\text{H}_2\text{O}$  and 2-methylimidazole to let  $\text{Fe}_3\text{O}_4@\text{TbBd}@\text{ZIF-8}$  composite form. The adsorption capacity of this composite was compared with that of  $\text{Fe}_3\text{O}_4@\text{TbBd}$ , being higher due to the hydrophilic affinity and the  $\pi$ - $\pi$  stacking interactions of ZIF-8 with the analytes, as well as to the pore filling effect which enhanced the van der Waals forces. Seven mg of it was dispersed in 10 mL of pork extract for the VA-m- $\mu$ -dSPE of 8 sedative drugs after previous treatment of the samples with ACN, NaOH and tert-butyl methyl ether. ACN was used as elution solvent (1 mL), obtaining good recovery values (79–114%) and LODs in the range 0.7–3.2  $\mu\text{g/L}$ . The material could be used up to 6 times after proper washing.

The last way to synthesise m-MOFs is the sealing technique, in which modified m-NPs are added to the MOFs precursor, giving rise to the coordination of organic ligands and metallic ions in the MOFs [38–40]. In general, MOFs suffer of low water stability, a fact that Niu et al. [38] tried to resolve by obtaining a ternary nanohybrid. Attapulgite (ATP) modified  $\text{Fe}_3\text{O}_4$  ( $\text{Fe}_3\text{O}_4@\text{ATP}$ ) was mixed with Zn nitrate and then 2-methylimidazole was added to obtain  $\text{Fe}_3\text{O}_4@\text{ATP}@\text{ZIF-8}$ . The authors made a comparison of the extraction efficiency of 6 benzoylurea insecticides by  $\text{Fe}_3\text{O}_4@\text{ATP}$ ,  $\text{Fe}_3\text{O}_4@\text{ZIF-8}$  and  $\text{Fe}_3\text{O}_4@\text{ATP}@\text{ZIF-8}$ , obtaining the better results for  $\text{ATP}@\text{Fe}_3\text{O}_4@\text{ZIF-8}$ . This is probably due to the enhanced hydro-stability that ATP provides, increasing the number of adsorption sites. Thirty mg of the composite was used for the VA-m- $\mu$ -dSPE of the selected pesticides in 8 mL of tea infusions using 2 mL ACN as the elution solvent. The phase could be used up to 5 times and provided good results in terms of recovery (79–114%) and LODs in the range 0.7–3.2  $\mu\text{g/L}$ . Another work in which the m-MOF nanocomposite was obtained by the sealing method is that developed by Tadjarodi and Abbaszadeh [39], in which  $\text{Fe}_3\text{O}_4$  particles were modified with 4-(5)-imidazoledithiocarboxylic acid (DTIM) and then made react with trimesic acid in DMF/EtOH. After the addition of a Cu(II) acetate solution, the  $\text{Fe}_3\text{O}_4@\text{DTIM}@\text{MOF-199}$  composite was obtained and used for Hg(II) extraction from fish and canned tuna (0.5 g) after acid digestion of the samples using 1.1 M thiourea as the elution solvent (3.5 mL), obtaining a LOD of 10 ng/L and recovery values in the range 95–102%. The sorbent could be reused up to 12 times and the effect of potentially interfering ions (K(I), Na(I), Ca(II), Mg(II), Al(III), Fe(III), Cr(III), Mn(II), Pb(II), Zn(II), Ag(I), Ni(II), Co(II), Cd(II),  $\text{CrO}_4^{2-}$  and  $\text{AsO}_4^{3-}$ ) was assayed and even at high concentrations, they did not affect the extraction of Hg(II) at pH = 6.0. Also in another occasion [40], magnetite NPs were mixed with tetraethyl orthosilicate (TEAS) in  $\text{NH}_4\text{OH}$  solution to form  $\text{Fe}_3\text{O}_4@\text{SiO}_2$  and then made react with 3-(chloropropyl)trimethoxysilane (3-CPTS) in toluene and later with 1-(2-pyridylazo)-2-naphthol (PAN) in MeOH:triethylamine (TEA) to form  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{PAN}$ . Then, they were mixed with benzene 1,4-dicarboxylic acid ( $\text{H}_2\text{BDC}$ ) and  $\text{Cr}(\text{NO}_3)_2$  to give the nanocomposite  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{PAN}@\text{MIL-101}$ . The extraction capabilities of raw MIL-101(Cr),  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{PAN}$  and  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{PAN}@\text{MIL-101}$  were compared, providing the latter the best performance due to the combination of two facts: its higher surface area and the presence of PAN in the m-NPs as a proper chelator, which enhances the complex formation between nitrogen atoms and Sn(IV). Furthermore, the MIL-101(Cr) action as spacer was also noted, which prevents  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{PAN}$  aggregation, as well as the cation-exchange interactions between the negative sites of MIL-101(Cr) and hydrated Sn(IV) ions. The sorbent was used for the UA-m- $\mu$ -dSPE of Sn(IV) from canned tuna fish, canned cherry and tomato paste (1 g sample) after acid digestion. Sn(II) could also

be determined by oxidising it into Sn(IV). Only 0.75 mL of 1.25 M HCl was used as the elution solvent, obtaining a LOD of 5.0 ng/L and recovery values between 87–96%.

Apart from the aforementioned works, there are others in the literature which combine the use of m-MOFs with other systems to improve the extraction of the analytes [41,42]. This is the case of the work developed by Senosy et al. [41] in which ZIF-8 modified magnetic GO was employed to extract a group of triazole fungicides in honey and fruit juices. Bare Fe<sub>3</sub>O<sub>4</sub> m-NPs were modified with (3-aminopropyl) triethoxysilane (APTES) in order to provide them with -NH<sub>2</sub> groups. Then, GO powder was dispersed in DMF and *n*-hydroxyl succinimide (NHS) and (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) were added together with the Fe<sub>3</sub>O<sub>4</sub>@APTES particles to finally form Fe<sub>3</sub>O<sub>4</sub>@APTES-GO. Once dispersed in MeOH, Zn(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O was added to give rise to the Fe<sub>3</sub>O<sub>4</sub>@APTES-GO@ZIF-8 nanocomposite. After dilution with water of the honey (10 g in 100 mL) and juice samples (1:2, *v/v*), 16 mg of the phase were added to 30 mL of extract and submitted to m-μ-dSPE. MeOH was used as elution solvent (0.5 mL), obtaining a good recovery (72–111%) and LODs in the range 0.014–0.109 μg/L. The presence of GO sheets provided a better dispersion of the phase in aqueous solution. Another interesting work concerning m-MOFs combined with other phases is that developed by Du et al. [42], who described the synthesis of a Fe<sub>3</sub>O<sub>4</sub>@MOF-199-embedded 2-ethylhexylacrylate (EHA)/divinylbenzene (DVB)/methyl methacrylate (MMA) polymerised high internal phase emulsion (polyHIPE) m-MOF composite by *in situ* polymerisation. PolyHIPEs have been employed in the last decade as sorbent materials due to their high specific surface area, high interconnected pore network and well-defined porosities; however, they showed low permeability and poor mechanical behavior if not combined with a more stable structure. The authors mixed the monomers MMA, DVB and EHA and the surfactant Span 80 with a K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> solution which was dropwise added, followed by the addition of the previously synthesised Fe<sub>3</sub>O<sub>4</sub>@MOF-199. The prepared monolithic composites were cut into disks of 1.2 cm in diameter and 6.0 mm in thickness. The authors compared the surface area of the Fe<sub>3</sub>O<sub>4</sub>@MOF-199/(EHA/DVB/MMA)polyHIPE with conventional (EHA/DVB/MMA)polyHIPEs, obtaining a lower value, but showing an obvious better mechanical strength. Magnetic-stir cake sorptive extraction (m-SCSE) was developed with the cut disks for the determination of 4 tetracycline antibiotics in 10 mL of milk, egg, chicken muscle and kidney extract after proper treatment of the samples. LODs were between 1.9 and 13.9 μg/L for milk and egg and between 1.8 and 13.0 μg/kg for chicken muscle and kidney. Recovery values were in all cases higher than 87%.

### 2.1.3. Combined with Polymeric Materials

The presence of functional groups in polymers makes them ideal for their combination with m-NPs [46]. This fact, together with the stability of polymers in a wide range of pH, has become that combination very popular for the extraction of food samples [7]. It should be noted that, in contrast, the polymers are relatively unstable at high temperatures (a problem which is exacerbated by the possible catalytic behaviour of the metallic core) [47]. Some selected examples of the application of the mentioned combination are shown in Table 3 [48–57].

The interaction between polymers and m-NPs could occur through covalent or electrostatic (as a result of attractive magnetic force, steric hindrance and van der Waals interactions) mechanisms. The inclusion of polymers, as happens with other coatings, passivates the surface of m-NPs and avoids agglomeration [47]. If coating occurs simultaneously with the synthesis, particle growth is limited [47].

Both natural (agarose, chitosan, dextran, short-chain amylose) and synthetic polymers including non-imprinted polymer (NIP), such as polypyrrole, polydopamine (pDA), poly(diallyl dimethylammonium chloride), polystyrene, etc., MIPs and ion-imprinted polymers (IIPs) have been combined with m-NPs for food analysis. Normally, natural polymers are attached through electrostatic interaction whereas covalent bonding is involved for synthetic polymers [58]. A wide variety of analytes, including pesticides, dyes, antibiotics, vitamins, hormones, endocrine disruptors, antioxidants, mycotoxins, metals and other contaminants and natural organic compounds, have been extracted by m-polymeric NPs from different food matrices, comprising vegetables, fruits, beverages, cereals and derivatives, milk and dairy products, honey, meat and fish, among others.

