Metal–Organic Framework-Based Composites for the Detection and Monitoring of Pharmaceutical Compounds in Biological and Environmental Matrices

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Abstract The production of synthetic drugs is considered a huge milestone in the healthcare sector, transforming the overall health, aging, and lifestyle of the general population. Due to the surge in production and consumption, pharmaceutical drugs have emerged as potential environmental pollutants that are toxic with low biodegradability. Traditional chromatographic techniques in practice are time-consuming and expensive, despite good precision. Alternatively, electroanalytical techniques are recently identified to be selective, rapid, sensitive, and easier for drug detection. Metal–organic frameworks (MOFs) are known for their intrinsic porous nature, high surface area, and diversity in structural design that provides credible drug-sensing capacities. Long-term reusability and maintaining chemo-structural integrity are major challenges that are countered by ligand–metal combinations, optimization of synthetic conditions, functionalization, and direct MOFs growth over the electrode surface. Moreover, chemical instability and lower conductivities limited the mass commercialization of MOF-based materials in the fields of biosensing, imaging, drug release, therapeutics, and clinical diagnostics. This review is dedicated to analyzing the various combinations of MOFs used for electrochemical detection of pharmaceutical drugs, comprising antibiotics, analgesics, anticancer, antituberculosis, and veterinary drugs. Furthermore, the relationship between the composition, morphology and structural properties of MOFs with their detection capabilities for each drug species is elucidated.
Keywords  Metal organic framework · Pharmaceutical detection · Drug detection · Electrochemical sensing

1 Introduction

The production of synthetic drugs is a huge milestone in the healthcare sector, transforming the overall health, aging, and lifestyle of the general population. The surge in production and consumption of these drugs gave rise to their emergence as potential environmental pollutants found in water and soil samples. The high toxicity and low biodegradability of these antibiotics trigger adverse effects on human health and the ecosystem. In addition, the presence of such pharmaceutical compounds in the aquatic environment causes toxicity to microorganisms and aquatic vertebrates and affects the growth of green algae. Besides the environmental threats, the release of pharmaceutical residues into our ecosystem can trigger the growth of antibiotic-resistant bacteria. This will lower the susceptibility of common bacteria to current antibiotics, reducing their effectiveness in preventing and curing infections. Due to these factors, it is vital to develop sensitive and selective sensor systems to consistently monitor the presence of synthetic drug residues in our environment. To date, the conventional strategies adapted for drug detection are ultra-high-performance liquid chromatography with tandem mass spectrometry, high-performance liquid chromatography (HPLC), thin-layer chromatography, and enzyme-linked immunosorbent assay (Demir & Silah, 2020). Generally, the traditional detection methods are highly precise but require elaborate instrumentation and analytical procedure, causing them to be time-consuming and expensive. Alternatively, in recent times, research ventures have been undertaken to employ electrochemical methods for antibiotic detection (Aftab et al., 2020; Alsaiari et al., 2021). The electrochemical approach offers various benefits, such as efficient drug sensors, including short analysis time, facile procedure, cost-effectiveness, and low limits of detection (Ghanbari & Norouzi, 2020; Shaterian et al., 2020; Tavana et al., 2020). In these electrochemical sensors, an electrode composed of active chemical species serves as the transduction element. The interaction between the chemical compositions and the analyte of interest brings about the electrical output used for detection analysis.

MOFs are a class of organometallic complexes, which are crystalline compounds constructed from the metal core and organic ligands. The attractive sensing properties of MOFs are due to their large specific surface area, porous nature, accessibility for electrolytes, and facilitated diffusion of reactants. Over the last 5 years, the application of metal–organic frameworks as the potential active material for gas and chemical sensors began to gain traction. Within this timeframe, several studies have been reported highlighting the potential of metal–organic frameworks as the active ingredient for the electrochemical detection of various classes of synthetic drugs. In this chapter, we will review the materials that are suitable for the manufacture of sensors, the chemical nature of drugs, and the techniques utilized to characterize the sensors. Firstly, the different electrochemical methods adapted for the detection of such drug molecules are discussed. This is followed by elucidation of the material composition used for MOF-based electrochemical drug sensors. In the final section, recent kinds of literature on electrochemical drug detection employing MOFs are presented according to various classes of pharmaceutical compounds.

2 Electrochemical Procedure for Detection of Pharmaceutical Products

2.1 Linear Sweep Voltammetry (LSV)

In LSV, the working electrode is immersed into the analyte-containing solution and the potential of the working electrode is scanned from a lower limit to an upper limit. Typically, the initial potential is set at a point at which no electrochemical process occurs between the electrode and analyte. Upon a gradual shift in the working electrode potential, the process of analyte oxidation or reduction begins to take place. Throughout this procedure, the current response is recorded and later plotted into a current against voltage plot as shown in Fig. 1(a). The plot evolves from a zero-current point (at which no electrochemical process occurs) to a sharp increase in a current response attributed to an electrochemical reaction at the electrode surface. The current increment due to Faradaic reactions reaches a maximum point, beyond which the current value begins to drop. This is because, beyond a certain point, the diffusion layer at the electrode surface has grown significantly, hence impeding the access of the analyte to the electrode layer. Figure 1(a) highlights some of the significant
information, such as peak current and peak potential, that can be derived from a LSV curve.

For reversible processes, the peak current can be deduced based on the following equation:

$$i_p = 2.69 \times 10^8 n^3/2 S D^{1/2} \nu^{1/2} C$$

(1)

where $n=$ number of electrons, $S=$ surface area of the working electrode in cm$^2$, $D=$ diffusion coefficient in cm$^2$s$^{-1}$, $\nu=$ sweep rate in Vs$^{-1}$, and $C$ is the molar concentration of the analyte in mol/L. From this equation, it is evident that the value of peak current depends linearly on the analyte concentration and the square root of the scan rate. Thus, in the electrochemical detection of drugs, the LSV plots are performed at various sweep rates to study the impact of the sweep rate on the behavior of the analyte at the electrode interface. Usually, a linear plot is obtained for the logarithm of peak current versus the logarithm of scan rate, and the slope of the plot is used as an

![Fig. 1](image-url)

**Fig. 1** a Typical current versus voltage plot for LSV, b general current against voltage plot for CV, c potential-time profile for DPV, d potential-time plot for SWV, and e electrochemical drug sensing. Reprinted from Ko et al. (2020) with permission from American Chemical Society
indicator to explain possible mechanisms at the electrode surface. Apart from that, the linear dependence of peak current on the concentration of analyte is particularly useful for the evaluation of an electrochemical sensor. The peak currents of a series of standard analyte solutions are obtained from LSV and the peak current versus concentration is plotted to evaluate the linearity of the fabricated electrochemical sensor. The calibration curve derived from the analysis can then be used for the quantitative determination of the unknown concentration of analyte based on the peak current value detected.

2.2 Cyclic Voltammetry (CV)

CV is the most widely used voltammetric technique for any electrochemical sensing system as it provides useful information about the redox potential and electrochemical reaction rates between the electrode and analyte of choice. As depicted in Fig. 1(b), CV involves scanning the potential of the working electrode from a lower limit \( V_1 \) to an upper limit \( V_2 \). However, unlike LSV, upon reaching the maximum potential, the scan is reversed, and the potential is swept back to \( V_1 \). Based on the current against voltage plot of both the forward and reverse scans, the reversibility of an electrochemical process can be deduced. In the forward scan, the potential sweep occurs towards more positive values, favoring the oxidation of the analyte, reaching the maximum current at anodic peak potential. The potential is then extended to a more positive value to attain a steady-state environment, following which the reverse scan is performed, scanning the potential to a more negative value. The minimum current occurs at the cathodic peak potential, which indicates the reduction of the oxidized analyte species.

Like LSV, the peak current values in CV are dependent on the concentration of analyte and thus can be used to establish the linearity between analyte concentration and current response. Another vital parameter in CV is the scan rate, which dictates the time taken to sweep from the lower and upper limit potentials. Since different chemical processes (such as adsorption and diffusion) require different durations, the CV plots of a system are often performed at various scan rates to provide information on the mechanism of the electrochemical process involved. According to Laviron’s equation, the relationship between peak potentials and the scan rate of the CV cycle is as follows:

\[
E_{pa} = E^{\circ} + \frac{2.303RT}{(1 - \alpha)nF} \log v \tag{2}
\]

\[
E_{pc} = E^{\circ} + \frac{2.303RT}{\alpha nF} \log v \tag{3}
\]

\[
\log k_s = \alpha \log(1 - \alpha) + (1 - \alpha) \log \frac{\log RT}{nFv} - \frac{\alpha(1 - \alpha)nF\Delta E_p}{2} \cdot 303RT \tag{4}
\]

where \( \alpha \) is the charge transfer coefficient, \( n \) is the number of electron transfers, \( v \) is the scan rate, and \( k_s \) is the heterogeneous electron transfer rate constant.

2.3 Differential Pulse Voltammetry (DPV)

DPV is basically very similar to LSV, in which the working electrode is scanned over an upper and lower limit potential profile. However, in DPV, a sequence of voltage pulses is applied over the incremental baseline potentials. In this procedure, the current response is measured right before the pulse is applied and right after the pulse ends. The difference between these values is then plotted in the current against the voltage plot. The plot utilizes second derivative functions of the current–voltage relation, which is usually in larger values, therefore, allowing better isolation of the Faradaic signals from the background current. Due to this reason, the DPV method vastly improves the sensitivity of electrochemical detection systems and performs better for the simultaneous detection of multiple analytes, producing well-resolved peak currents for different analytes. In most cases, three basic parameters, namely, modulation amplitude, modulation time, and step potential, need to be optimized to produce the most effective electrochemical sensing procedure. Modulation amplitude is the height of the potential pulse and typically ranges between 5 and 100 mV. Step potential is the difference between the incremental baseline potentials and modulation time is the duration of potential pulse application. Figure 1(c) outlines the various parameters involved in the execution of DPV.

2.4 Square Wave Voltammetry (SWV)

SWV involves a procedure in which the potential of the working electrode is scanned through a series of forward and reverse pulses over the incremental baseline potentials (Fig. 1(d)). The current response is the difference between the currents in the forward and the
reverse pulse. In addition to incredible sensitivity due to a greater signal-to-noise ratio, SWV can be performed at higher scan speeds without compromising the peak resolution. In the experimental procedure of SWV, the frequency of the square wave is varied to modify the interval time. Thus, the selection of suitable frequency is an important criterion to produce credible data points.

3 Types of Drugs

In this section, we discuss MOF-based electrochemical detection of different classes of pharmaceutical drugs.

3.1 Antibiotics

3.1.1 Nitroimidazole (NMZ)

NMZ is a drug incorporated with the nitro group at the 5-position of a imidazole. Its IUPAC name is 5-nitro-1H-imidazole. It has a well-known potential for treatment against various bacterial and protozoan infections (Mital, 2009; Souza et al., 2022). Its derivatives are reported for anti-fungal activities (Günay et al., 1999). NMZ demonstrated two reduction peaks in acidic media. The first peak involved four electrons converting the $\text{NO}_2$ group into hydroxylamine, and the second peak was produced by the reduction of hydroxylamine into $\text{–NH}_2$ (Brett et al., 1997). 1-Methyl-4-nitro-2-brominemethylimidazole was reduced on a glassy carbon electrode (GCE) modified with multi-walled carbon nanotubes (MWCNTs) using adsorptive stripping voltammetry (AdSV) with a detection limit (DL) and quantification limits (QL) of $4.41 \times 10^{-6}$ and $6.21 \times 10^{-6}$ mol L$^{-1}$, respectively (Jara-Ulloa et al., 2011). Wheel-shaped Tb-derived MOF was engineered by Yang et al. for the determination of NMZ from aqueous systems using fluorescence spectroscopy. $[\text{Tb}_2(\text{COO})_4]$ subunit was extended with C$_5$-symmetric 3,3’,3”-[1,3,5-benzenetriyltris(carbonylimino)]tris-benzoate hydrothermally with DL of $1.59 \times 10^4$ M$^{-1}$ (Yang et al., 2020). Duo et al. reported two-dimensional magnetic bimetallic nanosheets for magnetic solid phase extraction of NMZ from water by using HPLC. Ni was used to control the composition and morphology of the sensor. The DL shown by this sensor was 0.025–0.05 $\mu$g L$^{-1}$ (Duo et al., 2021).

3.1.2 Ciprofloxacin (CIP)

The scientific name of CIP is 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazine-1-yl)-quinoline-3-carboxylic acid belongs to an antibiotic class of drugs which is effective for a variety of bacterial infections in joints, skin, urinary, and respiratory tract. It is also administered in typhoid. CIP is taken orally, intravenously, or in the form of drops in the ears and eyes. It inhibits the function of DNA gyrase, which ultimately breaks both strands of DNA in bacteria (Liu et al., 2022; Walters et al., 1999). The electrochemical activity of CIP is due to the inherent piperazine ring in it, which is oxidizable. Fotouhi and coworkers reported a simple electrochemical technique for quicker and quantitative detection of CIP on MWNTs film electrodes in the concentration range of 40–1000 µM, and DL was 6 µM (Fotouhi & Alahyari, 2010). Kingsley et al. designed a CIP sensor based on a CuZn/ferrite nanoparticle-modified electrode, resulting in a DL of 2.58 µM. Aforesaid sensors functioned by monitoring the electro-oxidation signal (Kingsley et al., 2016). Similarly, Feng et al. reported sensitive and selective CIP detection from contaminated water using Cu$^{+2}$ anodic stripping voltammetry (ASV). Zr (IV) derived NH$_2$-UiO-66 composites and reduced graphene oxide (rGO) were employed as working electrodes. In the presence of CIP, Cu(II) oxidation current declined to owe to the formation of a stable CIP-Cu(II) complex. Trace levels of CIP can be detected by using NH$_2$-UiO-66 as a sensor up to 6.67 nM (Fang et al., 2019). Rani and coworkers stated Cu-MOF for CIP detection from water with modified GCE by DPV with a limit of detection (LOD) of $20 \times 10^{-6}$ mol L$^{-1}$. Moreover, from tap water, 94% of CIP was recovered by this method (Rani et al., 2020). Similarly, ppm level CIP estimation in urine was studied by making Ga-MOF functionalized by Eu(III) (Al Sharabati et al., 2022; Wang & Yan, 2020).

