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Improved food additive analysis by ever-increasing nanotechnology

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Improved food additive analysis by ever-increasing nanotechnology

Cover Page Footnote

Jing Zhang and Shui Hu contributed equally to this work.

Improved food additive analysis by ever-increasing nanotechnology

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Abstract

Improper use of food additives may lead to potential threat to human health, making it important to develop sensitive and selective method for their detection. Nanomaterials with unique chemical and electrochemical properties show extensive applications in the design of food additive sensing systems. In this review, we summarize the recently adopted electrochemical and optical analysis of food additives based on nanomaterials. Detection of typical food additives (colorants and preservatives) by using different sensing mechanisms and strategies are provided. In addition, determination of illegal food additives is also briefly introduced. Finally, this review highlights the challenges and future trend of nanomaterial-based food analysis system.

Keywords: Nanomaterials, Food colorants, Food preservatives, Illegal additives, Detection

1. Introduction

As the changing population and lifestyle, there are increasing requirements on food quality and texture. To enhance the appearance, fragrance, taste, or storage of food, additional ingredients, usually called as food additives, are generally applied in food industry. According to their functions, these food additives can be classified into different species, including colorants, preservatives, sweeteners, thickeners, emulsifiers, raising agents, and acidity regulators, etc [1]. Reasonable use of these food additives not only improves the color and taste of food, but also boosts the nutritional value. Unfortunately, improper use of some food additives leads to a potential threat to human life and health [2,3]. In addition, some food additives have been demonstrated as potential disease triggers. For example,

Lakshmi *et al.* found that indigo carmine colorant may cause permanent damage to the cornea and conjunctiva [4]. Ma *et al.* also reported that excessive intake of indigo carmine has mutagenic effects and may lead to tumors [5]. Furthermore, some synthetic chemicals with high toxicities have also been used as illegal food additives, which cause serious food accidents. Therefore, the development of simple and effective method to monitor the content of food additives is extremely important for protecting Human beings.

To accomplish successful detection of food additives, many methods based on liquid chromatography, mass spectrometry, and electrochemistry have been reported [6–12]. For instance, Harp *et al.* reported the determination of seven certified colorants using liquid chromatography [13]. In comparison with sole liquid chromatography technique, the combination of liquid chromatography and

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mass spectrometry provides higher sensitivity toward food additive analysis. Using this coupling technique, Hao *et al.* has proposed a sensitive and selective method for tertiary butylhydroquinone (typical preservative) detection [9]. Despite of the analysis of food additives using these conventional detection techniques, there are still some drawbacks, including complicated sample preparation, complicated analytical steps, and time-consuming testing. In addition, the sensitivities of some systems do not suffice the demand of food quality evaluation. And thus, the exploration of new systems with simplicity and high sensitivity for food additive is still charming.

Nanomaterials with large specific surface area and unique chemical/electrochemical properties are widely used as sensing probes, nanocatalysts, nanodrugs, and so on [14–20]. In last two decades, profiting from the ever-increasing nanoscience and nanotechnology, a number of facile and sensitive detection techniques toward food additives have been developed [21–23]. A brief summary of nanomaterial-based detection systems toward food additives would benefit the researchers to choose proper method in the future work. In this review, we essentially focus on recent advances in food additive analysis using nanomaterials that have been reported since 2016. Detection of two kinds of extensively used food additives, including colorants and preservatives, is discussed. In addition, the analysis of illegal food additives based on nanotechnology is also introduced. Finally, challenges and future outlooks of nanomaterial-based food additive analysis are discussed.

2. Food colorant detection

Food colorants control the aesthetic appearance of food, which makes food more attractive and plays an important role in the choice of food [24]. Thus, food colorants are essential for food manufacturing industry because they can excite the purchase interest of consumers. Many colorful compounds can be used as food colorants, including sunset yellow, allura red, lemon yellow, erythrosine, carmine, amaranth, tartrazine, acid orange, and so on [25–36]. In general, natural food colorants are harmless or even beneficial to the human body. Through the genotoxicity evaluation, Hobbs *et al.* found that gardenia blue as natural food colorant does not pose genotoxic concern [37]. Nevertheless, the high cost of natural colorants leads to the wide circulation of many bright colored synthetic chemicals with high stability and low cost. These synthetic colorants are usually organic reagents prepared by artificial

chemical synthesis. They are mainly used in the coloring of carbonated drinks, fruit juice drinks, confectionery wine, confectionery, candy, hawthorn products, pickled vegetables, ice cream, jelly, chocolate, cream, instant coffee, and other foods. However, it should be noticed that many food colorants (especially synthetic food colorants) are suspected of carcinogenesis and have been strictly limited in use. To avoid food colorant contamination, a few methods have been reported by using nanomaterials as signal reporters [38,39]. In view of the usage of these food colorants, analysis of them in soft drinks and other foods are concluded.

2.1. Colorants analysis in soft drinks

Soft drink is defined as the natural or artificial beverage with low alcohol content (<0.5%, mass ratio). In addition to the high cost, natural colorants are easy to change color or fade in the processing of soft drinks. Therefore, water-soluble synthetic colorants are usually used to improve the sensory quality of soft drinks, which increases the buyer's preference. The common soft drinks include carbonated drinks, juice drinks, vegetable juice drinks, tea drinks and bottled drinking water drinks, and so on. In order to achieve rapid and sensitive detection of artificial colorants in soft drinks, nanomaterials have been widely used as accumulators or optical reporters. For example, Bakheet *et al.* reported a fluorimetric Allura red detection system in soft drinks by using poly(ionic liquid) immobilized magnetic nanoparticles as the adsorbent [40]. In this report, the author adopted magnetic solid phase extraction technology, which greatly shortened the analysis time. Compared with conventional solid-phase extraction fillers, this method only requires small amount of adsorbent and short equilibrium time to achieve low-concentration micro-extraction. Such high extraction capacity and extraction efficiency are majorly due to the large specific surface area and short diffusion distance of nanoparticles. Because of the good stability and hydrophobicity of polyionic liquids, the authors used free radical copolymerization to fix polyionic liquids (PILs) on the surface of magnetic nanoparticles ($\text{Fe}_3\text{O}_4@\text{SiO}_2$) to obtain adsorbents ($\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{PILs}$). Moreover, Allura red can be firmly adsorbed on the PIL by $\pi-\pi$ hydrophobic dispersion and weak dipole interaction mechanism because of the azo and aromatic structures, which greatly improves the separation rate. Finally, magnetic solid phase extraction was combined with fluorescence spectrophotometry, they successfully achieved Allura red analysis under the optimized conditions, with a limit of

detection (LOD) of 0.002 $\mu\text{g/mL}$. And good linearity was observed in concentration range from 0.01 to 0.50 $\mu\text{g/mL}$. Additionally, the proposed method could be applied for Allura red analysis in candies and beverages samples with acceptable deviations. The same is the principle of extraction. Swapnil Tiwari *et al.* in order to detect tartrazine in soft drinks, the silver nanoparticles were modified with hydrophobic ligands, and then the tartrazine was extracted by single drop microextraction. Finally, the satisfactory results were obtained by combining with diffusion reflection Fourier transform infrared spectroscopy [41].

As can be seen from the above reports, combining the excellent surface adsorption activity of nanoparticles with traditional detection methods is currently an effective method for detecting food colorants in soft drinks. Among the traditional detection methods, the electrochemical method has been widely used due to its portability, high sensitivity, low cost and short analysis time [42–46]. In this detection method, the glassy carbon electrode (GCE) has become a popular working electrode by virtue of its good conductivity and high chemical stability. As a kind of chemically modified electrode, it will be more and more popular to modify glassy carbon electrode with nanomaterials to improve its electrochemical performance. When choosing the materials to modify the GCE, carbon nanotubes have unique physical and chemical properties, which can promote the electron transfer of electroactive substances, and show better selectivity and more obvious electrocatalysis for the target compounds. Among the carbon nanotubes, multi-walled carbon nanotubes (MWCNTs) have outstanding tensile strength, excellent electrical conductivity, high chemical stability, and can produce good electron transfer rate. Compared with the bare electrode, their films have considerable surface enhancement effect, which can significantly improve the sensitivity of the sensor. For example, P. Sierra-Rosales *et al.* used 1,3-dioxolane as the dispersant and modified the glassy carbon electrode with MWCNTs to obtain an electrochemical sensor with high stability and good repeatability. It showed high sensitivity and reproducibility in the detection of tartrazine, sunset yellow and carmoisine in soft drinks [29]. After surface functionalization of MWCNTs modified electrode with molecularly imprinted polymer through the electropolymerization of acrylamide in the presence of sunset yellow template, Arvand *et al.* developed a selective electrochemical method for sunset yellow [47]. The good specificity is attributed to the molecular recognition of molecularly imprinted polymer, which rules out the interference of