**Table 3.** Recent applications of magnetic polymeric nanomaterials as sorbents in food analysis.

Analytes	Matrix	Nanomaterial	Extraction Technique	Determination Technique	Recovery %	LOD	Reference
Acrylamide	Potato chips (2 g)	Fe <sub>3</sub> O <sub>4</sub> @dextran@MIP (20 mg)	SLE, m-μ-dSPE	HPLC-UV	84–97	20 μg/L	[48]
6 Phenyl pesticides	Apple, pear, cucumber, lettuce and cherry tomato (50 g)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @poly (phenylene ethynylene) framework (20 mg)	UAE, m-μ-dSPE	UHPLC-MS/MS	80–119	0.27–3.1 ng/L	[49]
Malachite green	Fish (5 g)	CdTe QDs/Fe <sub>3</sub> O <sub>4</sub> @MIP (0.8 mg)	UAE, m-μ-dSPE	FD	102–109	0.014 μmol/L	[50]
22 Oestrogenic compounds	Cow, goat, sheep and human milk (1.5 mL)	Fe <sub>3</sub> O <sub>4</sub> @pDA (80 mg)	m-μ-dSPE	UHPLC-MS/MS	70–120	0.55–11.8 μg/L <sup>a)</sup>	[51]
3 Acaricides	Grape, apple and peach juice (8 mL)	1-hexadecyl-3-methylimidazoliumbromide-coated ATP@polyaniline-polypyrrole@Fe <sub>3</sub> O <sub>4</sub> (1 mg)	m-MHSPE	HPLC-DAD	76–95	0.16–0.57 μg/L	[52]
Clonazepam and norazepam	Herbal health food (0.5 g)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @MIP (-)	SBSE	HPLC-UV	90–103	0.01 μg/mL	[53]
Cd(II) and Pb(II)	Fish and shrimp (0.5 g), broccoli, apple, lettuce and mushroom (1 g)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @polyaminoquinoline (21 mg)	MAE, m-μ-dSPE	FAAS	86–102	0.1–0.7 ng/mL	[54]
5 Polar acidic herbicides	Rice (5 g)	Fe <sub>3</sub> O <sub>4</sub> @polyethyleneimine@r-GO (5.4 mg)	SLE, m-dSPE	HPLC-DAD	87–103	0.67–2.00 ng/g	[55]
Ag (I)	Rice, potato and tomato (1 g)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @TiO <sub>2</sub> @IIP (40 mg)	m-dSPE	FAAS	98–100	0.5 ng/mL	[56]
<i>Bactrocera oleae</i> sexual pheromone	Olive oil (10 mL)	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @MIP (50 mg)	m-dSPE	GC-MS	95–99	3.2 μg/L	[57]

ATP: attapulgit; DAD: diode array detector; FAAS: flame atomic absorption spectrometry; FD: fluorescence detection; GC: gas chromatography; HPLC: high performance liquid chromatography; IIP: ion imprinted polymer; LOD: limit of detection; MAE: microwave assisted extraction; m-μ-dSPE: magnetic-micro-dispersive solid-phase extraction; m-MHSPE: mixed hemimicelles solid-phase extraction; MIP: molecularly imprinted polymer; MS: mass spectrometry; MS/MS: tandem mass spectrometry; pDA: polydopamine; QD: quantum dot; r-GO: reduced-graphene oxide; SBSE: stir bar sorption extraction; SLE: solid-liquid extraction; UAE: ultrasound assisted extraction; UHPLC: ultra-high performance liquid chromatography; UV: ultraviolet.

Polymers are frequently combined with other materials (in addition to m-NPs) to improve extraction capacity, physical properties or to facilitate interaction. Thus, examples can be found in the literature of the combination with SiO<sub>2</sub> [49,53,54,56,57], carbonaceous materials [55,59], ionic liquids (ILs) [52] and quantum dots (QDs) [50]. It should be mentioned that, keeping in mind that the extraction mechanism involves different interactions when multi-material composites are used, some of the applications mentioned in this section could also be included in the preceding ones.

Silanisation is a typical method to modify m-NPs due to the low price, and chemical, mechanical and thermal inertness and stability [46,58]. Moreover, the chemistry of silica is well known and, thus, different arrangements are allowed (for example the combination of successive porous and non-porous layers). This total knowledge about silica facilitates an easier further modification, whereas the functionalisation of magnetite could sometimes be difficult. This is the reason why a high percentage of the applications that use polymers (and particularly MIPs) employed Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub> as a substrate.

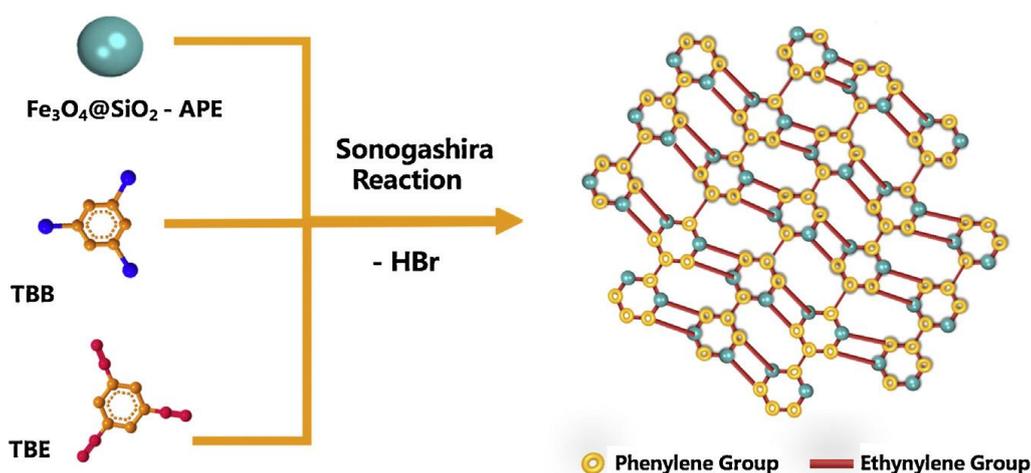
The combination with carbonaceous materials not only allows the possibility of including functional groups at the carbonaceous surface without disrupting the electronic network but also increases the adsorption sites of such material adding a further interaction mechanism, apart from the  $\pi$ - $\pi$  stacking offered by the carbon skeleton. Moreover, the dispersion in water of the carbonaceous m-NPs is enhanced. As an example, Li et al. [55] synthesised polyethyleneimine modified reduced graphene oxide m-NPs through self-assembling via electrostatic interaction of positive charged polyethyleneimine magnetite NPs and negative charged graphene oxide sheets. Fe<sub>3</sub>O<sub>4</sub> NPs were synthesised via a solvothermal method and polyethyleneimine composite was obtained via a crosslinking reaction. GO was exfoliated with deoxygenated water and ultrasounds and then mixed with magnetic polyethyleneimine NPs. Subsequently, GO was reduced with NaBH<sub>4</sub>. After being characterised by TEM, FT-IR, XRD, TGA, zeta potential analysis and VSM, the obtained material was employed for the extraction of polar acidic herbicides (dicamba, 2,4-dichlorophenoxy acetic acid, 4-chloro-methyl-phenoxy acetic acid, 2-(2,4-dichlorophenoxy) propionic acid, 2,4,5-trichlorophenoxy acetic acid) from rice by m-dSPE with good results (recovery: 87.41–102.52%, LODs: 0.67–2.00 ng/g). The optimal conditions for parameters affecting extraction efficiency were obtained through a multivariate experimental design (i.e., response surface methodology) and the method proved to be comparable or even superior to other previous methods developed with the same aim.

Yang et al. [52] developed a magnetic mixed hemimicelles dSPE using an IL-coated ATP@polyaniline-polypyrrole@Fe<sub>3</sub>O<sub>4</sub> composite for the analysis of acaricides in fruit juice. The mechanism of the mixed hemimicelles dSPE involves the adsorption of ionic surfactants (ILs in this case) on metal oxides. At concentrations lower than the critical micelle, a single (hemimicelles) or double-layer (admicelles) is formed. The use of hemimicelles in SPE implicates high extraction efficiency, high breakthrough volumes and easy elution of the analytes. However, the protocol requires relatively high analysis times for the transference of the solvent to the column, due to the formation of these micellar structures. Thus, the use of dSPE procedures can overcome this disadvantage. In the mentioned application [52], the ATP@polyaniline-polypyrrole@Fe<sub>3</sub>O<sub>4</sub> was mixed with water and sonicated to form the magnetic fluid and added to the fruit juice. Then, 50  $\mu$ L of 1-hexadecyl-3-methylimidazolium bromide was added and sonicated for 2 min to trap the analytes in the hemimicelles. Factors affecting extraction efficiency (sorbent type, amount of composite, volume of IL, sample pH, extraction time and desorption conditions) were optimised and suitable recovery values (76–95%), LODs (0.16–0.57  $\mu$ g/L) and sorbent-to-sorbent repeatability (1.83–4.24%) were obtained. Compared with other methods employed to extract acaricides, the developed protocol reduced the analysis time between 3 and 32 times.

The use of QDs is based on their noteworthy optical properties, including the broad absorption spectra, the size tenability, the narrow symmetric emission, and the photostability. The use of a co-nucleus of CdTe QDs and magnetite produced a fluorescent sorbent the combination of which with MIPs allowed the detection of malachite green (triphenylmethane dye) in fish [50]. The concentration of malachite green was determined through the ratio of fluorescence intensities of the m-NPs in the

absence and presence of malachite green (quencher) using its quenching constant. This fluorescent material, synthesised by reverse microemulsion, provided a LOD of 0.014  $\mu\text{mol/L}$  and recovery values in the range 103–109%. Selectivity of the method was evaluated with leucomalachite green, crystal violet and brilliant green and NIP m-NPs.