3.1.3 Metronidazole (MNZ)

MNZ is marketed as flagyl with IUPAC name, 2-(2-methyl-5-nitro-1H-imidazole-1-yl) ethanol. It malfunctions the DNA of bacteria and microbes by inhibiting the formation of nitroso radicals. It is used to treat a variety of bacterial and protozoal diseases like endocardium inflammation, bacterial vaginosis, giardiasis, trichomoniasis, and amebiasis (Ceruelos et al., 2019). It is administered orally as a cream or intravenously as an
injection. In animals, MNZ is employed as a feed additive, but it causes cancer, which is why it is banned in the European Union (EU) (Han et al., 2014). Overdosage of MNZ in humans causes toxicities and optic and peripheral neuropathies (Prabhakaran et al., 2015). Baikeli et al. reported NO$_2$ group in MNZ functions as an active redox center and is useful for electrochemical sensing. They also modified the GCE surface with Fe, N, and Co-doped carbon to improve selectivity and sensitivity (Baikeli et al., 2020a). Electrochemically, MNZ-graphene nanoflakes DL was reported at 0.015 nM. The peak potential was observed at $-0.32$ vs Ag/AgCl (Meenakshi et al., 2018). Baikely et al. also prepared ZnCo/C composites by carbonization of ZnCo-MOFs based on ZIF-8 and ZIF-67, then modified GCE for electrochemical detection of MNZ in pharmaceutical samples with LOD of 17 nM in a 0.05–100 µM range concentration (Baikeli et al., 2020b). Another selective and sensitive platform for MNZ detection is carbon nanofibers modified Au nanoparticles with a greater linear response in the range of 0.1–2000 µM with a DL of 0.024 µM. The results were reproducible to detect MNZ from tap water (Zhang et al., 2022).

### 3.1.4 Vancomycin (VAN)

VAN is a glycopeptide antibiotic for treatment against various pathogenic bacteria. It is recommended for intravenous delivery. Moreover, its oral delivery has shown poor absorption. Complicated infections of joints, skin, bloodstream meningitis, endocarditis, and bones are treated by VAN (Liu et al., 2011). It is chosen for serious staphylococcus infections. VAN prevents the appropriate synthesis of the cell wall in gram-positive bacteria, but it is inactive against gram-negative bacteria (Hammes & Neuhaus, 1974; He et al., 2021). Blidar et al. presented VAN sensing based on graphene-gold nanocomposites. VAN is directly detected in the oxidation domain while indirectly via reduction with a 0.29 µM of DL (Blidar et al., 2019). Molecularly imprinted polymer (MIP) nanoparticles were also reported for the detection of VAN by using vinyferocene and ferrocenylmethyl methacrylate in varying quantities and characterized by CV. Electrochemically, VAN exposure alters the redox properties of the ferrocene group owing to retardation in electron transfer (Mazzotta, et al., 2016). A Cu(II) benzene-1,3,5-tricarboxylate MOF was modified with poly (acrylic acid) and reported as an electrochemical sensor for VAN in water, serum, and spiked urine with DL of 1 nM (Gill et al., 2020; Mendes et al., 2020).

#### 3.1.5 Enrofloxacin (ENRO)

ENRO is member 6-flouro-7-piperazinyl-4-quinolones, hence named as 1-cyclopropyl-7-(4-ethylpiperazin-1-yl)-6-fluo-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (Wolfson & Hooper, 1985). It is an antibiotic drug marketed as Baytril. ENRO demonstrated bactericidal action in both gram-positive and gram-negative bacteria. It is active in stationary as well as the growth phase of bacteria. However, its activity is concentration dependent and effective against vibrio, salmonella, Aeromonas, Proteus, shigella, etc. (Mitchell, 2006). ENRO is inactive against anaerobes. It is also employed in cattle, rabbits, pigs, chickens, sheep, and dogs to manage bacterial infections (Navalon et al., 2002). However, several usages of fluoroquinolones are supposed to be the reason for arthritis in dogs, so food and drug administration called for selective and sensitive techniques for robust ENRO detection (Hampshire et al., 2004). Among numerous electro-analytical methods, AdSV is a useful technique to determine fluoroquinolones at the nM level (Jara-Ulloa et al., 2011). Navalon et al. reported that AdSV coupled with a static mercury drop electrode proved to be a sensitive and selective method with DL of 1–5 ng mL$^{-1}$ to determine ENRO (Navalon et al., 2002). Recently, aptamers are also reported as detection probes containing MOF skeleton in the electrochemical estimation of ENRO. For example, semiconducting Co$_3$Ni$_{13-}$-(2,3,6,7,10,11-hexaaminotriphenylene)$_2$ MOF was constructed by Song et al. that demonstrated superior ENRO detecting performance in serum, river water, and milk with extremely low DL 0.2 fg mL$^{-1}$ (Song et al., 2021).

#### 3.1.6 Furazolidone (FZD)

FZD is nitro furan based monoamine oxidase inhibitor antibacterial agent with generic name 3-[(5-nitrofuran-2-yl)methylideneamino]-1,3-oxazolidine-2-one (Timperio et al., 2003). It has broader activity against infections caused by parasites, bacteria, and protozoa. The action mechanism involved cross-linking anchored in bacterial DNA. It is used to treat salmonellosis, helicobacter, and cholera (Machado, Silva & Viriato, 2008). Moreover, it is used in veterinary medicine and aquafarming. Extensive exposure to FZD can cause mutagenesis, carcinogenesis, and liver and kidney failure. It is harmful to DNA
and can stop the growth and the cell cycle. Its standard dose for adults is 100 mg kg\(^{-1}\) (Yan et al., 2018).

Hwa et al. reported functionalized carbon black incorporated with tungsten carbide for the FZD sensor using CV and DL of 0.6 nM (Hwa et al., 2019). Similarly, hexagonal zirconium phosphate nanoplates were prepared by hydrothermal method for FZD sensing represented DL of 1.2 nM (Kokulnathan et al., 2020). Another study reported SnS\(_2\)-SnO\(_2\)/graphene composites pasted over GCE viable to detect a trace amount of FZD using CV analysis. The optimum working potential was −0.516 V, and LOD was 1.42 nM (Amalraj et al., 2020). Niu et al. formulated Co/Ni-MOF, followed by the synthesis of NiCo\(_2\)O\(_4\)@C/GCE for FZD analysis in honey and milk using DPV. A8.47 and 35 nM DL were reported for FZD (Niu et al., 2021).

### 3.1.7 Monensin (MNS)

MNS is a polyether-based antibiotic drug extracted from *Streptomyces cinnamonensis*. It is also known as rumensin. The structure of MNS was reported by Agtarap et al. in 1967 (Agtarap et al., 1967). It is an ionophore belonging to crown ethers that can make complexes with monovalent metal ions such as Li(I), Ag(I), K(I), Na(I), and Ti(I). MNS transports these ions across lipid membranes via electro-neutral exchange (Pinkerton & Steinrauf, 1970). It is used in the beef industry for coccidiosis prevention and enhancement in the manufacturing of propionic acid (Matsuoka et al., 1996). MNS ingestion by humans from edibles can cause necrosis, muscle rhabdomyolysis, and food safety concerns. So, the permissible limit of MNS was set to 2–50 µg kg\(^{-1}\) by the EU (Blain et al., 2017). In the laboratory, it is used to block Golgi bodies (Zhang et al., 1996). Derivatives of MNS are reported for the development of ion-selective electrodes (Kallen et al., 1993). Hu et al. synthesized Zn/Ni-ZIF-8800@graphene in chitosan and then coated it on GCE, followed by electrochemical deposition of gold nanoparticles (AuNPs). The deposited AuNPs amplified electrical signals. DPV was used to detect MNS in milk DL, up to 0.11 ng mL\(^{-1}\) (Hu et al., 2019). Similarly, it was detected in horse feed by Rudnicki’s group using SWV. The best SWV signal was obtained at −1.50 V vs Ag/AgCl/KCl. LOD was 1.27×10\(^{-8}\) mol L\(^{-1}\) (Rudnicki et al., 2018).

### 3.1.8 Nitrofurazone (NFZ)

NFZ belongs to the nitrofuran group with the generic name \((2E)-2-[(5-nitro-2-furyl)methylene]hydrazine\) carboxamide. It is a yellowish and crystalline material with the trade name Furacin used for topical antibiotic gel. In humans, it is used for a variety of skin infections, burns, wounds, and ulcers. It is typically recommended for dogs, cows, cats, and livestock as an antibacterial ointment for cutaneous burns, wounds, infections, and ulcers. Its mode of action is not understood but is believed to interfere with DNA synthesis and glycolysis. A quicker estimation of NFZ was reported by Ye et al. by utilizing polyfurfural-rGO on GCE using the DPV technique (Ye et al., 2018). A selective and sensitive NFZ electrochemical sensor on gold nanorods was established, where NFZ was electro-reduced by an irreversible mechanism using amperometry and DPV. The DL for DPV quantification was 0.18 µmol L\(^{-1}\) (Rahi et al., 2015). Another novel NFZ sensor fabricated with cross-linked DUT/tubular polypyrrole can also be used for ornidazole detection (Wang et al., 2020a). Cheng et al. fabricated GCE with (BC/Cr\(_2\)O\(_3\)/Ag/MIP) NFZ sensor in biological fluids by using DPV with a DL of 3×10\(^{-9}\) M combination of Cr\(_2\)O\(_3\) based MOF, AgNPs, and biomass carbon composite have shown excellent activity and surface area. Moreover, MIP was developed by methacrylic acid and acrylamide (Cheng et al., 2020).

### 3.1.9 Tetracycline (TET)

TET is an oral antibacterial medicine extensively used to cure malaria, acne, plague, brucellosis, syphilis, and cholera. It disturbs translation and hence protein synthesis in bacteria. It has a broader spectrum of activities against aerobic, anaerobic, gram-positive, and negative bacteria. TET is also recommended for the treatment of peptic ulcers that are caused by bacteria. It is employed as biomarker to detect mineralizing in bones. In wildlife, it is utilized as a biomarker to detect vaccine consumption in baits (Olson et al., 2000). Abuse of TET has serious implications for humans, such as drug resistance, allergic reactions, toxicity, and growth retardation in bones in hypersensitive individuals (Gan et al., 2014). Safe limits of TET established by EU in edibles like in eggs 440 nM, in milk, and 220 nM in muscle tissues (Guo & Gai, 2011). So, Specific detection of TET is
necessary. TET electrochemical carbon-based sensor was fabricated by Wong et al. by combining the carboxylic group with MWCN in presence of graphene. This sensor was successfully employed to estimate TET concentration in river water, urine, and pharmaceutical samples using adsorptive stripping DPV with DL $3.6 \times 10^{-7}$ mol L$^{-1}$ (Wong et al., 2015).

Tang et al. designed a TiO$_2$-MoS$_2$@Au composite and then thiolated it with a DNA aptamer to get an electrochemical aptasensor that showed DL $5 \times 10^{-11}$ M (Tang et al., 2018). Likewise, a highly selective DNA aptamer was prepared by Kim et al. that can recognize minor structural changes in TET and its derivatives. The minimal DL of this sensor was 10 nM. The binding of aptamer with TET was investigated by CV and SWV (Kim et al., 2010).

Song et al. synthesized NH$_2$-MIL-101(Fe)/CNF@AuNPs aptasensor derived from Fe-MOFs for sensing TET in tap water and polluted water. APTASensor was designed by a combination of hydrothermal, pyrolysis, and electro-deposition methods. Furthermore, it displayed excellent current and impedance response. The minimum LOD was 0.01 nM (Song et al., 2022). Ln-MOFs were tested for sensing 27 antibiotics in water, but the reported sensor exhibited ultra-sensitive activity for TET and Oxytetracycline (OTC) recognition only through the inner filter process. LOD for TET and OTC were reported at 2.77 and 1.95 nM (Li et al., 2020). A recent study led by Song et al. explored an aptasensor that was derived from Fe-based MOFs for TET monitoring from real water samples. Lower DL was 0.01 nM. The reported sensor could be utilized to monitor TET levels from environmental water samples in the future (Song et al., 2022).

3.1.10 Chloroamphenicol (CAP)

CAP is the first antibacterial drug that contains a nitro group and is derived from dichloroacetic acid. It has several generic names, preferred name is D-threo-2, 2-dichloro-N-[3-hydroxy-a-(hydroxymethyl)-p-nitrophenethyl]-acetamide, but in literature D (-) threo-2-dichloroacetamido-1-p-nitrophenyl1,3-propanediol is common. CAP has bactericidal activity against almost all families of bacteria in the concentration range of 1–10 µg per mL (McLean et al., 1949). It is used as eye ointment and intravenously administered for typhoid fever. It inhibits protein synthesis by disrupting in peptidyl transferase enzyme present in bacterial ribosomes. Furthermore, it is used to promote growth in animals (Yan et al., 2015). It has serious side effects such as gray baby syndrome, depression of bone marrow, aplastic anemia, etc. (Wu et al., 2015).

The permissible limit for CAP is 0.3 µg per kg in animal-derived foods. Xiao et al. performed the transformation of GCE by exfoliated porous carbon and then investigated CAP by SWV. The calculated DL was $2.9 \times 10^{-9}$ mol L$^{-1}$ (Xiao et al., 2017). DL of CAP incorporated in graphene nanoflakes was 0.038 nM with a reported peak potential $-0.51$ vs Ag/AgCl (Meenakshi et al., 2018). Fe-doped MOF (Fe/ZIF-8) was prepared, followed by carbonization in the N$_2$ atmosphere and obtained doped carbon nanoparticles for GCE modification. The modified GCE exhibited a larger surface area (1221.19 m$^2$ g$^{-1}$ and was characterized by LSV for determination of MNZ and CAP. Fe-MOF provided a larger surface area, stability, and higher activities. Both antibiotics were satisfactorily detected in phosphate buffer solution (PBS) and water system. The author deduced that the NO$_2$ group in CAP and MNZ is a redox-active center for their electrochemical performance (Baikeli et al., 2020a). Wei et al. reported Zr-based MOF decorated by poly 3,4-ethylenedioxythiophene films for CAP sense. The performance of the modified electrode was examined by CV and DPV. The stated sensor represented good conductivity and accurate detection in real samples with a DL of 0.0018 µM (Wei et al., 2021).

3.2 Analgesics

3.2.1 Diclofenac (DCF)

It is a non-steroidal anti-inflammatory drug (NSAID) for the treatment of pain with the brand name Voltaren. Its generic name is [2-(2,6-dichloroanilino) phenyl]acetic acid. It can be taken orally or injected rectally. DCF is also available in the form of skin ointment. Medically, it is used for pain, dysmenorrhea, and inflammatory diseases. It prevents the formation of prostaglandins by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) and provides pain relief for about 8 h.

