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Review

Metal–Organic Frameworks (MOFs) Based Analytical Techniques for Food Safety Evaluation

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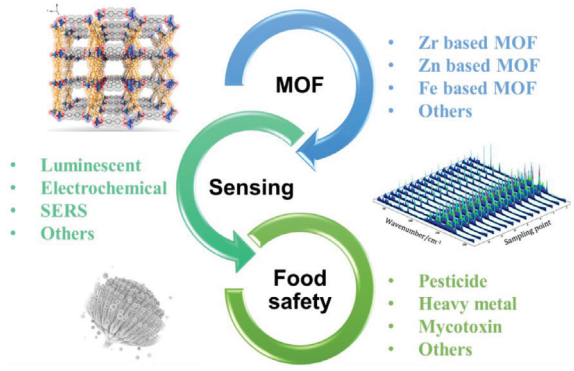
ABSTRACT

As the supply chain of food around the world has become more and more globalized and complicated, food safety issue has attracted considerable concern owing to the widespread pollution of the whole ecosystem and the extent of their impact on the well-being of human beings. Correspondingly, a variety of analysis approaches to detecting and even adsorbing contaminants in food have been extensively explored and investigated. Among them, Metal-Organic Frameworks (MOFs) as potential versatile sensing materials have been utilized in the construction of multitude of sensing platforms with excellent performance to monitor different pollutants of food, including pesticide residues, heavy metals, mycotoxins and so on. Herein, we briefly introduce the progress of the MOFs-based sensing techniques, and then present the typical contributions of representative sensing platforms in detection of pesticides, heavy metals and other contaminants. Finally, we evaluate and discuss the future perspectives and challenges of MOFs in food contaminant analysis.

GRAPHICAL ABSTRACT



1. INTRODUCTION

Food, both raw and produced, is an essential part of human life. The imbalanced distribution/supply of food across different regions and people's increasing demand of greater diversity of food have promoted the development of food supply chain dispersed all over the world [1]. In the meanwhile, food with multiple or specific functions have been manufactured and promoted as supplement to daily food [2,3]. Along with this complicated scenario has food safety issue emerged in recent years.

As summarized by the World Health Organization, more than 200 illnesses that people may suffer in the world are food-borne, which may lead to severe pains to long-term fatal diseases like cancers that could endanger everyone [4]. The significance of food safety has achieved increasing recognition through the policy and regulation making at both national and international levels, owing to its close linkage to the health and well-being of all the individuals [5]. On the one hand, in the current globalized economy, food supply chains inevitably go beyond the regional markets. Contamination of food by various sources at any point during food production, distribution

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and preparation may affect people across national borders [6–8]. On the other hand, the modern agriculture has been revolutionized by the development of biotechnology with large number of biochemical substances applied in the whole food supply chain from land to table. Among them, pesticide residues and heavy metals have attracted great attentions of all the stakeholders with consideration of the risks and hazards that may bring to the consumer. Pesticides are effective in eliminating insects and treating many plant diseases, their residues are notorious for severe damages to the respiratory system, nervous system, reproductive system and the immune system of human bodies and irreversible adverse effects on the bio-system [9,10]. Heavy metals as other pollutants have threatened food safety through water system. Due to their low degradability and notorious toxicity, research into sensing platforms of ultra-low level heavy metal ions is of great significance [11,12]. Also, Ochratoxin A (OTA) is a highly toxic mycotoxin prevalent in corn, beans, and a series of food related products, which may threaten human life [13,14]. Malachite green is another organic compound that has been illegally used excessively in agriculture as a fungicide [15,16]. Therefore, the urgent and upgraded demand of diagnosing, controlling and even removing pesticide residues, heavy metals and other contaminants (e.g. mycotoxin, malachite green, melamine) from fresh food or products has promoted the advancement of relevant technologies to control and ensure food safety.

In recent years, a variety of tailored Metal-Organic Frameworks (MOFs) have been constructed and used as the sensory materials for the establishment of facile and sensitive detection systems [17,18]. The versatility of MOFs have been observed in its application in detecting pesticide residues, heavy metals, and other toxic substances with high selectivity and accuracy in food and environmental samples [8,19]. Compared with the traditional analytical techniques based on liquid chromatography, gas chromatography or mass spectrometry requiring complex equipment and high-level technical personnel in food analysis, MOF-based sensing techniques might have shown great flexibility, convenience and potential for on-site detection [20–23]. This review will report typical novel MOFs-based sensing techniques for detecting contaminant residues in food and discuss its contributions to food safety by referring to specific application examples in recent 5-year studies.

2. VARIOUS TYPES OF MOFs

Recent studies have reported a variety of MOFs, many of which displayed excellent performance in accurate detection of diverse target pollutants with high selectivity, repeatability and short response time, which cater for the great demand of tailed sensors [19,24–26]. As composites constructed through incorporating specific metal ions/clusters with organic ligands/linkers, MOFs with uniform structures and high porosity possess chemical and physical merits of both inorganic and organic materials. Considering the multitude of the combinations of metal ions and organic ligands, it is important to understand the categories and classification of the MOFs used for food safety evaluation (Tables 1–3). The metal ions commonly seen in the MOFs applied in detection of food contaminants include zirconium, zinc, iron, europium, terbium and so on.

2.1. Zr-based MOFs

Zirconium-based MOFs (Zr-MOFs) constitute one of the major types of MOFs. A series of Zr-MOFs have been utilized and performed well in fluorescent sensing, analyte detection, as well as bio-imaging [27]. For instance, a functionalized MOF for determination of cadmium ion was initially fabricated by incorporating

Table 1 | List of MOF-based sensing techniques for pesticide detection

No	Pesticide	MOFs	Ligand	Sensing category	Limit of detection	Sample matrix	References
1	Parathion-methyl	Zr-MOF	H_4TCPB	Luminescence	0.438 nM (0.115 μg/kg)	Lettuce and cowpea	[45]
2	Parathion	$[Cd(atc)(H_2O)_2]_n$	atc	Electrochemical	0.1 ng/mL	Rice	[46]
3	Chlorpyrifos	$Tb(tftpa)_{1.5}(2,2'\text{-bpy})(H_2O)$	H_2tftpa	Fluorescence	0.14 ppb	ethanol	[47]
4	Parathion-methyl	ZnPO-MOF	H_4TCPB	Luminescence	0.456 nM (0.12 g/kg)	Irrigation water	[74]
5	2,6-Dichloro-4-nitroaniline (DCN)	$[Zn_2(bpdc)_2(BPyTPE)]$	BPyTPE and H_2bpdc	Fluorescence	0.13 ppm	–	[49]
6	DCN	$[Ag(CIP^-)]$	HCIP	Fluorescence	0.17 μM (~105 ppb)	–	[50]
7	DCN	$[[Cd(tptc)_{0.5}(bpz)(H_2O)]\cdot 0.5H_2O]_n$	H_4tptc and bpz	Luminescence	112 ppb	–	[37]
		$[Cd(tptc)_{0.5}(bpy)]_n$	H_4tptc and bpy		638 ppb		
8	2,6-Dichloro-4-nitroamine (2,6-Dich-4-NA)	$[Zn_3(DDB)(DPE)]\cdot H_2O$	H_5DDB and DPE	Fluorescence	0.27 μM (~166 ppb)	Carrot, grape and nectarine extracts	[51]
9	Thiram	Ag@ZIF-8	Hmim	SERS	0.1 μM	Apple	[52]
10	Thiram	Fe_3O_4-Au@MIL-100(Fe)	H_3BTC	SERS	15 nM	Water	[75]
11	Paraquat	$[Zn_2(cptpy)(btc)(H_2O)]_n$	Hcptpy and H_3BTC	Luminescence	9.73 μM	–	[31]
12	Atrazine	$Cu_2(BTC)_2$@SiO_2	H_3BTC	Electrochemical	0.01 nM	Water	[36]
13	Acetamiprid	AuNP/MOF-199	H_3BTC	SERS	0.02 μM	–	[76]
		AuNP/UiO-66	PTA, H_2BDC		0.009 μM		
		AuNP/UiO-67	H_2bpdc		0.02 μM		

