Dopamine is a neurotransmitter that plays a critical role. Accurate dopamine detection is required both clinically and in medicine. A molecular imprinting (MIP) based electrochemical sensor is an extremely effective approach for detecting specificity. MIP is capable of effectively avoiding interference from other molecules, which compensates for the limited selectivity of conventional sensors in practical detection. This article discusses the many types and modification approaches for electrochemical sensors based on MIP. Then, we summarize the electrochemical MIP sensor-based dopamine sensor. Additionally, we emphasize how various additives might improve the sensing capability of conventional imprinted films. Finally, we discussed possible future directions for this field's development.

**Keywords:** Neurotransmitter; Dopamine; Molecular imprinting; Graphene; Electrodeposition

**1. INTRODUCTION**

Dopamine is a catecholamine neurotransmitter found in nerve tissue and bodily fluid that plays a critical role in brain function. Its distribution in certain parts of the human brain has an effect on pituitary endocrine function coordination and is directly tied to neural activity [1,2]. Dopamine is a significant cause of schizophrenia and Parkinson's disease. Additionally, dopamine stimulates the heart and improves blood flow to the kidneys, making it effective in the treatment of ischemic, cardiogenic, and septic shock [3–5]. As a result, the research of dopamine analysis methods is critical for neurophysiological function, disease diagnosis, and drug quality control [6].

The technique of spectroscopy can be used to determine the quantity of trace quantities of dopamine in the blood. The absorbance at 520 nm was determined using a ferrous sulphate-tartrate
solution as chromogen [7–10]. The absorbance and concentration of dopamine hydrochloride were found to have a strong linear relationship in the range of 2 to 10 g/L. To minimize hypotension in certain patients receiving clinical hemodialysis for renal insufficiency, dopamine is continuously supplied via micropump, and the concentration of dopamine in the blood is within this linear range at the normal dosage [11–14]. This establishes a theoretical foundation for dopamine dose control in clinical hemodialysis. Simultaneously, the chromogenic agent tetrachlorobenzoquinone was employed, and the quantity of dopamine could also be measured at 480 nm [15].

Chemiluminescence has increased in popularity as a result of its high sensitivity, simplicity, and quickness, and is frequently used in analytical work. Dopamine hydrochloride strongly inhibits the luminol-potassium ferricyanide chemiluminescence reaction system in alkaline media [16,17]. Thus, dopamine hydrochloride can be detected by suppressing reverse flow chemiluminescence. This technique is quick, precise, and has a large linear range [18,19]. It can be used to determine the concentration of dopamine hydrochloride in injections of dopamine hydrochloride. In a sulfuric acid environment, potassium permanganate oxidizes dopaminergic acid to generate a chemiluminescence system [20,21]. The luminescence intensity was linearly related to the dopamine concentration in the range 1.25 to 25.0 mg/L, and the detection limit of the approach was 1.00 mg/L [22]. In an acidic environment, potassium permanganate can oxidize formaldehyde and generate chemiluminescence. When dopamine was added to the system, the system's luminescence signal was greatly increased [23–25].

Due to the superior fluorescence analysis properties of CdTe quantum dots, they have been utilized as fluorescent reagents in the labeling and very sensitive analysis of metal ions and bioactive compounds. Dopamine hydrochloride can be used to greatly sensitize the fluorescence intensity [26,27]. CdTe quantum dots can be employed as fluorescent probes to assess the dopamine hydrochloride content of organic drug components using this method [28]. Dopamine hydrochloride has a substantial quenching impact on the fluorescence system catalyzed by haemoglobin in alkaline media, necessitating the development of a new approach for the measurement of dopamine hydrochloride using enzyme-catalyzed fluorescence spectrometry [29]. This method has a detection limit of 8.2 nM. The approach is straightforward, sensitive, and selective, and has been successfully used to quantify dopamine hydrochloride in pharmaceutical preparations [30–32].