A biosensor for electrochemical sensing of DCF was designed by amino-functionalized diclofenac binding aptamer (DBA) on GCE. Depending upon
the concentration of DCF, the conformation of DBA changes; hence, charge transfer decreases, which can be determined by voltammetry and electrochemical impedance spectroscopy (EIS). Aptamer showed DL of 2.7 × 10⁻⁷ M. Aforesaid aptamer equally worked for serum samples (Kashefi-Kheyrabad & Mehrgard, 2012). Functionalized MWCN were employed as DCF sensors with modified gold and platinum nanoparticles. Electrochemical properties were examined by CV and DPV representing 0.3 µM LOD (Eteya et al., 2019). A novel carbon nano-structural electrode was prepared to detect DCF. Electro-oxidation of DCF was studied by CV and the effect of concentration is determined by SWV, which exhibited a DL of 3.41 × 10⁻⁸ M (Honakeri et al., 2020). Malekzadeh et al. devised Zr/MOF/MIP sensor for simultaneously finding DCF and paraaminobenzoic acid (PABA). Zr/MOF enhanced the surface area of the electrode upon testing by CV and DPV in potassium ferrocyanate solution. Electro-sensor proved to be sensitive, selective, stable, and reproducible in detection from pharmaceutical and commercial samples. (Malekzadeh et al., 2020). Epoxy matrix imparted HKUST-1-carbon MOF were utilized to tailor electrodes for simultaneous and selective detection of DCF and ibuprofen using CV, chronoamperometry (CA), and multi-pulsed amperometry (MPA) in pharmaceutical and water systems (Motoc et al., 2016). A study conducted by Malekzadeh et al. by using the electro-polymerization method for the detection of DCF. They prepared Zr-MOF/MIP. The MOF was characterized by X-ray diffraction (XRD), scanning electron microscope (SEM), Fourier transform infrared spectroscopy (FTIR), and CV. DPV technique was used to evaluate sensor response. A 0.1 µM DL, selectivity, reproducibility, and longer stability exhibited by the electrochemical sensor for DCF (Malekzadeh et al., 2020).

3.2.2 Ibuprofen (IBP)

IBP is an NSAID with a scientific name of (RS)-2-[4-(2-methylpropyl)phenyl]propanoic acid. Pain, inflammation, migraines, and fever are treated by IBP. It can be taken by mouth or intravenously injected. IBP demonstrates its activity in 1 h. It is a weaker anti-inflammatory drug as compared to other NSAIDS. Like other NSAIDs, it also retards the activities of COX enzymes to decrease the formation of prostaglandins. Lysine salt is used in some countries, which are faster in pain relief due to improved solubility of IBP (Beaver, 2003). Inhalation of IBP in solution form for COVID-19 treatment is ongoing research in Argentine and Cordoba.

Manea et al. synthesized Ag-functionalized nanofiber and Ag-modified natural zeolites as a sensor for IBP by using DPV revealing that Ag-functionalized nanofiber-based sensors are excellent for IBP detection (Manea et al., 2012). MWNTs were employed as IBP sensors, for example, Ag-modified zeolite MWCN-epoxy electrode reported by Motoc et al. (Motoc et al., 2013). Motoc et al. also devised HKUST-1-carbon MOFs incorporated with epoxy matrix electrodes for selective and simultaneous detection of DCF and IBP in pharmaceutical and water samples using CV, CA, and MPA techniques. The reported LOD for DCF and IBF using CV were 100 and 21.70 µg L⁻¹, respectively (Motoc et al., 2016). Mondol et al. developed Zr-based MOF for the adsorption of IBP from water, which demonstrated a good adsorption capacity of 213 mg/g, the Zr-based MOF was successfully recycled without any notable loss in adsorptive capacity (Mondol et al., 2022).

3.2.3 Acetaminophen (AAP)

The common name of AAP is paracetamol, with a scientific name of N-(4-hydroxyphenyl) acetamide. It has antipyretic, anti-inflammatory, and pain-relieving activity. However, its anti-fever action is still unclear (Ludwig & McWhinnie, 2019). It decreases body temperature by 0.2–0.3 °C upon standard dosage (Chiumello et al., 2017). AAP is employed for post-surgical pain, dental pain, migraines, cancer pain, lower back pain, neuropathic pain, and a cure for influenza. But AAP is inferior in pain relieving than IBP. A combination of AAP and IBP is more potent and superior in pain relieving than taking both drugs alone (Moore & Hersh, 2013).

Shi et al. fabricated a sensitive sensor, Au@Pt/Au, supported by reduced graphene/polydopamine to detect AAP by using CV with 0.31 µM LOD (Shi et al., 2020). Similarly, a study was reported in which reduced graphene was employed for AAP oxidation over GCE in CV with DL of 2.13 nM (Adhikari et al., 2015). Manjunatha et al. modified graphite electrodes by MWCN for AAP detection by CV and
demonstrated DL of $5 \times 10^{-7}$ mol L$^{-1}$ (Manjunatha et al., 2011). Lu et al. formulated a sensing system for the estimation of AAP, dopamine, and xanthine with Co$_3$O$_4$/FeCo$_2$O$_4$ decorated with BC. The electrode was fabricated via BC/Co$_3$O$_4$/FeCo$_2$O$_4$ and tested by DPV. This system satisfactorily worked for real samples (Lu et al., 2021). Ni fabricated MOFs were also used and reported for the estimation of AAP in blood, serum, and urine. Ni-MOF was used to synthesize high-surface Ni/C composites. The lower LOD was $4.04 \times 10^{-2}$ µM (Guo et al., 2021). A different method for AAP detection was stated by Guo et al. They doped Ni with nanoporous carbon followed by the fabrication of Ni/C-MOF for estimation and detection of AAP. CV and DPV were used to determine the electrochemical performance of Ni/C-MOF toward AAP. This research would be a promising way to develop AAP sensors with high performance (Guo et al., 2021).

### 3.3 Anticancer Drugs

#### 3.3.1 Imatinib (IMA)

IMA is an anticancerous drug sold under the brand name Gleevec. It is a 2-phenyl amino pyrimidine derivative that is taken orally with 98% bioavailability. Its scientific name is 4-[[4-methylpiperazin-1-yl]methyl]-N-(4-methyl-3-[[4-(pyridine-3-yl)pyrimidin-2-yl]amino]phenyl]benzamide. Specifically, IMA is a chemotherapeutic drug to treat cancer of white blood cells (WBCs), lymph line of blood cells, leukemia abnormality in the 22nd chromosome, gastrointestinal stromal tumors, higher eosinophil count in blood, mast cell disease, and myelodysplastic syndrome (Moen et al., 2007). IMA inhibits numerous tyrosine kinase enzymes by the occupation of TK sites (Hantschel et al., 2008). Electrochemical sensing of IMA in human urine was performed by using SWV using carboxylic group modified MWCN, exhibiting 7 nM LOD (Rodríguez et al., 2018). Wu et al. biosynthesized Ag-graphene nanocomposites and employed them as modifiers over GCE, displaying 10 nM DL (Wu et al., 2021). Ghapanvari et al. developed Fe$_3$O$_4$ nanoparticles supported by MWCN and polyacrylonitrile as electrode materials with a LOD of 0.4 nM (Ghapanvari et al., 2020). A promising method for IMA analysis in urine and serum samples was developed by the Rezvani Jalal group. They in situ constructed HKUST-1 MOF on graphene oxide (GO) nanoribbons. CV was used to test the capability of the fabricated GCE electrode. HKUST-1 constructed on GO has better performance and activity than simple HKUST-1/GCE. With a DL of 0.006 µmol L$^{-1}$ (Rezvani Jalal et al., 2020), Pour and his coworkers modified GCE with MWCNTs/Cu-MOF and exhibited excellent catalytic responses for IMA with reproducibility, accuracy, and stability. This sensor not only presented a LOD of 4.1 nM but also detected IMA in human blood serum, urine, and pharmaceutical tablets (Pour et al., 2021).

#### 3.3.2 Idarubicin (IDA)

It is a 4-dimethoxy-anthracycline analog of daunorubicin. Its scientific name is (1$S,3S$)-3-acetyl-3,5,12-trihydroxy-6,11-dioxo-1,2,3,4,6,11-hexahydropyracen-1-yl 3-amino-2,3,6-trideoxo-α-L-lyxo-hexopyranoside. IDA is an antitumor antibiotic drug administered intravenously. It is marketed with the brand names Zavedos and Idamycin. Myeloid, lymphoblastic, and...
myelogenous leukemia are treated by IDA. It has a higher solubility than its parent drug, daunorubicin. It prevents the uncoiling of DNA by penetrating it and delays the cell cycle. Together with cytosine arabinoside, it is used as a first-line treatment for acute myeloid leukemia. IDA detected by developing a nano-sensor based on ruthenium/vulcan carbon nanoparticles were dispersed over GCE. Nano-sensor was characterized by CV and EIS displayed limit of quantification (LOQ) and LOD of $2.8 \times 10^{-8}$ M and $9.25 \times 10^{-9}$ M, respectively (Kaya et al., 2020). TiO$_2$ nanoparticles supported on carbon nanofibers are also reported for the detection of IDA. The sensor was characterized by SWV. Modified electrode oxidized IDA with DL of 3 nM (Arkan et al., 2017). Kurbanglu et al. modified GCE and pyrolytic graphite electrodes (PGE) with MWCN for IDA detection. LOD for GCE and PGE were $1.87 \times 10^{-8}$ M and $3.75 \times 10^{-8}$ M, respectively (Kurbanoglu et al., 2013). MOF-based detection of IDA is also reported. For example, a per-lite/CoO/rGO@MO-199 composite was synthesized for IDA detection in urine, blood, and spike sample. Carbon paste electrode (CPE) was fabricated with per-lite/CoO/rGO@MO-199 and tested by DPV with a LOD of 1.5 nM. MOF-199 provided a larger surface area, and better conductivities are imparted by rGO (Dehdashtian et al., 2019). The group of Dehdashtian fabricated an IDA sensor that is composed of per-lite, rGO, cobalt oxide, and Cu containing MOF-199. The prepared sensor was used for CPE modification. In DPV analysis, the sensor showed a linear range of 5–1000 nM and DL of 1.5 nM with excellent IDA detection in real samples (Dehdashtian et al., 2019).

3.4 Antituberculosis Drugs

3.4.1 Isoniazid (INZ)

It is isonicotinic acid hydrazide with the generic name pyridine-4-carboxyhydrazide, used for latent and acute tuberculosis treatment. It is taken orally or injected into muscles. INZ is firstly synthesized in 1952, and the World Health Organization (WHO) regarded it as an important medicine for humans (Chakraborty et al., 2015). It is the first-line treatment for tuberculosis coupled with ethambutol, rifampicin, streptomycin, and pyrazinamide. It prevents the synthesis of the mycolic acid, a necessary component in the cell wall of mycobacteria. It can also be administered with rifampicin to treat non-tuberculosis mycobacteria like avium complex (Mdluli et al., 1998). MWCN was prepared for electrochemical sensing of INZ. DPV was applied as a sensing technique demonstrated $5 \times 10^{-7}$ M DL. Moreover, the higher resolution of voltammetric peaks allows the detection of INZ in presence of ascorbic acid (AA) (Shahrokhian & Amiri, 2007). Balasubramanian et al. reported modification of electrodes with B/N are doped with mesoporous carbon (MC) showing promising detection of INZ using amperometry with 1.5 nM LOD (Balasubramanian et al., 2019). Qian et al. designed an electrochemical sensor for INZ detection based on graphene nanomaterials with a DL of 0.03 µM (Qian et al., 2021). A precise sensor has been introduced by Wang et al. for the determination of INZ in mouse serum and tablets derived from NiO@ZnO MOF. Synthesis was carried out by reaction of Zn(II) and Ni(II) with terephthalic acid. Stronger activity and good conduction exhibited by the aforesaid mentioned sensor in DPV characterization with an anodic peak at 0.22 V and DL of 0.25 µM (Wang et al., 2020b). A molecularly imprinted film generated on Cu-MOF/MC is a reliable and accurate candidate for GCE modification for the determination of INZ and RIF from serum, urine, and blood samples using DPV. The minimal LOD were 0.37 nM for INZ and 0.38 nM for rifampin (Rawool & Srivastava, 2019). MOF-derived accurate and reproducible NiO and ZnO hollow microspheres were developed by Wang et al. to sense INZ. NiO@ZnO spheres were characterized by CV and DPV. The fabricated sensor not only demonstrated good conductivity but also gave a strong peak for INZ at a potential of 0.2 V against saturated calomel electrode (Wang et al., 2020b).

3.4.2 Pyrazinamide (PZM)

PZM, or pyrazine-2-carboxamide medicine, was synthesized in 1936 but widely used in 1972 for tuberculosis management. It is taken orally but not recommended for latent tuberculosis (Hussain et al., 2021). PZM is always used with rifampicin and INZ. PZM is antiuricosuric drug (Ichida et al., 2004). It is a prodrug that is converted into pyrazinoic acid and changes the neutral pH in bacillus to acidic which ceases growth of mycobacteria (Whitfield et al., 2015). Electrode modification is performed for electrochemical detection of PZM. For instance, Chokkreddy et al. fabricated GCE with silver nanoparticles, 1-ethyl-3-methylimidazolium tetrafluoroborate ionic liquid, and rGO. Electrode sensing was tremendous at pH 6 in acidic conditions to reduce PZM at $-0.82$ V vs SCE. DL and QL were 0.0102 µM and 0.3658 µM, respectively.
(Chokkareddy et al., 2021). Chokkareddy et al. designed ionic liquid assimilated MWCN as support for nanoparticles of Co-ferrite decorated over GCE. The modified electrode was characterized by CV and DPV that can be used for simultaneous detection of ethambutol and PZM. The calculated LOD for PZM was 0.010 µM (Chokkareddy & Kanchi, 2020). Yan et al. modified GCE by using co-based MOF embedded in MC. Co-MOF-74 was used for INZ and PZM recognition in human serum and urine samples by imparting improved oxidation in INZ and enhanced reduction in PZM in voltammogram (Yan et al., 2019). PZM was detected by Chokkareddy et al. by modification of GCE with the ionic and novel liquid-based sensor. GCE was fabricated by Ag nanoparticles, rGO, and 1-ethyl-3-methylimidazolium tetrafluoroborate liquid. DPV and CV were employed for the determination of the PZM reaction at the electrode surface. Optimum electrochemical detection of PZM was observed at −0.82 V potential and pH 6. The method was claimed to be very sensitive with DL of 0.0102 µM (Chokkareddy et al., 2021).

3.4.3 Rifampicin (RIF)

It is also named as a rifampin antibacterial and antituberculosis drug that demonstrated activity against several types of bacterial diseases, such as tuberculosis, mycobacterium avium complex, leprosy, and legionnaires (Lee et al., 2017). RIF is used alone for latent tuberculosis and combined with ethambutol and PZM for acute tuberculosis therapy. It shortens treatment duration and prevents resistance development (Ntie-Kang et al., 2014). It is effective against a variety of bacteria, protozoa, and some viruses (Sodeik et al., 1994). Sensor for the detection of RIF was fabricated by the group of Amidi. They modified GCE with poly-melamine followed by electro-deposition of AuNPs. The sensor was characterized by CV and EIS. There are two peaks for RIF observed at 0.09 and 0.70 V in PBS with 0.03 µM DL (Amidi et al., 2017). A report represented an ultra-sensor for RIF in which TiO2 nanoparticles were incorporated in rGO and modified GCE were subjected to electrochemical detection allowing 0.03 µM DL (Reddy et al., 2021). C-dots@CuFe2O4 were developed for the simultaneous determination of RIF and INZ. Moreover, DL 0.022 µmol L−1 for RIF and 0.041 µmol L−1 for INZ was reported (Shiri et al., 2017). A molecularly imprinted film generated on CMOF/MC is a reliable and potential contender for GCE adaption for analyzing INZ and RIF from serum, blood, and urine samples using DPV. The minimum DL was 0.37 nM for INZ and 0.38 nM for RIF (Rawool & Srivastava, 2019). In a recent study, Sagar et al. explored rGO and CuO MOF for RIF detection. These researchers modified GCE by rGO@CuO sensor and observed a three-fold increment in current values during electrochemical characterization of the sensor by CV and DPV. Sensors have shown very low DL 5–11 nM and remarkable stability (Sagar et al., 2022).