Among the polymeric coating, microporous organic polymers can be an interesting alternative. Generally speaking, microporous organic polymers are composed of lightweight elements linked by covalent bonds that can be obtained from many different building blocks using different chemical reactions. Such polymers can be designed to obtain desirable properties and are characterised by the presence of pores smaller than 2 nm [60]. This kind of polymer can be classified on the following categories: Hyper-cross-linked-polymers, polymers of intrinsic microporosity, covalent organic frameworks, conjugated microporous polymers and porous aromatic frameworks. These kinds of materials have been used in many different research fields including sample preparation for food analysis. In this regard, their combination with m-NPs has provided good results [49,61]. For example, Lei et al. [49] synthesised magnetic poly(phenylene ethynylene)-conjugated microporous polymer microspheres for the extraction of 6 phenyl pesticides (meptyldinocap, picoxystrobin, mandipropamid, fenpropidine, ethoxyquin and pyraclostrobin) from fruits (apple and pear) and vegetables (cucumber, lettuce and cherry tomato). For this purpose,  $\text{Fe}_3\text{O}_4$  NPs were prepared by coprecipitation and treated with tetraorthosilicate to obtain  $\text{SiO}_2$  covered m-NPs. The conjugated three-dimensional network structure of poly(phenylene ethynylene) frameworks (Figure 3) was obtained by mixing  $\text{Fe}_3\text{O}_4@ \text{SiO}_2$ -aminophenylacetylene particles with 1,3,5-tribromobenzene, 1,3,5-trialkynylbenzene in dimethyl formamide, bis(triphenylphosphine) palladium(II) chloride, CuI, triethylamine and toluene/water (1:1 *v/v*). m-NPs, characterised by TEM, SEM, IR, magnetic analysis and  $\text{N}_2$  adsorption proved to have a size of 500 nm. After validation of the method, the sorbent was applied in a dissipation study. After spraying lettuce and tomato, samples were collected and analysed between 2 h and 21 days. The half-life time for these compounds was in the range between 1.3–11.0 days. Finally, the method was applied to the analysis of apples and lettuces after sinking them in vinegar, 2% salt water, 2% soda water and water. Baking soda solution demonstrated to be the more efficient method to remove these harmful molecules.



**Figure 3.** Synthesis of magnetic conjugated microporous polymer with conjugated three-dimensional network structure. Reprinted from [49] with permission from Elsevier, 2020.

The inclusion of MIPs is particularly interesting in sample preparation because of their inherent high selectivity. However, this selectivity can play a negative role if a multi-residue methodology is needed. Moreover, MIPs are frequently characterised by a heterogeneous distribution of the binding sites with poor site accessibility, low attaching capacity, incomplete template removal and slow binding kinetic. These drawbacks could be partially overcome by combining them with m-NPs, instead of

using MIPs in the bulk state. Thus, it is not surprising that these kinds of mixture were used for food complex matrices. This way, a selective sorbent with superparamagnetism and good stability is obtained. Without any doubt, the great majority of applications of m-NPs combined with polymers for the analysis of foods have used a MIP [48,50,53].

Another interesting alternative derived from the imprinted polymer technology is the use of IIPs. As happens with MIPs, IIPs offer mechanical and chemical stability, easy preparation, low cost and high affinity and selectivity for the separation, pre-concentration or removal of target ions. Analogously to MIPs, the main drawback is the limited active surface, so the inclusion of m-NPs helps to overcome this problem. The base molecules to construct the IIPs are ligands. For instance, Jalilian and Taheri [56] obtained  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{TiO}_2$  as magnetic support and synthesised the IIP using Ag(I)-2,4-diamino-6-phenyl-1,3,5-triazine complex as the template molecule, methacrylic acid as the functional monomer, 2,2'-azobisisobutyronitrile as the radical initiator and ethylene glycol dimethacrylate as crosslinker. The composite was employed for the extraction of silver from 1 g of rice, potato and tomato after acidic digestion with 10 mL concentrated  $\text{HNO}_3$  followed by the addition of 2 mL of 30%  $\text{H}_2\text{O}_2$ . The extraction, performed with 40 mg of the magnetic material, provided recovery values in the range of 97.5–100.5% and ideal selectivity in presence of coexisting ions (Na(I), K(I), Pb(II), Cd(II) and Ni(II)). The composite was also employed for the analysis of radiology film, tap, well and waste water and could be re-used 8 times.

Finally, it should be mentioned that although m-dSPE was the most common extraction technique, this kind of particle was also adequate for other methodologies [52,53]. In this regard, Li et al. [53] developed a stir bar coated with  $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{MIP}$  NPs for the extraction of clonazepam and norazepan from herbal health food matrices (recovery values: 89.8–103.3%, LOD: 0.01  $\mu\text{g}/\text{mL}$ ) and Yang et al. [52], as it was previously mentioned, employed a 1-hexadecyl-3-methylimidazolium bromide-coated  $\text{ATP@polyaniline-poly pyrrole@Fe}_3\text{O}_4$  composite in m-mixed hemimicelles SPE.

## 2.2. Recent Applications in Sensors

### 2.2.1. Optical Sensors

The operating principle of optical sensors is the existence of transducers that transform optical signals (ultraviolet, visible, infrared radiation, etc.) emitted by a chemical/biological/physical reaction into data [1,62]. Table 4 shows a selection of recent applications of optical sensors to the food analysis field [63–72], including sensors using colorimetry [63,64], fluorescence [65,66], chemiluminescence [67,68], surface plasmon resonance (SPR) [69,70] and surface-enhanced Raman spectroscopy (SERS) [71,72].

Colorimetric sensors are based on the change of colour that can be detected by the naked eye and they have attracted interest because they are simple and fast and provide real-time detection [1,62]. This is the case of the work that Seddaoui and Amine developed for the detection of immunoglobulin G (IgG) for identifying meat adulteration [63]. Authors coated  $\text{Fe}_3\text{O}_4$  m-NPs with pDA and then covalently immobilised standard pig IgG onto the  $\text{pDa@Fe}_3\text{O}_4$  particles ( $\text{pDa@Fe}_3\text{O}_4@\text{standard pig-IgG}$ ). The non-reacted groups were blocked with bovine serum albumin (BSA) and then the pig meat-extracted proteins were added together with anti-pig IgG polyclonal antibody (pAb) conjugated with horseradish peroxidase (HRP). In this way, a competitive assay took place between purified IgGs and porcine IgGs for the binding sites of peroxidase-labelled Ab. Porcine IgG was monitored by optical density of the reaction product at 450 nm in the presence of peroxidase substrate. This magneto-immunoassay allowed the detection of 0.01% pork in meat mixtures in a simple, sensitive and selective way. Another interesting work based on colorimetric sensing was that developed by Guan et al. [64], in which a sensor based on gold and m-NPs, as an enzyme mimetic of HRP, was constructed for the detection of cholesterol in egg yolk. Gold NPs were synthesised by an eco-friendly method based on the reduction with orange peel aqueous extract of chloroauric acid ( $\text{HAuCl}_4$ ), and then made to react with amino-modified  $\text{Fe}_3\text{O}_4$  m-NPs to obtain an  $\text{Au@Fe}_3\text{O}_4$  m-NPs solution. Saponification of egg yolk was accomplished by addition of 2 M KOH and 10 mL EtOH and after dilution with

water, liquid-liquid extraction (LLE) with ether was carried out and finally, the extract evaporated and reconstituted with EtOH. One hundred  $\mu\text{L}$  of cholesterol oxidase (1 g/L) and 300  $\mu\text{L}$  of the sample extract in 500  $\mu\text{L}$  of 10 mM phosphate buffered saline (PBS) were incubated at 37 °C and after 30 min, 100  $\mu\text{L}$  of 0.1 g/mL Au@Fe<sub>3</sub>O<sub>4</sub> solution and 3 mL of 0.1 M HAc-NaAc buffer solution were added. The reaction was inhibited with 2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and absorbance of the supernatant was measured at 420 nm. Au@Fe<sub>3</sub>O<sub>4</sub> can catalytically oxidise ABTS in the presence of H<sub>2</sub>O<sub>2</sub> to produce a typical green colour, with H<sub>2</sub>O<sub>2</sub> coming from the reaction of cholesterol oxidase with cholesterol. The LOD was determined in 7.9  $\mu\text{M}$  and recovery values ranged from 99% to 107%.