Additionally, high performance liquid chromatography (HPLC) is a universal approach for detecting dopamine. HPLC has received considerable interest in the investigation of catecholamines due to its high separation rate [33]. HPLC-fluorescence detection is a highly successful and commonly used technology [34]. Catecholamines have an inherent fluorescence that can be used to detect them during HPLC separation. The results indicate that this procedure is straightforward, precise, and specific [35,36].

Due to the presence of two easily oxidized phenolic hydroxyl groups in the dopamine molecule, it exhibits electrochemical activity and may thus be detected using an electrochemical approach [37,38]. On gold, platinum, or GCE electrodes, however, the dopamine overpotential was large, and the electrode responsiveness was sluggish [39]. Additionally, it or the reaction product rapidly adsorbs on the electrode surface, resulting in passivation of the electrode and diminished sensitivity. Additionally, the oxidation peak potentials of contemporaneous substances such as adrenaline, vitamin C, and uric acid.
are comparable to those of dopamine in particular biological samples, resulting in considerable interference with dopamine detection [40–42]. As a result, the topic of selective dopamine detection has emerged as a hot and hard area of research in dopamine detection. Recent research has demonstrated that chemically modified electrodes can detect the selective enrichment and penetration of analytes efficiently by lowering the overpotential and enhancing the mass transfer rate of dopamine [43–46]. As a result, the use of chemically modified electrodes to analyze the electrochemical activity of dopamine has sparked considerable interest.

2. MOLECULARLY IMPRINTED ELECTROCHEMICAL SENSOR

Due to their high sensitivity, low cost, easy downsizing, and on-line detection capabilities, bioelectrochemical sensors are widely employed in chemistry, life science, materials research, and clinical medicine [47,48]. Biomolecules (such as enzymes and antibodies) have been used as particular recognition elements for sensors in environmental detection, biomedicine, and food analysis in recent decades, and their exceptional sensitivity and specificity have garnered widespread attention [49–51]. However, due to biomolecules' low physical and chemical stability, biosensors' practicability and commercialisation are severely hampered. The advantage of MIPs technology is that it has highly specific recognition sites and the ability to incorporate solid phase polymerization supports concurrently [52–55]. As a result, molecularly imprinted materials have a number of advantages over biosensitive materials, including high specificity, mass manufacture, resilience to biodegradation, and recurrent usage. As a result, MIPs as a sensitive material for sensors have emerged as a significant area of research in electrochemical sensing technology [56–58].

MIPs sensor is a new biosensor based on MIPs. Sensors are composed mostly of recognition components and transducers. MIPs are frequently employed as the recognition element or to change the recognition element in molecularly imprinted sensors [59]. When the target molecule precisely binds to MIPS, the ensuing physical and chemical changes are translated to electrical or other signals via the transducer components [60–62]. The analysis and detection of the target material can be accomplished by establishing a quantitative relationship between the output signal and the quantity change of the target material [63].

Electrochemical sensors are classified into capacitive, piezoelectric, current, and impedance sensors, among others, based on the type of electrical signal detected. Among them, the capacitance type first appeared, and the capacitance change of MIPs material prior to and following binding to the target material was directly evaluated qualitatively or quantitatively [64–66]. Piezoelectric sensors are primarily composed of quartz crystals with piezoelectric resonance characteristics, as demonstrated by the molecularly imprinted quartz crystal microbalance sensor and electrochemical crystal microbalance sensor [67]. Impedance sensors are based on capacitive sensors. This technique is suitable for studying the electrode's surface process and adsorption mechanism [68,69]. The current sensor is one of the most frequently utilized. Current sensors can be calibrated electrochemically using a variety of techniques, including square wave voltammetry (SWV), differential pulse stripping voltammetry (DPV), cyclic voltammetry (CV), and linear sweep voltammetry (LSV). There are two primary detection methods for
molecularly imprinted current-type sensors: for electrically active chemicals that are suited for direct detection, sensors can detect them directly [70–72]. Electroactive compounds are frequently utilized as electrochemical probes for non-electroactive chemicals. The electrochemical probe's reaction was examined during the process of the target occupying and leaving the imprinted site [73,74]. Nano-imprinted particles based on molecular imprinting technology have also been developed in recent years, and these nano-imprinted particles are critical in the development of biological and electrochemical sensors [75,76].