H_4TCPB, 1,2,4,5-Tetrakis(4-carboxyphenyl) benzene; atc, 2-aminoterephthalic acid; BPyTPE, (E)-1,2-diphenyl-1,2-bis(4-(pyridin-4-yl)phenyl)ethene; H_2bpdc, 4,4′-biphenyldicarboxylic acid; H_5DDB, 3,5-di(2′,4′-dicarboxylphenyl)benzoic acid; DPE, 1,2-di(4-pyridyl)ethylene; HCIP, 4-(4-carboxylphenyl)-2,6-di(4-imidazol-1-yl)phenyl)pyridine); H_4tptc, *p*-terphenyl-2,2″,5″,5‴-tetracarboxylate acid; bpz, 2-(1*H*-pyrazol-3-yl)pyridine, bpy, 2,2′-bipyridine; H_3BTC, benzene-1,3,5-tricarboxylic acid; PTA, H_2BDC, terephthalic acid; H_2tftpa, tetrafluoroterephthalic acid; Hcptpy, 4-(4-carboxyphenyl)-2,2′:4′,4″-terpyridine; Hmim, 2-methylimidazole.

Table 2 | List of MOF-based sensing techniques for heavy metal detection

No	Heavy metal	MOFs	Ligand	Sensing category	Limit of detection	Sample	References
1	Hg^{2+}	$[Zn(OBA)\text{-}(DPT)_{0.5}]\cdot DMF$ (TMU-34(-2H))	H_2OBA and DPT	Luminescent	1.8 μM in water 6.9 μM in acetonitrile	Water	[55]
2	Hg^{2+} Pb^{2+}	$Zn_2(dbtdcO_2)_2(tppe)$ (LMOF-263)	$H_2dbtdcO_2$ and tppe	Luminescent	3.3 ppb 4.9 ppb	–	[56]
3	Hg^{2+}	ssDNA labeled UiO-66-NH_2	$H_2BDC\text{-}NH_2$	Luminescent	17.6 nM	–	[57]
4	Hg^{2+}	$Tb(TATAB)\cdot(DMF)_4(H_2O)(MeOH)_{0.5}$	H_3TATAB	Luminescent	4.4 nM	Natural water	[58]
5	Fe^{3+}	$UO_2(C_8H_3O_6N)\cdot DMF$	H_2L	Luminescent	6.3 ppb	–	[60]
6	Fe^{3+} Cr^{3+}	$[[Eu_2(pdba)_3(H_2O)_3]\cdot 2H_2O]_n$ $[[Eu_3(pdba)_4(H_2O)_4]\cdot 5H_2O]_n$	H_2pdba	Luminescent	1.0 μM	–	[34]
7	Fe^{3+}	$[Zr_6O_4(OH)_8(H_2O)_4(L^1)_2]$ (BUT-14) $[Zr_6O_4(OH)_8(H_2O)_4(L^2)_2]$ (BUT-15)	H_4L^1 H_4L^2	Luminescent	3.79 μM (212 ppb) 0.286 μM (16 ppb)	–	[61]
8	Fe^{3+}	$[Zr_6O_4(OH)_4(C_8H_2O_4S_2)_6]\cdot DMF\cdot 18H_2O$ $[Zr_6O_4(OH)_4(C_{10}H_6O_4S_2)_6]\cdot 4.8DMF\cdot 10H_2O$ $[Zr_6O_4(OH)_4(C_{15}H_8O_4S_2)_6]\cdot 4DMF\cdot 21H_2O$ $[Zr_6O_4(OH)_4(C_{20}H_{10}O_4S_2)_6]\cdot 2.5DMF\cdot 11H_2O$	H_2TDC H_2DMTDC H_2MPTDC H_2DPTDC	Luminescent	1.26 μM 0.86 μM 0.93 μM 0.34 μM	–	[77]
9	CrO_4^{2-} and $HCrO_4^-$	$[Eu_7(mtb)_5(H_2O)_{16}]\cdot NO_3\cdot 8DMA\cdot 18H_2O$ Eu-MOF	H_4mtb	Luminescent	0.56 ppb 2.88 ppb 1.75 ppb	Deionized water lake water seawater	[63]
10	$Cr_2O_7^{2-}$	$[Cd(TIPA)_2(ClO^{4-})_2]\cdot(DMF)3(H_2O)$	TIPA	Luminescent	8 ppb	–	[64]
11	Cd^{2+}	UiO-66-NH_2@ PANI	$H_2BDC\text{-}NH_2$	Electrochemical	0.3 μg/L	Lake water, tap water, saliva and urine	[29]
12	Cd^{2+}	Eu^{3+}@UiO-66(Zr)–$(COOH)_2$	H_4btec	Luminescent	0.06 μM	Tap water and lake water	[28]
13	Pb^{2+}	$(Fe\text{-}P)_n$-MOF-Au-GR	Tmpp	Electrochemical	0.02 nM	Water, fruit juice and solid samples	[78]
14	Cu^{2+}	BPEI-CQDs/ZIF-8 composite	Hmim	Luminescent	80 pM	River water	[30]
15	Bi^{3+}	$[Al_8(OH)_4(OCH_3)_8(BDC(OH)_2)_6]\cdot x\ H_2O$ (CAU-1-$(OH)_2$)	$H_2BDC(OH)_2$	Luminescent	2.16 μM	Water	[79]
16	Co^{2+}	$[[Cd_{1.5}(TPO)(bipy)_{1.5}]\cdot 3H_2O]_{2n}$	H_3TPO	Luminescent	0.31 μM	–	[80]
17	UO_2^{2+}	$[Tb(BPDC)_2]\cdot(CH_3)_2NH_2$ (DUT-101)	H_2bpdc	Luminescent	8.34 μg/L	Water	[35]