other chemicals. With the proposed electrochemical system, they realized sunset yellow sensing in the concentration range from 0.05 to 100 μM , with a LOD of 5.0 nM. Polydopamine with good electron transfer capability has been widely used as the surface coating material for electrodes. Using dopamine as the monomer, Yin *et al.* reported the surface functionalization of MWCNTs modified electrode with polydopamine (molecularly imprinted polymer) in the presence of sunset yellow template [48]. The modified electrode is capable of sunset yellow sensing with excellent specificity because of the highly matched imprinted cavities, as shown in Fig. 1. Surface coating of polydopamine not only enhances the capture of sunset yellow, but also promotes the electron transfer, which leads to high sensitivity. Using this electrode, electrochemical detection of sunset yellow was achieved in the concentration range of 2.2 nM–4.64 μM , with a LOD of 1.4 nM ($S/N = 3$). This LOD is much lower than most previously reported works. The prepared sensor was successfully used to detect sunset yellow in real spiked samples. The combination of MWCNTs with gold nanoparticles (AuNPs) is an attractive material with a wide size range and size dependent optical, magnetic, electronic and chemical properties. Chitosan (CHIT) has good adhesion, high mechanical strength, excellent film-forming ability and non-toxic, and is easy to be chemically modified because of its rich amino groups. Rovina *et al.* Modified GCE with graphene (GO), MWCNTs and AuNPs *via* CHIT to obtain the electrode (CHIT/GO/MWCNTs/AuNPs/GCE) [49]. The electrode was applied to the determination of sunset yellow in soft drinks in the concentration range of 10–90 mg/mL, LOD of 0.032 mg/mL, showing excellent sensitivity.

In addition to MWCNTs, other nanomaterials (bimetallic nanoparticles, transition metal oxides, graphene oxide, etc.) can also be used as good candidates for electrode modification and electrochemical activity enhancement [27,30,36,50]. For example, in order to detect amaranth in soft drinks, Wang *et al.* prepared a porous graphene material-graphene nanomesh (GNM) to modify the glassy carbon electrode (GCE) to obtain GNM/GCE electrode [27]. In addition, in order to prove that this porous nanomaterial modified electrode has higher electrochemical performance, the author compared it with reduced graphene oxide (RGO) modified glassy carbon electrode (RGO/GCE) and bare glassy carbon electrode (GCE). Because the introduction of macroporous density into graphene sheet is not only conducive to the adsorption of amaranth growth molecules to the working electrode surface through the pores, but also conducive

to the rapid diffusion of electrons in the electrochemical detection process, the electrochemical activity of GNM/GCE is significantly higher than that of RGO/GCE and bare GCE. In addition, Parisa S. Dorraji *et al.* synthesized a ZnO/cysteic acid nanocomposite to modify the glassy carbon electrode (GCE) and can be used to simultaneously determine sunset yellow and tartrazine in soft drinks [30]. In this report, Cysteine is formed by electrochemical oxidation of L-cysteine on the surface of glassy carbon electrode (GCE), and is used as a suitable polymer framework to make ZnO nanofilms uniformly deposited on the electrode surface. The fabricated modified electrode facilitated the electron transfer of sunset yellow and tartrazine, resulted in increased oxidation currents. Ding *et al.* prepared a nano-hybrid of electrochemically reduced graphene oxide (MnO₂ NRs-ERGO) decorated with manganese dioxide nanorods, which was used to modify the glassy carbon electrode (GCE) [51]. Because of the strong catalytic activity of MnO₂ NRs and the high adsorption capacity and excellent conductivity of ERGO, the

modified glassy carbon electrode showed excellent analytical performance such as high sensitivity, high selectivity and low cost. Moreover, it was used to detect sunset yellow (SY) in soft drinks with wide linear range and low detection limit. Zhao *et al.* developed a molecularly imprinted copolymer sensor (MIP-PMDB/POPD-GCE) by electropolymerizing m-dihydroxybenzene (m-db) and o-phenylenediamine (o-PD) and then directly fixing the copolymer on the surface of glass carbon electrode (GCE) [32]. Due to the fact that the copolymer is filled with nanopores which can bind tartrazine molecules, tartrazine in soft drinks can be determined quickly.

In addition to glassy carbon electrode, carbon paste electrode, graphene electrode and metal electrode can also be used for the detection of colorants in soft drinks [26,28,31,35,39,52]. For example, Ya *et al.* simply synthesized a Zinc oxide nanoflower (ZnONF) to modify the carbon paste electrode to obtain a zinc oxide nanoflower modified carbon paste electrode (ZnONF/CPE), which was used to detect sunset yellow in soft drinks.

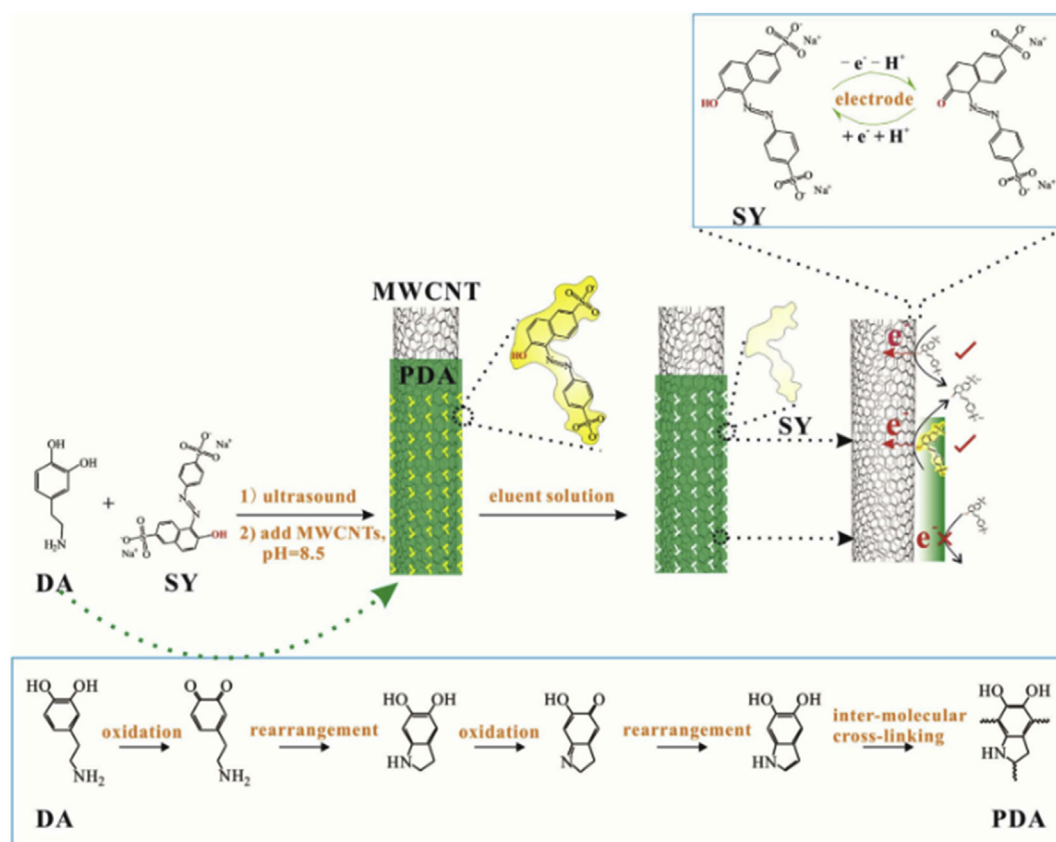


Fig. 1. Schematic preparation of MWCNT@polydopamine (PDA) and sunset yellow (SY) sensing. Reprinted with permission from Ref. [48] with permission from the Elsevier, Copyright 2018.