The imprinted polymer attachment on the transducer is a critical step that impacts the electrochemical sensor's performance [77–80]. The permanence of imprinted material on the transducer surface, as well as its effect on the electrode surface or substrate conductivity, will affect the transducer's detection performance. The following procedures are used to manufacture molecularly imprinted electrochemical sensors:

1. Drop coating method: the method is primarily concerned with selecting the proper dispersion system. MIPS is distributed in a dispersion fluid and then drips directly onto the electrode surface. After the solvent evaporates, M Stiffess S will be distributed and adhere to the electrode surface [81]. While the drop coating method is the easiest, the MIPS modification layer is sometimes too thick or uneven, impairing conductivity and reducing the effectiveness of recognition site generation.

2. In-situ polymerization: similar to the in-situ polymerization approach used to prepare chromatographic filled columns, the imprinted material is directly polymerized on the surface of the detection or separation unit using an initiator and crosslinking agent [82,83]. In general, imprinted polymer films are formed directly on the electrode surface for molecularly imprinted electrochemical sensors. On the surface of the transducer element, a modified layer with a broad area and adjustable thickness can be efficiently created [84]. However, because the redox products of template molecules in the system are difficult to remove, if employed on the electrode surface, the electrode renewal process may be troublesome.

3. Method of self-assembly: it is based on the covalent adsorption of functional groups. It is typical to use sulphydryl groups and gold, platinum, or oxide surface chemical adsorption to ensure that the imprinted material forms a homogeneous, stable, and ordered modification layer on the electrode surface [85]. While the self-assembly strategy is not constrained by the transducer components' ability to produce a homogeneous surface modification layer, there is a concern about the modification's stability against the base in certain inert conditions.

4. Electropolymerization: a solution including template molecules and functional monomer is created first, and then an electrochemical technique is utilized to directly initiate monomer polymerization [86]. This approach is unique in that the MIPs layer can develop directly on the electrode surface, with a thin, homogeneous, and adjustable thickness. In comparison to bulk polymerization, electropolymerization requires no initiator or crosslinking agent. It is more straightforward to manage the thickness of the polymer sheet, which may often reach the nanoscale scale. As a result, electropolymerization appears to be a promising approach for fabricating MIPs sensor-imprinted films [87].

Molecularly imprinted electrochemical sensors have demonstrated vast application prospects in environmental detection, food analysis, biological analysis, and clinical medicine following decades of
development [88]. Molecularly imprinted electrochemical sensors are being utilized to detect environmental contaminants, pesticides, perform drug analysis, and determine bioactive molecules. Tang et al. [89] used divinylbenzene as a crosslinking agent, diallyl barbiturate as a functional monomer, and cestrin as a template molecule to develop imprinting sensors for triazine herbicides and their metabolites. Sun et al. [90] employed dopamine as a functional monomer and bovine hemoglobin as a template to create an imprinted film on the surface of magnetic Fe₃O₄ nanoparticles that was effectively used to detect bovine hemoglobin electrochemically. Hu et al. [91] used the sol-gel process to create an imprinted electrode on polyaniline/multiwalled carbon nanotubes and a P-cyclodextrin substrate for L-phenylalanine detection. Zhong et al. [92] synthesized pyrrole-phenylboric acid and used it as a functional monomer to create electropolymerized imprinted sensors for dopamine detection. Through borate ester linkages, functional monomers interact with dopamine. By immersion and cyclic voltammetry, the produced polymer can rapidly remove template molecules from H₂SO₄ solution, demonstrating strong selectivity and anti-interference capabilities.