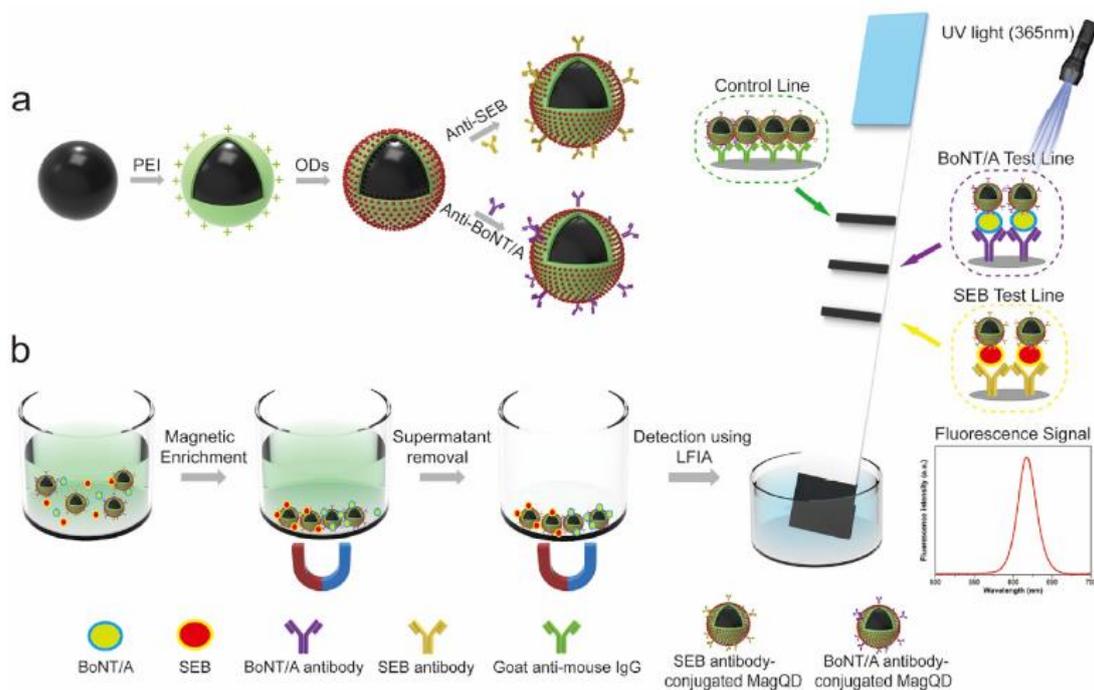
Fluorescence sensors are normally highly sensitive and selective [1,62]. Li et al. [65] used a lanthanide-doped upconversion NPs (UCNPs)-based sensor to analyse *E. coli* in pork meat after alkaline peptone treatment to precipitate macroaggregates and seston. An *E. coli* Apt was linked to m-NPs and acted as a capture probe, while conjugated DNA (cDNA) linked to UCNPs worked as a signal probe. The whole m-NPs@Apt@cDNA@UCNPs platform, in the presence of *E. coli*, showed a decrease in the fluorescence emission at 662 nm. The method was demonstrated to be specific in the presence of other bacteria (*S. aureus* and *S. typhimurium*), showed good recovery values (97–107%) and had a LOD of 10 colony forming units (CFU)/mL. Wang and co-workers [66] described a lateral flow assay (LFA) strip using dense carboxylated QDs on the surface of polyethyleneimine (PEI) modified Fe<sub>3</sub>O<sub>4</sub> m-NPs to capture and enrich two toxins, botulinum neurotoxin type A (BoNT/A) and staphylococcal enterotoxin (SEB), and serve as fluorescent labels. Figure 4 shows a scheme of the magnetic-quantum dots (m-QDs) preparation. Briefly, Fe<sub>3</sub>O<sub>4</sub> were prepared from FeCl<sub>3</sub> with EG and diethylene glycol (DEG) using sodium acetate as alkali source and polyvinylpyrrolidone (PVP) as stabiliser. Then, the m-NPs were coated with PEI and afterwards, carboxyl-functionalised CdSe/ZnS QDs were absorbed on the Fe<sub>3</sub>O<sub>4</sub>@PEI surface. Immuno-Fe<sub>3</sub>O<sub>4</sub>@PEI@QDs were prepared conjugating BoNT/A or SEB Ab onto the Fe<sub>3</sub>O<sub>4</sub>@PEI@QDs surface by carbodiimide reaction. The figure also shows the mechanism of the method using two test lines, BoNT/A and SEB mAb and one control line (polyclonal goat anti-mouse IgG), which was applied to milk and grape juice without sample treatment, obtaining good recovery values (82–95%) and a LOD of 2.52 ng/L for BoNT/A and 2.86 ng/L for SEB.

Chemiluminescence-based sensors have attracted interest due to their advantages, such as simplicity, low cost, wide linear range and good sensitivity [1,62]. Regarding its coupling with m-NPs for their use in food analysis, two recent papers are highlighted in this review. Jie et al. [67] developed a magnetic enzyme chemiluminescence immunoassay (MECLIA) using Fe<sub>3</sub>O<sub>4</sub>@Au particles to detect fumonisin B<sub>1</sub> in corn and wheat. Sample extraction was accomplished with MeOH/water (75:25 v/v) and the PBS diluted extract was submitted to the MECLIA. Fe<sub>3</sub>O<sub>4</sub>@Au particles were synthesised by reduction of Au(III) onto Fe<sub>3</sub>O<sub>4</sub> NPs previously generated by coprecipitation. Then, they were coated with fumonisin B<sub>1</sub>-ovalbumin for binding with fumonisin B<sub>1</sub> Abs and put on a microplate of a 96 microplate reactor. HRP-IgG was conjugated with fumonisin B<sub>1</sub> Abs and in luminol-H<sub>2</sub>O<sub>2</sub> medium, HRP-IgG catalysed luminol oxidation by H<sub>2</sub>O<sub>2</sub>, giving a high chemiluminescence signal. Recovery values in the range 98–110% and a LOD of 0.027  $\mu\text{g/L}$  were obtained. Cross-reactivity was assayed with other toxins, showing a very good specificity. On the other hand, Hao and co-workers [68] detected *Salmonella typhimurium* in pork through a quite complex sensitive steady-state chemiluminescence aptasensor based on rolling circle amplification. Avidin, as *S. typhimurium* Apt, was immobilised in Fe<sub>3</sub>O<sub>4</sub> m-NPs, so the target molecule could be trapped by them (recognition molecules and capture probes). Then, Co(II) enhanced N-(aminobutyl)-N-(ethylisoluminol) (ABEI) functionalised flowerlike gold NPs (AuNFs) and cDNA complex (Co(II)/ABEI-AuNFs-cDNA) were used as signal probes to produce and enhance chemiluminescence signal. *p*-iodophenol (PIP) was added to form an ABEI-AuNFs-PIP-H<sub>2</sub>O<sub>2</sub> steady-state chemiluminescence system. Pork samples were treated with 0.01 M phosphate buffer solution (5 g, 10 mL) and after centrifugation, the supernatant was submitted to the chemiluminescence assay. The LOD was estimated in 10 CFU/mL and recovery values ranged between 87% and 101%. The use of m-NPs in this work helped to produce a rapid separation and purification, reducing the assay time.

**Table 4.** Novel applications of magnetic nanoparticles based on optical sensors in food analysis.

Analytes	Matrix	Nanomaterial	Determination Technique	Recovery %	LOD	Reference
IgG	Pork meat (2 g)	Fe <sub>3</sub> O <sub>4</sub> @pDA	Colorimetry	-	0.01%	[63]
Cholesterol	Egg yolk (1 g)	Fe <sub>3</sub> O <sub>4</sub> @Au	Colorimetry	99–107	7.9 µM	[64]
<i>Escherichia coli</i>	Pork meat (25 g)	Fe <sub>3</sub> O <sub>4</sub> @Apt@cDNA@UCNPs	Fluorescence	97–107	10 CFU/mL	[65]
BoNT/A, SEB	Milk, grape juice (1 mL)	Fe <sub>3</sub> O <sub>4</sub> @PEI@CdSe/ZnSQDs	Fluorescence	82–95	2.52–2.86 ng/L	[66]
Fumonisin B <sub>1</sub>	Corn, wheat (5 g)	Fe <sub>3</sub> O <sub>4</sub> @Au	Chemiluminescence	98–110	0.027 µg/L	[67]
<i>Salmonella typhimurium</i>	Pork meat (5 g)	Fe <sub>3</sub> O <sub>4</sub> @Apt	Chemiluminescence	87–104	10 CFU/mL	[68]
Estradiol	Milk (1 mL)	estradiol-mAb-m-NPs	SPR	88–114	0.814 µg/L	[69]
<i>Salmonella enteritidis</i>	Egg shell (5 g)	Ab@Fe <sub>3</sub> O <sub>4</sub>	SPR	93–113	<14 CFU/mL	[70]
<i>Salmonella typhimurium</i>	Egg white, cheese, packaged juice (-)	FP-m-NPs	SERS	86–115	10 cells/mL	[71]
Aflatoxin B <sub>1</sub>	Peanut oil (5 g)	Fe <sub>3</sub> O <sub>4</sub> -chitosan-Apt	SERS	95–109	0.54 ng/L	[72]

Ab: antibody; Apt: aptamer; BoNT/A: botulinum neurotoxin type A; cDNA: complementary DNA; CFU: colony forming unit; FP-m-NPs: functionalised polymeric magnetic nanoparticles; IgG: immunoglobulin G; LFIA: lateral flow immunoassay; mAb: monoclonal antibody; m-NP: magnetic nanoparticle; NP: nanoparticle; pDA: polydopamine PEI: polyethylenimine; QD: quantum dot; SEB: staphylococcal enterotoxin B; SERS: surface-enhanced Raman spectroscopy; SPR: surface plasmon resonance; UCNPs: lanthanide -upconversion nanoparticle.



**Figure 4.** (a) Scheme of antibody (Ab)-modified magnetic-quantum dots (m-QDs) preparation and (b) mechanism of m-QDs-based lateral flow immunoassay (LFIA) strip for simultaneous and sensitive detection of two protein toxins. Reprinted from [66] with permission from Elsevier, 2020.