Under the best conditions, the detection limit is 0.10 $\mu\text{g/L}$. Due to the large specific surface area and high accumulation efficiency of ZnONF, the electrochemical oxidation of sunset yellow was enhanced by ZnONF modified carbon paste electrode (ZnONF/CPE) [52]. Wu *et al.* used one-pot hydrothermal to fix the ZnO/RGO/ZnO nanocomposite in situ on the zinc foil, and used the obtained ZnO/RGO/ZnO@Zn directly as the electrode material to detect sunset yellow in soft drinks, and It shows an ultrahigh sensitivity of 20.25 $\mu\text{A } \mu\text{M}^{-1} \text{ cm}^{-2}$, a low LOD (3 nM), a wide linear detection ranging from 0.01 to 5 μM [39]. By casting a double-stranded spiral copper (I) onto the surface of a single-walled carbon nanotube modified screen-printed electrode, Nuñez-Dallos *et al.* reported the voltammetry of amaranth red and tartrazine in soft drinks [31]. Using this method, amaranth red and tartrazine can be detected at 30 nM and 60 nM (S/N = 3), respectively. The small relative standard deviation (3.5%, $n = 7$, three different electrodes) proves the high accuracy of the proposed method. In addition, the organic molecule β -cyclodextrin can also be used to modify the electrode to enhance the electrochemical detection in soft drinks due to its good adsorption capacity [36,53]. Although the most commonly used method for detecting colorants in soft drinks is to modify the working electrode with nanotechnology, in recent years, some methods other than electrochemical sensing have been reported to better detect colorants in soft drinks [54–57]. Among them, surface enhanced Raman spectroscopy (SERS) as a highly sensitive nanotechnology can also be used to detect colorants in soft drinks. For example, Ou *et al.* used gold nanorods (Au NRs) as SERS substrates and proposed a system to detect Allure red or sunset yellow in soft drinks [55]. In their work, they found that the aspect ratio of gold nanorods is crucial for SERS signals, and the strongest Raman signal enhancement is achieved by special Au NRs (aspect ratio = 2.4 or 1.8). He *et al.* chose cysteamine to modify the gold nanoparticle SERS substrate, and then detected the acid pigment with weak surface affinity in soft drinks [56]. Because cysteamine has a positively charged group $-\text{NH}_3^+$, it can electrostatically interact with acidic pigments, and hydrogen carbonate bonds between the calcium carbonate and the pigment molecules, making the pigment molecules closer to the surface of the gold nanoparticles. Experimental results show that the method still has good reproducibility under complex conditions, and the results can be detected very quickly and sensitively.

2.2. Colorants analysis in other foods

As food cosmetics, food colorants can also be used for other foods, *e.g.*, meat, cake, and candy. It is noticed that food colorants not only provide attractive color, but also help to preserve water. However, according to food colorants regulations, synthetic colorants are not able to be used in meat and its processed products. In this case, only few natural colorants could be applied in meat processing. For example, Carminic acid (CA) is extensively used as a typical red and natural food colorants for meat products. However, the allowable concentration range of CA in foodstuff is set to be 25–500 mg/kg by the Standardization Administration of China (GB 2760-2014). Therefore, in order to detect CA, Yuan *et al.* learned that small-sized layered double hydroxides (LDHs) can increase the intensity of the chemiluminescence (CL) of the Luminol- H_2O_2 system by more than 950 times [58]. The enhanced chemiluminescence is due to the synergistic effect of the positively charged layer and the intercalated carbonate. The former attracts luminol dianions and increases their local concentration, while the latter forms carbonates and promotes the formation of emissive 3-aminophthalate anions. Therefore, combined with the negative charge nature of CA, the author proposed a sensitive chemiluminescence detection CA method based on the LDH-luminol- H_2O_2 system (Fig. 2) [59]. The surface adsorption of CA causes the positively charged center of the LDH layer to be occupied, which hinders the approach of the Luminol dianion. Similarly, the reducing power of CA inhibits the formation of free radicals, which reduces the interaction between luminol divalent anions and free radicals. In addition, the UV-vis absorption range of CA overlaps with the chemiluminescent emission of the luminescent 3-aminophthalate anion, resulting in the occurrence of chemiluminescent resonance energy transfer. As a result, the synergy of occupied active sites, reduction of free radicals and CL resonance energy transfer leads to quenching of CL emission. Based on this mechanism, they achieved the detection of CA in dried pork slices within a concentration range of 0.5–10 μM , with a LOD of 0.03 μM . They also studied the repeatability of the proposed CL sensor. During 11 repeated measurements of 2 μM CA, the calculated relative standard deviation was 2.9%, which proved the accurate CA analysis of the designed system. Indeed, the chemiluminescence spectrophotometry used in this report as a traditional detection method has the advantages of low background noise, fast response and simple instrument [60,61], it has been widely used in combination

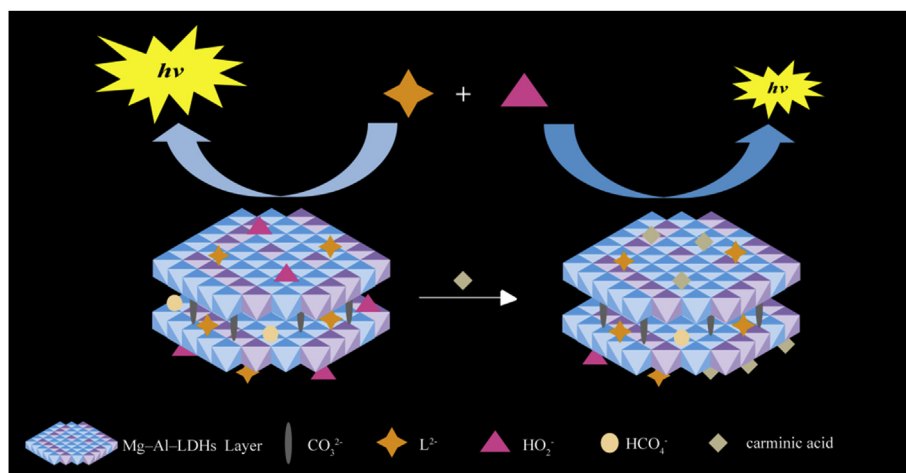


Fig. 2. Schematic representation of the sensing principle of LDH-luminol- H_2O_2 system for the detection of CA. Reproduced from Ref. [59] with permission from The American Chemical Society, Copyright 2018.

with the increasingly developed nanotechnology [58,59,62].

Electrochemical methods with high sensitivities have also been applied for the detection of food colorants. For example, Arvand *et al.* prepared homogeneous bimetallic nickel tin oxide hollow nanospheres by template method to modify carbon paste electrode to obtain a new electrode (Ni–Sn-oxide NSs/CPE) [34]. The results show that the electrode has higher sensitivity than bare carbon paste electrode in the detection of erythrosine in commercial food such as candy and jelly. This is because the active sites of the reaction are greatly increased due to the high specific surface area of bimetallic hollow nanospheres, and the synergistic action of the two metals can make the electron transfer in Ni–Sn-oxide NSs easier. However, the specific mechanism of the electrode for the detection of erythrosine in the article needs further study. Zhao *et al.* used molecular imprinting technology for electrochemical sensing to specifically detect the food pigment erythrosine [33]. In order to improve the sensitivity and stability of the reduced graphene oxide on the surface of the glassy carbon electrode, the author used sodium citrate as a reducing agent and stabilizer, using 2-aminoethanol (2-AET) functionalized, uniformly distributed gold nanoparticles (AuNPs) modified reduced graphene oxide (RGO); in order to improve the selectivity of the sensor, the author used erythrosine as template molecules to obtain molecularly imprinted cavities on the modified electrode surface. Using this method to detect food coloring shows high selectivity and sensitivity. Pogacean *et al.* prepared the nanocomposites by mixing graphene oxide with TiO_2 –Ag nanoparticles, and then used it to modify the gold

electrode to detect amaranth also showed good sensitivity [25]. In addition, chitosan as an easily modified organic molecule can also be used to modify glassy carbon electrodes to better detect food colorants [63].