3.5 Veterinary drugs

3.5.1 Marbofloxacin (MBF)

MBF belongs to the class of fluoroquinolone bactericidal synthetic veterinary drugs derived from a carboxylic acid. Its IUPAC name is 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyridol(3,2,1-ij)(4,2,1)benzoxadiazin-6 carboxylic acid. It is sold under the trade names Zeniquin, Marbovet, and Forcyl. MBF is used to cure respiratory, fungal, skin, urinary, and mammary gland infections in dogs and cats. It demonstrated broad-spectrum activity against gram-positive and gram-negative bacteria in growth and stationary phases (Spreng et al., 1995). Impairment of DNA gyrase is believed to be MBF’s mechanism of action (Siengdee et al., 2019). Bacterial exposure to MBF causes their mortality in 20 min. MBF is administered orally and topically. Abdel-Atty et al. presented a novel and sensitive CPE by doping yttrium with Mn2O2 for MBF detection utilizing the SWV technique. An irreversible electrochemical oxidation pattern was demonstrated by MRB at 1.10 V vs Ag/AgCl. The minimal DL was 2.4×10−9 M. The method was applicable for MRB detection in milk, meat, and bovine samples (Abdel-Atty et al., 2020). A similar method was demonstrated by Min et al. by GCE modification with nafion for accurate detection of MBF in serum vs Ag/AgCl at a potential of +0.15 V with reported DL of 5×10−9 mol L−1 (Min et al., 2009).

3.5.2 Alprazolam (APZ)

It is marketed under the brand name Xanax. It is a combination of benzodiazepines and triazole to get triazolobenzodiazepines derived from APZ (Chouinard, 2004). Therefore, its IUPAC name is 8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a] (Demir & Silah, 2020; Shaterian et al., 2020) benzodiazepine. It is a short-span
potent tranquilizer to manage anxiety and panic disorders. APZ is also employed for the treatment of nausea due to chemotherapy and is taken by mouth. APZ has common side effects of depression, tiredness, headaches, sleepiness, etc. APZ has its receptor site in the nervous system that produces a calming effect by regulating the function of GABA. APZ and bromazepam (BMZ) were comparatively detected by CV and DPV techniques in Britton–Robinson buffer at pH 3. CPE phenomenon for APZ and BMZ was diffusion and adsorption, respectively. LOQ reported was $4.2 \times 10^{-7}$ moldm$^{-3}$ for APZ and $3.8 \times 10^{-7}$ moldm$^{-3}$ for BMZ (Samiec & Navrátilová, 2017).

3.5.3 Phenylbutazone (PBZ)

It is a common NSAID medicine administered mainly to horses and dogs for the management of pain and fever. However, its use for humans is prohibited owing to suppressing the production of WBCs and aplastic anemia. Scientifically, it is named as 4-butyl-1,2-diphenyl-pyrazolidine-3,5-dione. From a chemistry perspective, PBZ is crystalline in nature and structurally belongs to a heterocyclic system prepared by simple lactamization of hydrazobenzen with n-butylmalonate in the presence of a base. In dogs, chronic and arthritis pains are managed by PBZ. For dogs, continuous renal and blood monitoring is necessary for longer exposure to PBZ. It is a common NSAID for horses due to its analgesic and antipyretic action (Schoonover et al., 2005). PBZ provides pain relief from infectious injuries, arthritis, and laminitis and controls inflammation. Meucci et al. explored DPV experiments for quantitative analysis of PBZ and flunixin meglumine in plasma. Graphite-based screen printed electrode was used with LOQ 0.01 µgmL$^{-1}$ for both inx meglumine in plasma. Graphite-based screen printed electrodes with AuNPs and functionalized MWCNTs. GPE was characterized by CV, DPV, and EIS techniques. The effect of interference compounds such as AA, uric acid, and citric acid was also investigated. A linear response was observed in the range of 12–100 and 100–3000 nM. The amount of TMD was calculated in tablets, urine, and blood serum accurately(Kolahi-Ahari et al., 2020). A chemiluminescent system based on the oxidation of rhodamine 6 G was developed by

3.5.4 Amoxicillin (AMOX)

AMOX is an antibiotic used for the treatment of urinary, respiratory, and skin infections in cats, dogs, birds, ferrets, and reptiles. AMOX is marketed as Amoxicil, Bimox, Novamoxin, etc. Its IUPAC name is (25S,5R,6R)-6-[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-1-thiazabicyclo[3.2.0]heptane-2-carboxylic acid. It is essential medicine on the WHO list. It can be taken by mouth as a capsule, suspension, or chewable tablet. This drug absorbs rapidly in 1–2 h without outward effects. Gradual recovery can be noticed after a few days. Mesoporous Zn-MOFs incorporated with Cu(II) were fabricated on GCE by the electrochemical procedure. The resulting Cu/Zn-MOF was explored for electrochemical determination of AMOX in 0.1 M NaOH solution. AMOX was oxidized by Cu/Zn-MOF with a significant catalytic rate $K_{cat} = 3.9 \times 10^5$ cm$^3$ mol$^{-1}$ S$^{-1}$. Sensor presented robust response, excellent stability, wider linear range of 1–205 µM higher sensitivity 0.0256 µA µM$^{-1}$ cm$^{-2}$, DL 0.36 µM, and reproducible results. AMOX was estimated successfully from blood, urine, and tablets (Habibi et al., 2021). Recently, a mesoporous platform based on Cu/Zn-MOF was reported for the fabrication of GCE to detect AMOX. The results indicated an excellent linear response range of 1–205 µM, DL 0.36 µM. Higher stability, sensitivity, rapid response, and reproducibility (Habibi et al., 2021).

3.5.5 Tramadol (TMD)

TMD is branded with the name Ultram and scientifically named 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol. TMD is administered for moderate to severe pains. It can be taken orally or in the form of an injection. As a zoologic medicine, TMD is used for the treatment of postsurgery pain relieving, injurious, and chronic cancer pains in camels, goats, dogs, rabbits, cats, rats, raccoons, and small mammals (Souza & Cox, 2011). A cost-effective and selective sensor for the quantification of TMD was reported by the Kolahi-Ahari group. They modify graphite pencil electrodes with AuNPs and functionalized MWCNTs. GPE was characterized by CV, DPV, and EIS techniques. The effect of interference compounds such as AA, uric acid, and citric acid was also investigated. A linear response was observed in the range of 12–100 and 100–3000 nM. The amount of TMD was calculated in tablets, urine, and blood serum accurately(Kolahi-Ahari et al., 2020). A chemiluminescent system based on the oxidation of rhodamine 6 G was developed by
Yousefzadeh et al. Cu nanocluster’s MOF was explored to enhance emissions. Selective response of TMD was guaranteed by utilizing MIP-Fe3O4@SiO2 NPs prior to chemiluminescence analysis. Thus, a highly selective TMD quantification was carried out with a DL of 0.80 nM using Cu-based MOFs (Yousefzadeh et al., 2019). A summary of MOF-based pharmaceutical and drug detection has been shown in Fig. 2.

4 MOF-Based Electrochemical Sensors for Detection of Pharmaceuticals

4.1 Pristine MOF

MOFs are crystalline compounds constructed from the metal core and organic linkers, which have been the new alternative material proposed for electrochemical detection applications. The attractions of MOFs as active material in electrochemical drug sensors are reflected in their unique characteristics, including their adjustable crystalline porous frameworks and tuneable chemical constituents and structures, which originate from the diverse combinations of metal centers and organic ligands. Typically, the synthesis of MOF involves three main chemical species, metal salt, organic linker, and solvent. Since the deduction of MOF structure is primarily contingent on the coordination between the metal centers and organic ligands, a plethora of studies has been dedicated to comprehending the effects of these two components on the topology of the material. Traditionally, MOF was first synthesized using water as the solvent in a hydrothermal method. The mixture of the metal salt, organic ligand, and water will be sealed in a closed container (usually being a Teflon-lined autoclave) and heated for a specific amount of time which could go from several hours to days. This later evolved into the solvothermal method in which organic solvents replaced an aqueous system. The hydro and solvothermal methods were conducive to the crystal growth of the MOFs but the procedure is time-consuming and difficult to be scaled up for mass production. General schematics of MOF synthesis by the solvothermal method have been shown in Fig. 3(i).

Since time and reproducibility are the concerning factors in the hydrothermal synthesis of MOFs, few alternative techniques were introduced to resolve the issue. Microwave-assisted MOF synthesis, for instance, was found to be effective in reducing the reaction during MOF synthesis while retaining the quality of the product obtained. Using microwave ovens specifically designed for chemical synthesis, this technique provides better control over crucial...
reaction parameters such as irradiation power and solution temperature, hence enabling the production of MOFs with similar crystallinity, particle size, and morphology. Sabouni et al. compared the properties of indium-benzenetricarboxylic acid (In-BTC) based MOFs synthesized using solvothermal and microwave heating (Sabouni et al., 2012). The microwave method was indeed the more rapid and facile method, which produced the desired product within 10 min compared to 5 days with the use of a solvothermal procedure. Besides the reduction of reaction times, microwave heating was also reported to favor the formation of smaller MOF particles as highlighted in Fig. 3(ii).

Another technique that could compete with the advantages offered by microwave heating is the sonication method, which applies high-energy ultrasound to the reaction mixture. Some of the added benefits of employing the sonication method for MOF synthesis include short reaction time, ambient temperature requirement, and environmental sustainability. This method is also useful for the synthesis of small-sized MOF particles, as the crystal size obtained is more often smaller than that achieved by microwave irradiation. The sonochemical synthesis method was reported to promote accelerated nucleation, which quickly depletes the nutrient for the particle growth in the substrate mixture and therefore results in uniform and smaller crystals (Jung et al., 2010).

4.2 Carbon/MOF Composites

4.2.1 MC/MOF Composites

Typically, in their native state, MOFs are known to exhibit poor electrical conductivity and low mechanical and thermal stability. These shortcomings can significantly restrict the effectiveness of MOF as an electrochemical sensor for drug molecules. Hence, to rectify these issues, MOFs are often combined with other materials of high conductivity and stability that have been developed in recent years. The composites of carbon-based materials with MOFs have been a particularly successful approach adopted in the pursuit of improving the electroconductivity and chemical stability of the electrochemical sensors. By far, in the literature, a variety of carbon derivatives have been explored to fabricate an electrochemical sensing interface with customizable functionality with respect to the analyte drug of interest.

Generally, porous carbon materials can be categorized according to their pore diameters as microporous (pore size < 2 nm), mesoporous (2 nm < pore size < 50 nm), and macroporous (pore size > 50 nm), respectively. Among these species, MC is a highly ordered carbon structure that has excellent features in terms of surface area, pore diameter tunability, and excellent electron transfer ability. Due to these factors, MC is widely used in various surface area-dominated

![Fig. 3 Synthesis method of MOF via hydrothermal procedure](image-url)
processes such as catalysis, energy storage, and sensing. Incorporation of mesoporous carbon into MOF composites is usually done by pre-synthesizing the MC, which is then added to the precursor solutions in MOF synthesis. This approach usually results in morphological structures in which the MC serves as connecting particles between the MOF crystals. For instance, Rawool et al. fabricated Cu-MOF/MC composites as an active material for the simultaneous detection of rifampicin and isoniazid (Rawool & Srivastava, 2019).

As shown in Fig. 4, the field emission scanning electron microscope (FESEM) images indicate that the Cu-MOF has a rod-shaped structure while MC shows an interconnected network of spherical particles with sizes varying from 30 to 40 nm. Upon the formation of the Cu-MOF/MC composites, the rod-shaped structure of Cu-MOF is unaffected and instead is merely enveloped by a large network of MC. The presence of the spherical MC particles within the interstitial spaces between MOF crystals allows facilitated conductivity of electrons, which improves the efficiency of electrochemical response. The TGA curves of pristine Cu-MOF and Cu-MOF/MC composites were compared in this study, from which it is evident that the weight loss observed in the case of Cu-MOF/MC is less as compared to that of pristine Cu-MOF. Hence, it is concluded that the inclusion of MC in Cu-MOF contributed to the enhancement of the thermal stability of the overall composite.

4.2.2 Graphene/MOF Composites

In recent times, electrochemical sensors fabricated from the synthesis of composites combining MOF and graphene-based materials have been attempted and proven to be effective in improving the intrinsic properties of the sensing material. Graphene is technically a single-atom-thick sheet of sp² carbons arranged hexagonally to form a honeycomb structure. Another widely used material in electrochemical sensors is GO, which is chemically oxidized graphene forming a similar monolayer structure with high oxygen content. GO is usually prepared via the chemical oxidation of graphite using oxidation agents via Hummer’s method. Owing to its oxygen containing-functional groups, GO is particularly useful to accommodate chemical interaction with biomolecules and pharmaceutical compounds. When GO is chemically, thermally, or electrochemically reduced to decrease its oxygen content, the resulting product is known as rGO. Since all these members of the graphene family differ in terms of surface properties, hydrophilicity, conductivity, and size, the choice of graphene-based materials employed in the MOF composite need to be designed according to the analyte species.

The incorporation of graphene into MOF to form the desired composites can be achieved by two means. Firstly, the graphene material and MOF are synthesized independently. Both of these materials are then dispersed into a common solvent medium followed by sonication to achieve homogeneity. Wang et al. adopted this method to form a composite of Cu-terephthalic acid-based MOF (Cu-TPA) with GO (Wang et al., 2014). From the SEM images of the sonication-prepared Cu(TPA)-GO composite, it was concluded that the MOF crystals in the composite retained their original cubic shape and had been coated well with GO. Interestingly, the aqueous solution of Cu-TPA had very poor solubility and dispersibility in water, proven by the formation of light blue sediments on the bottom of the vial within 20 min. However, upon mixing with GO, the MOF formed a homogeneous brown dispersion without any precipitate, and in fact, this homogeneous dispersion could be maintained for a month. This study indicates that MOF composites with GO could effectively improve the solubility and dispersibility of MOF in comparison to its native form.

