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A Review: Electrochemical Determination of Dopamine

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Abstract

In the last few decades, researchers are attracted to nanomaterials and their reactivity due to their high surface area. The electrochemical sensors were developed by using this huge number of nanomaterials and used for the determination of drug/biomolecules. Dopamine is a naturally occurring biogenic compound and an important neurotransmitter. The normal concentration of dopamine mediates the functioning of the central and peripheral nervous system but the concentration in excess can create different diseases. Due to the presence of a high concentration of electro-active interferents such as uric acid, ascorbic acid, and paracetamol, etc. The detection of dopamine electrochemically in real samples is challenging. To overcome this problem, nanomaterials were used to modify the electrochemical sensor to enhance the sensitivity and selectivity of the electrode. In this brief review, of most extensively used materials for the fabrication of a modified electrode to detect dopamine are considered. The characteristics of the materials which improve the electro-catalytic activity of modified surfaces have also been emphasized. The reports are limited up to the electrochemical methods dealing with the detection of dopamine, in the presence of uric acid and ascorbic acid simultaneously.

Keywords: Dopamine;Nano-Particles Modified Electrodes;Electrochemical Detection;Electrocatalytic Activity;Neurotransmitters;

Introduction

Bio-fluid has lots of small molecules, for the detection of these drug molecules in bio-fluids, the monitoring of drugs is essential and has a pivotal role in monitoring drug quality. Dopamine 4-(2-aminoethyl) benzene-1,2diol, (DA), a naturally occurring biogenic compound, known for its inhibitory neurotransmitter, is produced in the "Dargic neurons" in the ventral tegmental area (VTA) of the midbrain, strongly associated with reward mechanisms in the brain like memory, locomotion, learning, and behavior of cognition. As a hormone, it mediates the functioning of the central and peripheral nervous system [1-2] during physical activities but also is responsible for emotion and the endocrine system. Lower concentration of DA can produce burning mouth syndrome [3], restless leg syndrome [4], Senile dementia, fibromyalgia [5-6], and rarely depression [7]. Depletion of DA in the cerebral region may lead to Parkinson's disease [8] while a high concentration of DA, resulted because of addiction to cocaine, heroin, nicotine, alcohol and long-term smoking, etc., may act on the sympathetic nervous system and result from unusual blood pressure and an incensement in heart rate. Various analytical techniques such as titrimetry [9], high performance liquid chromatography [10 -12], spectrophotometry [13], chemiluminesence [14], gas-chromatography-mass spectrometry [15] and ultraviolet spectrophotometry [16] are developed to detect PCM and DA in biological fluids and tablets. These developed techniques are inconvenient in the routine analysis because of the tedious extraction process. Recently developed electrochemical techniques [17-23] have attracted researchers to use these types of molecules in biofluids, as they are cheap, highly selective, easy to handle, and less time-consuming. Literature reports suggested that nanomaterials having porous morphology and high surface area were traditionally employed for electrode material to detect of bio-molecules as well as drug molecules [24 -25]. Some electrodes have been reported for the detection of these molecules [26 - 27]. Here in this review we objectively look into the most efficient and promising results capable to detect DA in presence of UA and AA or their simultaneous detection Properties of modified surfaces that initiate their electro-catalytic activity towards target analyzes have been critically summarized. Best analytical approaches are sorted out based on the following figure of merits:

sensitivity, selectivity, simplicity in sample pretreatment, simplicity and stability of modification, a signal enhancement compared to bare electrode, linear working concentration range, a separation between oxidation potentials of peaks, and limit of detections. [Figure 1]
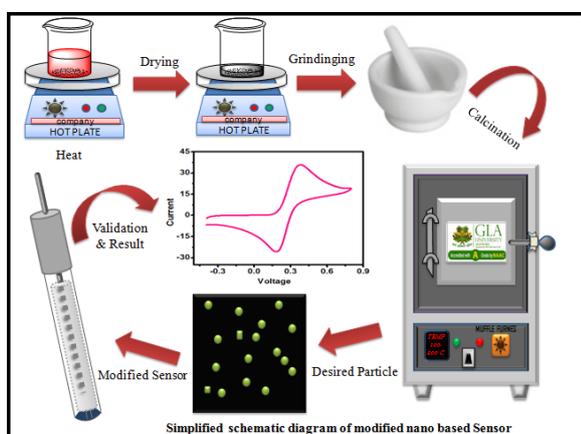

Figure-1: Schematic diagram of a Nano-based modified sensor

Modified Electrodes for Detection of DA:

To determine dopamine in drug molecules as well as in a biological fluid sample, a large number of electrodes have been used. Some of which recently developed electrode/ electrode materials have been cited like J b Raoof et. al developed MWCNTs modified carbon paste electrode for DA. They prepared a carbon paste electrode (CPE) modified by multiwall carbon nanotubes (MWCNTs) and banana tissue. The developed electrode was exploited to detect dopamine. The modified electrode was good in selectivity toward DA in the presence of ascorbic acid (AA). The differential pulse voltammetry (DPV) technique was used to investigate the surface of the modified electrode towards the electrochemical determination of DA. The detection limit (3σ) was 2.09 μM for DA with a linearity range from 10-30 μM was recorded at the surface of the developed electrode. After 20 days of preparation, the electrode was showing relatively good stability [28], Srikanth Cheemalapati et. al [29] presented a report on multi-walled carbon nanotubes (MWCNT)/graphene oxide (GO) nanocomposite. The nanomaterial was prepared by the dispersion of MWCNT homogeneously for the determination of DA and PCM simultaneously. Wrapping of MWCNT with GO sheets was confirmed by TEM analysis. The MWCNT/GO nanocomposite exhibited superior electro-catalytic activity towards the oxidation of DA and PCM, in comparison to either pristine MWCNT or GO. The synergetic effect of MWCNT & GO was the main reason for the simultaneous detection of DA and PCM. In this report, the electrochemical analysis was studied by cyclic voltammetry, differential pulse voltammetry, and amperometry. The nanocomposite modified electrode exhibited electro-catalytic oxidation of DA and PCM in the linear response range from 0.2 to 400 μmol L^{-1} and 0.5 to 400 μmol L^{-1} with the detection limit of 22 nmol L^{-1} and 47 nmol L^{-1} respectively. The proposed sensor exhibited remarkable selectivity, sensitivity, stability with consistency, and precision; In 2017, DongwonKim et. al [30] published work on the determination of dopamine (DA) and acetaminophen (AC) using activated graphene-Nafion modified glassy carbon electrode (AG-NA/GCE). In that report, they prepared, AG by a simple and facile method of thermal activation of graphene oxide (GO) with potassium hydroxide (KOH) to improve

pore volume and specific surface area. For the characterization of surface morphology and pore structure of AG, the field-emission scanning electron microscope, transmission electron microscopy, Raman spectroscopy, and nitrogen isothermal adsorption-desorption technique was used. The electroanalytical performance of the AG-NA/GC electrode toward the oxidation of DA and AC was analyzed via cyclic voltammetry and differential pulse voltammetry. The result displayed excellent selectivity and sensitivity toward an analysis of DA and AC with low detection limit values of 0.33 and 0.031 μM (S/N = 3) for DA and AC, respectively. For the real sample analysis, the human urine sample was diluted and used for analysis, Justin Claude Kemmegne-Mbouguen et. al [31] reported work in 2017. They modified the carbon paste electrode by using Cameroonian smectite clay and a metal-free meso-tetra (4-carboxyl phenyl) porphyrin and used for the detection of DA, acetaminophen, and tyrosine simultaneously. The developed electrode (TCPP–Sa/CPE) displayed extended linear ranges, high sensitivities, and selectivity's, and low limits of detection for DA (0.1 μM), AC (0.2 μM), and Tyr (0.7 μM) using square wave voltammetry; In a report of Dandan Chen et al. [32] a Nanoporous platinum-yttrium alloy (NP-PtY) was fabricated by dealloying ribbons of a PtYAl alloy. They used this Nano-porous platinum-yttrium alloy to modify the graphene electrode to form the glassy carbon electrode and used as an electrochemical sensor for the highly sensitive and detection of dopamine selectively. The sensor, best operated at 0.16 V vs. SCE, has a linear range covering the 0.9 to 82 μM concentration range, a 0.36 μM detection limit (at S/N = 3), and good selectivity over tyramine, tryptamine, phenethylamine, uric acid, and ascorbic acid. It gave satisfactory results in the determination of DA in spiked samples of urine; Zeid Abdullah Alothman et al. [33] reported the development of acid-functionalized multi-wall carbon nanotubes (f-MWCNTs) modified glassy carbon electrodes for the simultaneous determination of DA & PCM. In the DPV technique both, DA and AP give sensitive oxidation peaks at 125 mV and 307 mV, respectively. Under the optimized experimental conditions (such as supporting electrolyte pH, accumulation time and scanning rate, etc.) DA and AP give linear response over the range of 3–200 μmol L^{-1} (r = 0.992) and 3–300 μmol L^{-1} (r = 0.989), respectively. The lower detection limits were 0.8 for DA and 0.6 μmol L^{-1} for AP. G. P. Keeley et al. developed a sensor for simultaneous electrochemical determination of DA and PCM based on thin pyrolytic carbon films. In this article, they described the determination of DA and PCM using CV and DPV. Good selectivity, stability, and reproducible simultaneous measurement of the two compounds are achieved using thin pyrolytic carbon (PyC) films as working electrodes. This carbon electrode can detect dopamine in the range 18 to 270 μM, with a 2.3 μM limit of detection (LoD), while simultaneously sensing paracetamol in the range 15 to 225 μM (LoD 1.4 μM). A 225 mV separation between the two competing signals is realized [34], Y Liu et. al reported a work, of synthesized amino-group functionalized mesoporous Fe_3O_4 nanoparticles by using the solvothermal method. Pd-loaded amino-group functionalized mesoporous Fe_3O_4 nanoparticles (Pd@Fe_3O_4) were made with ethanol as a reducing agent. Pd@Fe_3O_4 modified the glassy carbon electrode (GCE) displayed remarkable electrochemical catalytic activities towards dopamine (DA) owing to the synergetic effect between Pd and Fe_3O_4. The electrochemical behavior of Pd@Fe_3O_4/GCE towards DA was experimented using square wave voltammetry and the selective determination of DA was carried out at a high concentration of uric acid. A wide concentration range (0.96–107 μmol/L) and low detection