H_2OBA, 4,4′-oxybis(benzoic acid); DPT, 3,6-di(pyridin-4-yl)-1,2,4,5-tetrazine; H_3TATAB, 4,4′,4″-*s*-triazine-1,3,5-triyltri-*p*-aminobenzoic acid; $H_2dbtdcO_2$, dibenzo[*b*,*d*]thiophene-3,7-dicarboxylic acid-5,5-dioxide; Tppe, 1,1,2,2-tetrakis(4-(pyridin-4-yl)phenyl)ethane; $H_2BDC\text{-}NH_2$, 2-aminoterephthalic acid; H_4mtb, 4-[tris(4-carboxyphenyl)methyl]benzoic acid; PANI, polyaniline; H_4btec, 1,2,4,5-benzenetetracarboxylic acid; Tmpp, (5,10,15,20-tetrakis(4-methoxyphenyl)porphyrinate); H_2L, 9*H*-carbazole2,7-dicarboxylic acid; H_2pdba, 4′-(1*H*-pyrazol-3-yl)-[1,1′-biphenyl]-3,5-dicarboxylic acid; H_2TDC, thieno[2,3-*b*]thiophene-2,5-dicarboxylic acid; H_2DMTDC, 3,4-dimethylthieno[2,3-*b*]thiophene-2,5-dicarboxylicacid; H_2MPTDC, 3-methyl-4-phenylthieno[2,3-*b*]thiophene-2,5-dicarboxylic acid; H_2DPTDC, 3,4-diphenylthieno[2,3-*b*]thiophene-2,5-dicarboxylic acid; H_4L^1, 5′,5‴-bis(4-carboxyphenyl)-[1,1′:3′,1″:3″,1‴:3‴,1⁗-quinquephenyl]-4,4⁗-dicarboxylic acid; H_4L^2, 4,4′,4″,4‴-(4,4′-(1,4-phenylene)bis(pyridine-6,4,2-triyl))-tetrabenzoic acid; TIPA, tri(4-imidazolylphenyl) amine; $H_2BDC(OH)_2$, 2,5-dihydroxyterephthalic acid; H_3TPO, tris(paracarboxylphenyl) phosphine oxide.

Table 3 | List of MOF-based sensing techniques for other contaminants detection

No	Target analytes	MOFs	Ligand	Sensing category	Limit of detection	Sample matrix	References
1	Aflatoxin B_1	$Zn_2(bpdc)_2(tppe)$ (LMOF-241)	Tppe and H_2bpdc	Luminescent	46 ppb	–	[69]
2	Ochratoxin A	Fe_3O_4/g-C_3N_4/HKUST-1	H_3BTC	Luminescent	2.57 ng/mL	Corn	[70]
3	Melamine	$[Zn_8(ad)_4(BPDC)_6O\cdot 2Me_2NH_2$, 8DMF, $11H_2O]$	H_2bpdc	Electrochemiluminescent	0.038 nM	Milk and infant formula powder	[73]
4	Methenamine	Au@MIL-101	H_2BDC, PTA	SERS	0.5 nM	Vermicelli	[32]
5	Malachite Green	Fe_3O_4-Au@MIL-100(Fe)	H_3BTC	SERS	4.4 nM	Water	[75]
6	Malachite Green	Au@MIL-100(Fe)	H_3BTC	SERS	8 nM	Fish	[33]

Eu^{3+} into the UiO-66(Zr)–$(COOH)_2$ [28]. This MOF demonstrated excellent fluorescence response toward various concentrations of Cd^{2+} with high fluorescence intensity in aqueous solutions. The Limit of Detection (LOD) of this MOF was found to be as low as 0.06 μM. In the preparation of conductive electrochemical sensor, another Zr-based MOF UiO-66-NH_2 was coated by the polymer Polyaniline (PANI) with high conductivity [29]. The modified electrode UiO-66-NH_2@PANI with a core/shell structure showed high sensitivity and selectivity in the detection of trace cadmium ions with LOD at 0.3 μg/L.

2.2. Zn-based MOFs

Another major type of novel MOFs is Zinc-based MOFs (Zn-MOFs). Among them, Zeolitic imidazolate framework (ZIF-8) MOFs are very common in the synthesis of different sensing electrodes. These zeolitic imidazole-based MOFs possess the advantages of MOFs (i.e., high porosity and surface area, transition metal centers, and tailored linkers) with high stability, chemical robustness, and framework diversity. An as-prepared fluorescent (FL)-functionalized MOFs [i.e., branched poly-(ethylenimine)-capped carbon quantum dots (BPEI-CQDs)/ZIF-8] was fabricated by encapsulating a highly fluorescent amine-capped carbon-based quantum dots into ZIF-8 MOFs [30]. These composites have been tested to be excellent sensors of Copper ions with their outstanding sensitivity and selectivity, with a very low detection limit of 80 pM. Another good example is a 3D-structured MOF obtained by assembling d^{10}-electronic-configuration Zn^{2+} ions with two trigonal ligands an elongated terpyridine-carboxylic acid ligand, 4-(4-carboxyphenyl)-2,2′:4′,4″-terpyridine (Hcptpy), and an auxiliary ligand, 1,3,5-benzenetricarboxylic acid (H_3BTC) [31]. This MOF has been found to be highly selective and sensitive in the detection of paraquat in aqueous solution.

2.3. Fe-based MOFs

Iron-based MOFs (Fe-based MOFs) have been utilized for the establishment of MOF-based Surface-enhanced Raman scattering (SERS) assays, and applied in the analysis of different food contaminants, especially the small molecular environmental pollutants. In recent studies, the core-shell structures with Au Nanoparticle (AuNP) core and Fe-based MOFs [e.g. MIL-100 (Fe), MIL-101 (Fe)] have been established in the SERS sensing platforms for the detection of residual methenamine [32] and malachite green [33].

2.4. Other Metal-based MOFs

There are also other metal ions utilized in the construction of functional MOFs. Lanthanide-based MOFs (i.e. Eu^{3+} and Tb^{3+}) demonstrated their great merits as sensing materials owing to the electron transitions of Ln (III) ions. Two Europium-based MOFs (Eu-MOFs) were reported to have fascinating selectivity toward Fe^{3+} and Cr^{3+} with their excellent luminescence performance and high stability in water [34]. Another terbium MOF showed high selectivity and sensitivity toward mercury ions in aqueous solution [35]. Furthermore, calcium-, copper- and other metal-based MOF were successfully developed for the detection of pesticide, heavy metal, mycotoxin and related contaminants in real samples [36–38].

3. APPLICATIONS IN FOOD CONTAMINANT ANALYSIS

3.1. Pesticide Residues

3.1.1. Detection of OPPs

Organophosphorus Pesticides (OPPs) are the major type of pesticides used worldwide with their efficiency in improving the yield of the modern agriculture [39]. Consequently, the widespread or even excessive use has led to pesticide poisoning accidents and accumulated residues in soil, ground water and food that are essential to human beings [40]. Therefore, there is an urgent need to develop facile and reliable analytical methods of detecting OPP residues for the food safety and human health [41–44]. To detect trace amount of OPPs in real food and environmental samples, a facile and low-cost Zr-MOF was established [45]. This 3D rod-like luminescence probe with strong hydro-stability, photostability and thermal stability in aqueous solutions was synthesized through the solvothermal method by using Zr (IV) and 1,2,4,5-tetrakis (4-carboxyphenyl) benzene (H_4TCPB). This Zr-MOF presents excellent selectivity toward parathion-methyl due to its intrinsic advantage of exceptionally strong adsorption ability. Its luminescence quenching response toward parathion-methyl was plausibly owing to the photoexcited transfer. In the test of real food samples (lettuce and cowpea), this zirconium-luminescent MOF (Zr-LMOF) performed high selectivity toward parathion-methyl with a low LOD of 0.438 nM (Figure 1A). In another pesticide sensing platform established based on a nano-MOF mainly for detection of parathion, 2-Aminobenzylamine (2-ABA) modified on indium tin oxide was selected as the solid ligand for the synthesis of this MOF formulated as $[Cd(atc)(H_2O)_2]_n$. This MOF showed excellent performance in detecting parathion in a rice sample with a LOD as low as 0.1 ng/mL [46]. Lanthanide-based MOF (Ln-MOF) probe were prepared by using tetrafluoroterephthalic acid (H_2tftpa) as the organic ligand for the detection of chlorpyrifos and Di-*n*-butyl phthalate (DBP) for the first time. This luminescence sensor displayed high sensitivity toward chlorpyrifos in ethanol and DBP in seawater with the detection limits of 0.14 and 2.07 ppb, respectively [47].