The alternative method for graphene/MOF composite preparation is to introduce the graphene material during the synthesis of the MOF itself. In this approach, the graphene suspension is added to the solution containing MOF precursors dissolved homogeneously during the last stage of the MOF preparation by hydrothermal process. This method of preparation is deemed to form a better connection between graphene and MOF particles in the composite. For example, in a 2014 study, conductive graphene-like layers were assimilated into copper-benzene tricarboxylic acid-based MOF, also known as HKUST-1 (Alfè et al., 2014). A pre-determined amount of graphene-like layers were added into a DMF solution containing copper salt and 1,3,5 benzenetricarboxylic acid, with subsequent hydrothermal treatment to form the composite. Figure 5 highlights the SEM images of the native HKUST-1 and HKUST-1/graphene layer composites with varying amounts of graphene-like layers. While the pristine form of the MOF depicted the appearance of octahedral crystals with smooth surfaces, the surface of the composites shows a “lace-like” arrangement in the vicinity of the carbonaceous layers embedded within HKUST-1.
crystals. Such interlayered formation of composites is more likely to be attained when the graphene material is added prior to MOF formation.

4.2.3 MWCNTs/MOF Composites

The most recent addition of the carbon family in electrochemical sensing applications is the carbon nanotubes (CNT), which are cylindrical molecules comprised of rolled-up graphene sheets. Single-walled carbon nanotubes (SWCNT) are formed when a graphene sheet is rolled to form a single tube with a diameter less than 1 nm, whereas multi-walled carbon nanotubes (MWCNT) consist of multiple concentrically interlinked nanotubes with diameters up to 100 nm (Alfè et al., 2014).

MWCNT are the more widely used variety for electrochemical sensors, and the method of forming

Fig. 4 (i) FESEM images of A Cu-MOF, B MC, and C Cu-MOF/MC; TEM images of D Cu-MOF, E MC, and F Cu-MOF/MC; EDS mapping of G C, H O, and I Cu elements. Reprinted from Rawool and Srivastava (2019) with permission from Elsevier
MWCNT/MOF composites is very much similar to graphene as discussed above. Due to the three-dimensional nature of CNTs, they are found to be able to prevent the agglomeration of MOF particles and, thus, allow better access for the analytes to more active sites in the sensor. Figure 5 depicts the morphology of UiO-66-NH2 MOFs and their composites with MWCNT (Wang et al., 2021). The MWCNTs were found to fill up spaces between MOF crystals and form wire-like linkages between one octahedral crystal to another. This type of distribution is advantageous for any electrochemical system as it provides facilitated pathways for charge carriers to improve the overall charge transport within the composite material.

4.3 Metal/MOF Composites

MOFs consist of organic ligands that are coordinated by a covalent bond to the metal. These are superior as compared to traditional porous materials in diversity, flexibility, surface area, and porosity. An additional advantage of MOFs is their physicochemical properties can be tailored by changing metal, ligand, or temperature during synthesis (Sanchez et al., 2011). MOFs displayed Langmuir surface area greater than 10,000 m² g⁻¹ and exhibited excellent electrochemical performance owing to the presence of metal, ligand, or both as electro-active species (Kempahanumakkagari et al., 2018). Zhai et al. first time coated N-doped porous carbon (PC) with Ag-MOF for the determination of cysteine in milk with better recovery. The PC@Ag-MOF modified electrode was characterized by CV and LSV, which represented good electrochemical signals and higher conductivities (Zhai et al., 2020). Studies were reported to prepare metal-MOFs with a feasible hybrid framework. For instance, Ni-MOF was fabricated for a solid-state supercapacitor with excellent charge densities (Meng et al., 2018a). Ag-based ZIF-67 was designed by Meng et al. for the oxidative detection of glucose (Meng et al., 2018b).

Cu-based MOF was reported by a group of Rani for GCE modification to detect CIP. The sensibility of the electrode was monitored by using DPV with 20×10⁻⁶ mol L⁻¹ DL (Rani et al., 2020). A research report published by Liu and co-workers represented the detection of ampicillin (AMP) using Co-MOF@terephthalonitrile. This electro-sensor was tested by CV and EIS and successfully determined AMP from

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**Fig. 5** The micromorphology and structure of octahedral UiO-66-NH₂ (A SEM image and C TEM image) and UiO-66-NH₂@MWCNTs materials (B SEM image and D TEM image) Reprinted from Wang et al. (2021) with permission from Elsevier
serum, milk, and river water with extremely low DL 0.217 fg mL⁻¹ (Liu et al., 2019a). Malekzadeh et al. devised a new sensor based on Zr/MOF/MIP for the simultaneous detection of DCF and PABA. Zr/MOF increased the surface area of the electrode upon testing by CV and DPV in a solution of potassium ferrocyanate. Electro-sensor proved to be sensitive, selective, stable, and reproducible (Malekzadeh et al., 2020). Several metal nanoparticles/MOFs and metal oxides/MOFs are also reported for the electrochemical detection of numerous drugs.

### 4.3.1 Metal Nanoparticle/MOF

It is imperative to engineer appropriate electrocatalysts and their support material for the detection of a variety of analytes. MOFs as support manage the shape and size of metal nanoparticles (NPs). Electroactive metal NPs/MOF of Au, Ag, Cu, Pt, and Pd are well reported in the literature. However, there are three main approaches to anchor metal NPs in MOFs. In the first approach, metal NPs/MOFs are prepared and encapsulated in composites. For instance, AuNPs/ZIF-8 was devised by the insertion of AuNPs in MOF for hydrazine and AA detection (Luo et al., 2019). In this method, AuNPs distribution is poor, resulting in low reproducibility. Hosseini et al. reported Cu-MOF and Au-SH-SiO₂ that performed proficient electrolytic oxidation of hydrazine and L-cysteine at pH of 5 and 7, respectively (Hosseini et al., 2013a, 2013b). The second strategy is to fabricate metal NPs in cavities of MOFs. For example, the hydrothermal method was used for the preparation of Zn-MOF and then anchored with Ag NPs that represented superior electro-activity for H₂O₂. Similarly, AuNPs/ZnMOF, AgNPs/Fe-MOF, and CuNPs/Zn-MOF were prepared as electro-sensors. However, reduction inculcates destruction in MOF structure (Braglia et al., 2017; Yadav et al., 2016; Zhang, et al., 2019). The third method employs a one-pot strategy to design metal NPs/MOF to detect the desired molecule. In this technique, metal NPs distribution and MOF structure can be regulated during synthesis (Yang et al., 2017). Newly, PtNPs were prepared by one-pot encapsulation for NaBH₄ oxidation (Ling et al., 2016). Chokkareddy, et al. modified GCE with AgNPs/1-ethyl-3-methylimidazolium tetrafluoroborate by ionic liquid and rGO. Electrode sensing was remarkable at pH 6 in acidic media for the reduction of PZM at −0.82 V. The reported QL and DL were 0.3658 and 0.0102 µM, respectively (Chokkareddy et al., 2021).

### 4.3.2 Metal Oxide/MOF

MOF improves stability by escalating electro-catalytic cycles, transporting micro-molecules and preventing NPs agglomeration. This section will discuss metal oxide/MOFs for electrochemical sensing of pharmaceuticals. Wang et al. explored Fe₃O₄ NPs@ZIF-8/rGO for dopamine detection over modified GCE. The reported sensor selectively detected dopamine in serum and urine even in presence of AA (Wang et al., 2015a). CuOₓ NPs@ZIF-8 was reported as a highly selective electro-sensor for the estimation of H₂O₂ by Yang et al. The stated electro-sensor showed sufficient stability and uniform distribution of CuOₓ NPs (Yang et al., 2016). The electrode was modified by the Arkan group with TiO₂ NPs@ carbon nanofibers for the determination of IDA using SWV. Tailored electrode oxidized IDA with DL of 3 nM (Arkan et al., 2017). Tang et al. constructed a TiO₂-MoS₂@Au composite and then thiolated it with a DNA aptamer to get an electrochemical aptasensor for TET estimation, representing a DL of 5 × 10⁻¹¹ M (Tang et al., 2018). Another article presented ultra-sensor TiO₂ NPs@rGO for RIF sensing at customized GCE when subjected to electrochemical detection allowed 0.03 µM DL (Reddy et al., 2021). Zhan et al. fabricated ZnO@ZIF-8 for electrochemical sensing of AA and H₂O₂. It was revealed that ZnO performed as a template by providing Zn(II) for the production of ZIF-8 (Zhan et al., 2013). Gao et al. assembled a highly electro-active, ultra-sensitive, stable, and selective electro-sensor NiO@Ni-MOF for luteolin detection. The calculated LOD was 3 pM. The reported ultra-sensor was successfully established for luteolin estimation in real samples as well (Gao et al., 2020).

### 4.4 Polymer/MOF

Polymers are flexible and malleable materials that can be processed easily, while MOFs are brittle and crystalline in nature. Therefore, polymers are hybridized with MOFs for attaining desired properties of both types of materials. Researchers stated that polymers regulate MOFs features like growth and frameworks. On the other hand, manipulation in polymer structure is attained by MOFs (Kalaj et al., 2020). These hybrid materials extended the utility
of polymer MOFs in numerous fields, such as drug delivery, water purification, gas absorption, and electrochemical sensing. In electrochemical sensing, polymer MOFs can be applied for MIP, designing of matrix mixed membranes (MMMs), and polymer templates (Kalaj et al., 2020). Single-step electro-polymerization of o-phenylenediamine and pyrrole was carried out by Yan et al. for CIP recognition with a DL of 65.7 pM (Yan et al., 2017). Nanomaterials can also be incorporated into polymers to enhance sensitivity. For example, GCE was tailored by poly (methacrylic acid) containing MWCNTs in it for the detection of norfloxacin (Liu et al., 2019b). GCE can be transformed by grafting polymer with NPs of MC to analyze ofloxacin (Tan et al., 2014). Similarly, Arnaboldi et al. designed a cost-effective enantiopure and selective electrode that exhibited unique peaks for dextro and levo floxacin by deposition of chiral oligomer film on GCE (Arnaboldi et al., 2015). Polymer matrix membranes were reported for heparin detection by designing ion-selective electrodes. Polyvinyl chloride embedded tetradodecylmethylammonium chloride was used for heparin detection (Ma et al., 1992).

### 4.4.1 Conducting Polymer/MOF

Conducting polymers impart stability and sufficient conductivity in materials. Electro-sensor constructed by a combination of conductive poly (3,4-ethylenedioxythiophene) NTs enfolded with porphyrin-based MOF-525. The sensor was coated on the surface of GCE and displayed amazing electro-activity with DL of 0.04×10⁻⁶ M (Huang et al., 2017). Ma et al. stated coated polyaniline on a stable surface matrix of UiO-66-NH₂. The composite resulted in UiO-66-NH₂@polyaniline being used for the detection of cadmium ions. Sensor-modified electrode exhibited reproducible results and LOD was 0.3 µg L⁻¹ (Wang et al., 2017). Mahato et al. fabricated poly (N-[4H-1,2,4-triazol4-yl]acrylamide) with PVC for generating a membrane for electrode modification to detect six different aliphatic alcohols. Interestingly, the sensor distinguishedly responded for each alcohol with a stability of 1000 s (Mahato et al., 2017).

### 4.4.2 Molecularly Imprinted/MOFs

A technique by which model-shaped cavities are generated within a polymer matrix is known as molecular imprinting. It incorporates a system for substrate recognition as the enzyme recognizes its specific substrate. A molecular imprinting polymer is a polymer possessing in-built cavities that have affinity and selectivity for specific target molecules only. MIP is able to distinguish between the original compound and its derivatives. Two strategies are involved to design MIP, one is self-assembly, while the other is linking of monomer to molecular imprint by covalent bonding (Bui & Haupt, 2010). MIP designing can be explored for pharmaceutical recognition of cocaine, ephedrine, cefitoxime, L-cysteine, VAN, DCF, etc. Smolinska-Kempisty et al. fabricated a novel MIP-based sensor for the detection of cocaine. PVC was used as a polymer for molecular imprinting followed by the designing of an ion-selective membrane. The reported sample quantified cocaine in blood samples (Smolinska-Kempisty et al., 2017). The voltammetric sensor reported for ephedrine recognition by Mazzotta et al. for the first time, the imprinted polymer was synthesized and anchored within poly (pyrrole) followed by loading over GCE. The sensing capability was analyzed by CV (Mazzotta et al., 2008). Excellent cefitoxime sensing performance has been shown by MIP derived from poly (cysteine) made by the electro-polymerization method. MWCNTs were covered over GCE to enhance the surface area and then coated prepared MIP sensor. The detectability of the MIP-sensor was analyzed by DPV with LOD 1×10⁻¹⁰ mol L⁻¹ (Ali et al., 2021).

Aswini et al. prepared a carbon paste electrode for the examination of methacrylic acid-based MIP that was characterized by CV, DPV, and EIS for its response toward L-cysteine with 9.6 nM LOD. Moreover, tailored electrodes efficiently determined L-cysteine in water and blood (Aswini et al., 2014). MIPNPs were stated for VAN identification via ferrocenylmethyl methacrylate and vinylferrocene in variable amounts characterized by CV. VAN disclosure in the electrochemical cell changes the redox activity of the ferrocene group due to limited electron transfer (Mazzotta et al., 2016). Malekzadeh et al. developed Zr-MOF/MIP by electro-polymerization technique for DFC sensing. PABA and DFC were employed as a template and functional monomers. Detection capability was evaluated by CV and DPV in a solution of potassium ferrocyanide. The DL obtained was 0.1 µM. A relative comparison of imprinted and nonimprinted Zr-MOFs was carried out, depicting the superior performance of Zr-MOF/MIP (Malekzadeh et al., 2020). Zhang et al. prepared a nanoscaled MIP membrane that
was selective in simazine recognition (Zhang et al., 2017).

4.5 MOF Biocomposites

MOFs have distinctive properties that include porosity, diverse functionalities, higher surface area, and tunability. Therefore, MOFs are capable contenders to immobilize different biomolecules by acting as support to stabilize and reuse biomolecules. However, the integration of biological molecules such as enzymes, peptides, nucleic acids, phages, and antibodies not only impart specificity, selectivity, and sensitivity but also broaden the target spectrum (Qiu et al., 2019).

MOF biocomposites can be categorized as enzyme-MOF, nucleic acid-MOF, antibody-MOF, peptide MOF, etc. (Qiu et al., 2019). Biocomposites can be prepared by encapsulation, infiltration, or bioconjugation method. Moreover, bioconjugation is subdivided into surface adsorption, covalent attachment, and pore infiltration technique (Doonan et al., 2017).

Enzyme-biocomposites are widely studied for the detection of glucose. For instance, Dong et al. modified carbon paste electrodes by surface adsorption using Ag@Zn(C$_7$H$_4$O$_2$S) MOF along with immobilizing mixture of myoglobin and glucose oxidase. The fabricated electrode was characterized by CV, EIS, and amperometry with a DL of 0.08 µM. Furthermore, fabricated electrodes responded linearly for H$_2$O$_2$ and NO$_2^−$ (Dong et al., 2016). Bisphenol A (BPA) is a compound that disturbs the endocrine system. Wang et al. formulated Cu-MOF and selected tyrosinase as a model enzyme for rapid and ultra-sensitive recognition of BPA by amperometry showing a DL of 0.013 µM (Wang et al., 2015b). Similarly, Bisphenol E (BPE) was detected by using chitosan-based metal-MOF (Lu et al., 2016).