SPR sensors are refractometric sensors based on the changes in the refractive index on the sensor surface because of chemical, biological or physical events [1,62]. Jiu et al. [69] analysed estradiol in milk using a SPR biosensor system using m-NPs as amplifying elements. Anti-estradiol mAb was conjugated with m-NPs (Nanomag-D spio 20 nm NPs coated by dextran matrix and protein A) via protein A. Chitosan was coated on the sensor surface to immobilise the antigen estradiol-BSA using glutaraldehyde. Estradiol present in the sample could competitively bind estradiol-BSA and anti-estradiol-mAb and, therefore, cause a decrease of the SPR signal due to the diminution of estradiol-BSA and anti-estradiol-mAb concentration. m-NPs showed good capability of amplifying SPR signal, which resulted in a high sensitivity for estradiol detection. The method could be applied to milk samples after extraction of estradiol with ethyl acetate and the authors demonstrated its selectivity against other analogue molecules (diethylestilbestrol, dienestrol, hexestrol or estrone). They also compared the results obtained with this enhanced sensor with a traditional SPR sensor based on CS modified chip and an enzyme-linked immunosorbent assay (ELISA), showing in general better results. The LOD was 0.814  $\mu\text{g/L}$  and the recovery values were in the range 88–114%. Another interesting work dealing with SPR sensors was that developed by Liu et al. [70], who worked on a SPR immunosensor to analyse *Salmonella enteritidis* in eggshell after simple buffer extraction. First, Ab- $\text{Fe}_3\text{O}_4$  m-NPs were used to recognise and isolate, by an external magnetic field, the bacteria from the sample matrix. Afterwards, *S. enteritidis*-Ab- $\text{Fe}_3\text{O}_4$  conjugates were put on the sensor surface modified with anti-*S. enteritidis* pAb. *S. enteritidis*-Ab- $\text{Fe}_3\text{O}_4$  m-NPs worked both as carriers of the target analyte from the sample to the sensor surface, and also to increase the refractive index changes. Selectivity studies were carried out in the presence of *Escherichia coli* K12 ER2738 and *Lactobacillus* LK-3, obtaining an SPR signal more than 5500 times higher than for the other bacteria. A LOD lower than 14 CFU/mL was obtained with recovery values between 93% and 113%. The method was compared with SPR immunosensor based on direct detection (without m-NPs), clearly obtaining a higher concentration range and a 1000-times better LOD.

SERS sensors have become interesting due to their high sensitivity and specificity [1,62]. Chattopadhyay and co-workers [71] described a SERS immunosensor for detecting *Salmonella*

*typhimurium* in egg white, cheese and packaged juice (after proper PBS buffer extraction, except for juice) using functionalised polymeric m-NPs (FP-m-NPs), synthesised by in situ emulsion polymerisation of 3 monomers (styrene, MMA and 2-(methacryloyloxy)ethyl acetoacetate) along with stabilised Fe<sub>3</sub>O<sub>4</sub> NPs, as capture probe. This probe contained diketonic functionalities in its surface that covalently linked with amino groups in Ab against *Salmonella* structural antigen (CSA-1-Ab). Au-NPs@CSA-1-Ab and 4-mercapto benzoic acid and 5,5'-dithiobis(succinimidyl-2-nitrobenzoate) (DTNB) as external Raman reporter molecules (RRM), were used as signal probes. Capture and signal probes linked the target bacteria generating Raman signal. The LOD was calculated in 10 cells/mL and recovery values ranged 86–115%. Yang et al. [72] developed a quite complex SERS aptasensor based on the use of Apt modified CS modified Fe<sub>3</sub>O<sub>4</sub> superparamagnetic particles (Fe<sub>3</sub>O<sub>4</sub>-CS-Apt) as capture probes for aflatoxin B<sub>1</sub>; while gold nanotriangles (GNT)-5,5'-dithiobis(2-nitrobenzoic acid) (DTNB)@Ag-DTNB-Apt were used as the Raman reporter probes. This gave rise to the detection platform GNT-DTNB@Ag-DTNB-Apt-aflatoxin B<sub>1</sub>-Apt-CS-Fe<sub>3</sub>O<sub>4</sub>, which was applied to real peanut oil samples, obtaining recovery values between 95% and 109% and a very low LOD of 0.54 ng/L. Authors also demonstrated the selectivity of the method against aflatoxin B<sub>1</sub> in the presence of other toxins such as ochratoxin A and aflatoxin G<sub>1</sub>.

### 2.2.2. Electrochemical Sensors

The particular characteristics of m-NPs in terms of large surface area, physicochemical nature, electrochemical and magnetic properties, as well as their easy modification make them adequate candidates as transducers in electrochemical sensors. Indeed, they have been used in different applications in the field of food analysis as can be observed in Table 5, in which some of the most relevant applications have been compiled [16,73–78]. These kinds of systems involve the use of reference, work and counter electrodes. It is in the latter in which the use of nanostructures and, particularly, m-NPs plays an important role to increase the sensitivity and selectivity of the detection system. This fact is related to their capability to enhance the signal as result of their good conductivity and the establishment of specific interactions with target analytes, including biomolecules [1,62]. In the field of food analysis the application of electrochemical sensors has been performed for the evaluation of both inorganic species [16,75,76] and organic compounds, including proteins, hormones, contaminants, etc. [73,74,77,78] in matrices of different nature such as seafood, fish and meat [73,79], milk [76–78], vegetables [74], oil, tea and sugar [16] or fruit juice [75].

Electrochemical sensors are based on the electrochemical signal changes associated with the result of a chemical reaction between the target analytes and a recognition element located at the electrode. Among the elements used in the last few years in the area of food analysis there is a great variety including Abs [73,76], peptides combined with specific recognition structures, based on MIPs [77], polymers [78], DNA based Apts [74,79] or enzymes [75]. However, the evaluation of metallic species was carried out using a nanostructure-modified carbon paste electrode (CPE) without additional elements. In this case, Mohamed et al. [16] developed a simple procedure to carry out the evaluation of Cu(II) in oil, sugar and tea samples using differential pulse anodic stripping voltammetry (DP-ASV), after sample pre-treatment using an acidic extraction for oil samples and a combination of heating at 525 °C followed by acidic extraction for sugar and tea samples. The nanostructure was constituted by CoFe<sub>2</sub>O<sub>4</sub> NPs since this metal oxide has a high surface area, as well as a porous spinel structure with adequate characteristics for the determination of heavy metals. Results showed very good performance of the prepared electrode, obtaining a high recovery (99%) and a low LOD (0.085 µg/L), as well as great stability, acceptable selectivity, excellent repeatability and reproducibility.

Despite the fact that Apts and Abs provide very specific interactions with the target analytes and lead to high selectivity, their combination with additional specific elements has also been developed in this field. An interesting example that illustrates such an approach is the work carried out by Han et al. [77], in which the combination of a peptide, glutathione (GSH) and a MIP was applied for the recognition of estradiol in milk powder samples using a glassy carbon electrode (GCE) modified by Au and Fe<sub>3</sub>O<sub>4</sub> NPs. In this case, the authors combined the advantages of the great specificity given by

the linker elements with the benefits of using a magnetic system to simplify the procedure reaching also high selectivity. As can be seen in Figure 5, GSH was bound to the Au@Fe<sub>3</sub>O<sub>4</sub> NPs for electrode preparation. Then, estradiol, used as template, was linked to this one by specific interactions prior to polymerisation to create the MIPs. For analysis performance, the electrode set up was assembled by the location of an external magnet on the GCE and introduced in the sample solution containing the MIP. After differential pulse voltammetry (DPV) measurements the magnet was removed and the estradiol@MIP was again released to the initial solution. Authors demonstrated that the incorporation of the MIP element increased the selectivity of the sensor even when similar chemical structures such as estriol or estrone were present. In addition, the use of Au NPs avoids Fe<sub>3</sub>O<sub>4</sub> NPs oxidation and aggregation, increasing device stability, and also enhances the conductivity of the material.

Depending on the electrochemical signal measurement mode, different kinds of sensors can be selected. In general terms, different modalities of amperometric [73,74] and voltammetric [75–78] sensors have been applied recently in this area based on the evaluation of the variation of the current potential in the work electrode, as a result of a redox transformation that involves the target analyte and the recognition element [1]. In this sense, differential pulse voltammetry has been the most used [76–78], although cyclic voltammetry (CV) [75], DP-ASV [16], and square wave stripping voltammetry (SWSV) [79] have also been tested, providing good sensitivity.

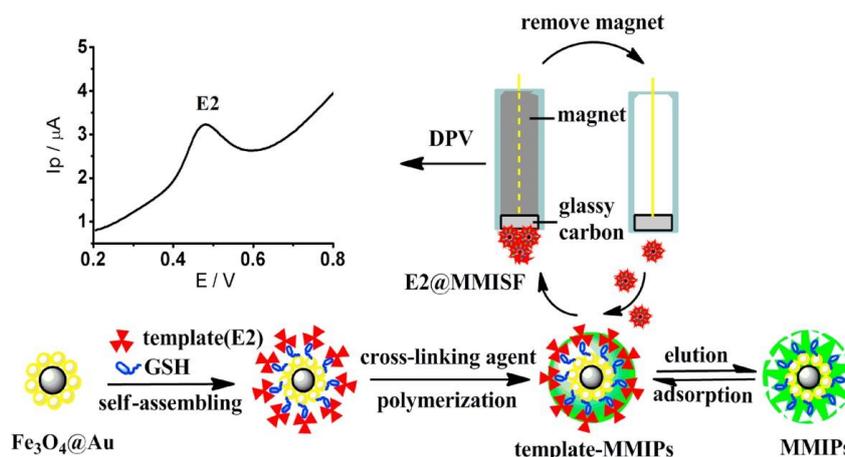
Regarding the type of transducer, Fe<sub>3</sub>O<sub>4</sub> NPs have been the m-NPs mostly used [73–78], however, CoFe<sub>2</sub>O<sub>4</sub> was also tested [16] as a modifier of sensor platforms in combination with recognition elements. In some cases, the combination with other nanomaterials has also shown very good results, including graphene [78] and GO [75], metal NPs [74,77,79] or QDs [79]. This strategy allows increasing the specificity of the interaction with the target analytes and improving the electrochemical features of the modified sensors as it was pointed out by Chen et al. [79]. In this work, authors developed a sensor based on Au@Fe<sub>3</sub>O<sub>4</sub> NPs using a strand DNA Apt modified with PbS and CuS QDs for the analysis of chloramphenicol and polychlorinated biphenyl-72 (PCB72) in fish, using SWSV. The determination was based on one-step substitution reaction between the Apt(DNA)@QDs nanotracers and the target analytes on the sensor system. When such a replacement took place, Apt(DNA)@QDs were released into the solution and they could be simultaneously detected by SWSV of Cu(II) and Pb(II). The QDs acted as electrochemical tracers thanks to their well-defined oxidation potential which allowed enhancing the electrochemical signal. This fact, together with the advantages already mentioned about the combination of Au and Fe<sub>3</sub>O<sub>4</sub> NPs, led to a very sensitive method with an LOD of 0.057 µg/L. Apart from that, Apt(DNA)@QDs were linked to the magnetic composite by a dendric complex constituted by a large number of HRP and secondary Abs that provided a great number of enzyme sites where the nanotracer can be bound, increasing the number of active points and, consequently, the effectiveness of the sensor which provided recovery values in the range 96–105%, even with such a complex samples like fish matrices.