3.1.2. Detection of 2,6-dichloro-4-nitroaniline

2,6-Dichloro-4-Nitroaniline (DCN) as a typical organochlorine pesticide with extremely high toxicity. Its poor degradability leads to long-term pollution of the environmental surroundings and food produced consequently [48]. Although there have been many common analytical methods used in the DCN detection, most of them have rigid requirements in finance and manpower. Therefore, to detect low concentration of DCN in agricultural products with facial and low-cost methods, a novel and reversible sensing strategy was established with a new synthesized luminescent MOF in the pillar-layer-interpenetration structure $[Zn_2(bpdc)_2(BPyTPE)]$ (Figure 1B). This composite with satisfactory aggregation-induced emission characteristics exhibits exceptionally high quantum yield of 99%. This MOF has been proved to be remarkably selective toward nitroaniline and consequently sensitive in detecting trace residues of DCN with a linear range of 0.95–16.92 ppm and a low detection limit of 0.13 ppm [49]. Another luminescent sensor for detecting DCN was an Ag-based MOF synthesized through the solvothermal method by utilizing the multifunctional solid ligand 4-(4-carboxylphenyl)-2,6-di(4-imidazol-1-yl)phenyl)pyridine). The MOF formulated as $[Ag(CIP^-)]$ demonstrated high selectivity and sensitivity toward DCN with a low LOD (0.17 μM, ~105 ppb) based on its strong luminescence quenching effect [50]. Using *p*-terphenyl-2,2″,5″,5‴-tetracarboxylate acid as the ligand,

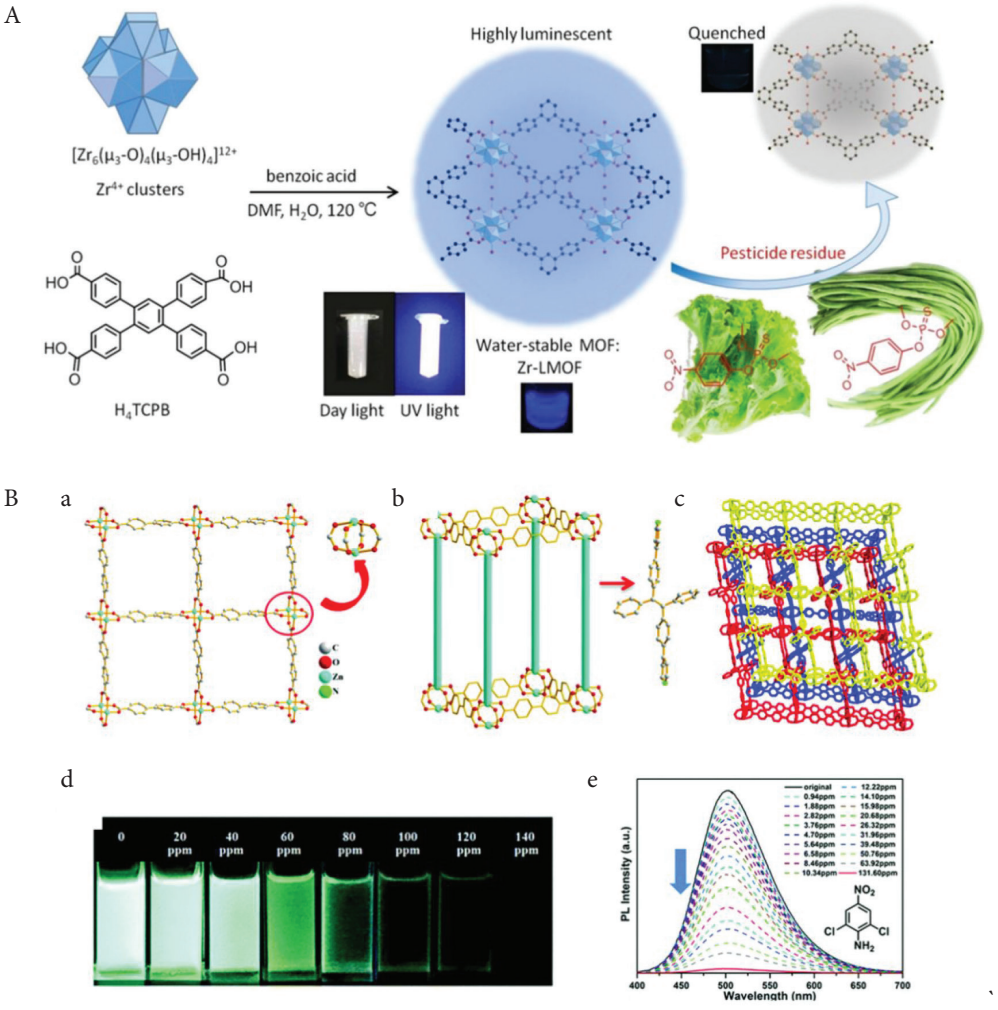

Figure 1 | (A) Schematic diagram for synthesis of water-Stable Zr-LMOF and its application for organophosphorus pesticide sensing. (B) Topological representation of rhombic 4^4 two-dimensional paddle-wheel layer with an indicated structure of paddle-wheel secondary building unit $[Zn_2(COO)_4]$ (a); Single net of $[Zn_2(bpdc)_2(BPyTPE)]$ viewed along the *a*-axis (b); The overall crystal structure demonstrating the threefold interpenetration and 1D pore running along the *b*-axis (c); Fluorescence photos of $[Zn_2(bpdc)_2(BPyTPE)]$ in suspensions with gradually increased 2,6-Dichloro-4-nitroaniline (DCN) (d); Fluorescence titration of $[Zn_2(bpdc)_2(BPyTPE)]$ in a dichloromethane suspension of DCN with different concentrations (λ_{ex} = 365 nm).

Fan et al. [37] reported to develop the first cadmium (II)-based MOFs for detection of DCN and Cr (VI) anions simultaneously. In particular, both of the crystalline compounds, i.e. $[[Cd(tptc)_{0.5}(bpz)(H_2O)]\cdot 0.5H_2O]_n$ (1), and $[Cd(tptc)_{0.5}(bpy)]_n$ (2), could sensitively identify DCN with LOD being 112 and 638 ppb respectively. As a multifunctional luminescence probe, this MOF could detect CrO_4^{2-}, $Cr_2O_7^{2-}$ and nitrofurantoin simultaneously. Further, a 3D-structured Zn-based MOF with excellent sensing performance was reported toward 2,6-dichloro-4-nitroamine, Cr (III/VI), Fe (III) and Mn (VII) in aqueous solution [51]. There are six nuclear clusters in this crystalline composite, $[Zn_3(DDB)(DPE)]\cdot H_2O$ (1), which is bridged by DPE and H_5DDB ligands. The nature of this structure results in predominant stability of this composite in water and acid. Its high quenching efficiency was possibly attributed to the competition for adsorption between MOF and analyte, electron molecular internal energy transfer, and photoexcited transfer as well. As the first multi-responsive luminescence-based sensor, this MOF material qualifies to be an ideal sensory material in detection of DCN in real carrots, grapes and nectarine extracts samples (LOD, 0.27 μM).