Although research on how to develop new nanomaterials to modify working electrodes (glass carbon electrodes, carbon paste electrodes, graphene electrodes, metal electrodes, etc.) is currently the most popular direction for the detection of soft drinks and food colorants other than soft drinks, SERS also occupies a proper place in the detection of food colorants due to its fast, sensitive and non-destructive testing characteristics [64,65]. In comparison with ordinary Raman systems, the signals of Raman reporter on the surface of nanoparticles can be greatly enhanced through the surface plasmon resonance-induced electromagnetic enhancement and/or charge transfer mediated chemical enhancement [66,67]. To apply SERS technique into the detection of food colorants, the key issue is to obtain a substrate with high SERS activity. Generally speaking, since the random distribution of hot spots on the SERS substrate will cause the SERS signal to show poor repeatability, it is necessary to fabricate nanostructures with uniform gaps. Wu *et al.* prepared gold nanoparticles with a diameter of 80 nm into a single layer of uniform gold nanoparticle film by solvent driven self-assembly [68]. Using this film as a SERS substrate, the sensitive analysis of sunset yellow and tartrazine in ppm level was realized. In addition, the author also used it to detect illegal food additives including ciprofloxacin, diethylhexyl phthalate and azodicarbonamide. Wu *et al.* used ascorbic acid to reduce silver nitrate, in the presence of a polyvinylpyrrolidone (PVP)

surfactant, regulates the generation of uniform flower-like silver nanoparticles for SERS substrate analysis to detect carmine in food additives [69]. Using the same method to produce uniform flower-shaped silver nanoparticles, Ai *et al.* used this silver nanoparticles as a SERS substrate to study four food colorants (food blue, tartrazine, sunset yellow and acid red) [70]. Experimental results show that the LOD of the four colorants is as low as 100 nM (of which tartrazine's LOD is close to 10 nM). This shows a very high sensitivity for the detection of international standard food coloring. However, not all target analytes can be detected simply by using metal nanoparticles as the substrate, because metal nanoparticles have weak adsorption to some analyte molecules, making it difficult for analyte molecules to access metal nanoparticles [71]. In addition, silver nanoparticles have a tendency to oxidize, so it is difficult to be a long-term SERS substrate [72]. Therefore, when we choose the SERS method to detect food additives or other target analytes, we should take into account the characteristics of the target molecule, and if necessary, modify the nano-substrate to improve its adsorption [73]. In the past four years, most of the relevant reports have used electrochemical methods or SERS. I think this must be inseparable from the word “adsorption”. To improve the traditional detection methods with nanotechnology is to make full use of the high specific surface area of nanoparticles to increase the adsorption of target molecules, so as to improve the sensitivity of traditional methods. This is the case with electrode modification, the selection of suitable SERS substrate, even the traditional high performance liquid chromatography (HPLC) [74]. Partial detection methods for food colorants were summarized in Table 1.

3. Food preservative detection

Food contains lots of organic compounds, and its time-dependent spoilage is inevitable. Putrescent foods are extremely toxic to Human health and even cause death. Thus, the storage of food is one of the key issues in food industry. Based on the spoilage process, food spoilage primary includes two pathways: contamination by microorganism and oxidation-induced degradation. To extend the food storage period, some chemical compounds are added as ingredients, called as food preservatives [75]. According the function mechanism, these food preservatives can be generally divided two classes, antimicrobial and antioxidant. Antimicrobial preserves food by inhibiting or killing

Table 1. Summary of detection methods toward food colorants.

#	Material	Strategy	Target analytes	Linear range (μM)	LOD (μM)	Ref.
1	graphene nanomeshes/GCE	electroanalysis	amaranth	5.0×10^{-3} –1.0	7.0×10^{-4}	[27]
2	poly (p-aminobenzenesulfonic acid)/zinc oxide nanoparticles/CPE	electroanalysis	tartrazine	0.0349–5.44	0.08	[28]
3	ZnO/cysteic acid nanocomposite/GCE	electroanalysis	sunset yellow	0.1–3.0	0.03	[30]
4	MIP-PmDB/PoPD-GCE	electroanalysis	tartrazine	0.07–1.86	0.01	[32]
5	graphene with 2-aminoethanethiol functionalized gold nanoparticles	electroanalysis	erythrosine	5.0×10^{-3} –1.1	3.5×10^{-3}	[33]
6	nickel-tin oxide hollow nanospheres/CPE	electroanalysis	erythrosine	0.1–100	2.1×10^{-3}	[34]
7	PEDOT:PSS/AuNPs/CA/SPCE	electroanalysis	carmine	9.0×10^{-3} –3.9	6.05×10^{-3}	[35]
8	three-dimensional β-cyclodextrin functionalized graphene aerogels/GCE	electroanalysis	Ponceau 4R	0.001–1.0	3.0×10^{-4}	[36]
9	ZnO/RGO/ZnO foil	electroanalysis	sunset yellow	0.05–5	3×10^{-3}	[39]
10	MIP/ε-MWCNTs/GCE	electroanalysis	sunset yellow	0.05–100	0.005	[47]
11	molecularly imprinted polydopamine-coated multi-walled carbon nanotubes/GCE	electroanalysis	sunset yellow	2.2×10^{-3} –4.64	1.4×10^{-3}	[48]
12	electrochemically-reduced graphene oxide nanosheets decorated with MnO ₂ nanorods-GCE	electroanalysis	sunset yellow	0.01–2 2–10 10–100	0.002	[51]
13	positively charged Au NPs-embedded MIHs	SERS	new red	1.64–164	0.164	[57]
14	layer doubled hydroxide–luminol–H ₂ O ₂ system	chemiluminescence	carmine acid	0.5–10	0.03	[59]
15	flower-shaped Ag NPs	SERS	carmine	0.01–1000	0.01	[69]

bacteria/fungus through the denaturation of microbial protein, destruction of cell wall, suppression of enzymatic activity, etc. Many organic and inorganic chemicals can be used as food antimicrobial, including potassium sorbate, sodium benzoate, nitrite, and sulfite, etc [18]. While antioxidant protects food by hindering the oxidation of certain constituents, *e.g.*, fats. Chemicals with good reducing ability are applied as antioxidants, such as butylated hydroxyanisole, butylated hydroxytoluene, tertiary butylhydroquinone, ascorbic acid, polyphenols [75]. Notice that the added food preservatives must be nontoxic, thus the contents need to be strictly limited based on food safety rules. Recent studies indicated that the excess uptake of food preservatives leads to various diseases and even cancer [76–79]. Mohammadzadeh-Aghdash *et al.* summarized the interaction between food preservatives and serum albumin and revealed that the interaction leads to the activation of inflammatory paths and acceleration of diabetes [80]. Taking this into consideration, the development of sensitive detection methods toward food preservatives is of significance to ensure food safety and Human health. In this section, detection methods on antimicrobial and antioxidant were briefly introduced.

3.1. Antimicrobial

Similar to the colorant's detection, electrochemical and optical detection methods are also applicable to food preservatives analysis. And the detection sensitivity and selectivity could be improved with the introduction of nanomaterials. Gold working electrode functionalized with *p*-amino thiophenol and Au NPs has been applied to the electrochemical

detection of nitrite, a typical inorganic food preservative [81]. After processing of electrode, nitrite oxidation on the electrode surface with a characteristic peak potential of 0.76 V was observed. And the current was found to be proportional to the nitrite concentration. With this system, nitrite detection showed good linearity in concentration range of 0.5–50 $\mu\text{g/mL}$ nitrite and a LOD of 0.12 $\mu\text{g/mL}$. Beyond electrochemical activity, nitrite has some special reactivity toward some oxidant. It is well known that it can react with hydrogen peroxide and produces generate peroxynitrous acid under acidic conditions. The highly reactive peroxynitrous acid can oxidize surface protecting agent, and cause aggregation of nanomaterials. Using this tactic, Yuan *et al.* reported a fluorescence turn-off method to detect nitrite with hyperbranched polyethyleneimine protected silver nanoclusters (hPEI-Ag NCs) [82]. The sensing was performed under acidic condition in the presence of excess hydrogen peroxide. The surface coating with hyperbranched polyethyleneimine is critical to accomplish the sensing application. That is because the hyperbranched molecular structure endows high stability of Ag NCs toward hydrogen peroxide or sole nitrite. However, the generated peroxynitrous acid destroys the hyperbranched polyethyleneimine and leads to the formation of Ag NC aggregates, which subsequently causes the fluorescence quenching (Fig. 3). Based on this system, nitrite detection was achieved with a LOD of 100 nM, which is much lower than maximum contamination level in drinking water set by the U.S. Environmental Protection Agency. In addition, this method utilizes a specific reaction, and other anions including F^- , Cl^- , Br^- , I^- , $\text{C}_6\text{H}_5\text{CO}_2^-$, SCN^- , N_3^- , IO_3^- , IO_4^- , BrO_3^- , ClO_4^- , citrate $^{3-}$, EDTA $^{2-}$,

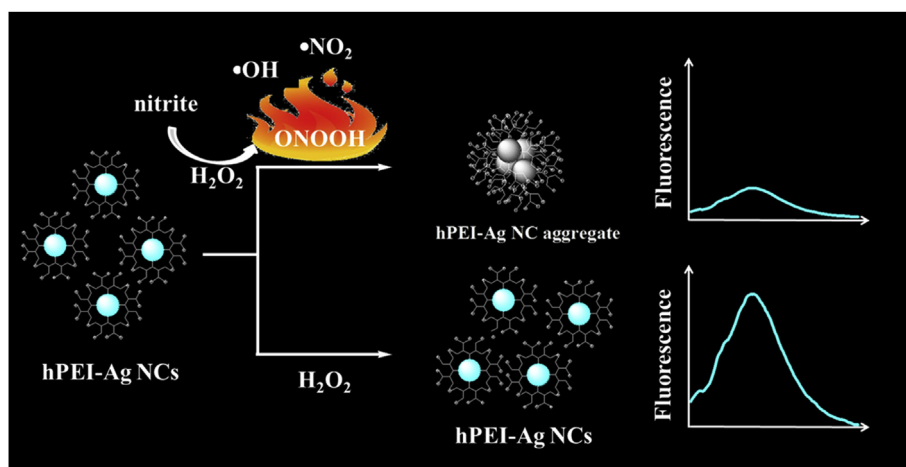


Fig. 3. Schematic illustration of nitrite induced aggregation of hyperbranched polyethyleneimine protected silver nanoclusters (hPEI-Ag NCs) and fluorescence quenching. Reproduced from Ref. [82] with permission from The Royal Society of Chemistry, Copyright 2016.