limit (0.41 μmol/L, S/N = 3) for the determination of DA were obtained [35], in one another reports, the Au electrode was modified with thioglycolic acid (TGA) capped CdTe quantum dots. CdTe quantum dots played the role of an efficient electron-conducting tunnel in electron transfer between DA and Au electrode. The increment in peak current is attributed: (a) electrostatic attraction between cationic DA and anionic quantum dots, (b) high surface area, and (c) high conductivity of QDs. However, the TGA capped QDs provided a better platform for the oxidation of DA [36]. Yuting Yan et. Al [37] developed an electrode, which was used for sensitive and selective detection of DA. The AuNP-RGO modified electrode resulted in the enhancement of ECL signals about 5-fold as compared to bare GCE. Moreover, onset positive potential was decreased and ECL intensity was amplified by an increase in the concentration of DA. An interference analysis was performed by taking double concentrations of UA and AA relative to DA, D Yuan et. al set a one another example, the reduced GO/MWCNTs/AuNPs was used to modify GCE for ECL detection of dopamine based on peroxydisulfate solution. The ECL signal of peroxydisulfate solution was investigated at reduced GO/MWCNTs/AuNPs/GCE and it was enhanced with an increase in DA concentration. The response was linear in the range between 0.20 to 70μM. The applicability of the ECL sensor was again tried by analysis of DA in hydrochloride injection, human urine, and serum [38]. S. Liu et. al proposed a promising electrochemiluminescence (ECL) sensing strategy with dual-stabilizers-capped CdSe quantum dots (QDs) as ECL emitters. The dual-stabilizers-capped CdSe QDs were covalently immobilized onto p-aminobenzoic acid-modified glass carbon electrode with ethylenediamine as a linking molecule. The proposed sensor could accurately quantify dopamine from 10.0 nM to 3.0 μM with a detection limit of 3.0 nM in practical drug, human urine, and cerebrospinal fluid samples without any signal amplification techniques. This strategy seems promising to fabricate ECL sensors with high sensitivity and spectral selectivity [39], Yogendra et. al [40] reported The perovskite-type lanthanum ortho ferrite nano-particles (LaFeO$_3$) based electrochemical sensor and used to detect dopamine. For this work, the lanthanum ortho ferrite nano-particles (LaFeO$_3$) were synthesized by the combustion technique using sugar and ethanolamine with lanthanum oxide and ferric nitrate. After characterization through FESEM and TEM, the crystallite size was found to be 40 to 46 nm with a cubic crystal structure. To check the electrochemical properties of the modified sensor electrode (LaFeO$_3$/GP), the cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques were used. During the experiment, the phosphate buffer solution having pH 6.0 was employed, maintaining the scan rate 100mVs-1 and 50mVs-1 for cyclic voltammetry and differential pulse voltammetry, respectively, Yogendra et.al [41] recently reported the graphite-based electrochemical sensor modified by Nano-sized praseodymium ferrite (np-PrFeO3) materials for the detection of dopamine. The crystallite sizes of synthesized nanoparticles (nps) were in the range from 40-45 nm with a cubic crystal system. Cyclic voltammetry and Differential pulse voltammetry techniques were used to study the electrochemical property and were observed to be superior to earlier reports. The limit of detection of dopamine at PrFeO3/GP electrode was 600 nM with 5 to 200 μM for linearity range, Yogendra et al., in 2019, [42] reported some very efficient electrodes for the detection of paracetamol and dopamine, the electrodes were developed from Nano-sized material of cobalt ferrite (np-CoFe$_2$O$_4$) and manganese ferrite (np-MnFe$_2$O$_4$). Characterization of size, shape, and morphology of nanomaterials was performed by XRD, FESEM, and EDS techniques.