3.1.3. Detection of other pesticides

Recently, necklace-like Ag@ZIF-8 core/shell heterostructure nanowires were established for the pesticide detection, the synthesis process of which only requires two major steps [52]. This heterostructure substrate exhibited exceptionally high SERS enrichment factor up to 4.2×10^7 for crystal violet molecules, which could remain stable for almost 2 months. Moreover, this substrate displays high sensitivity toward thiram with difference concentrations in trace amount on apple peels (LOD, 0.1 μM). For nitrogen heterocycles detection, a 3D luminescent MOF with the formula $[Zn_2(cptpy)(btc)(H_2O)]_n$ was synthesized by incorporating two ligands Hcptpy and H_3BTC with Zn (II) for detecting Paraquat in aqueous solutions (Figure 2) [31]. This compound with (3,3,4,4)-connected topology showed strong stability in air and water. An excellent luminescence quenching response was observed with a very low LOD value at 9.73 μM, which was probably owing to interactions and energy transfer between the composite and the analytes. And the good reusability of this luminescence probe qualifies it to be a desirable candidate as a fluorescent chemical sensor.

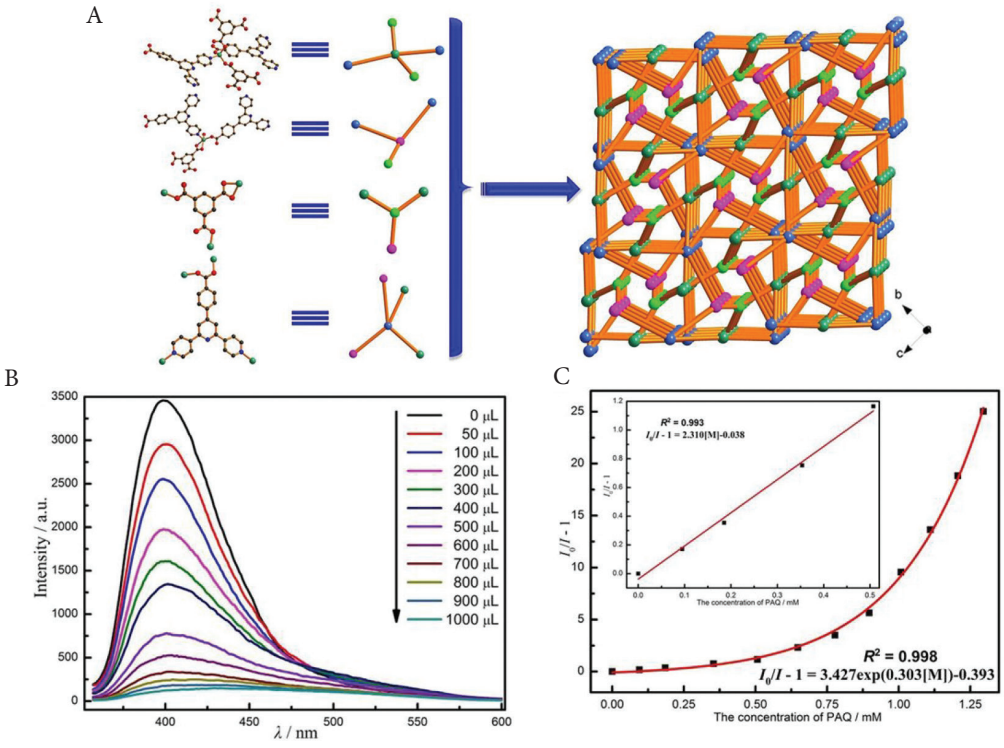

Figure 2 | (A) Schematic representation of the (3,3,4,4)-connected topology in $[Zn_2(cptpy)(btc)(H_2O)]_n$; (B) Concentration-dependent emission spectra of probe in the presence of paraquat (λ_{ex} = 340 nm); (C) Fitting curve for a nonlinear Stern–Volmer plot. Schematic illustration of the formation process of Ag@ZIF-8 nanowires and SERS detection.

More interestingly, one thins films $Cu_3(BTC)_2$@SiO_2/BDC-PANI were synthesized by coating $Cu_3(BTC)_2$@SiO_2 on organic ligand H_3BTC (98%). These thin films were then utilized in the assembly of the conductometric sensing platform for detection of atrazine. This electrochemical immunosensor showed high sensitivity with a LOD as low as 0.01 nM in aqueous solution [36].

3.2. Detection of Heavy Metals

3.2.1. Mercury

Because mercury is of extreme toxicity and high solubility in water, very low level of concentration of mercury ions in the ground water system will undeniably cause fatal and long-lasting risks to the human life and the environment [53,54], considerate attention in relevant studies have been attracted to develop facile, instant and low-cost sensing approaches to detect and even remove this widespread heavy metal at very low concentrations. A Zn-based MOF formulated as $[Zn(OBA)\text{-}(DPT)_{0.5}]\cdot DMF$ (TMU-34(-2H)) was synthesized through the photoluminescence method by utilizing 4,4′-oxybis(benzoic acid) as the organic ligand and 3,6-di(pyridin-4-yl)-1,2,4,5-tetrazine as the spacer. Its exceptionally sensitive and accurate detection (LOD in water: 1.8 μM; LOD in acetonitrile: 6.9 μM) within short response time (15 s) toward Hg^{2+} could be attributed to both the different signal transductions of the tetrazine-functionalized motifs and the double solvent sensing method used [55]. A series of facile Zn-based LMOFs, i.e. $Zn_2(ofdc)_2(tppe)$ (LMOF-261), $Zn_2(hfdc)_2(tppe)$ (LMOF-262), $Zn_2(dbtdcO_2)_2(tppe)$ (LMOF-263) were established by Rudd et al. [56] to work as both sensor and adsorbent of Hg^{2+} from aqueous solutions (Figure 3A–3C). The Powder X-ray diffraction (PXRD) pattern results confirm their similar isoreticular structures. The needle-shaped crystalline composite LMOF-263 was solvothermal synthesized by incorporating a tppe chromophore ligand and a sulfone-functionalized co-ligand dibenzo[*b*,*d*]thiophene-3,7-dicarboxylic acid 5,5-dioxide. Its intrinsic stability toward water and high fluorescence quantum yield (89.2%) qualifies it as a desirable sensory material (Figure 3E). The LMOF-263 exhibited high sensitivity and selectivity toward Hg^{2+} with satisfactory quenching efficiency at very low concentration (3.3 ppb). Furthermore, it performed remarkably in selectively capturing and removing the Hg^{2+} from water within 30 min. The sulfur and oxgen in the LMOF plays a key role in the interactions between Hg^{2+} and the sulfone moiety (Figure 3F). This sensing strategy provides a practical remediation alternative to solve environmental crisis. Another novel biosensing platform for detection for mercury ions was developed by using the combination of the MOF UiO-66-NH_2 and a T-rich FAM-labeled ssDNA [57]. This hybrid system utilizing T–Hg^{2+}–T specific interactions for Hg^{2+} assay exhibited excellent sensing performance with a low LOD at 17.6 nM. In addition, due to the high affinity of mercury ions to nitrogen atoms, 4,4′,4″-*s*-triazine-1,3,5-triyltri-*p*-aminobenzoic acid was also utilized as the organic ligand for the synthesis of terbium-based MOFs for sensitive luminescent sensing of mercury ions in aqueous solutions. Its detection limit was as low as 4.4 nM in natural water [58].