As can be seen in this section, electrochemical sensors based on m-NPs allow the preparation of very simple and easily handled procedures as a result of the magnetic properties of this nanomaterial. These characteristics, in combination with the great surface area of NPs, as well as the great conductivity of these materials, the specificity given by the use of selective recognition elements and the benefits of including some other nanomaterials in the same applications, make the use of this kind of approaches an excellent alternative for the development of sensitive and selective strategies for the evaluation of a huge number of organic and inorganic compounds, even in very complex matrices as occurs with food samples.

**Table 5.** Novel applications of magnetic nanoparticles based on electrochemical sensors in food analysis.

Analytes	Matrix	Nanomaterial	Determination Technique	Recovery %	LOD	Reference
Tropomyosin	Pork, beef, chicken, shrimp and squid (1 g)	Ab@Fe <sub>3</sub> O <sub>4</sub>	Amperometry	-	47 ng/L	[73]
Genetically modified organisms (RR soybean and lectin gene target)	Soybean (-)	Apts(DNA)@Amercaptophexanoic acid@Au@Fe <sub>3</sub> O <sub>4</sub> @ GCE	Chronoamperometry	-	0.02–0.05 nM	[74]
H <sub>2</sub> O <sub>2</sub>	Orange juice (10 mL)	HRP@chitosan@GO@Fe <sub>3</sub> O <sub>4</sub> @Pt	CV	99	48.08 $\mu\text{A}/(\mu\text{M}(\text{cm})^2)$ .	[75]
Cu(II)	Oil (25 g), sugar and tea (10 g)	CoFe <sub>2</sub> O <sub>4</sub> @CPE	DP-ASV	98	0.085 $\mu\text{g/L}$	[16]
Tetracycline	Milk (15 g)	Ab@carboxyl-Fe <sub>3</sub> O <sub>4</sub> @chitosan@AuElectrode	DPV	96–108	0.0321 $\mu\text{g/L}$	[76]
Estradiol	Milk powder (-)	MIP@GSH-Au@Fe <sub>3</sub> O <sub>4</sub> @GCE	DPV	87–91	2.76 nm/L	[77]
Penicillin	Milk (-)	PEDOT–Au@graphene–Fe <sub>3</sub> O <sub>4</sub> @ GCE	DPV	96–105	0.057 $\mu\text{g/L}$	[78]
Chloramphenicol, PCB72	Fish (5g)	Apt (DNA)@QDs@ AuNPs @ Fe <sub>2</sub> O <sub>4</sub>	SWSV	92–102	0.33–0.35 ng/L	[79]

Ab: antibody; Apt: aptamer; CPE: carbon paste electrode; CV: cyclic voltammetry; DP-ASV: differential pulse anodic stripping voltammetry; DPV: differential pulse voltammetry; EIS: electrochemical impedance spectroscopy; GCE: glassy carbon electrode; GO: graphene oxide; GSH: glutathione; HRP: horseradish peroxidase; LOD: limit of detection; MIP: molecularly imprinted polymer; PCB72: polychlorinated biphenyl 72; PEDOT: poly(3,4-ethylenedioxythiophene); QD: quantum dot; RR: event-specific roundup ready; SWSV: square wave stripping voltammetry.



**Figure 5.** Scheme of a MIP@GSH-Au@Fe<sub>3</sub>O<sub>4</sub>@GCE preparation and differential pulse voltammetry (DPV) measurement performance for the analysis of estradiol in milk powder samples. Reprinted from [77], with permission from Elsevier, 2020.

### 2.2.3. Other Types of Sensors

Apart from the popular optical and electrochemical sensors, other interesting options based on m-NPs have been applied for food analysis. The main interest of these alternative sensors lies in the use of a different transduction principles (i.e., quartz crystal microbalance (QCM) [80,81], magnetic relaxation switching (MRS) [82–84], photoelectrochemistry [85,86]) or/and their particular arrangement (i.e., portable and low-cost sensors based on screen-printed electrode (ScPE) [73,85,87–92], lateral flow strip (LFS) [93–96], microfluidic platforms [86,97–99], and smartphone analysis [95,100,101]). Some selected examples of these kinds of devices are included in Table 6 [80,81,85,86,94,95,98,100,101].

QCM sensors are mass-sensitive transducers with a thin plate of quartz attached to gold electrodes. The application of alternate electrical current to the quartz crystal promotes a high-frequency vibration with a resonant frequency. The change in the resonant frequency is linearly related to the change in the mass loaded. This kind of sensor is frequently employed for the detection of viruses and bacteria [102]. Thus, it is not surprising that one of the very few applications in food analysis was devoted to the detection of *Campylobacter jejuni* in chicken carcasses and ground turkey meat [80]. In that application, bacterial cells were trapped by magnetic nanobeds with a rabbit anti-*C. jejune* pAb coating. Then, the mouse anti-*C. jejuni* pAb immobilised on the electrode surface of the sensor bound with magnetic beads and Au NPs, conjugated with goat anti-rabbit IgG pAb, was introduced into the sensor to amplify the signal via binding the coated magnetic nanobeds. Some important parameters, such as the LOD (20–30 CFU/mL) and detection time (30 min), were determined.

Moreover, the specificity was evaluated by a cross-reactivity test of six non-target foodborne pathogens (*Campylobacter coli*, *Salmonella Typhimurium*, *Salmonella Enteritidis*, *Listeria monocytogenes*, *E. coli* and *Staphylococcus aureus*) and results demonstrated that the inclusion of the Ab-coated magnetic nanobeds increased the specificity and the effective capture and separation of selected bacteria from food matrices. Apart from the analysis of cells, the QMC sensors with m-NPs have also been employed for the direct detection of molecules in food [81]. In this regard, Chen et al. [81] analysed ractopamine (a  $\beta$ -adrenergic agonist used to treat pulmonary diseases, but also to increase protein deposition and fat mass) in pig fodder samples. For this purpose, amine-functionalised m-NPs were synthesised, functionalised with  $\beta$ -cyclodextrin and then directly adsorbed onto the surface of the quartz crystal using a magnet. After that, the particles were incubated with the appropriate amount of anti-ractopamine Ab and a more compact enzyme-linker Ab conjugate (PowerVision). This sensor provided a LOD of 0.01 ng/mL with recovery values in the range of 92–110% and good consistency with ELISA results.

**Table 6.** Novel applications of magnetic nanoparticles in other kinds of sensor.

Analytes	Matrix	Nanomaterial	Determination Technique	Recovery %	LOD	Reference
<i>Staphylococcus aureus</i>	Milk (1 mL)	Staphylococcus aureus peptide modified magnetic beads	CV, SWSV	102	3 CFU/mL	[85]
17- $\beta$ -estradiol	Milk, prawn, fish and chicken (1 g)	Fe <sub>3</sub> O <sub>4</sub> @ anti-estradiol monoclonal antibody Fe <sub>3</sub> O <sub>4</sub> @ goat anti-mouse antibody	Image software	-	0.2 ng/mL	[94].
<i>Escherichia coli</i> O157:H7	Broth and milk (1 mL)	Streptavidin-conjugated magnetic beads	Smartphone illumination sensor	-	1000 CFU/mL	[100]
<i>Salmonella Typhimurium</i>	Chicken (25 g)	Streptavidin conjugated magnetic beads@ monoclonal antibodies against <i>Salmonella Typhimurium</i>	Image software with smartphone	85–110	16 CFU/mL	[101]
3 Antibiotics	Milk (-)	Polystyrenebeads@m-NPs (carboxylic acid and amine functionalized with sizes between 30 and 1000 nm)	NMR	96–120	8.5 pg/mL–0.5 ng/mL	[82]
<i>Campylobacter jejuni</i>	Pure culture, chicken carcasses and ground turkey meat (25 g)	Magnetic nanobeads coated with rabbit anti- <i>C. jejuni</i> polyclonal antibody and AuNPs conjugated with goat anti-rabbit immunoglobulin G polyclonal antibody	QMC	-	20–30 CFU/mL	[80]
$\beta$ -coglutin	Lupine (-)	Fe <sub>3</sub> O <sub>4</sub> @Au core-shell	Image software with smartphone	-	8 fM	[95]
Aflatoxin B <sub>1</sub>	Peanut (5 g)	Anti-aflatoxin B <sub>1</sub> antibody-modified magnetic beads and carbon quantum dots functionalized MnO <sub>2</sub> nanosheets	Photoelectrochemical	-	2.1 pg/mL	[86]
Ractopamine	Pig fodder (1 g)	Fe <sub>3</sub> O <sub>4</sub> @ $\beta$ -CD	QMC	91–110	0.01 ng/mL	[81]
Altenariol monomethyl ether	Apple, cherry and orange (5 g)	Fe <sub>3</sub> O <sub>4</sub> @BSA-altenariol monomethyl ether -	UV Image software with smartphone	91–94	7 pg/mL	[98]

$\beta$ -CD:  $\beta$ -cyclodextrin; BSA: bovine serum albumin; CFU: colony forming units; CV: cyclic voltammetry NMR: nuclear magnetic resonance; NP: nanoparticle; QMC: quartz crystal microbalance; SWSV: square wave voltammetry.