The crystallite sizes of synthesized nanoparticles (nps) were in the range from 10 to 12 nm with a cubic crystal system. These particles were utilized as electrodes modified with graphite to detect paracetamol and dopamine through CV and DPV simultaneously. The minimum detection limit of paracetamol and dopamine at the CoFe$_2$O$_4$/GP electrode was 250 nM and 350 nM while at the MnFe$_2$O$_4$/GP electrode it was 300 nM and 400 nM, respectively. Both the electrodes were operated in the linearity range from 3 μM to 200 μM & 3 μM–160 μM for paracetamol and 3 μM–180 μM & 5 μM to 200 for dopamine, respectively. Ahmad Manbohi et al. [43] developed, electrochemical microfluidic paper-based analytical Nano-sensor (EμPAN) a sensitive, selective, fast, and low-cost technique for dopamine detection. The wax-based stamping technique was used for patterning of microfluidic structure on chromatography paper. In this work, a mixture of graphite-chitosan-poly ethylene glycol (PEG) was used as the bare working electrode and counter electrode, and silver ink was employed as a quasi-reference electrode. The electrochemical behavior of these electrodes was studied using 5mM K$_3$[Fe (CN)$_6$] in 0.5M KCl. The linear range and limit of detection of dopamine were 0.5–120 μM and 0.01 μM, respectively. To show the applicability of the EμPAN, this device was exploited to determine DA in blood and urine samples, Yun-Shuai Bi et al. [44] reported a hexagonal boron carbon nitride hybrid (h-BCN) is developed by in situ high-temperature solid-state reaction and subsequent chemical reduction with hydrazine. The XRD and TEM analysis was used to show that the h-BCN features interlayered structures with two characteristic d-spacing of 0.33 and 0.21 nm. The obtained h-BCN exhibited significant electrochemical sensors for dopamine and uric acid. The cyclic voltammetric and amperometric experiments revealed a good linear relationship between current densities and concentrations of dopamine (DA) of 10-300 μM and uric acid (UA) of 10-500 μM, with high sensitivities of 0.14 μA/μM and 0.32 μA/μM and detection limits of 5 μM and 2 μM, respectively, Lei Cheng et al. [45] worked on a hybrid and hierarchical nanocomposite. The nanocomposites were prepared by the growth of zeolitic imidazolate framework-8 (ZIF-8) on the template of ionic liquid (IL, [Bmim] [BF4]) functionalized reduced graphene oxide (IL-RGO). XRD, FESEM, FTIR, and Raman spectroscopy were used to characterize the structure and morphology of IL-RGO/ ZIF-8 nanocomposite. The results revealed RGO sheets to have refrained from restacking by IL, and ZIF-8 nanoparticles grew well on the surface of IL-RGO. A very high sensitive sensor to detect DA can be achieved due to the synergetic effect of large surface area and good catalytic activity of ZIF-8 and good electrical conductivity of IL-RGO. The modified electrode exhibits good electrocatalytic activity and electroconductive properties towards DA which were investigated by cyclic voltammetry, differential pulse voltammetry, and electrochemical impedance spectroscopy. The linear response range of DA was from $1 0 \times 10^{-7}$ to $1 0 \times 10^{-4}$ mol/L with a low detection of limit $3 5 \times 10^{-8}$ mol/L. Also, the sensor was shown to provide satisfactory stability for the determination of DA, Mathieu Ouellette et al. [46] reported fast identification electrochemically and quantification of neurotransmitters in the ever-growing field of neuro electronics, they focused on the facilitation of for the detection of dopamine electrochemically by functionalizing commercially available electrodes by depositing the thin film of gold nanoparticles. The effect of buffer solution, fiber material, concentration, and cyclic voltammetry (CV) cycle number, were tested during neurotransmitter detection. In each case, having no drastic change of outcome of the functionalization process, the selectivity towards dopamine was improved. An increment