3. MOLECULAR IMPRINTED SENSOR FOR ELECTROCHEMICAL DETECTION OF DOPAMINE

Pyrrole is the most often utilized molecularly imprinted sensor material. A MIP-based electrochemical sensor for the identification and detection of dopamine was successfully developed by electropolymerizing pyrrole–phenylboronic acid as a novel monomer [93]. When paired with the imprinting effect of MIP, pyrrole–phenylboronic acid may form a cyclic boronic ester bond with dopamine, imparting on the sensor a twofold recognition capability for dopamine. In comparison to sensors constructed with pyrrole or phenylboronic acid as the electropolymerized monomer, the present sensor exhibited an amazingly high imprinting factor for dopamine. Additionally, o-phenylenediamine [94], p-aminothiophenol [95] are often utilized molecularly imprinted materials.

MIP synthesized electrochemically on a pencil graphite electrode was used to demonstrate sensor capabilities in the organic synthesis of a new functional thia-bilane structure [96]. Tripyrane 1 was converted to thia-bilane monomer by a reaction with nitrovinylthiophene 2 and molecular iodine. The thia-bilane monomer was electropolymerized to add dopamine to the polymeric framework. To test the MIP electrode, urea, tryptophan, ascorbic acid, and glucose were introduced. Apart from its outstanding sensitivity and selectivity, stability, repeatability, and durability, this monomer was designed specifically for electrochemical molecular imprinting technology.

Carbon material can be used to improve the detection effect of MIPs. MIP films were created by electropolymerizing pyrrole in the presence of dopamine after electrodeposition of carboxyl-functionalized multi-walled carbon nanotubes onto a GCE surface. [97]. The pH, monomer concentration, number of electropolymerization cycles, and scan rate for sensor preparation were optimized. When compared to other structurally comparable compounds, the MIP-based sensor demonstrated superior detection capability for dopamine. The carbon aerogel was made using the sol–gel method with ambient pressure drying [98]. For the detection of dopamine, a new electrochemical
sensing platform with electrocatalytic activity and molecular identification capabilities was developed using molecularly imprinted polypyrrole on a carbon aerogel surface.

Along with carbon nanotubes, graphene is a popular substance. Mao et al. [99] discussed the development of a novel graphene sheet/Congo red-MIPs composite (GSCR-MIPs) for use as a molecular recognition element in the fabrication of a dopamine electrochemical sensor. Due to the template molecules' high affinity, they were absorbed at the GSCR surface and subsequently employed to copolymerize methacrylic acid and ethylene glycol dimethacrylate preferentially. Potential scanning was demonstrated to extract dopamine molecules from the imprinted polymers screen, enabling the removal of dopamine to occur quickly and completely. In compared to traditional MIPs, the GSCR-MIPs exhibited not only faster desorption and adsorption kinetics, but also increased dopamine selectivity and binding capacity. As a demonstration, a highly sensitive and selective electrochemical sensor for the detection of dopamine was successfully constructed using the synthesized GSCR-MIPs nanocomposites. Liu et al. [100] reported the development of a MIPs electrochemical sensor based on a graphene–chitosan composite. The MIPs-GR sensor was constructed by electrodepositing a dopamine–graphene–chitosan composite film on the GCE and then removing the dopamine by electrochemical induced elution. Due to the excellent electrical characteristics, unique two-dimensional structure, and large surface area of graphene, the built sensor demonstrated a very sensitive reaction to dopamine oxidation with an increased current signal and rapid response time. Another study suggested the creation of a composite of SiO$_2$-coated graphene oxide and MIPs via a novel graphene oxide-based imprinting technique [101]. SiO$_2$-coated graphene oxide sheets were synthesized through the sol–gel technique in a water–alcohol mixture. Prior to polymerization, the vinyl groups on the graphene oxide/silica surface were chemically changed with -methacryloxypropyl trimethoxysilane, enabling selective polymerization on the graphene oxide/silica surface. Then, by copolymerizing graphene oxide/SiO$_2$–MIPs with functionalized graphene oxide/SiO$_2$, dopamine, methacrylic acid, and ethylene glycol dimethacrylate, a novel graphene oxide/SiO$_2$–MIPs composite was successfully created. The DPV current responsiveness of the graphene oxide/SiO$_2$–MIPs sensor was approximately 3.2 times that of the non-imprinted polymers.