3.2.2. Iron

Iron is a widespread heavy metal contaminant in water. Due to the hazards it may cause to human health, the recommended permit limit of Fe in drinking water is as low as 0.3 ppm [59]. Several

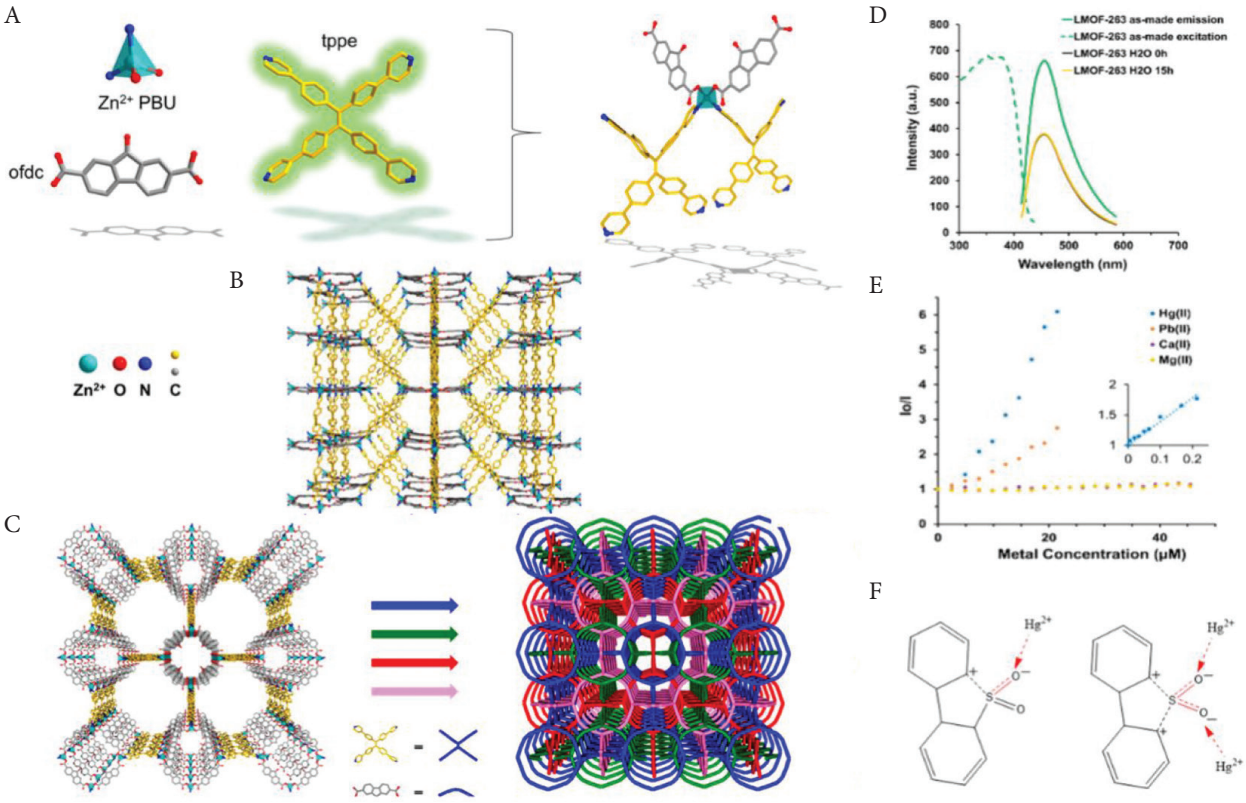

Figure 3 | (A) The primary building unit of LMOF-261, depicting a pseudotetrahedrally coordinated Zn center bound to two tppe ligands and two ofdc linkers; (B) An individual net of the LMOF-261 framework viewed along the *b*-axis; (C) The same net depicted down the *c*-axis and simplified LMOF-261 depicting fourfold interpenetration; (D) LMOF-263 optical emission in the solid-state and as a suspension in water; (E) Stern–Volmer curves (λ_{ex} = 365 nm) for metal ions (inset, Hg^{2+} detection at low concentrations); (F) Interaction mechanism of Hg^{2+} with the sulfone functional group.

fluorescence-based MOFs have been constructed for the detection of Fe^{3+} ions by overcoming challenges caused by the low water stability of iron. A depleted uranium-based MOF, $UO_2(C_8H_3O_6N)\cdot DMF$ was produced for the first time [60]. This compound was synthesized through solvothermal reactions to possess remarkable stability in aqueous media. This compound exhibits excellent selectivity toward iron ions (LOD 6.3 ppb) even with the interference of other ions. The luminescence quenching response of this composite was probably due to the competitive adsorption between Fe^{3+} and fluorescence probe. The nature of high selectivity and sensitivity of this sensory material made it promising for heavy metal detection. Two different water-stable Eu-MOF fluorescent sensors formulated as $[[Eu_2(pdba)_3(H_2O)_3]\cdot 2H_2O]_n$ (1) and $[[Eu_3(pdba)_4(H_2O)_4]\cdot 5H_2O]_n$ (2) were designed for detection of Fe^{3+} as well as Cr^{3+} in real environmental conditions [34]. The precursor compound terephthalic acid at different concentration was utilized in the synthesis of the sensing materials. To detect Fe^{3+} in aqueous solutions with powerful sensitivity and strong water stability, two Zr (IV)-based MOFs BUT-14 and BUT-15 were established with two similar ligands (i.e. H_4L^1 and H_4L^2) with minor difference in the functionalization. Between the two, BUT-15 demonstrated great repeatability and sensitivity (LOD 0.286 μM) with stable fluorescent quenching efficiency [61].

3.2.3. Chromate

The extensive chromate wastes have brought threats to the environment and subsequent hazards to human well-being [62]. MOFs have also been developed to detect the chromate anions in the natural water systems so as to purify water [63,64]. An Eu (III)-based luminescent MOF $[Eu_7(mtb)_5(H_2O)_{16}]\cdot NO_3\cdot 8DMA\cdot 18H_2O$ was constructed with a 3D structure for the detection of chromate anions in aqueous solutions [63]. Its outstanding sensing performance under real environments has been verified in the detection of chromate in deionized water, natural lake water and seawater. In the luminescence and analytical experiments, the detection limits reached as remarkably low as 0.56, 2.88 and 1.75 ppb in the three different types of environmental water respectively (Figure 4). A highly stable luminescent porous cationic framework $[Cd(TIPA)_2(ClO^{4-})_2]\cdot(DMF)3(H_2O)$ was synthesized with a 2D layer. These structures were further constructed 3D structure through parallel packing, which exhibited high sensitivity and selectivity against $Cr_2O_7^{2-}$ in aqueous solutions. Remarkably, the detection limit was as low as 8 ppb [64].