MRS sensors in combination with m-NPs have also been employed for the analysis of food samples [82–84]. The sensor is based on the change in the spin-spin relaxation time produced on the surrounding water molecules as a result of the modifications on the dispersed and aggregate states of m-NPs when an analyte appears in the magnetic field. The changes of spin-spin relaxation time depend on the amount of the target compound in the sample. These changes are measured through nuclear magnetic resonance (NMR). Among the applications in food analysis, the determination of bacterial populations is frequent [83,84], although organic individual compounds such as antibiotics (i.e., chloramphenicol, sulfonamide and oxytetracycline) have been also studied [82]. For example, Xianyu et al. [82] developed a biosensor for analysing three antibiotics belonging to different families (amphenicols, sulphonamides and tetracyclines) in milk. For this purpose, they developed a method based on click chemistry to assemble different sizes of polystyrene beads and magnetic nanoparticles to prepare core-satellite structures that enable the MRS assays. The click chemistry-mediated MRS was compared with traditional MRS. The LOQs obtained with the click-mediated sensor (8.5 pg/mL for chloramphenicol and 0.5 ng/mL for sulfonamide) were between 72 and 100 times better. The selectivity using antibiotic analogues (thiamphenicol, cephalosporin, tetracycline, sulfadimidine and gentamicin) for detection of chloramphenicol was tested and results showed that only the target compound produced an appreciable effect on the magnetic signal. As can be deduced, the analysis of antibiotics using m-NPs is an important topic [103]. Thus, it is expected that the number of publications within food analysis in this regard will increase in the next few years.

Regarding the transduction principle, it is also worth mentioning the so-called photoelectrochemical sensors [85,86]. Photoelectrochemical sensing is based on the use of light as the excitation source and photocurrent generated on the electrode as the detection signal. This combination joins the advantages of both methods. These sensors are inherently sensitive with a low background signal and a fast response. Moreover, the system is simple, easily miniaturised, consumes low energy, and has a low cost. As an example, Lin et al. [86] developed a photoelectrochemical immunoassay for the detection of aflatoxin B<sub>1</sub> in peanut samples. With this aim, anti-aflatoxin B<sub>1</sub> Ab-modified magnetic beads were used as support for the immunoreaction, glucose oxidase labeled aflatoxin B<sub>1</sub>-BSA conjugates as the tag with competitive immunoassay format and carbon QDs functionalised MnO<sub>2</sub> nanosheets for the visual and photoelectrochemical evaluation. After the modification of the electrode surface with carbon QDs functionalised MnO<sub>2</sub>, the anti-aflatoxin B<sub>1</sub> Ab-modified magnetic beads were flowed through the detection cell and collected on the electrode with a magnet. Then, the sample extract and the glucose oxidase labeled aflatoxin B<sub>1</sub>-BSA conjugates were injected simultaneously and reacted for 60 min to complete the competitive-type immunoreaction. After that, the glucose substrate was flowed and reacted for 15 min. The formation of immunocomplexes involves the oxidation of glucose generating H<sub>2</sub>O<sub>2</sub> (which reduced MnO<sub>2</sub> to Mn(II)). In this way, the QDs are dissociated from the electrode and the photocurrent is reduced. The obtained sensor showed a LOD of 2.1 pg/mL with good reproducibility (RSDs in the range 4.3–10.7%) and acceptable accuracy. The method was compared with ELISA and both techniques provided similar results.

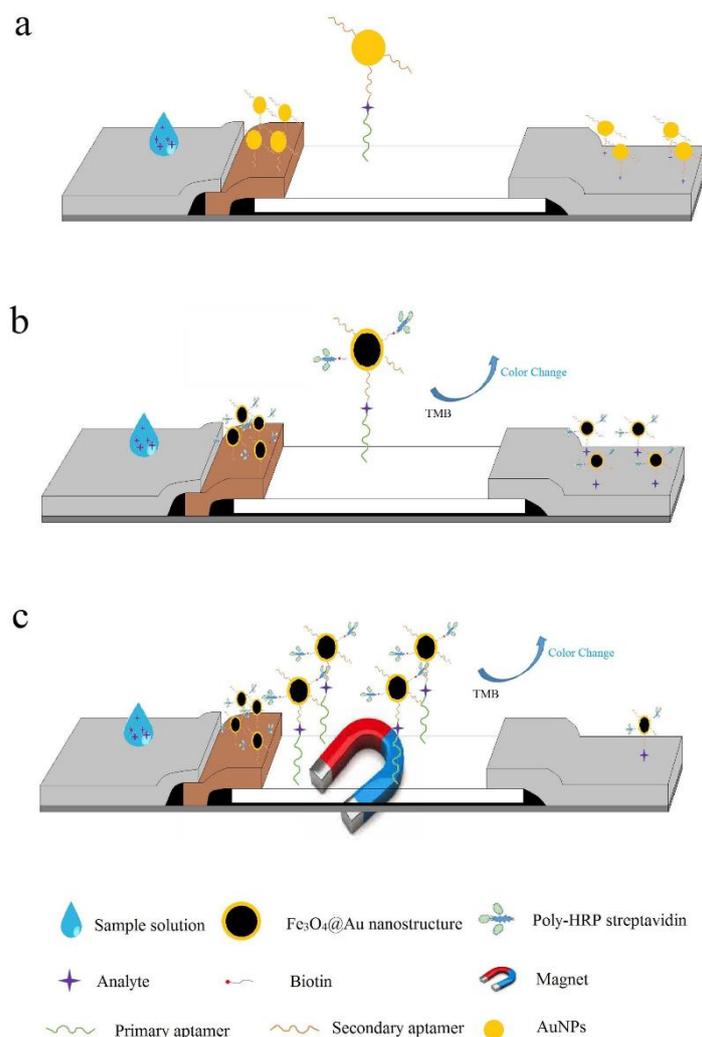
The use of low-cost and portable platforms for sensor operations has attracted growing interest since no expensive and easy-to-handle devices are required [1]. It should be mentioned that the different sensors described in this part are based on the detection options previously described. However, due to their particular arrangement and interesting advantages, a separate description is included here. Among the different strategies, the use of ScPE in combination with m-NPs has been the most popular for the analysis of food [73,83,87–92]. ScPEs are planar systems with the three electrodes of the electrochemical cell arranged on a plastic, ceramic, textile or paper substrate. The minimal sample consumption of these devices, together with other advantages such as a mass-scale production, simplicity, selectivity, disposable use and flexibility, justifies their popularity [104]. In combination with m-NPs, ScPE has been used for the analysis of allergens [73],  $\beta$ -agonists [87], mycotoxins [92], bacteria [88], pesticides [89,90], polybrominated diphenyl ethers [91], and biogenic amines in seafood [73], meat [87,91], cereals [92], beverages [88,89], vegetables [90], milk [91], fish [91]

and eggs [91]. For this purpose, functionalised m-NPs are coated with a suitable substrate and trapped at the ScPE surface with a magnet at the backside.

LFS is a rapid, portable, simple and inexpensive system based on separation at strips as a result of the sample flow produced by capillary action. For this purpose, samples are deposited at the initial sample pad and, after flowing to the adsorbent pad through the strip, the signal is measured. Frequently, such separation is provided by an immunochromatographic phenomenon on specific molecules immobilised on two lines (control and analysis). However, sometimes this system can be less sensitive than other methods. This may be why not many LFS assays are commercially available. This kind of sensor has been employed together with m-NPs to analyse biogenic amines [93], oestrogenic compounds [94], globulin proteins [95] and botulinum neurotoxins [96] in beverages [93,96], milk [94,96], fish [94], meat [94] and legumes [95]. The main advantage of the introduction of m-NPs is the drastic increase in sensitivity and reduction of the LOD. In this regard, Wu et al. [95] applied three different LFS sensors (a conventional method, a sensitised system and a magnetically immobilised Apt (Figure 6)) for the detection of  $\beta$ -coglutin in lupine. In the classical version, the analyte was placed on the sample pad and flowed longitudinally by capillary action. The strip-immobilised Apt formed a sandwich-type immunocomplex (Apt-antigen-Apt) as analytes conjugated with AuNPs-secondary Apt. The detection was based on the colour developed by the AuNPs in the test zone (Figure 6a). In order to increase the detectability of Au-NPs, the sensitised probe was modified with HRP. The addition of 3,3',5,5'-tetramethylbenzidine allows a quick reaction with HRP creating a blue enhanced signal (Figure 6b). Finally, the inclusion of a magnet under the strip to trap the Fe<sub>3</sub>O<sub>4</sub>@Au core-shell NPs allowed an increase in the amount of analyte conjugated with the immobilised Apt (Figure 6c). The combination of magnetic concentration with enzyme amplification (through HRP) increased detection sensitivity by more than 1000 times (LOD 8 fM). Cross-reactivity with  $\alpha$ ,  $\gamma$ , and  $\delta$  lupin coglutins was tested and significant changes were not detected with these coglutins.

Microfluidic platforms integrate separation, identification and determination in microfluidic channels in a compacted, flexible and modular format. Moreover, its combination with magnetic NPs allows benefiting from the advantages of these materials. Thus, it is not surprising that microfluidic chips using immunomagnetic separation [97,98], electrochemical, magnetic [99] or optical detection [98], have been developed. In these applications, the microfluidic chips were fabricated according to the particular needs and were mainly applied for the analysis of bacteria [97,99], although organic compounds (such as mycotoxins [98]) were also analysed.