Additionally, Nobel metal nanoparticles are frequently employed to increase MIP. For instance, gold nanoparticles doped MIPs were employed to produce a very sensitive biomimetic MIP sensor for dopamine sensing [102]. AuNPs, unique functional monomers with aniline groups on the surface, were produced in the presence of dopamine and p-aminophenylthiol and utilized to electropolymerize MIPs films on the electrodes. The sensors created on the basis of AuNPs-doped MIPs conductive sheets are capable of successfully removing interference from ascorbic and uric acids. In another study, the molecular recognition element of an electrochemical sensor for the detection of dopamine was constructed using a novel core-shell combination of AuNPs and SiO$_2$ MIPs [103]. The introduction and mixing of AuNPs with biocompatible porous sol-gel materials is the technique's primary benefit over previous blot recognition technologies. Due to the template molecules' high affinity, they are initially adsorbed on the surface of AuNPs and subsequently joined to the polymer membrane via hydrogen bonds and interactions between the template molecules and the silane monomer. CV was employed to remove dopamine molecules from the imprinted membrane, enabling for a rapid and effective extraction of dopamine. In comparison to earlier interferents, the AuNPs@SiO$_2$-MIPs sensor exhibited not only high selectivity for dopamine but also a large linear range over dopamine concentration. Additionally,
the novel electrochemical sensor was successfully employed to detect dopamine in dopamine hydrochloride injections and human urine samples, revealing that it was a versatile sensing instrument capable of detecting dopamine selectively in real-world samples.

**Table 1.** Comparison of detection limit and detection linear range of MIPs based dopamine electrochemical sensor.

<table>
<thead>
<tr>
<th>Sensor</th>
<th>Linear range</th>
<th>LOD</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thia-bilane</td>
<td>0.05 μM to 250 μM</td>
<td>20 nM</td>
<td>[96]</td>
</tr>
<tr>
<td>Carbon nanotube/polypyrrole</td>
<td>0.625 μM to 100 μM</td>
<td>60 nM</td>
<td>[97]</td>
</tr>
<tr>
<td>Graphene/Congo red</td>
<td>0.1 μM to 830 μM</td>
<td>100 nM</td>
<td>[99]</td>
</tr>
<tr>
<td>MWCNT/copoly(MAA-co-TRIM)</td>
<td>0.5 μM to 200 μM</td>
<td>0.5 μM</td>
<td>[104]</td>
</tr>
<tr>
<td>Aniline moiety</td>
<td>0.228 μM to 140 μM</td>
<td>0.228 μM</td>
<td>[105]</td>
</tr>
<tr>
<td>APTES</td>
<td>2 μM to 800 μM</td>
<td>2 μM</td>
<td>[106]</td>
</tr>
<tr>
<td>o-aminophenol</td>
<td>0.02 μM to 0.2 μM</td>
<td>1.98 nM</td>
<td>[107]</td>
</tr>
<tr>
<td>Graphene–chitosan</td>
<td>1 nM to 80 nM</td>
<td>0.01 nM</td>
<td>[100]</td>
</tr>
<tr>
<td>Pyrrole–phenylboronic acid</td>
<td>50 nM to 0.1 μM</td>
<td>33 nM</td>
<td>[93]</td>
</tr>
<tr>
<td>o-phenylenediamine</td>
<td>0.5 mg/L to 7.0 mg/L</td>
<td>0.11 mg/L</td>
<td>[94]</td>
</tr>
<tr>
<td>Graphene oxide/SiO₂</td>
<td>50 nM to 160 μM</td>
<td>30 nM</td>
<td>[101]</td>
</tr>
<tr>
<td>Carbon nanotubes/graphene aerogels/polypyrrole</td>
<td>5 nM to 20.0 μM</td>
<td>1.67 nM</td>
<td>[108]</td>
</tr>
<tr>
<td>Metallic microrod</td>
<td>0.2 pM to 80 nM</td>
<td>0.763 pM</td>
<td>[109]</td>
</tr>
<tr>
<td>CS film/ZnO NPs@C/3D-KSC</td>
<td>0.12 nM to 152 μM</td>
<td>0.039 nM</td>
<td>[110]</td>
</tr>
<tr>
<td>ZnO nanotubes</td>
<td>0.02 μM to 5 μM and 10 μM to 800 μM</td>
<td>-</td>
<td>[111]</td>
</tr>
<tr>
<td>Poly(acrylamidophenylboronic acid)</td>
<td>50 nM to 2 μM</td>
<td>20 nM</td>
<td>[112]</td>
</tr>
<tr>
<td>Poly(5-amino 8-hydroxy quinoline)/reduced graphene oxide</td>
<td>-</td>
<td>32.7 nM</td>
<td>[113]</td>
</tr>
<tr>
<td>Gold/polypyrrole</td>
<td>40 nM to 10 μM</td>
<td>-</td>
<td>[114]</td>
</tr>
<tr>
<td>Aptamer-MIP</td>
<td>50 nM to 10 μM</td>
<td>47 nM</td>
<td>[115]</td>
</tr>
<tr>
<td>Graphene@carbon nanotube foam</td>
<td>2 fM to 1 pM</td>
<td>0.667 fM</td>
<td>[116]</td>
</tr>
<tr>
<td>Polypyrrole/carbon nanotubes</td>
<td>50 pM to 5 μM</td>
<td>10 pM</td>
<td>[117]</td>
</tr>
<tr>
<td>ETD</td>
<td>0.02 μM to 0.107 μM</td>
<td>4.4 nM</td>
<td>[118]</td>
</tr>
</tbody>
</table>
4. CONCLUSION AND PERSPECTIVES