NO_3^- , SO_3^{2-} and SO_4^{2-} , didn't show any visible interference. The good recoveries and small relative standard deviation values proved the practical application of the proposed platform for nitrite analysis in lake water, tap water and seawater samples.

Sulfite has also been widely used as the antimicrobial, which can inhibit the enzymatic activity of some microorganisms. Using methyl green attached Eu, Sm, Mn-doped CaS nanoparticles, Wang *et al.* reported a sensitive sulfite detection platform based on recovery of upconversion luminescence [83]. The sensing mechanism was shown in Fig. 4, methyl green quenched the luminescence of CaS nanoparticles through fluorescence resonance energy transfer (FRET) mechanism. Introduction of sulfite destroys the molecular structure of methyl green and breaks up FRET process, leading to the enhancement of luminescence. With the use of portable luminescence reader, they achieved sensitive sulfite sensing with a LOD of 2 ng/mL, which is lower than that with commercial test strips (0.05 $\mu\text{g/mL}$). Using nitrobenzofurazan response motif anchored structurally asymmetric naphthorhodamine as the probe; Jin *et al.* realized fluorimetric sulfite detection in water and wine samples [84]. With the integration of the nucleophilicity of sulfite and the electrostatic attraction mediated reaction kinetics, selective sulfite analysis was achieved with a LOD of 70 nM. In addition, this probe was applied for imaging intracellular and endogenous sulfite.

3.2. Antioxidant

There are tens to hundreds of antioxidants, which can be used as food preservative. Based on their sources, they can be divided into natural, synthetic and biological antioxidants. Most of them are phenol compounds. Utilizing chemical/electrochemical redox reaction, many works have been reported for the detection of various antioxidants [77,85–89]. For example, using hyperbranched hPEI-Ag NCs as the signal reporters, Yuan *et al.* achieved tea polyphenol (natural antioxidant) was detected based CL technique [62]. The sensing mechanism is that hydroxyl radicals oxidized Ag NCs and induce the emission of CL signal (Fig. 5). However, the hydroxyl radicals could be effectively scavenged by tea polyphenols. As a result, the CL intensity decreased. The decreased CL intensity was proportional to the concentration of tea polyphenols. With this method, they realized linear determination of tea polyphenols in the concentration range of 2.52–76.2 μM . In addition, practical application of the proposed system was verified by

detecting tea polyphenols content in three tea samples (green tea, black tea and oolong tea). According to the results, the highest content of tea polyphenols was detected in green tea.

Based on electrochemical strategy, Sandeep *et al.* also reported the detection of polyphenols (catechol) using graphene nanoribbons/AgNPs/polyphenol oxidase composite modified graphite (Gr) electrode [90]. In this report, polyphenol oxidase (PPO) or catechol oxidase is a copper-containing oxidoreductase enzyme that can catalyze the oxidation of catechol to the corresponding o-quinone. If an enzyme is to be used to modify the electrode, the key is to choose a suitable substrate to fix the enzyme on the electrode without changing the active site of the enzyme. The author chose graphene nanoribbons (GNRs) as the matrix because GNRs have more open-ended structures than graphene and carbon nanotubes, which provide them high density of reaction edges and large active surface area that helps to bind enzyme *via* electrostatic or π – π interaction. In addition, because silver nanoparticles are often used as modifiers for biosensors due to their high quantum electron transfer and catalytic properties, and the capping residues on their surface can effectively clamp GNR and PPO enzymes, retaining all the properties of the enzyme, the author chose AgNPs to modify the matrix to further improve the sensitivity and conductivity of GNR. The Gr/GNRs/AgNPs/PPO sensor obtained by modifying the graphite electrode with this method has a lower detection limit (0.03 μM) and a wider linear range (2–2300 μM) for detecting catechol. Ascorbic acid is also an efficient natural antioxidant, which shows strong reducing ability and can be used in various areas. The detection of ascorbic acid based on optical techniques has also been reported in last few years. Using metal oxides or metal hydroxides as the nanocatalysts, colorimetric sensing of ascorbic acid was achieved [91,92].

In comparison with natural antioxidants, synthetic antioxidants usually show stronger toxicity, making the detection of these synthetic antioxidants important. Up to now, many electrochemical methods toward these synthetic antioxidants have been explored with the combination of molecularly imprinted polymer. Yue *et al.* reported the rapid detection of tertiary butylhydroquinone using Pd–Au bimetallic nanoparticles decorated reduced graphene oxide (rGO) electrode with the surface functionalization of molecularly imprinted polymer [86]. The molecularly imprinted polymer was in-situ generated with tertiary butylhydroquinone as the template molecule. As expected, selective tertiary butylhydroquinone detection was achieved by

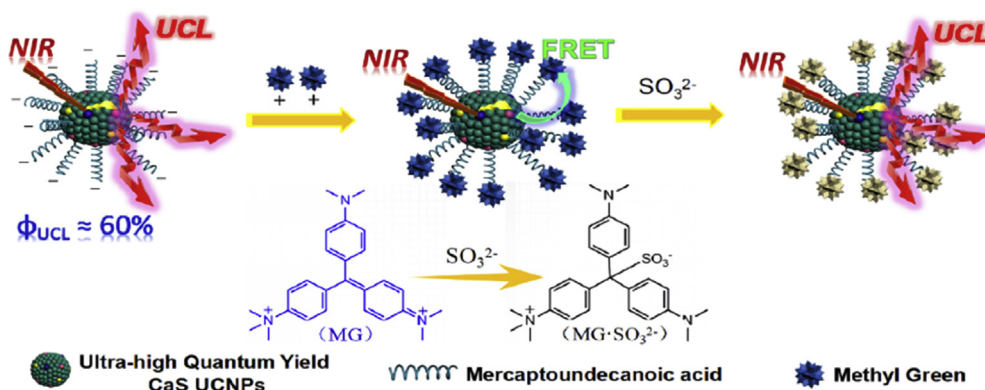


Fig. 4. Schematics of upconversion luminescence (UCL) turn-on sulfite detection using methyl green functionalized upconversion nanoparticles (UCNPs). Reprinted from Ref. [83] with permission from the American Chemical Society, Copyright 2018.

integrating electrochemical analysis. For tertiary butylhydroquinone sensing, the proposed method provided the linear range of 0.5–60 $\mu\text{g/mL}$ with a LOD of 0.046 $\mu\text{g/mL}$. By decorating Au NPs and molecularly imprinted polymer onto the surface of three-dimensional graphite paper electrode, Fan *et al.* greatly enhanced the detection sensitivity toward tertiary butylhydroquinone [77]. With such a design, tertiary butylhydroquinone was detected in the concentration range of 80 nM–100 μM , with a LOD of 12 nM. The large surface area of three-dimensional graphite paper plays an important role on the enhanced sensitivity. Organic electrochemical transistor has also been applied for the electrochemical detection of antioxidant. After the modification of gate electrodes with poly(diallyldimethylammoniumchloride) and MWNTs, Xiong *et al.* reported the electrochemical sensing of gallic acid at very low concentration (10 nM) [93]. This system possesses small operating voltage in comparison with traditional electrochemical

methods, and provides a promising tool for portable gallic acid analysis in actual tea beverages.