of 92% of oxidation current for dopamine and a lowering of 66% for ascorbic acid serotonin was noticed under the best condition. Moreover, dopamine sensing was achieved in tandem with home-made triple electrodes and an in-house built potentiostat at a high scan rate mode According to Da-Seul Kim et al. [47] dopamine is a key molecule in neurotransmission and has been known to be responsible for several neurological diseases. Hence, its sensitive and selective detection is important for the early diagnosis of diseases related to abnormal levels of dopamine. They reported a new cylindrical gold nanoelectrode (CAuNE) platform fabricated via sequential laser interference lithography and electrochemical deposition. Among the fabricated electrodes, CAuNEs with a diameter of 700 nm, 150 s deposited, was found to be the best for electrochemical dopamine detection. The linear range of the CAuNE-700 nm was 1–100 µM of dopamine with a limit of detection (LOD) of 5.83 µM. Moreover, owing to the homogeneous periodic features of CAuNEs, human neural cells were successfully cultured and maintained for more than 5 days in vitro without the use of any extracellular matrix proteins and dopamine was detectable in the presence of these cells on the electrode, In another report, an efficient and simple designed nanohybrid made to detect ascorbic acid, dopamine, and uric acid individually and simultaneously. This nanohybrid is a combination of chemically reduced graphene oxide (CRGO) and redox poly (para-phenylene) (Fc-ac-PP) modified in a lateral position with ferrocenyl group CRGO/Fc-ac-PPP. Due to the synergetic effect of CRGO/Fc-ac-PPP Nano-hybrid and redox attached ferrocene, yielded large conductivity, surface area, and better catalytic properties. Moreover, this Nano-composite is capable of detecting AA, DA, and UA in a co-existence system with defined and separated redox peaks oxidation individually & simultaneously. The linear response ranges for AA, DA and UA, when detected simultaneously, are 0.1–10000 _M, 0.0001–1000 _M, and 0.1–10000 _M, respectively, and the detection limits (S/N = 3) are 0.046 _M, 0.2 nM and 0.013 _M, respectively. The proposed sensor exhibited acceptable results in real spiked urine samples for measuring the abnormally high or low concentration of AA, DA, and UA in vivo [48], A high-performance poly (aniline boronic acid) nanocomposite electrode containing DNA-functionalized carbon nanotubes and nitrogen-doped graphene was electrochemically fabricated and employed for highly sensitive and selective detection of dopamine. The covalent anchoring between boronic acid receptors on the electrode surface and diols of dopamine in the electrolyte solution changed the electrochemical properties of the polyaniline backbone, which was exploited as a transduction mechanism for non-oxidative, sensitive, and selective detection of dopamine. The electrodeposited polymer on the electrode substrate with boronic acid functionalities demonstrated minimal affinity towards dopamine interferents; e.g. ascorbic acid. This minimal affinity is because of very weak interactions of boronic acid diols with diols of ascorbic acid. For the detection of dopamine biomolecules in a physiologically-relevant environment cyclic voltammetry and differential pulse voltammetry were employed. The separation of the oxidation peak potentials of dopamine and ascorbic acid was measured to be 300mV for poly (aniline boronic acid) nanocomposites containing DNA-functionalized carbon nanotubes and nitrogen-doped graphene. The optimal mass ratio of DNA functionalized carbon nanotubes to nitrogen-doped graphene was investigated to be 1:3. This high resolution in voltammetry peaks allows selectively determining of dopamine. The detection limit of dopamine is measured to be as low as 6 nM for these 229 specific nanocomposite electrodes. Besides its high