The detection limit and detection linear range of a dopamine electrochemical sensor based on MIPs are compared in Table 1. Due to the numerous benefits of MIP hybridization, there is an increasing trend toward using MIP composites rather than MIP alone. Additionally, creating a composite material with acceptable qualities necessitates extreme caution. The use of diverse nanostructures into sensor design is critical since it can result in high sensitivity when combined with MIPs. However, synthesizing suitable nanomaterials with the desired morphology and size is extremely difficult, as various studies have demonstrated that a threshold size for nanomaterials, particularly nanoparticles, must be created in order to attain exceptional performance. Due to the MIPs' high selectivity, interference with the dopamine sensor is also decreased. Numerous manufactured sensors demonstrated intuitive operation, good reusability, and low cost. The issue of decreased sensitivity due to the MIP layer's non-conductivity was also addressed in the majority of research, and by utilizing various types of conductive signaling substrates, ultrasensitive electroanalytical detection in the nanomolar range was achieved. Additionally to these studies, the performance of certain techniques for dopamine detection, such as the low detection limits of sensor responses in the pico-molecular range, demonstrates the method's promise. Only a few MIP-based sensors have been validated in clinical samples, and in the majority of cases, these sensors have not been validated using established procedures. However, with the exception of a few research, the analytical applicability of these sensors for dopamine detection in real-time trials has not been examined, which may shed information on the accuracy of the dopamine sensors or methodologies established. To optimize their benefits and develop marketable dopamine sensors, researchers must conduct real-time studies of their sensors' effectiveness. Despite great interest and extensive study into the development of dopamine sensors/methods, very few commercial products are available in this field. Their commercialization is complicated by a lack of cost-effective bioreceptors, the utilization of ecologically friendly functional monomers, and storage stability. This issue becomes considerably more critical when developing medical diagnostic gadgets. Numerous steps remain to be taken to complete the development and commercialization of MIP-based dopamine sensor systems, as their application in clinical settings is still in its infancy. As a result, a new generation of diagnostic devices based on sensor technology is urgently needed that can integrate sampling, processing, and analysis to handle the most prevalent diagnostic difficulties.

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