Gong et al. encapsulated microperoxidase-11 in Al-based porous coordination MOF to modify electrodes for H$_2$O$_2$ sensing. The electrode was examined by CV and DPV, which revealed encapsulation of microperoxidase enhanced the capability of the electrode toward H$_2$O$_2$ sensing with a LOD of 0.09 µM (Gong et al., 2017). Nucleic acid-biocomposites are reported to devise aptamers for the detection of various compounds. For example, Su et al. assembled an efficient aptamer for cocaine detection by CV and DPV. The aptamer was formulated by Zr-based MOF implanted in Au nanoclusters. The stated DL was 0.44 pg mL$^{-1}$ (Su et al., 2017). Likewise, Chen et al. detected CAP and oxytetracycline (OTET) by using SWV. The aptamer was constructed on nanostructured MOF and represented DL values of 33 and 48 fM for CAP and OTET, respectively (Chen et al., 2017).

5 Current Challenges and Solutions

The high surface area, porosity, and diversity in structural design endow MOFs with prospects to provide credible drug-sensing capacities. At the inception stage, researchers struggled to compensate for poor conductivity and mechanical stability of MOFs used in electrochemical sensing. However, in recent times, these factors have been solved by exploring novel ligand–metal combinations, post-synthesis MOF functionalization, and optimization of synthetic conditions. The more complex challenge in employing MOF-based electrochemical sensors for drug detection lies in maintaining the structural and chemical integrity of the MOFs for reproducible application. Since the activity of MOF is highly dependent on its structure, any collapse within the framework, particularly upon repeated association with the target molecule, will lead to non-reusability of the developed system. Therefore, the reproducibility and long-term reusability of MOF-based sensors need to be highlighted in upcoming studies. Probing the morphological and topological changes experienced by the MOFs upon sustained exposure to the analyte in the electrochemical setup is an essential technique to comprehend the electrochemical stability of the material. In fact, such an approach of characterizing MOFs before and after usage in the desired system is a common practice in other MOF-based applications such as gas sensors, supercapacitors, and electrocatalytic water splitting.

From a production viewpoint, the synthesis of MOFs, especially those comprising complex, novel ligands, is highly expensive and time-consuming. Most of the unique MOF structures consume a few days to be synthesized and requires highly pristine organic ligands, which are not practically viable for scaled-up production. Further functionalization procedures on the fabrication of MOF-based composite will also cause the synthesis process to be tedious. For studies involving electroactive MOFs, it is crucial to ensure the background signal is
minimized as much as possible to amplify signal intensity at low analyte concentration. Fabrication of electrochemical drug sensors via direct growth of MOF on the electrode surface is proving to be an effective technique. However, the literature on the mechanism of MOF crystal growth in such in-situ methods is still limited. Therefore, more emphasis needs to be given to the theoretical analysis of binder-free MOF synthesis. This will aid in establishing the correlation between the mechanism, topology, and detection activity of the MOFs.

6 Concluding Remarks and Future Perspectives

MOFs are innovative and emerging platforms for the electrochemical detection of pharmaceuticals. This review highlights developments in the employment of MOF-based materials for the electrochemical sensing of different classes of synthetic drugs. Herein, several key points have been identified to influence the performance of MOF-based electrochemical sensors. The high surface area, porosity, and diversity in structural design endow MOFs to provide credible drug-sensing performance. The synthesis method adopted for the fabrication of MOF is significant in determining the topology, morphology, and electrochemical stability of the materials. In contrast to pristine MOF, materials combined with carbon structures or metallic species exhibited better electrochemical signals and conductivity. However, the production of MOFs from the novel and complex ligands increases production time and cost. It is essential to develop more conductive, stable, reproducible, reliable, and selective MOF materials for drug sensing applications. To achieve this, the fundamental interaction between the MOF host and pharmaceutical compounds needs to be studied in an extensive manner. For potential commercialization, the MOF synthesis process should be facile and reproducible. Furthermore, the sensing mechanism of MOFs is still unclear, it is believed that they possess sensing sites that may act to generate redox signals for a specific analyte. The inclusion of biological molecules such as enzymes and aptamers in their

**Fig. 6** Variation in the composition of MOF used for pharmaceutical and drug detection
architecture would improve specific recognition of MOF-based materials. It is high time to address chemical stability and conductivity issues related to MOF-based materials to boost their applications in the fields of biosensing, multiple drug detection, therapeutics, clinical diagnostics, imaging, and controlled drug release. As far as electrochemical detection is concerned, in near future, MOF-based sensors are expected to be explored for on-site detection, cancer markers, multiple drug sensing, and in vivo detection of pharmaceuticals that will bring these materials to further elevations.

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**References**

Abdel-Atty, S., et al. (2020). The fabrication of a highly sensitive nano green carbon paste electrode modified with yttrium doped manganese oxide (Mn2O3/Y2O3) for electrochemical determination of marbofloxacin and its residues in bovine meat and milk samples. *Journal of the Electrochemical Society, 167*(10), 107509.

Adhikari, B.-R., Govindhan, M., & Chen, A. (2015). Sensitive detection of acetaminophen with graphene-based electrochemical sensor. *Electrochimica Acta, 162*, 198–204.

Aftab, S., et al. (2020). NH2-fMWCNT-titanium dioxide nanocomposite based electrochemical sensor for the voltammetric assay of antibiotic drug nadifloxacin and its in vitro permeation study. *Journal of Electroanalytical Chemistry, 859*, 113857.

Agtarap, A., et al. (1967). Structure of monensic acid, a new biologically active compound. *Journal of the American Chemical Society, 89*(22), 5737–5739.

Akbari, et al. (2022). Development of an electrochemical fentanyl nanosensor based on MWCNT-HA/ Cu-H3BTC nanocomposite. *Journal of Industrial and Engineering Chemistry, 114*, 418–426.

Al Sharabati, M., Sabouni, R., & Husseini, G. A. (2022). Biomedical applications of metal-organic frameworks for disease diagnosis and drug delivery: A review. *Nanomaterials (Basel, Switzerland), 12*(2), 277.

Alfè, M., et al. (2014). Synthesis and characterization of conductive copper-based metal-organic framework/graphene-like composites. *Materials Chemistry and Physics, 147*(3), 744–750.

Ali, M., et al. (2021). Sensitive MWCNT/P-Cys® MIP sensor for selective electrochemical detection of cefizoxime. *Journal of Materials Science, 56*(22), 12803–12813.

Alsaiari, et al. (2021). The application of nanomaterials for the electrochemical detection of antibiotics: A review. *Micromachines (Basel), 12*(3), 308.

Amalraj, A. J. J., Umesh, N. M., & Wang, S.-F. (2020). Synthesis of core-shell-like structure SnS2-SnO2 integrated with graphene nanosheets for the electrochemical detection of furazolidone drug in furoxide tablet. *Journal of Molecular Liquids, 313*, 113554.

Amidi, S., et al. (2017). Sensitive electrochemical determination of rifampicin using gold nanoparticles/poly-melamine nanocomposite. *Rsc Advances, 7*(64), 40111–40118.

Arkan, E., Paimard, G., & Moradi, K. (2017). A novel electrochemical sensor based on electropun TiO2 nanoparticles/carbon nanofibers for determination of Idarubicin in biological samples. *Journal of Electroanalytical Chemistry, 801*, 480–487.

Arnaboldi, S., et al. (2015). Inherently chiral electrode: The tool for chiral voltammetry. *Chemical Science, 6*(3), 1706–1711.

Aswini, K., Mohan, A. V., & Biju, V. (2014). Molecularly imprinted polymer based electrochemical detection of L-cysteine at carbon paste electrode. *Materials Science and Engineering: C, 37*, 321–326.

Baikeli, Y., et al. (2020a). Electrochemical determination of chloramphenicol and metronidazole by using a glassy carbon electrode modified with iron, nitrogen co-doped nanoporous carbon derived from a metal-organic framework (type Fe/ZIF-8). *Ecotoxicology and Environmental Safety, 204*, 111066.

Baikeli, Y., et al. (2020b). Electrochemical determination of metronidazole using a glassy carbon electrode modified with nanoporous bimetallic carbon derived from a ZnCo-based metal-organic framework. *Journal of the Electrochemical Society, 167*(11), 116513.
Balasubramanian, P., et al. (2019). A novel, efficient electrochemical sensor for the detection of isoniazid based on the B/N doped mesoporous carbon modified electrode. *Sensors and Actuators b: Chemical*, 283, 613–620.

Beaver, W. T. (2003). Review of the analgesic efficacy of ibuprofen. *International Journal of Clinical Practice. Supplement*, 135, 13–17.

Blain, M., et al. (2017). Survival after severe rhabdomyolysis following monensin ingestion. *Journal of Medical Toxicology*, 13(3), 259–262.

Bildar, A., et al. (2019). Graphene–gold nanostructures hybrid composites screen-printed electrode for the sensitive electrochemical detection of vancomycin. *Coatings*, 9(10), 652.

Braglia, L., et al. (2017). Tuning Pt and Cu sites population inside functionalized UiO-67 MOF by controlling activation conditions. *Faraday Discussions*, 201, 265–286.

Brett, A. M. O., et al. (1997). Voltammetric behavior of nitroimidazoles at a DNA-biosensor. *Electroanalysis*, 9(14), 1132–1137.

Bui, B. T. S., & Haupt, K. (2010). Molecurally imprinted polymers: Synthetic receptors in bioanalysis. *Analytical and Bioanalytical Chemistry*, 398(6), 2481–2492.

Ceruelos, A. H., et al. (2019). Therapeutic uses of metronidazole and its side effects: An update. *European Review for Medical and Pharmacological Sciences*, 23(1), 397–401.

Chakraborty, et al. (2015). Tuberculosis drug development: History and evolution of the mechanism-based paradigm. *Cold Spring Harbor Perspectives in Medicine*, 5(8), a021147.

Chan, H., & Fogg, A. (1979). Voltammetric determination of phenylbutazone and oxyphenbutazone at a glassy carbon electrode. *Analytica Chimica Acta*, 109(2), 341–349.

Chen, M., et al. (2017). An electrochemical aptasensor for multiplex antibiotics detection using Y-shaped DNA-based metal ions encoded probes with NMOF substrate and CSRP target-triggered amplification strategy. *Analytica Chimica Acta*, 968, 30–39.

Cheng, J., et al. (2020). Molecurally imprinted electrochemical sensor based on biomass carbon decorated with MOF-derived Cr2O3 and silver nanoparticles for selective and sensitive detection of nitrofurazone. *Chemical Engineering Journal*, 398, 125664.

Chiumello, D., Gotti, M., & Vergani, G. (2017). Paracetamol in fever in critically ill patients—An update. *Journal of Critical Care*, 38, 245–252.

Chokkareddy, R., & Kanchi, S. (2020). Simultaneous detection of ethambutol and pyrazinamide with IL@ CoFe 2 O 4 NPs@ MWCNTs fabricated glassy carbon electrode. *Scientific Reports*, 10(1), 1–10.

Chokkareddy, R., et al. (2021). A novel ionic liquid based electrochemical sensor for detection of pyrazinamide. *Journal of the Iranian Chemical Society*, 18(3), 621–629.

Chouinard, G. (2004). Issues in the clinical use of benzodiazepines: Potency, withdrawal, and rebound. *Journal of Clinical Psychiatry*, 65, 7–12.

Dehdashtian, S., Hashemi, B., & Aeenmehr, A. (2019). The application of perlitic/cobalt oxide/reduced graphene oxide (PC-rGO)/metal organic framework (MOF) composite as electrode modifier for direct sensing of anticancer drug idarubicin. *IEEE Sensors Journal*, 19(24), 11739–11745.

Demir, E., & Silah, H. (2020). Development of a new analytical method for determination of veterinary drug oxyclozanide by electrochemical sensor and its application to pharmaceutical formulation. *Chemosensors*, 8(2), 25.

Dong, S., et al. (2016). Exploiting multi-function metal-organic framework nanocomposite Ag@ Zn-TSA as highly efficient immobilization matrixes for sensitive electrochemical biosensing. *Analytica Chimica Acta*, 934, 203–211.

Doonan, C., Ricco, R., Liang, K., Bradshaw, D., & Falcaro, P. (2017). *Accounts of Chemical Research*, 50, 1423–1432.

Duo, H., et al. (2021). Magnetic mesoporous carbon nanosheets derived from two-dimensional bimetallic metal-organic frameworks for magnetic solid-phase extraction of nitroimidazole antibiotics. *Journal of Chromatography A*, 1645, 462074.

Eteya, M. M., Rounaghi, G. H., & Deiminiat, B. (2019). Fabrication of a new electrochemical sensor based on AuPt bimetallic nanoparticles decorated multi-walled carbon nanotubes for determination of diclofenac. *Microchemical Journal*, 144, 254–260.

Fang, X., et al. (2019). Nanocomposites of Zr (IV)-based metal–organic frameworks and reduced graphene oxide for electrochemically sensing ciprofloxacin in water. *ACS Applied Nano Materials*, 2(4), 2367–2376.

Fotouhi, L., & Alahyari, M. (2010). Electrochemical behavior and analytical application of ciprofloxacin using a multi-walled nanotube composite film-glassy carbon electrode. *Colloids and Surfaces b: Biointerfaces*, 81(1), 110–114.

Gan, T., et al. (2014). Simple and novel electrochemical sensor for the determination of tetracycline based on iron/zinc cations–exchanged montmorillonite catalyst. *Talanta*, 121, 187–193.

Gao, F., et al. (2020). NiO@ Ni-MOF nanorays modified Ti mesh as ultrasensitive electrochemical sensing platform for luteolin detection. *Talanta*, 215, 120891.

Ghanbari, M. H., & Norouzi, Z. (2020). A new nanostructure consisting of nitrogen-doped carbon nanoonions for an electrochemical sensor to the determination of doxorubicin. *Microchemical Journal*, 157, 105098.

Ghapuvarri, M., et al. (2020). A modified carbon paste electrode based on Fe 3 O 4@ multi-walled carbon nanotubes@ polyacrylonitrile nanofibers for determination of imatinib anti-cancer drug. *Journal of Applied Electrochemistry*, 50(2), 281–294.

Gill, A. A., et al. (2020). A poly (acrylic acid)-modified copper-organic framework for electrochemical determination of vancomycin. *Microchimica Acta*, 187(1), 1–9.

Gong, C., et al. (2017). Microperoxidase-11@ PCN-333 (Al)/ three-dimensional macroporous carbon electrode for sensing hydrogen peroxide. *Sensors and Actuators b: Chemical*, 239, 890–897.

Gudin, M. T., et al. (2018). Neuromuscular blockade: Subarachnoid anesthesia. *Essentials of Regional Anesthesia* (pp. 213–232). Springer.