sensitivity and selectivity, the dopamine sensor we fabricated demonstrates very high stability and repeatability with a standard error calculated for n = 5 to be 5.23% [49], Dopamine homeostasis is a vital clinical diagnostic index, an excess level in the human body initiates certain serious diseases. Herein, a novel electrochemical sensing platform based on gold Nano- bipyramid/multi-walled carbon nanotube hybrids (AuNBP/MWCNTs) is developed to detect dopamine in human fluids. Using field emission scanning electron microscopy, it is observed that AuNBPs of about 60 nm with two pyramids are well dispersed on the surface of MWCNTs. Energy-dispersive X-ray spectrometry, X-ray diffraction, and X-ray photoelectron spectroscopy confirm that AuNBPs are self-assembled onto the surface of MWCNTs to form the hybrids. Cyclic voltammetry study reveals that the AuNBP/MWCNTs exhibit good electrocatalytic activity toward dopamine oxidation owing to the synergistic effects of AuNBPs and MWCNTs. Besides, both cyclic voltammetry and differential pulse voltammetry display three well-resolved and distinct oxidation peaks on the AuNBP/MWCNT-modified glassy carbon electrode. Based on AuNBP/MWCNTs, the newly developed electrochemical sensor is used to detect dopamine in the presence of ascorbic acid and uric acid over a wide linear range from 50 nM to 2.7 mM and a low detection limit of 15 nM (at S/N = 3). Quantitative analysis of DA in a real sample may be performed using the sensor [50]. A platinum–silver graphene (Pt–Ag/Gr) nanocomposite modified electrode was fabricated for the electrochemical detection of dopamine (DA). Electrochemical studies of the Pt–Ag/Gr nanocomposite to detect DA were done by CV and DPV. The results of CV analysis revealed that Pt–Ag/Gr/GCE enhanced electrocatalytic activity towards DA oxidation due to the synergistic effects between the platinum–silver nanoparticles and graphene. The DPV results showed that the modified sensor demonstrated a linear concentration range between 0.1 and 60 µM with a limit of detection of 0.012 µM. The Pt–Ag/Gr/GCE presented satisfactory results for reproducibility, stability, and selectivity. In addition, the sensor showed satisfactory recoveries in a real sample study [51]. The development of inexpensive and simple analytical tools is of practical significance for biological sample analysis. This work developed a simple and cost-effective electrochemical sensor that was covered with filter paper and modified by multi-walled carbon nanotubes (MWCNTs) for selective and sensitive dopamine (DA) detection in animal tissue extracts. Animal tissue samples were extracted with an acidified n-butanol (1 ml/g) homogenate in an ice bath suitable for electrochemical detection. A DA response is received at a very low potential (0.43 V vs. Ag/Ag Cl) and is not affected by noradrenaline (NE) or 5-hydroxytryptamine (5-HT). The correlation between analytical signals and the amount of assembled MWCNTs, as well as with the electrode area was also investigated. The amperometric reaction to DA is found to be linear in a concentration range of 2.5×10^{-8} M to 1×10^{-5} M, with a 5 nM detection limit (signal-to-noise ratio of 3) under optimized experimental conditions. The method was further applied to quantify DA in the brain and tendon tissues of rats. The new method proposed is inexpensive, simple, and rapid compared to those of other conventional methods. It is pertinent to note that the sensor is a disposable, single-use sensor; thus, for every experiment, the electrode is prepared "as new". According to the authors they presumed that this approach is an effective model for quantifying DA, which has great potential for future diagnostics of DA-related diseases [52], Dopamine, an important neurotransmitter in the central nervous system, coexist with uric acid and ascorbic acid. UA and AA can be oxidized easily, having potentials close to that of DA for electrochemical

analysis, resulting in overlapping voltammetric response. In this work, a novel molecularly imprinted (MI) electrochemical sensor was proposed for selective determination of DA (in the presence of up to 80-fold excess of UA and AA), relying on gold nanoparticles (Aunano)–decorated glassy carbon (GC) electrode coated with poly(carbazole (Cz)-co-aniline (ANI)) copolymer film incorporating DA as a template (DA imprinted-GC/P(Cz-co-ANI)-Aunano electrode, DA-MIP-Aunano electrode). The sensor for DA detection showed great electroactivity for analyte oxidation in a 0.2 mol L^{-1} pH 7 phosphate buffer solution. Square wave voltammetry (SWV) was performed within 10-4–10-5 mol L^{-1} of DA, of which the oxidation peak potential was observed at 0.16 V. The limit of detection (LOD) and limit of quantification (LOQ) were 2.0×10^{-6} and 6.7×10^{-6} mol L^{-1}, respectively. Binary and ternary synthetic mixtures of DA-UA, DA-AA, and DA-UA-AA yielded excellent recoveries for DA. Also, DA could be recovered quantitatively from a real sample of bovine serum spiked with DA and determined in concentrated dopamine injection solution. The developed SWV method was statistically validated against a literature potentiodynamic method using a caffeic acid modified-GC electrode [53]. In one more article, a rotating droplet system is used for the simultaneous detection of dopamine and serotonin. Carbon nanoparticles functionalized with sulfonic groups on the electrode surface enables potential discrimination between the neurotransmitters and the most common interferences, whereas the efficient and low-volume hydrodynamic system helps to lower the detection limit toward physiologically relevant concentrations. In this article, the authors presented the results with a 10 nM limit of detection for serotonin and a 100 nM to 2 μM linear response range from the system in a sample containing equimolar concentrations of dopamine and serotonin and 0.5 mM concentration of both uric and ascorbic acids. Demonstrating the practical applicability of this method, the authors measured the concentration of serotonin in 70 μL of mice blood serum samples without additional pretreatment [54]. A nano-composite of HKUST-1