Due to the advantages of small sample volume, high throughput, and low cost, simultaneous detection of multiple targets in a single run/volume have attracted growing attention. For the electrochemical assays, simultaneous detection of multiple antioxidants is possible with separated voltammetric peaks. As an example, Ng *et al.* proposed a fast and sensitive method for the simultaneous detection of tertiary butylhydroquinone, butyl hydroxyanisole and butylated hydroxytoluene [94]. The voltammetric peaks for tertiary butylhydroquinone, butyl hydroxyanisole and butylated hydroxytoluene were observed at 0.278 V, 0.503 V, and 0.747 V, respectively. This method allows the detection of tertiary butylhydroquinone, butyl hydroxyanisole and butylated hydroxytoluene at 0.5, 0.3, and 0.7 $\mu\text{g/mL}$. And the analysis of these antioxidants in ghee, sunflower oil and salad dressing was realized.

In addition, array-based sensing with the integration of principal component analysis and hierarchical cluster analysis is also capable of multiple targets analysis [95,96]. With this strategy, Bordbar *et al.* developed a colorimetric array for distinguishing 20 various food antioxidants [97]. In this work, Au NPs and Ag NPs synthesized by six different reducing and/or capping agents (sodium borohydride, chitosan, cetyltrimethylammonium bromide (CTAB), bovine serum albumin (BSA), glucose and polyvinyl pyrrolidone (PVP)) were used as the sensing elements. Interaction between individual antioxidant and these elements causes aggregation or morphological changes of Au NPs and Ag NPs, which generates unique response pattern (Fig. 6). After the acquirement of colorful imaging with a digital camera, the color information was

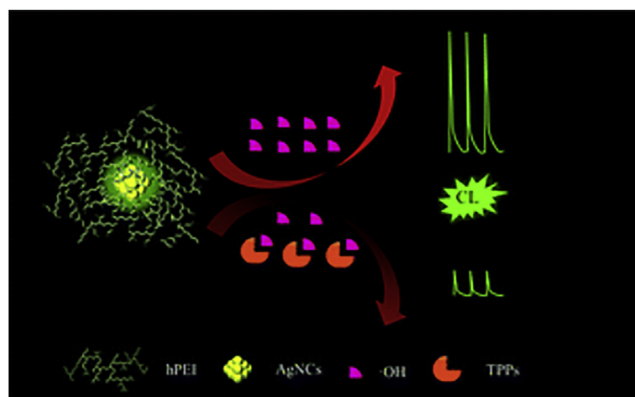


Fig. 5. The sensing mechanism is that hydroxyl radicals oxidized Ag NCs and induce the emission of CL signal. Reproduced from Ref. [62] with permission from The Royal Society of Chemistry, Copyright 2017.

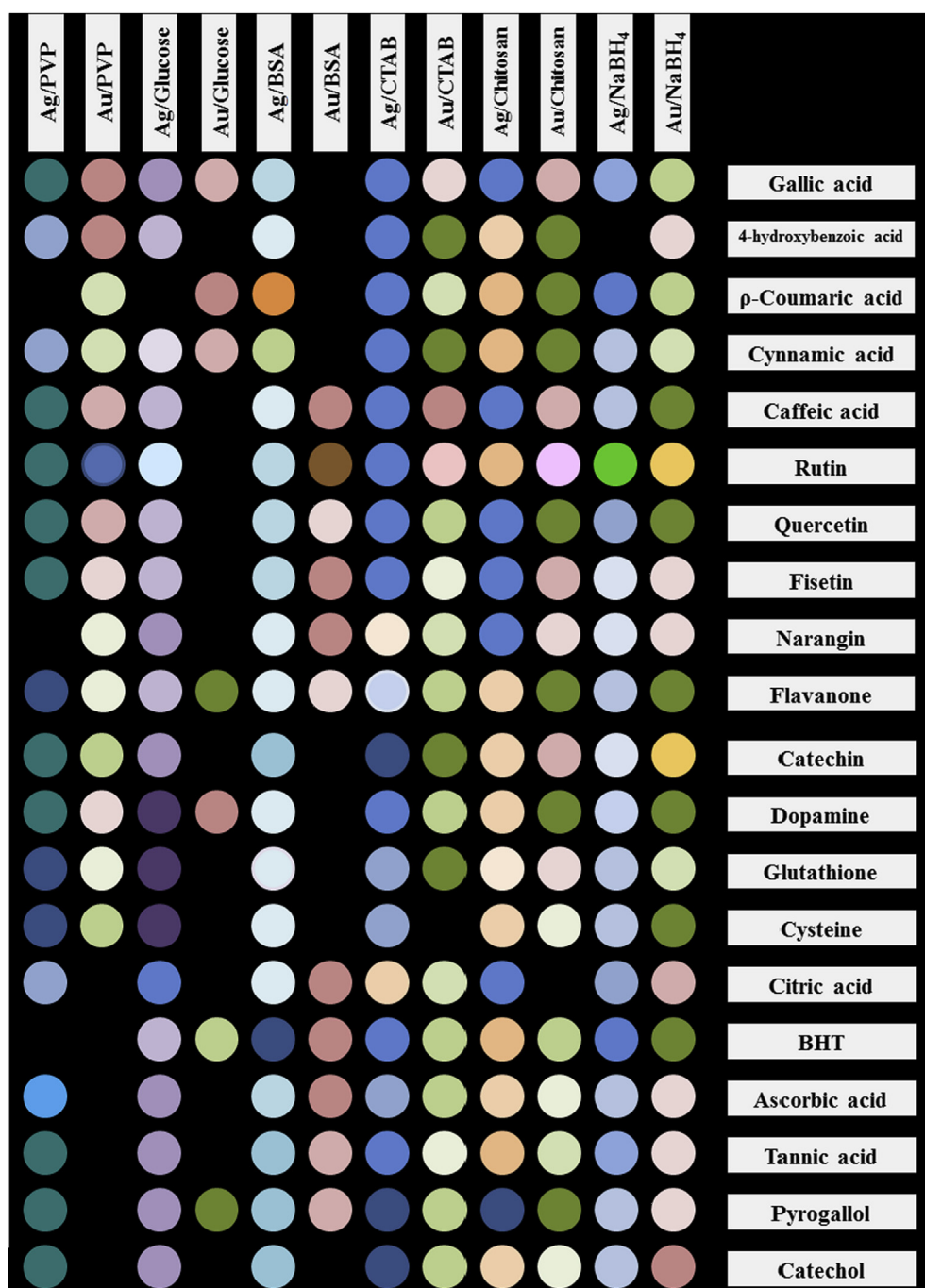


Fig. 6. Color difference maps of 20 types of antioxidant. Reprinted from Ref. [97] with permission from the Springer, Copyright 2018.

analyzed through principal component analysis and hierarchical cluster analysis. All repeated measurements were assigned into the same group, indicating the successful differentiation of these antioxidants. Interestingly, Euclidean Norm was proportional to the antioxidant concentration. Through the calibration, the LODs for gallic acid, caffeic acid, catechin, dopamine, citric acid, butylated hydroxytoluene, and ascorbic acid were

determined to be 4.2, 13, 53, 6.9, 47, 3.5, and 43 nM, respectively. Partial detection methods for food preservatives were summarized in Table 2.

4. Illegal food additives detection

In addition to above food additives, some special chemicals are also used to improve the storage or appearance of food. However, these chemicals,

Table 2. Summary of detection methods toward food preservatives.

#	Materials	Strategy	Target analytes	Linear range	LOD	Ref.
1	MIP/AuNPs/exfoliated graphite paper (EGP)	electroanalysis	tertiary butylhydroquinone	0.08–100 μM	0.07 μM	[77]
2	graphene quantum dots	fluorescence	ascorbic acid	1.11–300 μM	0.32 μM	[79]
3	gold nanoparticles/p-aminothiophenol/Au	electroanalysis	nitrite	0.5–50 $\mu\text{g/mL}$	0.12 $\mu\text{g/mL}$	[81]
4	nitrobenzofurazan anchored asymmetric naphthorhodamine	fluorescence	sulfite	2–100 μM	0.07 μM	[84]
5	CoSe ₂ nanoparticles and reduced graphene oxide/SPCE	electroanalysis	propyl gallate	0.075–460.15 μM	0.016 μM	[85]
6	PdAuNPs/ERGO nanocomposites	electroanalysis	tertiary butylhydroquinone	0.5–60 $\mu\text{g/mL}$	0.046 $\mu\text{g/mL}$	[86]
7	MoS ₂ /ZnO heterostructure	photoelectrochemical	propyl gallate	0.125–1470 μM	0.012 μM	[89]
8	graphene nanoribbons/AgNPs/polyphenol oxidase/graphite	electroanalysis	catechol	2–2300 μM	0.03 μM	[90]
9	poly(diallyldimethylammonium chloride) and carbon nanomaterials nanocomposites/Au	electroanalysis	gallic acid	1–10 μM	0.01 μM	[93]
10	gold and silver nanoparticles	colorimetric	all type of antioxidants	–	4.2 nM/53 nM	[97]

known as illegal food additives, are strictly limited because of their seriously harm to the public health. And most food safety incidents reported in past years are caused by illegally added industrial additives. To control food safety issues, these illegal food additives need to be strictly controlled. Therefore, the development of facile approaches for the detection of these illegal food additives is very important. With the combination of HPLC technique, several works for analyzing illegal food additives have been reported [98,99]. In this part, three well-known illegal food additives, including Sudan dye, clenbuterol and melamine, are discussed.