3.2.4. Other metal ions

Similarly, Cd^{2+}, Pb^{2+}, Co^{2+} and other ions were also detected by using MOF based sensing techniques (Table 2) [29,65,66]. For instance, a highly sensitive conductive electrochemical sensor for detecting cadmium ions was constructed by coating the UiO-66-NH_2 with the conductive PANI polymer. The excellent analytical performance of the core-shell structure UiO-66-NH_2@PANI could be attributed to the chelation mechanism between Cd^{2+} and amine groups on the electrode. Even with the presence of other ions, this modified electrode still displayed high sensitivity toward

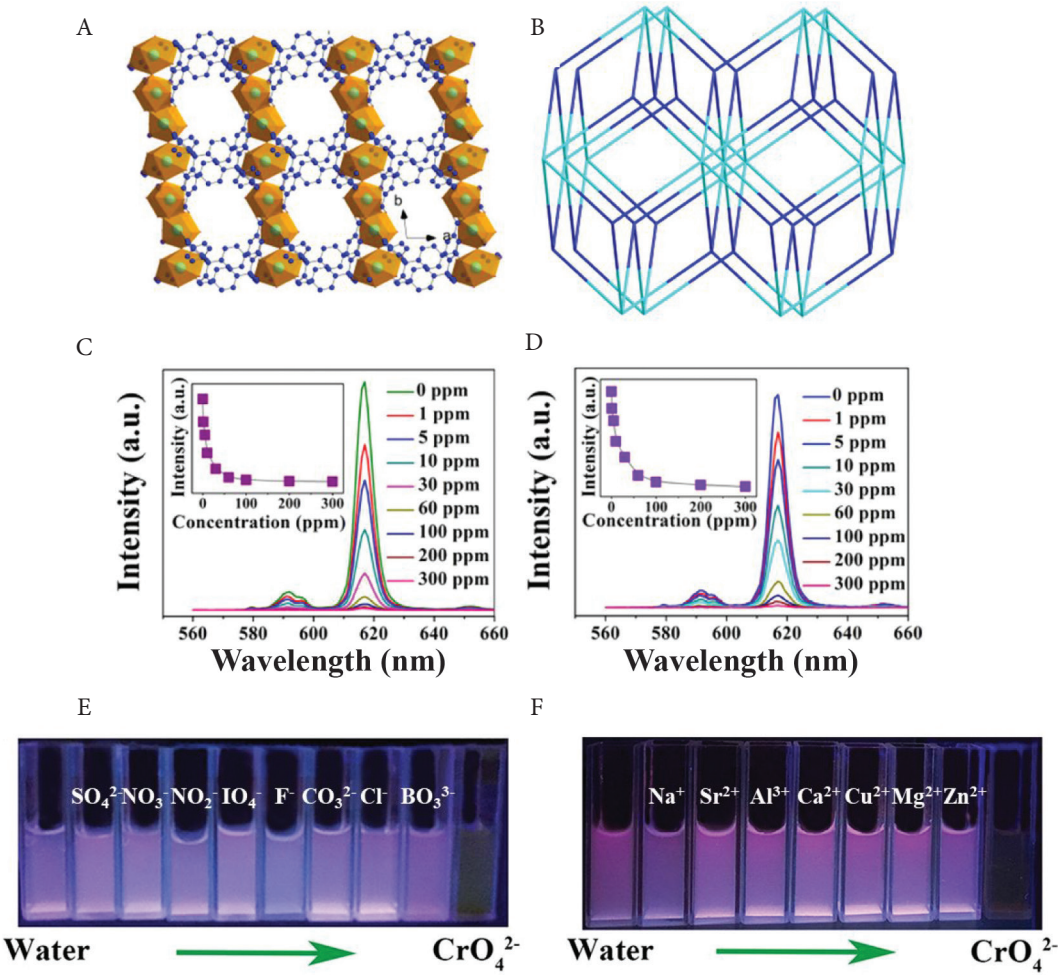

Figure 4 | (A) Three-dimensional (3D) network structure viewed along the *c*-axis of Eu-MOF. (B) Its topological structure to show the (4,8)-connected 3D framework. PL spectra of Eu-MOF in Dushu Lake water (C) and seawater (D), respectively, with a wide range of chromium concentrations. Inset showing the quenching process. Corresponding luminescence photograph of Eu-MOF immersed in different anion (E) or cation (F) solutions (excited at 365 nm).

trace amount of Cd^{2+} ions with LOD as low as 0.3 μg/L with a wider linear range from 0.5 to 600 μg/L and higher stability. Moreover, $[Tb(BPDC)_2]\cdot(CH_3)_2NH_2$ (DUT-101) as one kind of Tb-based MOFs with desirable stability in a 3D dual-channel structure was designed [35]. DUT-101 demonstrated high selectivity and sensitivity toward trace amount of UO_2^{2+} ions even in the mixture with different metal ions. The plausible sensing mechanism of this proposed strategy was the combination of the inhibition of fluorescence energy transfer and the improvement of electron molecular internal transition. Additionally, naked eye green fluorescent test papers were fabricated from this MOF, which could be used to detect UO_2^{2+} ions in drinking water with short response time.

3.3. Detection of Other Contaminants

There are many other contaminants that bring risks to food safety and human health, including environmental organic contaminants, mycotoxins among many others [67,68]. Here we selected a few representatives for a brief introduction (Table 3).

For mycotoxin detection, a rapid and selective sensing strategy at the ppb level was established by Hu et al. [69] (Figure 5). In the synthesis of this luminescent MOF, 1,1,2,2-tetrakis(4-(pyridin-4-yl)phenyl) ethane (tppe) and 4,4′-biphenyldicarboxylic acid were chosen to work as the ligands. The topological analysis of the LMOF-241 revealed its three-fold interpenetration without common symmetry operations (Figure 5D). Zn^{2+} ion selected ensured the strong ligand-based emission, which makes LMOF-241 an ideal sensory material. Probably owing to the electron transfer mechanism, this LMOF exhibits intense blue-green emission with desirable quantum yield at 92.7% (Figure 5F). And the tppe molecule as a strong fluorophore makes the selective emission quenching possible. With its intrinsic advantages of sensitivity and selectivity toward Aflatoxin B_1 (AFB_1), a detection method through luminescence quenching was developed with a detection limit as low as 46 ppb for sensing AFB_1 in aqueous solutions.

Hu et al. [70] also fabricated an easy and fast sensing material Fe_3O_4/g-C_3N_4/Hong Kong University of Science and Technology (HKUST-1) composite for OTA detection in corn sample. This as-synthesized polymer was obtained by linking Fe_3O_4 and g-C_3N_4 to the surface of HKUST-1 networks. HKUST-1 was selected to combine with the 2D structured g-C_3N_4 so as to inhibit the hydrophobicity and completely quench the fluorescence of the 5-carboxyfluorescein dye through photoinduced electron transfer.