(MOF) and electroreduction graphene oxide (ERGO) is prepared and used as an electrochemical sensor for the simultaneous determination of paracetamol and dopamine using one-step electrodeposition. The MOF/ERGO composite displays excellent electrochemical catalytic activities towards the paracetamol and dopamine, which is attributed to the synergistic effect of big surface area, porosity, and high electrocatalytic activity of the MOF and good conductivity of ERGO. The modified electrode could be applied to determine simultaneously paracetamol and dopamine in biochemical samples with wide linear ranges (0.2 μM to 160 μM for paracetamol and 0.2 μM to 300 μM for dopamine) and low detection limits (0.016 μM for paracetamol and 0.013 μM for dopamine). Meanwhile, the proposed sensor still displays high sensitivity, good selectivity, and excellent stability [55]. Dopamine detection is very sensitive, early diagnosis of some neurological disorder demands a highly selective approach. A new platform for electrochemical detection of DA accurately comprising a porous grapheme oxide (PGO)/gold nanoparticle (GNP)/pGO composite-modified indium tin oxide (ITO) is presented. The pGO was first synthesized and purified by ultrasonication followed by centrifugation, and it was functionalized on the surface of a GNP-immobilized ITO electrode. Due to the synergetic action of the pGO and GNPs, the 3D pGO-GNP-pGO-modified ITO electrode exhibited better detection performance of DA when compared with pGO- or GNP-modified ITO electrodes. The linear range of the sensing platform from 0.1 μM to 30 μM with a detection (LOD) of 1.28 nM, more precise than earlier reported electrodes have been observed. Moreover, the 3D pGO-GNP-pGO-modified ITO electrodes displayed the capability of detection even in the presence of several interfering molecules (e.g., ascorbic acid, glucose) also. The proposed platform of the 3D pGO-GNP-pGO-modified ITO electrode may be potential in the field of DA sensing devices and can be effectively utilized for early diagnosis of neurological related disorders [56]. All data are summarized in table 1.

S. No	Name of electrode	Detection limit	Linearity range	Ref.
1	MWCNTs modified carbon paste electrode	2.09 μM	10-30 μM	[28]
2	Multi-walled carbon nanotubes (MWCNT)/graphene oxide	22 nmol L^{-1}	0.2 to 400 μmol L^{-1}	[29]
3	Activated graphene-Nafion modified glassy carbon electrode	0.033 μM	NA	[30]
4	Cameroonian smectite clay and a metal-free *meso*-tetra (4-carboxyl phenyl) porphyrin modified carbon paste electrode	0.1 μM	NA	[31]
5	Nanoporous platinum-yttrium alloy	0.36 μM	0.9 to 82 μM	[32]
6	Acid functionalized multi-wall carbon nanotubes	0.8 μmol L^{-1}	3–200 μmol L^{-1}	[33]
7	Thin pyrolytic carbon films base electrochemical sensor	2.3 μM limit	18 to 270 μM	[34]
8	Palladium (Pd)-loaded amino-group functionalized mesoporous Fe$_3$O$_4$ nanoparticles based glassy carbon electrode	0.41 μmol/L	0.96–107 μmol/L	[35]
9	Au electrode modified with thioglycolic acid capped CdTe quantum dots	8.27 nM	0.025 μM to 3.0 μM	[36]
10	AuNP-RGO modified electrode	6.7 nM	0.02–40 μM	[37]