4.1. Sudan dyes

Sudan dyes, including Sudan I, Sudan II, Sudan III, Sudan IV, and Sudan black, are a group of oil soluble dyes, which are commonly used in plastics, rubber and paint. As synthetic dye, Sudan dyes possess bright red color and are very stable in comparison with natural colorants. Thus, they have been used for chemical colorant due to advantages of colorfastness and low price. However, Sudan dyes contain azo structure, which is suspected to be carcinogenic to human being. Recently, these Sudan dyes are utilized for food colouration by unscrupulous merchants. In consideration of their harm to Human being, Sudan dye as food additives have been severely prohibited according to the Food Standards Agency.

To detect Sudan dyes, many works based on electrochemical and optical sensing techniques has been reported [100–104]. For example, Ye *et al.* reported an electrochemical detection platform for the Sudan I sensing by using CuO nanoparticle-decorated 3D N-doped porous carbon (CuO/3DNPC) modified GCE electrode [102]. The potential of Sudan I become lower upon when approaching electrode, which enhances the current. Using this mechanism, they achieved selective Sudan I detection in a linear concentration range from 2.5 to 100 μM with between with a LOD of 0.84 μM . They also realized the detection of Sudan I in ketchup and chili sauces.

To enhance the detection sensitivity, Mahmoudi-Moghaddam *et al.* proposed a screen printed electrochemical sensor by using La³⁺-doped Co₃O₄ nanocubes as electrode substrate [100]. The catalytic character of La³⁺ greatly decreases the oxidation overpotential of Sudan I and enhances the peak current. With this advantage, Sudan I could be detected in the range of 0.3–300.0 μM . And the LOD toward Sudan I was calculated to be 0.05 μM . During the selectivity investigation, metal ions and

small molecules, including Ca^{2+} , Ni^{2+} , Mn^{2+} , Pb^{2+} , Mg^{2+} , Cr^{2+} , Zn^{2+} , CN^- , Br^- , K^+ , Li^+ , Ag^+ , SCN^- , sucrose, fructose, lactose, glucose, and urea, have no interference. In addition, Sudan I detection chili powder, tomato paste, and ketchup sauce have also been achieved. Similarly, using zinc oxide nanoparticles (ZnONPs) as the electrode material, Heydari *et al.* displayed the electrochemical Sudan III detection by integrating rotatable central composite design and response surface method [101]. With this combination, Sudan III detection was achieved in the linear dynamic ranges of 0.05–1.0 and 1.0–15.0 μM , with a LOD of 2.56 nM.

Using Ag NPs as the SERS substrate, Zhao *et al.* first reported a simple and effective SERS-based method for the detection of Sudan black B [103]. As shown in Fig. 7, they realized the Sudan black B sensing at a concentration of 0.05 $\mu\text{g/mL}$ in standard solutions. Interestingly, 0.1 mg/kg Sudan black B in black rice extracts was also detected using the proposed SERS-based method. From the perspective of saving resources, reducing costs and reducing environmental pressure, Hu *et al.* used tire-derived carbon dots as fluorescent sensors for sensitive detection of Sudan dyes [104]. Because the injection of nitrogen atoms into the carbon dots can lead to a change in the electronic environment and a significant increase in photoluminescence efficiency, the author used ammonium persulfate to oxidize the tire and dope with nitrogen atoms to make the prepared carbon dots have a high quantum yield of 23.8%. Because of the internal filtration effect, the carbon dots obtained after adding Sudan I–IV will have a significant decrease in fluorescence. This method is used to realize the sensitive detection of Sudan I–IV in chilli powder with the LODs are 0.17, 0.21, 0.53 and 0.62 μM for Sudan I, II, III and IV, respectively.

4.2. Clenbuterol

Clenbuterol is a well-known β_2 -adrenergic receptor agonist, which is used for the cure of chronic pulmonary and bronchial diseases. However, because of its capability to increase the lean meat rate and feed conversion rate of animals, clenbuterol is illegally used as a growth promoter and feed additive for livestock and poultry. Unfortunately, excessive clenbuterol residue in meat causes serious health problems, including cardiovascular diseases, central nervous diseases, and even acute poisoning. As a result, the monitoring of clenbuterol residue in meat samples is important to Human health. It is thus important to develop sensitive and selective method for clenbuterol sensing.

Toward this goal, a few systems have been explored based on electrochemical and optical response [105–109]. For instance, Zhang *et al.* reported an electrochemical sensor for clenbuterol detection by using polyoxometalate and zirconium dioxide nanocomposites as electrode material [106]. The used electrode material negatively shifts the oxidation potentials of clenbuterol and enhances the peak current. With this design, they achieved linear clenbuterol detection in the concentration range from 0.1 to 1000 μM , with a LOD of 5.03 nM. Using pork as the real sample, they realized clenbuterol with good recoveries (94.4–102.3%).

Beyond electrochemical sensing, optical analysis of clenbuterol has also been reported. Sun *et al.* proposed a SERS-based approach to detect clenbuterol by using GO/Au NPs as the SERS substrate [107]. Through controlling the depositing density of Au NPs, highly dense hot spots with strong electromagnetic coupling effect was produced. Using GO/Au NPs as the substrate, Raman signal of clenbuterol was enhanced 4.8 times in comparison with the use of sole Au NPs substrate. This proposed SERS-based method allows the selective clenbuterol detection with a LOD of 33.4 nM. Also based on gold nanoparticles, Muthaiah Shellaiah *et al.* developed a nanodiamond conjugated gold nanoparticles (ND@AuNPs) as colorimetric probe for the detection of clenbuterol in urine [108]. Through modifying nanodiamonds to have thiol groups, and then reacting with gold nanoparticles to obtain highly stable conjugates (ND@AuNPs). The complexation of the amide ($-\text{C}=\text{O}$ and $-\text{N}-\text{H}$) functional groups of ND@AuNPs with clenbuterol causes aggregation and changes the color from wine red to purple. This colorimetric method is used for selective detection of clenbuterol with a LOD of 0.49 nM.

To further improve the selectivity, immunofluorescence method for clenbuterol analysis has been developed. Conventional immunofluorescence technology requires complicated labeling procedure, which diminishes the sensing performances. To avoid labeling, Yao *et al.* proposed a competition strategy using S/N-doped carbon quantum dots and clenbuterol antibody [105]. In their work, clenbuterol antibody quenches the fluorescence of carbon quantum dots *via* amine–amine amine–amine coupling reaction. The introduction clenbuterol leads to the formation of stable clenbuterol antibody–clenbuterol complex, which liberates carbon quantum dots and enhances the fluorescence. This approach shows fluorimetric clenbuterol sensing in the concentration range from 0.07 to 1.7 ng/mL, with a LOD of 23 pg/mL. In addition,

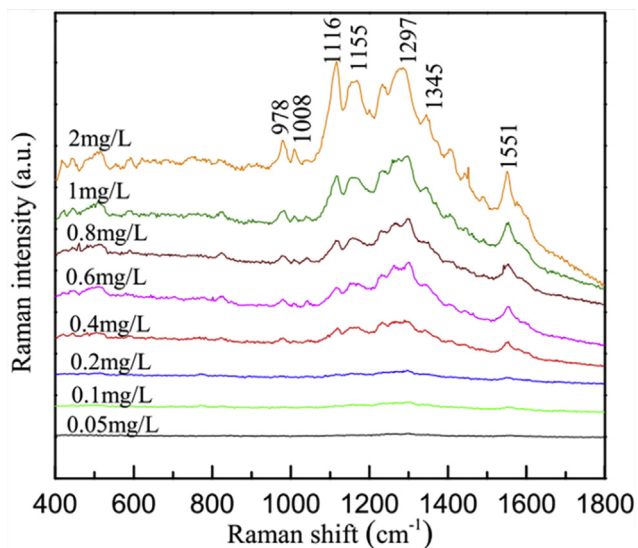


Fig. 7. Representative SERS spectra of Sudan black B standard solutions with different concentration. Reprinted from Ref. [103] with permission from the Elsevier, Copyright 2019.

nanoparticles and gold nanoclusters can also be used in immunofluorescence technology. For example, Peng *et al.* proposed a fluorescence immunoassay method combined with immunomagnetic separation [109]. In order to reduce the matrix effect, the author added immunomagnetic nanoparticles to the swine urine sample to separate the target substance immediately and effectively. Because it is loaded with Bovine serum albumin-gold nanoclusters (BSA-AuNCs) and artificial antigens, nanoflowers have the dual functions of fluorescence signal output and biological recognition. After adding this fluorescent-hybrid nanoflowers to the sample solution that has been magnetically separated, the fluorescence intensity of the supernatant obtained by magnetic separation is directly proportional to the concentration of clenbuterol. The assay has a linear response in the 0.5 ng/mL to 40 ng/mL clenbuterol concentration range, and 0.167 ng/mL limit of detection.