Güney, N. S., et al. (1999). 5-Nitroimidazole derivatives as possible antibacterial and antifungal agents. *Il Farmaco*, 54(11–12), 826–831.

Guo, Z., & Gai, P. (2011). Development of an ultrasensitive electrochemiluminescence inhibition method for the
determination of tetracyclines. Analytica Chimica Acta, 688(2), 197–202.

Guo, L., et al. (2021). Metal-organic framework precursors derived Ni-doping porous carbon spheres for sensitive electrochemical detection of acetaminophen. Talanta, 228, 122228.

Habibi, B., Pashazadeh, A., & Saghatforoush, L. A. (2021). Zn-mesoporous metal-organic framework incorporated with copper ions modified glassy carbon electrode: Electro catalytic oxidation and determination of amoxicillin. Microchemical Journal, 164, 106011.

Hammes, W. P., & Neuhaus, F. C. (1974). On the mechanism of action of vancomycin: Inhibition of peptidoglycan synthesis in Gaffkya homari. Antimicrobial Agents and Chemotherapy, 6(6), 722–728.

Hampshire, V. A., et al. (2004). Adverse drug event reports at the United States food and drug Administration Center for Veterinary Medicine. Journal of the American Veterinary Medical Association, 225(4), 533–536.

Han, J., et al. (2014). Detrimental effects of metronidazole on selected innate immunological indicators in common carp (Cyprinus carpio L). Bulletin of environmental contamination and toxicology, 92(2), 196–201.

Hantschel, O., Rix, U., & Superti-Furga, G. (2008). Target spectrum of the BCR-ABL inhibitors imatinib, nilotinib and dasatinib. Leukemia & Lymphoma, 49(4), 615–619.

He, S., et al. (2021). Metal-organic frameworks for advanced drug delivery. Acta Pharmaceutica Sinica B, 11(8), 2362–2395.

Honakeri, N. C., et al. (2020). Electrochemical behavior of diclofenac sodium at core-shell nanostructure modified electrode and its analysis in human urine and pharmaceutical samples. Sensors International, 1, 100002.

Hosseini, H., et al. (2013a). Au-SH-SiO2 nanoparticles supported on metal-organic framework (Au-SH-SiO2@Cu-MOF) as a sensor for electrocatalytic oxidation and determination of hydrazine. Electrochimica Acta, 88, 301–309.

Hosseini, H., et al. (2013b). A novel electrochemical sensor based on metal-organic framework for electro-catalytic oxidation of L-cysteine. Biosensors and Bioelectronics, 42, 426–429.

Hu, M., et al. (2019). Label-free electrochemical immunosensor based on AuNPs/Zn/Ni-ZIF-8-800@graphene composites for sensitive detection of monensin in milk. Sensors and Actuators b: Chemical, 288, 571–578.

Huang, T. Y., et al. (2017). Enhanced charge collection in MOF-525–PEDOT nanotube composites enable highly sensitive biosensing. Advanced Science, 4(11), 1700261.

Hussain, et al. (2021). Metabolism and hepatotoxicity of pyrazinamide, an antibactericidal drug. Drug Metabolism and Disposition, 49(8), 679–682.

Hwa, K.-Y., Sharma, T. S. K., & Karuppaiah, P. (2019). Development of an electrochemical sensor based on a functionalized carbon black/tungsten carbide hybrid composite for the detection of furazolidone. New Journal of Chemistry, 43(30), 12078–12086.

Ichida, K., et al. (2004). Clinical and molecular analysis of patients with renal hypouricemia in Japan-influence of URAT1 gene on urinary urate excretion. Journal of the American Society of Nephrology, 15(1), 164–173.

Jara-Ulloa, P., et al. (2011). Adsorptive stripping voltammetric determination of nitroimidazole derivative on multiwalled carbon nanotube modified electrodes: Influence of size and functionalization of nanotubes. Journal of the Brazilian Chemical Society, 22, 1271–1278.

Jung, D.-W., et al. (2010). Facile synthesis of MOF-177 by a sonochemical method using 1-methyl-2-pyrrrolidinone as a solvent. Dalton Transactions, 59(11), 2883–2887.

Kalaj, M., et al. (2020). MOF-polymer hybrid materials: From simple composites to tailored architectures. Chemical Reviews, 120(16), 8267–8302.

Kallen, K.-J., Quinn, P., & Allan, D. (1993). Monensin inhibits synthesis of plasma membrane sphingomyelin by blocking transport of ceramide through the Golgi: Evidence for two sites of sphingomyelin synthesis in BHK cells. Biochimica et Biophysica Acta (BBA)-Lipids and Lipid Metabolism, 1166(2–3), 305–308.

Kashefi-Kheyrabadi, L., & Mehrjadi, M. A. (2012). Design and construction of a label free aptasensor for electrochemical detection ofodium diclofenac. Biosensors and Bioelectronics, 33(1), 184–189.

Kaya, S. I., et al. (2020). Carbon-based ruthenium nanomaterial-based electroanalytical sensors for the detection of anticancer drug Idarubicin. Scientific Reports, 10(1), 1–12.

Kempahanumakkagari, S., et al. (2018). Metal–organic framework composites as electrocatalysts for electrochemical sensing applications. Coordination Chemistry Reviews, 357, 105–129.

Kim, Y.-J., et al. (2010). Electrochemical aptasensor for tetracycline detection. Bioprocess and Biosystems Engineering, 33(1), 31–37.

Kingsley, M. P., Kalambate, P. K., & Srivastava, A. K. (2016). Simultaneous determination of ciprofloxacin and paracetamol by adsorptive stripping voltammetry using copper zinc ferrite nanoparticles modified carbon paste electrode. RSC Advances, 6(18), 15101–15111.

Ko, M., et al. (2020). Employing conductive metal–organic frameworks for voltammetric detection of neurochemicals. Journal of the American Chemical Society, 142(27), 11717–11733.

Kokulnathan, T., et al. (2020). Development of an electrochemical platform based on nanoplate-like zirconium phosphate for the detection of furazolidone. ACS Applied Nano Materials, 3(5), 4522–4529.

Kolahchi-Ahari, S., Deimitian, B., & Roumagh, G. H. (2020). Modification of a pencil graphite electrode with multiwalled carbon nanotubes capped gold nanoparticles for electrochemical determination of tramadol. Journal of Electroanalytical Chemistry, 862, 113996.

Kurbanoglu, S., et al. (2013). Electrochemical investigations of the anticancer drug idarubicin using multiwalled carbon nanotubes modified glassy carbon and pyrolytic graphite electrodes. Electroanalysis, 25(6), 1473–1482.

Lee, et al. (2017). Role of rifampin for the treatment of bacterial infections other than mycobacteriosis. Journal of Infection, 75(5), 395–408.

Li, C., et al. (2020). Luminescent lanthanide metal-organic framework test strip for immediate detection of tetracycline antibiotics in water. Journal of Hazardous Materials, 384, 121498.
Ling, P., et al. (2016). Platinum nanoparticles encapsulated metal–organic frameworks for the electrochemical detection of telomerase activity. *Chemical Communications*, 52(6), 1226–1229.

Liu, C., et al. (2011). Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clinical Infectious Diseases*, 52(3), e18–e55.

Liu, X., et al. (2019a). Novel nanorarchitecture of Co-MOF-on-TPN-COF hybrid: Ultralowly sensitive bioplatform of electrochemical aptasensor toward ampicillin. *Biosensors and Bioelectronics*, 123, 59–68.

Liu, Z., et al. (2019b). Molecularly imprinted polymer decorated 3D-framework of functionalized multi-walled carbon nanotubes for ultrasensitive electrochemical sensing of Norfloxacin in pharmaceutical formulations and rat plasma. *Sensors and Actuators B: Chemical*, 288, 363–372.

Liu, H., Fu, T., & Mao, Y. (2022). Metal–organic framework-based materials for adsorption and detection of uranium(VI) from aqueous solution. *ACS Omega*, 7(17), 14430–14456.

Lu, X., et al. (2016). Response characteristics of bisphenols on a metal–organic framework-based tyrosinase nanosensor. *ACS Applied Materials & Interfaces*, 8(25), 16533–16539.

Lu, Z., et al. (2021). MOF-derived Co3O4/FeCo2O4 incorporated porous biomass carbon: Simultaneous electrochemical determination of dopamine, acetonaphthen and xanthine. *Journal of Alloys and Compounds*, 858, 157701.

Ludwig, J., & McWhinnie, H. (2019). Antipyretic drugs in patients with fever and infection: Literature review. *British Journal of Nursing*, 28(10), 610–618.

Luo, G., et al. (2019). A ZIF-8 derived nitrogen-doped porous carbon and nitrogen-doped graphene nanocomposite modified electrode for simultaneous determination of ascorbic acid, dopamine and uric acid. *New Journal of Chemistry*, 43(43), 16819–16828.

Ma, S. C., Yang, V. C., & Meyerhoff, M. E. (1992). Heparin-responsive electrochemical sensor: A preliminary study. *Analytical Chemistry*, 64(6), 694–697.

Machado, R. S., Silva, M. R. D., & Viriato, A. (2008). Fura-zolidona, tetraciclina e omeprazol: uma alternativa de baixo custo para erradicação de Helicobacter pylori em crianças. *Jornal de Pediatria*, 84, 160–165.

Mahato, et al. (2017). Poly(N-[4H-1,2,4-triazol-4-yl]acrylamide) with different ratio of poly(vinyl chloride) composite membrane for liquid phase sensing of alcohol. *Journal of Applied Polymer Science*, 134 (15), 44675.

Malekzadeh, M., et al. (2020). Development of a new electrochemical sensor based on Zr-MOF/MIP for sensitive diclofenac determination. *Analytical and Bioanalytical Electrochemistry*, 12(3), 402–414.

Manea, F., et al. (2012). Silver-functionalized carbon nanofiber composite electrodes for ibuprofen detection. *Nanoscale Research Letters*, 7(1), 1–4.

Manjunatha, R., et al. (2011). Electrochemical detection of acetaminophen on the functionalized MWCNTs modified electrode using layer-by-layer technique. *Electrochimica Acta*, 56(19), 6619–6627.

Matsuoka, T., et al. (1996). Review of monensin toxicity in horses. *Journal of Equine Veterinary Science*, 16(1), 8–15.

Mazzotta, E., et al. (2008). Development of a sensor prepared by entrapment of MIP particles in electrosynthesised polymer films for electrochemical detection of ephedrine. *Biosensors and Bioelectronics*, 23(7), 1152–1156.

Mazzotta, E., et al. (2016). Solid-phase synthesis of electroactive nanoparticles of molecularly imprinted polymers. A novel platform for indirect electrochemical sensing applications. *Sensors and Actuators B: Chemical*, 229, 174–180.

McLean, I., et al. (1949). Susceptibility of micro-organisms to chloramphenicol (chloromycetin). *The Journal of Clinical Investigation*, 28(5), 953–963.

Mdluli, K., et al. (1998). Mechanisms involved in the intrinsic isoniazid resistance of Mycobacterium avium. *Molecular Microbiology*, 27(6), 1223–1233.

Meenakshi, S., Sophia, S. J., & Pandian, K. (2018). High surface graphene nanoflakes as sensitive sensing platform for simultaneous electrochemical detection of metronidazole and chloramphenicol. *Materials Science and Engineering: C*, 90, 407–419.

Mendes, R. F., et al. (2020). Metal–organic frameworks: A future toolbox for biomedicine? *Chemical Society Reviews*, 49(24), 9121–9153.

Meng, H.-M., et al. (2018a). Aptamer-functionalized nanoscale metal–organic frameworks for targeted photodynamic therapy. *Theranostics*, 8(16), 4332.

Meng, W., et al. (2018b). A novel electrochemical sensor for glucose detection based on Ag@ ZIF-67 nanocomposite. *Sensors and Actuators B: Chemical*, 260, 852–860.

Meucci, et al. (2013). Determination of phenylbutazone and flunixin meglumine in equine plasma by electrochemical-based sensing coupled to selective extraction with molecularly imprinted polymers. *Sensors and Actuators B: Chemical*, 179, 226–231.

Min, S., X. Qin, and H. Xiao-ya, (2009) Determination of marbofloxacin in animal serum at a nafion-modified electrode [J]. *Chemical Sensors*, 2.

Mital, A. (2009). Synthetic nitroimidazoles: Biological activities and mutagenicity relationships. *Scientia Pharmaceutica*, 77(3), 497–520.

Mitchell, M. A. (2006). *Enrofloxacin*. *Journal of Equine Veterinary Science*, 15(1), 66–69.

Moen, M. D., et al. (2007). *Imatinib*. *Drugs*, 67(2), 299–320.

Mondal, et al. (2022). Adsorptive removal of carbamazepine and ibuprofen from aqueous solution using a defective Zr-based metal-organic framework. *Journal of Environmental Chemical Engineering*, 10(6), 108560.

Moore, P., & Hersh, E. (2013). Combining ibuprofen and acetaminophen for acute postoperative pain management: Translating clinical research to dental practice. *Journal of the American Dental Association*, 144(8), 898–908.

Motoc, S., et al. (2013). Electrochemical detection and degradation of ibuprofen from water on multi-walled carbon nanotubes-epoxy composite electrode. *Journal of Environmental Sciences*, 25(4), 838–847.

Motoc, S., et al. (2016). Electrochemical selective and simultaneous detection of diclofenac and ibuprofen in aqueous solution using HKUST-1 metal-organic framework-carbon nanofiber composite electrode. *Sensors*, 16(10), 1719.
Naghian, E., et al. (2020). A new electrochemical sensor for the detection of fentanyl lethal drug by a screen-printed carbon electrode modified with the open-ended channels of Zn (ii)-MOF. *New Journal of Chemistry, 44*(22), 9271–9277.

Navalon, A., et al. (2002). Determination of the antibacterial enrofloxacin by differential-pulse adsorptive stripping voltammetry. *Analytica Chimica Acta, 454*(1), 83–91.

Niu, X., Bo, X., & Guo, L. (2021). MOF-derived hollow NiCo2O4/C composite for simultaneous electrochemical determination of furazolidone and chloramphenicol in milk and honey. *Food Chemistry, 364*, 130368.

Ntie-Kang, F., et al. (2014). Perspectives on tuberculosis pathogenesis and discovery of anti-tubercular drugs. *Current Medicinal Chemistry, 21*(30), 3466–3477.

Olson, C. A., Mitchell, K. D., & Werner, P. A. (2000). Bait ingestion by free-ranging raccoons and nontarget species in an oral rabies vaccine field trial in Florida. *Journal of Wildlife Diseases, 36*(4), 734–743.

Ott, C. E., et al. (2020). Electrochemical detection of fentanyl with screen-printed carbon electrodes using square-wave adsorptive stripping voltammetry for forensic applications. *Journal of Electroanalytical Chemistry, 873*, 114425.