11	Reduced GO/MWCNTs/AuNPs	NA	0.20 to 70μM	[38]
12	Dual-stabilizers-capped CdSe quantum dots	3.0 nM	10.0 nM to 3.0 μM	[39]
13	Perovskite type lanthanum ortho ferrite nano-particles ($LaFeO_3$) based electrochemical sensor	600 nM	5–200 μmol	[40]
14	Graphite based electrochemical sensor modified by nano-sized praseodymium ferrite	600 nM	5–200 μmol	[41]
15	$CoFe_2O_4$/GP electrode	350 nM	3 μM–180 μM	[42]
	$MnFe_2O_4$/GP electrode	400 nM	5 μM to 200 μM	
16	Microfluidic paper-based analytical nanosensor	0.01 μM	0.5–120 μM	[43]
17	Hexagonal boron carbon nitride hybrid	5 μM	10-300 μM	[44]
18	IL-RGO/ZIF-8 nanocomposite	0.35 μM	0.1–100 μM	[45]
20	A thin film containing pre-formed gold nanoparticles.	1 mM	NA	[46]
21	Cylindrical gold nanoelectrode (CAuNE) platform fabricated via sequential laser interference lithography	5.83 μM	1–100 μM	[47]
22	CRGO/Fc-ac-PPP nanohybrid	0.2 nM	0.0001–1000μM	[48]
23	DNA-functionalized carbon nanotubes and nitrogen-doped graphene	6nM	0.007-1μM	[49]
24	AuNBP/MWCNTs	15 nM	50 nM to 2.7 mM	[50]
25	A platinum–silver graphene (Pt–Ag/Gr) nanocomposite modified electrode	0.012 μM	0.1 and 60 μM	[51]
26	Multi-walled carbon nanotubes (MWCNTs)	5 nM	0.025–10 μM	[52]
27	Molecularly Imprinted Poly(Carbazole-co -Aniline) Electrode Decorated with Gold Nanoparticles	2 μM	2 -6.7 μM	[53]
28	Carbon nanoparticles functionalized with sulfonic groups	10 nM	100 nM to 2 μM	[54]
29	MOF/ERGO composite	0.013 μM	0.2 μM to 300 μM	[55]
30	3D porous graphene oxide (pGO)/gold nanoparticle	1.28 nM	0.1 μM to 30 μM	[56]

A General overview of modification materials:

Detection of biological small molecule and quantification are presently obtaining the attention of scientist and medical practitioner. However, analytical methods of detection available are often expensive and time taking. Also, this can only be performed by trained personnel most of the time. To overcome those traditional lacks, chemically modified electrodes i.e. electrochemical sensors are some of the most promising alternative methods with low costs, shorter time, and a greater range of selectivity and sensitivity. In this review, we have discussed different types of materials being used to modify the electrodes for dopamine detection.

Challenges in real sample analysis:

Detection of a biological molecule, the presence of infectious pathogens, or contaminates in a real sample is necessary as these can lead to the serious problem of human health. To gain important information about human health, determination of different biomarkers, and small-molecule targets in body fluids found in blood and sweat. The concentration of some metabolites, ions, and proteins in sweat, saliva, tears, and urine have been established to track linearly with their respective concentrations in blood, meaning that real-time chemical monitoring of these targets using sensors is conceptually feasible [57]. But the reality is the challenges for the development of the tool as several limitations in detecting small molecules,

reusability, and sufficient stability for repetitive measurements [58]. Some challenges encountered in the electrochemical analysis are due to similar redox potentials of co-existing and high concentration interfering species in real biological samples which makes it difficult for dopamine level–analysis. Advanced modified electrodes which are mostly limited to proof of concept may be able to overcome the existing challenges [59]. Along with it, a critical problem remains in the sufficient selectivity of biosensors to be applied for real samples application is the presence of nontarget molecules with the unknown amount [60]. Few notable examples are there like glucose biosensors but the journey of biosensors from laboratories to clinical applications is still very limited. Therefore, in this research area, it is a challenging task to develop rapid, cost-effective, reliable, and specific sensors for the detection of small biological molecules. Over more than a decade, different research and development about electrochemical biosensors have been investigated, but till now in the medical market its penetration is slow as the reliability of the product is still under question despite various progression and achievement in this field. The consequent obstacles including optimization in sample preparation, analysis time, and device sensitivity are restricting the development of this field. Thus, electrochemical sensors are the forthcoming tool to provide fundamental, technical, and mechanistic studies in the field of detection of pathogens [61].

Conclusive Remarks

Herein we discussed the current status of investigation in this particular research area and provided our views on modified electrochemical sensors and various challenges that might be addressed and overcome by utilizing the modern nanoparticle-based technology before rapid use of the product for medical purpose for the betterment of the mankind. But to solve these challenges efficiently there is a need for combined expertise of different fields like electrochemists, biochemists, materials and electronic engineers, etc. Hopefully, the active approach towards solving the difficulties will help to enhance the reliability and sensitivity of dopamine chemical sensors discussed in this review.

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