4.3. Melamine

Melamine, a triazine nitrogen-containing heterocyclic organic compound, has high nitrogen content of 66.67%. Since normal technique for evaluating the protein content in food is based on Kjeldahl method, in order to increase the tested protein content, this chemical has been added to milk by some unscrupulous merchants. However, excessive uptake of melamine induces serious health problems, such as kidney disease, chronic nephritis and bladder cancer. Then, the exploration of rapid, sensitive, and

accurate method for detecting melamine in food, especially in milk is essential to Human health.

In view of its amino-contained structure, melamine shows high binding affinity to metal, like gold and silver. And thus, much effort has been dedicated to develop metal nanoparticle-based system for melamine detection [110–114]. For example, Ren *et al.* developed a competitive melamine immunosensor based on branched polyethyleneimine functionalized rGO and Au NPs modified electrode [112]. In this report, the author first assembled the negatively charged sodium 3-mercaptopropionate sulfonate to the Au electrode through the Au–S bond. On this basis, the positively charged branched polyethyleneimine functionalized reduced graphene oxide (BPEIGn) (prepared by a one-step catalytic reaction) is absorbed on the electrode surface through electrostatic interaction. Then, because the surface of BPEIGn is filled with many amino groups and positive charges, the negatively charged AuNPs are fixed on the electrode through covalent interaction and electrostatic adsorption. Subsequently, melamine is attached to the electrode surface by forming hydrogen bonds with polyethyleneimine. The flexible structure of branched polyethyleneimine and its abundant amino groups can enhance its interaction with melamine. Finally, using bovine serum albumin (BSA) to block non-specific absorption sites to obtain a melamine immunosensor modified electrode. It is precisely because of the principle of specific binding between antigen and antibody and the double amplification of BPEIGn and AuNPs that this sensor has excellent specificity and sensitivity. Therefore, using $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ solution as the working electrolyte, they achieved melamine analysis in the concentration range of 1×10^{-6} to $1 \mu M$, with a LOD of $2.66 \times 10^{-7} \mu M$.

Nie *et al.* proposed a bowl-like pore array that consists of hollow Au/Ag alloy nanoparticles, acting as hot-spots [111]. The designed bowl-like pore array showed high SERS activity toward melamine. Through the finite-difference time-domain simulations, the SERS enhancement mechanism was attributed to the surface plasmon resonance of alloy nanoparticles. The Raman shift 681 cm^{-1} that originates from the in-plane deformation modes of triazine ring was used as the reporting signal. The intensity of signal increased upon increasing melamine concentration from 1 nM to $10 \mu M$. To prove the practical application of this method, milk samples spiked with melamine was investigated. According to the results, melamine in milk could be detected as low as 0.1 ppm, which is 10 times lower

Table 3. Summary of detection methods toward illegal food additives.

#	Materials	Strategy	Target analytes	Linear range	LOD	Ref.
1	La ³⁺ -doped Co ₃ O ₄ nanocubes/SPE	electroanalysis	Sudan I	0.3–300.0 μ M	0.05 μ M	[100]
2	ZnO NPs/CPE	electroanalysis	Sudan III	0.05–15.0 μ M	0.00254 μ M	[101]
3	AuNPs	SERS	Sudan black B	0.05–2 μ g/mL	0.05 μ g/mL	[103]
4	sulfur and nitrogen doped carbon quantum dots	immunofluorescent	clenbuterol	0.07–1.7 ng/mL	23 pg/mL	[105]
5	polyoxometalate and ZrO ₂ nanocomposites hybrids material/GCE	electroanalysis	clenbuterol	0.1–1000 μ M	5.03×10^{-3} μ M	[106]
6	graphene oxide/gold nanocomposites	SERS	ractopamine	3.0–50 μ M	0.93 μ M	[107]
7	barium sulfate-coated CsPbBr ₃ perovskite nanocrystals	fluorescence	clenbuterol	0.05–1 μ M	3.34×10^{-2} μ M	[107]
			melamine	5.0–500.0 nM	0.42 nM	[110]
8	hollow Au/Ag alloy nanoparticles	SERS	melamine	0.001–10 μ M	0.001 μ M	[111]
9	branched polyethyleneimine functionalized reduced graphene oxide (BPEIGn)/AuNPs/Au	electroanalysis	melamine	1×10^{-6} –1 μ M	2.66×10^{-7} μ M	[112]
10	conjugated polymer nanoparticles (CPNs) and AuNPs	fluorescence resonance energy transfer (FRET)	melamine	0.1–1.5 μ M	0.0017 μ M	[114]

than the permission set by Food and Drug Administration (FDA).

Beyond electrochemical reactivity and SERS activity, Au NPs are also good fluorescence quenchers to organic and inorganic fluorophores. Using barium sulfate-coated CsPbBr₃ perovskite nanocrystals (CsPbBr₃ NCs@BaSO₄) as the fluorophore and Au NPs as the quencher, Li *et al.* reported a fluorescence turn-on method for the detection of melamine [110]. The approaching of Au NPs quenched the fluorescence from CsPbBr₃ NCs@BaSO₄ because of the intense electromagnetic local field around Au NP surface. Addition of melamine weakened the binding affinity between Au NPs and CsPbBr₃ NCs@BaSO₄, and subsequently enhanced the fluorescence. With use of this strategy, they realized sensitive melamine determination with a LOD of 0.42 nM. In addition, this method provided good stability toward melamine sensing with small relative standard deviation of 4.0%, and could be applied to the analysis of dairy product samples. Partial detection methods for illegal food additives were summarized in Table 3.

5. Conclusion and perspectives

In this review, we have displayed an overview on the recent progresses of nanomaterial-assisted food additives analysis based on optical and electrochemical techniques. The unique chemical and electrochemical properties of nanomaterial endow the sensitive detection of food additives including colorants, preservatives and illegal additives in food samples. These sensing systems usually show LODs at nM or μ M levels, which meet the permission of expected food additives set by FDA or EPA. With the combination of multiplex detection tactic and array-based sensing, a few examples accomplish the multiple targets analysis.

Although the present works achieve successful analysis of various food additives using nanomaterial-based optical and/or electrochemical systems, there are still some challenges need to be solved. First, the highly reactive surface of nanomaterials limits their use in complicated conditions. That is, some chemicals or substrates may have interference to the sensing of food additives. However, food extracts usually contain many compounds, including targets and potential interferents. To avoid the false results, an extra separation process might be helpful before analysis. Second, the design of food additives detection system with a universal strategy is lacking. For most systems, the sensing mechanisms are applicable for specific targets. Other food additives with diverse molecular

structures can not to be detected with similar systems. Thus, the exploration of a simple strategy for constructing versatile detection systems is appealing. In consideration of the molecular recognition nature, molecularly imprinted polymer technique may provide solution for this issue. By using different molecular templates, specific detection of various food additives with similar protocols is possible. Third, sole food additive is generally detected based on nanomaterial-assisted analysis. It is indicated in many works that food process is usually associated with different food additives. For example, colorants and preservatives exist at the same time. To further evaluate the food safety, the detection of multiple food additives from food samples needs to be finished in a single run/test. As mentioned above, electrochemical methods possess possibility to detect several food additives simultaneously through different voltammetric peaks. The overlap of adjacent voltammetric peaks may have negative effect. To realize multiple food additive analysis, array-based sensing might be a promising tool. There are several advantages to array-based sensing, including no demand of specific interaction, high-through, and wide signal input. In this case, to boost the analysis of multiple food additives, array-based detection with the combination of nanomaterials is worthy to be tried. With the assistance of microchip technology, portable analysis of multiple food additive with sensor array is also possible in near future.

Conflicts of interest

The authors declare no competing financial interest.

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