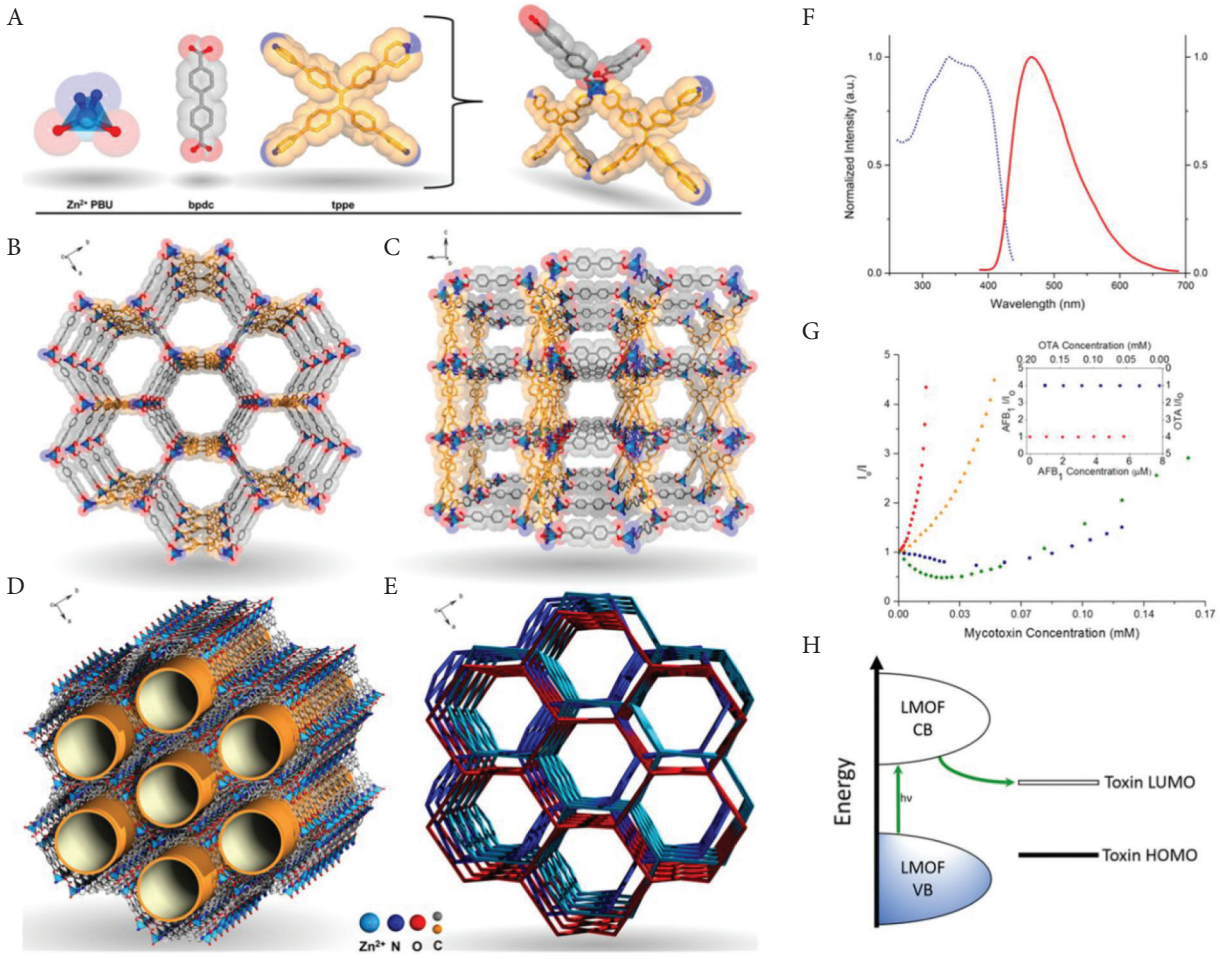

Figure 5 (A) Primary building unit of LMOF-241, showcasing a tetrahedrally coordinated Zn center bound to two tppe molecules and two bpdc molecules; (B) Single net of LMOF-241 framework viewed along the *c*-axis; (C) Single net of LMOF-241 framework viewed along the *b*-axis; (D) Overall crystal structure demonstrating the threefold interpenetration and 1D pore running along the *c*-axis; (E) LMOF-241 drawn as two-nodal (4,4)-c net (mog-type), with tppe and bpdc simplified as a 4-c node and 2-c node, respectively; (F) Excitation (dotted blue) and emission (solid red, λ_{ex} = 340 nm) spectra of LMOF-241 suspended in dichloromethane; (G) Stern–Volmer curves acquired at λ_{ex} = 340 nm and λ_{ex} = 410 nm (inset) for AFB_1 (red dot), AFB_2 (orange triangle), AFG_1 (green diamond), and OTA (blue square); (H) Schematic demonstrating electron transfer from LMOF-241 to mycotoxin LUMO, resulting in quenched emission.

Subsequently, the excellent performance of this sensing platform toward OTA was owing to the fluorescence enhancement. The detection limit of this sensory strategy was found to be as low as 2.57 ng/mL in real corn samples.

Melamine is another very common contaminant of food owing to its high nitrogen content [38,71,72]. In a recent study, a functionalized electrochemiluminescence sensor for facile and rapid detection of melamine was prepared through stabilizing $Ru(bpy)_3^{2+}$ in the bio-MOF-1 framework $[Zn_8(ad)_4(BPDC)_6O{\cdot}2Me_2NH_2, 8DMF, 11H_2O]$ [73]. This novel ECL sensor demonstrated high sensitivity toward melamine in a wide linear range (10^{-10}–10^{-4} M) with very low detection limit (0.038 nM), which also showed good repeatability in the real sample of milk and instant formula power. Cai et al. prepared a core–shell nanoparticle Au@MIL-101 through polymerizing Materials of Institute Lavoisier (MIL-101) around AuNPs@IP_6 for detecting methenamine particularly. This nanostructure demonstrated excellent SERS performance owing to great enhancement for Raman scattering. For its practical application in vermicelli samples, it showed very low LOD at 0.5 nM with a great linear range between 3.16×10^{-6} and 1.0×10^{-8} M [32].

4. CONCLUSION

In the current review, the recent technology advancements in MOFs-based sensor and their specific application in detection of pesticide residues, heavy metals and other toxic substances were summarized and reported.

The increasing demand of detecting health-or even life-threatening species in food, especially with great convenience and has been promoted by the enhanced awareness of assurance and improvement of food safety. MOFs with their intrinsic merits of modifiable pore structure, large surface area and "high density of active sites" have made them excellent candidates as the sensing materials for development of food contamination sensing platforms. In particular, the versatility of novel MOFs has been magnified by their combination with other functional materials with improved sensing performance. In general, the analytical methods for pesticide detection by using fluorescent MOF are developed based on the fluorescent quenching effect, which attributes to the energy transfer from composite to analyte or the competition between analyte and MOF of energy from light source. Electron transfer

between MOF and analyte is the major detection mechanism of electrochemical-based method. Similarly, energy transfer often exists in the sensing strategies due to the strong interactions between heavy metal ions and the specific moiety or atom in the MOFs. Furthermore, recognition element modification and signal amplification also have been used for sensitive and selective detection based on MOF.

Even with these progresses achieved, MOF application has been expected to overcome a series of limitations mainly caused by their water instability so as to improve their sensitivity, selectivity and reproducibility in aqueous conditions. Firstly, the optimization and utilization of the functional advantages of MOFs could be maximized to a greater extent for the application in the food industry through better understanding of the functionalities of MOFs, especially focusing on the development of MOF-based rapid methods suitable for food matrix (e.g. diagnostic kit and strip). Secondly, with consideration of the high possibility of multiple contaminants co-existing in food, multifunctional MOF materials are expected to be designed. Thirdly, the specificity of the MOFs-based sensing platforms is expected to improve, since most of the current MOFs could hardly detect a specific analyte from a family of pesticides with similar structures. Molecular imprinting technique, recognition unit incorporation, surface modification and related technologies could be integrated with MOF to greatly enhance the specificity and sensitivity of the analytical methods for targeted food contaminants. Furthermore, deepened understanding of the toxicology of MOFs should be obtained in the future studies, especially for those applied in the analysis of food and products closely related to human well-being. Last but not the least, more MOF materials with multifunction of sensing, capturing and removing target analytes simultaneously in food are expected to be developed.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTION

YX contributed in investigation, design, review and writing. YP contributed in investigation. ZG contributed in methodology. HH, COLU and YW contributed in conceptualization, supervision, editing and critical review.

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