Finally, regarding the use of sensors, their combination with smartphones should be highlighted [95,100,101]. That combination takes portability to another level involving a device that the vast majority of the population carries every day. Moreover, these devices are equipped with high-resolution cameras, potent processors, and allow wireless communication. Their use does not require extra and expensive instruments and most people are familiar with the management of apps. Although some applications are limited when using the smartphone as the analyser [95,101] through image-processing software, some innovative applications go beyond this. In this regard, Park et al. [100] developed a methodology that employed the smartphone in different steps of the analytical process. For evaluation of DNA amplicons in broth and milk, avidin-conjugated magnetic NPs and succinimide-linked sepharose were used with biotin primers. A portable low-power fan was modified for its use as a portable rotor and connected to the charging port of the smartphone. In this way, the centrifugal-based affinity ligand chromatography was performed. The change in distance produced during centrifugation as a result of the binding variation of NPs with DNA amplicons was optically measured using the illumination sensor of the smartphone with respect to the altered transmittance caused by the magnetic material. Thus, the detection by the naked eye acts as quick polymerase chain reaction (PCR) screening.



**Figure 6.** Schematic illustration of the principles of the traditional AuNPs-based lateral flow immunochromatographic assay method (a) the enzyme signal amplification-based based lateral flow immunochromatographic method (b) and the  $\text{Fe}_3\text{O}_4\text{@Au}$  NPs based lateral flow immunochromatographic method assisted with enzyme amplification and external magnetic field (c). Reprinted from [95] with permission from Elsevier, 2020.

### 3. Conclusions and Remarks about the Future

Food analysis is a topic of great concern and has a big impact on food systems and policies of countries around the world. The control of possible contaminants and naturally present compounds is essential. Current research in food science is intended to ensure a suitable detection of these molecules at extremely low concentrations in complicated matrices. For this reason, the development of sensitive advanced methodologies plays a predominant role in analytical chemistry research. Nanotechnology has arisen as an alternative for achieving this aim. In this regard, different NPs have been synthesised to overcome the problems of classical extraction methods. Among them, m-NPs have attracted great attention thanks to their interesting chemical, optical and magnetic properties, such as the easy isolation by magnets, simple functionalisation and/or coating, superparamagnetism, etc. The continuously growing number of publications centred on the synthesis and application of m-NPs suggest that interest in new magnetic particles continues. The practically unlimited possibilities for covalent or non-covalent modifications with high simplicity and relatively low cost ensure the synthesis of the suitable m-NPs for a particular application. In fact, several companies sell already-prepared m-NPs for analytical purposes. Thus, research on this topic is guaranteed within the next years.

The use of m-NPs has allowed the introduction of efficient sample extraction protocols and facilitated the application of the already well-known ones. Their extraordinarily high surface-area-to-volume ratio and their relatively easy functionalisation (which results in more selective sorbents) have propitiated this use. Different types of nanocomposite based on m-NPs have been applied. Carbonaceous modified NPs (including graphene and CNTs), MOF-based composites, polymeric modifications and surface functionalisation attachments have been reported in the literature. Moreover, combinations of two or more of these materials have become very popular, providing good recovery with simple, fast and more environmentally friendly processes. Moreover, cost and solvent consumption have been considerably reduced.

The particular electrical and magnetic properties of m-NPs make them exceptional transducers. For this reason, their use as substrates for building sensors has skyrocketed within food science. This kind of materials allowed the development of high throughput, real-time and portable detection methods. In this regard, the production of low-cost and portable sensors based on ScPE, LFS, microfluidic platforms and smartphone analysis implies a new paradigm. Such devices combine simplicity, rapidity and practicality while expensive instruments and complicated pre-treatment methodologies are not required. However, it should be mentioned that some challenges could be associated with the use of sensors in food analysis: sensitivity and repeatability depend on the sample preparation method and short shelf life reduces the detection efficiency.

The employment of miniaturised devices based on m-NPs is expected to increase in the next few years to develop highly efficient analytical systems with fast and accurate methodologies for sample preparation and analysis.

Finally, it should be noted that, from a green chemistry perspective, the analytical procedures involving m-NPs usually comprise short analysis time and a limited number of steps and require lower amounts of a sorbent that can be re-used without a significant loss in efficiency. Moreover, the volumes of loading and elution solvents are frequently reduced. However, the material preparation usually employs contaminant substances and/or generates harmful wastes. Furthermore, the recyclability of m-NPs is not always ensured. Thus, further profound studies are needed to ensure that m-NP-based methodologies are consistent with green chemistry principles.

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## Abbreviations

3-CPTS: 3-(chloropropyl)trimethoxysilane; 3Dgraphene: three-dimensional graphene; 4-bpmb: N,N-Bis[1-(pyridine-2-yl)ethylene]-benzene-1,4-diamine); 4-nbpy: bis-pyridin-4-ylmethylene -naphthalene-1,5-diamine; Ab: antibody; ABEL: N-(aminobutyl)-N-(ethylisoluminol); ABTS: 2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); ACN: acetonitrile; Apt: aptamer; APTES: (3-aminopropyl) triethoxysilane; ATP: attapulgit; AuNF: functionalised flowerlike gold nanoparticle;  $\beta$ -CD:  $\beta$ -cyclodextrin; Bd: bencidine; BDC: terephthalic acid; BoNT/A: botulinum neurotoxin type A; BSA: bovine serum albumin; C<sub>18</sub>: octadecylsilane; Cdna: conjugated DNA; CE: capillary electrophoresis; CFU: colony forming unit; CNT: carbon nanotube; COOH-MWCNT: carboxylated multi-walled carbon nanotubes; CPE: carbon paste electrode; CRM: certified reference material; CSA-1-Ab: *Salmonella* structural antigen; CV: cyclic voltammetry; DAD: diode array detection; DCM: dichloromethane; DEG: diethylene glycol; DMF: dimethylformamide; DMSO: dimethyl sulfoxide; DP-ASV: differential pulse anodic stripping voltammetry; DPV: differential pulse voltammetry; DSN: 5,5'-dithiobis(succinimidyl-2-nitrobenzoate); DTIM: 4-(5)-imidazolidithiocarboxylic acid; DTNB: 5,5'-dithiobis (2-nitrobenzoic acid); DVB: divinylbenzene; EDS: (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide; EG: ethylene glycol; EHA: 2-ethylhexylacrylate; EIS: electrochemical impedance spectroscopy; ELISA: enzyme-linked immunosorbent assay; ET-AAS: electrothermal atomic absorption spectroscopy; EtOH: ethanol; FAA: flame atomic absorption spectroscopy; FD: fluorescence detection; FP-m-NP: functionalised polymeric magnetic nanoparticle; FTIR: Fourier-transform infrared spectroscopy; GC: gas chromatography; GCB: graphitized carbon black; GCE: glassy carbon electrode; GNT: gold nanotriangle; GO: graphene oxide; GSH: glutathione; H<sub>2</sub>BDC: benzene 1,4-dicarboxylic acid; H<sub>2</sub>oba: 4,4'-oxybis(benzoic acid); HLB: hydrophilic-lipophilic balance; HPLC: high-performance liquid chromatography;

HRP: horseradish peroxidase; IgG: immunoglobulin G, IIP: ion-imprinted polymer; IL: ionic liquid; IR: infrared spectroscopy; LFA: lateral flow assay; LFIA: lateral flow immunoassay; LFS: lateral flow strip; LLE: liquid-liquid extraction; LOD: limit of detection; m- $\mu$ -dSPE: magnetic-micro-dispersive solid-phase extraction; MAA: methylacrylic acid; mAb: monoclonal antibody; MAE: microwave assisted extraction; MECLIA: magnetic enzyme chemiluminescence immunoassay; MeOH: methanol; m-FC: magnetic framework composite; MIP: molecularly imprinted polymer; MMA: methyl methacrylate; m-MHSPE: mixed hemimicelles solid-phase extraction; m-MOF: magnetic-metal-organic framework; m-NP: magnetic nanoparticle; MOF: metal-organic framework; m-QD: magnetic-quantum dot; MRS: magnetic relaxation switching; MS: mass spectrometry; MS/MS: tandem mass spectrometry; m-SCSE: magnetic-stir cake sorptive extraction; MWCNT: multi-walled carbon nanotube; ND: nanodiamond; NF: nanofiber; NH: nanohorn; NHS: n-hydroxyl succinimide; NIP: non-imprinted polymer; NMR: nuclear magnetic resonance; NP: nanoparticle; pAb: polyclonal antibody; PAE: phthalic acid ester; PAN: 1-(2-pyridylazo)-2-naphthol; PBS: phosphate buffered saline; PCB72: polychlorinated biphenyl-72; PCR: polymerase chain reaction; pDA: polydopamine; PEDOT: poly(3,4-ethylenedioxythiophene); PEI: polyethyleneimine; PIP: *p*-iodophenol; PolyHIPE: polymerised high internal phase emulsion; PSA: primary-secondary amine; PVP: polyvinylpyrrolidone; Q: single quadrupole; QCM: quartz crystal microbalance; QD: quantum dot; QqQ: triple quadrupole; QuEChERS: quick, easy, cheap, effective, rugged, safe; r-GO: reduced-graphene oxide; RR: event-specific roundup ready; SBSE: stir bar sorption extraction; ScPE: screen-printed electrode; SEB: staphylococcal enterotoxin; SEM: scanning electron microscopy; SERS: surface-enhanced Raman spectroscopy; SLE: solid-liquid extraction; SPE: solid-phase extraction; SPR: surface plasmon resonance; SWSV: square wave stripping voltammetry; Tb: 1,3,5-triformylbenzene; TEA: triethylamine; TEAS: tetraethyl orthosilicate; TEM: transmission electron microscopy; TGA: thermal gravimetric analysis; ThGA: thioglycolic acid; Tol: *p*-Tolyl isocyanates; UA: ultrasound assisted; UAE: ultrasound assisted extraction; UCNP: lanthanide-doped upconversion nanoparticle; UHPLC: ultra-high performance liquid chromatography; UV: ultraviolet; VA: vortex assisted; VA-m- $\mu$ -dSPE: vortex assisted-magnetic-micro-dispersive solid-phase extraction; VSM: vibrating-sample magnetometry; XRD: X-ray powder diffraction.

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