Pinkerton, M., & Steirnrauf, L. (1970). Molecular structure of monovalent metal cation complexes of monensin. *Journal of Molecular Biology, 49*(3), 533–546.

Plante, G. E., & Valiantzilie, T. B. (2010). Opioids for cancer pain: The challenge of optimizing treatment. *Metabolism, 59*, S47–S52.

Pour, B. H., et al. (2021). High sensitive electrochemical sensor for imatinib based on metal-organic frameworks and multiwall carbon nanotubes nanocomposite. *Microchemical Journal, 165*, 106147.

Prabhakaran, M. P., et al. (2015). Electrospaying technique for the fabrication of metronidazole contained PLGA particles and their release profile. *Materials Science and Engineering: C, 56*, 66–73.

Qian, L., et al. (2021). Graphene oxide-based nanomaterials for the electrochemical sensing of isoniazid. *ACS Applied Nano Materials, 4*(4), 3696–3706.

Qiu, Q., et al. (2019). Recent advances in the rational synthesis and sensing applications of metal-organic framework biocomposites. *Coordination Chemistry Reviews, 387*, 60–78.

Rahi, A., et al. (2015). Sonoelectrodeposition of gold nanorods at a gold surface–application for electrocatalytic reduction and determination of nitrofuranone. *Sensors and Actuators b: Chemical, 210*, 96–102.

Rani, R., et al. (2020). Copper based organic framework modified electrosensor for selective and sensitive detection of ciprofloxacin. *Electroanalysis, 32*(11), 2442–2451.

Rawool, C. R., & Srivastava, A. K. (2019). A dual template imprinted polymer modified electrochemical sensor based on Cu metal organic framework/mesoporous carbon for highly sensitive and selective recognition of rifampicin and isoniazid. *Sensors and Actuators b: Chemical, 288*, 493–506.

Reddy, Y. V. M., et al. (2021). An ultra-sensitive rifampicin electrochemical sensor based on titanium nanoparticles (TiO2) anchored reduced graphene oxide modified glassy carbon electrode. *Colloids and Surfaces a: Physicochemical and Engineering Aspects, 608*, 125533.

Rezvani Jalal, N., et al. (2020). In situ growth of metal–organic framework HKUST-1 on graphene oxide nanoribbons with high electrochemical sensing performance in imatinib determination. *ACS Applied Materials & Interfaces, 12*(4), 4859–4869.

Rodríguez, J., Castañeda, G., & Lizcano, I. (2018). Electrochemical sensor for leukemia drug imatinib determination in urine by adsorptive stripping square wave voltammetry using modified screen-printed electrodes. *Electrochimica Acta, 269*, 668–675.

Rudnicki, K., et al. (2018). Quantitative determination of the veterinary drug monensin in horse feed samples by square wave voltammetry (SWV) and direct infusion electrospray ionization tandem mass spectrometry (DI–ESI–MS/MS). *Microchemical Journal, 141*, 220–228.

Sabouni, R., Kazemian, H., & Rohani, S. (2012). Microwave synthesis of the CPM-5 metal organic framework. *Chemical Engineering & Technology, 35*(6), 1085–1092.

Sagar, P., Srivastava, M., & Srivastava, S. K. (2022). Electrochemical sensor for the anti-tuberculosis drug rifampicin on CuO@ rGO-nanocomposite-modified GCE by voltammetry techniques. *ChemistrySelect, 7*(33), e202202271.

Samiec, P., & Navrátilová, Z. (2017). Electrochemical behaviour of bromazepam and alprazolam and their determination in the pharmaceutical tablets Lexaurin and Xanax on carbon paste electrode. *Monatsshefte Für Chemie-Chemical Monthly, 148*(3), 449–455.

Sanchez, C., et al. (2011). Applications of advanced hybrid organic–inorganic nanomaterials: From laboratory to market. *Chemical Society Reviews, 40*(2), 696–753.

Schoonover, M. J., Jann, H. W., & Blaik, M. A. (2005). Quantitative comparison of three commonly used treatments for navicular syndrome in horses. *American Journal of Veterinary Research, 66*(7), 1247–1251.

Shahrokhi, S., & Amiri, M. (2007). Multi-walled carbon nanotube paste electrode for selective voltammetric detection of isoniazid. *Microchimica Acta, 157*(3), 149–158.

Shaterian, M., et al. (2020). Synthesis, characterization and electrochemical sensing application of CoFe2O4/graphene magnetic nanocomposite for analysis of atenolol. *Polyhedron, 182*, 114479.

Shi, L., et al. (2020). Reduced graphene/polydopamine-supported Au@ Pt/Au nanoparticles for electrochemical detection of acetaminophen. *International Journal of Electrochemical Science, 15*, 3922–3934.

Shiri, S., et al. (2017). An electrochemical sensor for the simultaneous determination of rifampicin and isoniazid using a C-dots@ CuFe 2 O 4 nanocomposite modified carbon paste electrode. *New Journal of Chemistry, 41*(24), 15564–15573.

Siengdee, E., et al. (2019). Determination of two fluoroquinolones and their combinations with hyaluronan effect in in vitro canine cartilage explants. *PeerJ 7*, e6553.

Smolinska-Kempisty, K., et al. (2017). New potentiometric sensor based on molecularly imprinted nanoparticles for cocaine detection. *Biosensors and Bioelectronics, 96*, 49–54.
Sodeik, B., et al. (1994). Assembly of vaccinia virus: Effects of rifampin on the intracellular distribution of viral protein p65. Journal of Virology, 68(2), 1103–1114.

Song, et al. (2021). A label-free enrofloxacin electrochemical aptasensor constructed by a semiconducting CoNi-based metal–organic framework (MOF). Electrochimica Acta, 368, 15760.

Song, J., Huang, M., Lin, X. H., Li, S. F. Y., Jiang, N., Liu, Y., Guo, H.-S. & Li, Y. J. C. E. J. (2022). Novel Fe-based metal–organic framework (MOF) modified carbon nanofiber as a highly selective and sensitive electrochemical sensor for tetracycline detection. Chemical Engineering Journal, 427, 130913.

Souza, M. J., & Cox, S. K. (2011). Tramadol use in zoologic medicine. Veterinary Clinics: Exotic Animal Practice, 14(1), 117–130.

Souza, et al. (2022). A comprehensive review on the use of Metal-Organic Frameworks (MOFs) coupled with enzymes as biosensors. Electrochem, 3(1), 89–113.

Spreng, et al. (1995). Antibacterial activity of marbofloxacin. A new fluoroquinolone for veterinary use against canine and feline isolates. Journal of Veterinary Pharmacology and Therapeutics, 18(4), 284-289.

Su, F., et al. (2017). Two-dimensional zirconium-based metal–organic framework nanosheet composites embedded with Au nanoclusters: A highly sensitive electrochemical aptasensor toward detecting cocaine. ACS Sensors, 2(7), 998–1005.

Tan, F., et al. (2014). Molecularly imprinted polymer/porous carbon nanoparticles as electrode sensing material for selective detection of ofloxacin. Materials Letters, 129, 95–97.

Tang, Y., et al. (2018). Electrochemical aptasensor based on a novel flower-like TiO2 nanocomposite for the detection of tetracycline. Sensors and Actuators b: Chemical, 258, 906–912.

Tavana, T., Rezvani, A. R., & Karimi-Maleh, H. (2020). Pt-Pd-doped NiO nanoparticles decorated at single-wall carbon nanotubes: An excellent, powerful electrocatalyst for the fabrication of an electrochemical sensor to determine nalbuphine in the presence of tramadol as two opioid analgesic drugs. Journal of Pharmaceutical and Biomedical Analysis, 189, 113397.

Timperio, A., Kuiper, H., & Zolla, L. (2003). Identification of a furazolidone metabolite responsible for the inhibition of amino oxidas. Xenobiotica, 33(2), 153–167.

Walters, J. D., Zhang, F., & Nakkula, R. J. (1999). Mechanisms of fluoroquinolone transport by human neutrophils. Antimicrobial Agents and Chemotherapy, 43(11), 2710–2715.

Wang, B., & Yan, B. (2020). A turn-on fluorescence probe Eu3+ functionalized Ga-MOF integrated with logic gate operation for detecting ppm-level ciprofloxacin (CIP) in urine. Talanta, 208, 120438.

Wang, X., et al. (2014). Highly dispersed and stable copper terephthalate metal–organic framework–graphene oxide nanocomposite for an electrochemical sensing application. ACS Applied Materials & Interfaces, 6(14), 11573–11580.

Wang, Y., et al. (2015a). Magnetic Fe3O4@MOFs decorated graphene nanocomposites as novel electrochemical sensor for ultrasensitive detection of dopamine. RSC Advances, 5, 98260–98268.

Wang, X., et al. (2015b). 3D metal-organic framework as highly efficient biosensing platform for ultrasensitive and rapid detection of bisphenol A. Biosensors and Bioelectronics, 65, 295–301.

Wang, Y., et al. (2017). A metal–organic framework and conducting polymer based electrochemical sensor for high performance cadmium ion detection. Journal of Materials Chemistry A, 5(18), 8385–8393.

Wang, Y., et al. (2018). Fabrication and characterization of metal organic frameworks/polyvinyl alcohol cryogel and their application in extraction of non-steroidal anti-inflammatory drugs in water samples. Analytica Chimica Acta, 1022, 45–52.

Wang, H., et al. (2020a). DUT-67 and tubular polypyrrole formed a cross-linked network for electrochemical detection of nitrofurazone and ornidazole. Analytica Chimica Acta, 1109, 1–8.

Wang, J., et al. (2020b). An electrochemical sensor based on MOF-derived NiO@ZnO hollow microspheres for isoniazid determination. Microchimica Acta, 187(7), 1–8.

Wang, X., et al. (2021). Rapid detection of cadmium ions in meat by a multi-walled carbon nanotubes enhanced metal-organic framework modified electrochemical sensor. Food Chemistry, 357, 129762.

Wei, C., Zhou, H., & Liu, Q. (2021). PCN-222 MOF decorated conductive PEDOT films for sensitive electrochemical determination of chloramphenicol. Materials Chemistry and Physics, 270, 124831.

Whitfield, M. G., et al. (2015). A global perspective on pyrazinamide resistance: Systematic review and meta-analysis. PLoS ONE, 10(7), e0133869.

Wolfson, J. S., & Hooper, D. C. (1985). The fluoroquinolone drugs used in veterinary medicine. Advances in Veterinary Science, 30, 207–270.

Wong, A., et al. (2015). Development and application of an electrochemical sensor modified with multi-walled carbon nanotubes and graphene oxide for the sensitive and selective detection of tetracycline. Journal of Electroanalytical Chemistry, 757, 250–257.

Wu, S., et al. (2015). Aptamer-based fluorescence biosensor for chloramphenicol determination using upconversion nanoparticles. Food Control, 50, 597–604.

Wu, Z., et al. (2021). Detection of imatinib based on electrochemical sensor constructed using biosynthesized graphene-silver nanocomposite. Frontiers in Chemistry, 9, 208.

Xiao, L., et al. (2017). Highly sensitive electrochemical sensor for chloramphenicol based on MOF derived exfoliated porous carbon. Talanta, 167, 39–43.

Yadav, D. K., et al. (2016). Electrochemical investigation of gold nanoparticles incorporated zinc based metal-organic framework for selective recognition of nitrite and nitrobenzene. Electrochimica Acta, 200, 276–282.

Yan, Z., et al. (2015). A “signal-on” aptasensor for simultaneous detection of chloramphenicol and polychlorinated biphenyls using multi-metal ions encoded nanospherical brushes as tracers. Biosensors and Bioelectronics, 74, 718–724.

Yan, C., et al. (2017). Electrochemical determination of enrofloxacin based on molecularly imprinted polymer...
via one-step electro-copolymerization of pyrrole and o-phenylenediamine. *Journal of Electroanalytical Chemistry, 806*, 130–135.

Yan, L., et al. (2018). Highly sensitive furazolidone monitoring in milk by a signal amplified lateral flow assay based on magnetite nanoparticles labeled dual-probe. *Food Chemistry, 261*, 131–138.

Yan, Y., et al. (2019). Rod-like Co based metal-organic framework embedded into mesoporous carbon composite modified glassy carbon electrode for effective detection of pyrazinamide and isonicotinyl hydrazide in biological samples. *Talanta, 205*, 120138.

Yang, J., et al. (2016). A novel Cu x O nanoparticles@ ZIF-8 composite derived from core–shell metal–organic frameworks for highly selective electrochemical sensing of hydrogen peroxide. *ACS Applied Materials & Interfaces, 8*(31), 20407–20414.

Yang, J., et al. (2017). Metal–organic framework derived hollow polyhedron CuCo2O4 functionalized porous graphene for sensitive glucose sensing. *Sensors and Actuators b: Chemical, 242*, 728–735.

Yang, H. W., et al. (2020). A Highly Stable (4, 8)-Connected Tb-MOF exhibiting efficiently luminescent sensing towards nitroimidazole antibiotics. *Zeitschrift Für Anorganische Und Allgemeine Chemie, 646*(1), 23–29.

Ye, F., et al. (2018). Polyfurfural-electrochemically reduced graphene oxide modified glassy carbon electrode for the direct determination of nitrofurazone. *Analytical Letters, 51*(5), 728–741.

Yousefzadeh, A., et al. (2019). Surface molecular imprinting and powerfully enhanced chemiluminescence emission by Cu nanoclusters/MOF composite for detection of tramadol. *Sensors and Actuators b: Chemical, 286*, 154–162.

Zhai, X., et al. (2020). Coating silver metal-organic frameworks onto nitrogen-doped porous carbons for the electrochemical sensing of cysteine. *Microchimica Acta, 187*(9), 1–8.

Zhan, W.-W., et al. (2013). Semiconductor@ metal–organic framework core–shell heterostructures: A case of ZnO@ZIF-8 nanorods with selective photoelectrochemical response. *Journal of the American Chemical Society, 135*(5), 1926–1933.

Zhang, G., Driouich, A., & Staehelin, L. (1996). Monensin-induced redistribution of enzymes and products from Golgi stacks to swollen vesicles in plant cells. *European Journal of Cell Biology, 71*(4), 332–340.

Zhang, J., et al. (2017). Electrochemical sensor based on molecularly imprinted composite membrane of poly (o-aminthiophenol) with gold nanoparticles for sensitive determination of herbicide simazine in environmental samples. *Sensors and Actuators b: Chemical, 249*, 747–755.

Zhang, L., et al. (2019). A non-enzymatic voltammetric xanthine sensor based on the use of platinum nanoparticles loaded with a metal-organic framework of type MIL-101 (Cr). Application to simultaneous detection of dopamine, uric acid, xanthine and hypoxanthine. *Microchimica Acta, 186*(1), 1–10.

Zhang, L., et al. (2022). An electrochemical sensor based on CNF@ AuNPs for metronidazole hypersensitivity detection. *Biosensors and Bioelectronics: X, 10*, 100102.

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