Metal and Metal Oxide Based Advanced Ceramics for Electrochemical Biosensors-A Short Review

G. Bala Subbaiah[1], K. Venkata Ratnam[1], S. Janardhan[1], K. Shiprath[1], H. Manjunatha[1]*, M. Ramesha[2], N. V. Krishna Prasad[3], S. Ramesh[3] and T. Anil Babu[3]

[1]Department of Chemistry, GITAM School of Science, GITAM University, Bengaluru, India, [2]Department of EECE, School of Technology, GITAM University, Bengaluru, India, [3]Department of Physics, GITAM School of Science, GITAM University, Bengaluru, India

Identifying and quantifying the biological concentrations of certain biomolecules such as dopamine, glucose, tyrosine, and cholesterol, etc. has become the basis for medical diagnosis in the treatment of a number of related diseases. In most cases, the concentrations of these biomolecules in biofluids like blood acts as a biomarker and becomes crucial in the treatment of diseases. On the other hand, advanced ceramics refers to oxides (alumina, zirconia), non-oxides: (carbides, borides, nitrides, silicides), Composites (particulate reinforced combinations of oxides and non-oxides), etc. This review article discusses recent developments in the field of electrochemical sensors developed using metal and metal oxide based advanced ceramics with an emphasis on developments in the field over the past five years. The article presents the key results, important findings, and interesting chemistry of biosensing advanced ceramic based electrochemical biosensors for some important biomolecules such as acetaminophen, glucose, and dopamine, etc.

Keywords: advanced ceramics, electrochemical biosensors, cyclic voltammetry, chronoamperometry, biomolecules such as dopamine, glucose, acetaminophen

INTRODUCTION

The development of electrochemical sensors for chemical and biological sensing has made remarkable advantages in recent years with various applications (Worsfold, 1995). The electrochemical detection mechanism has played a vital role in medical applications such as disease diagnosis. Due to the highly sensitive and selective nature of electrochemical sensors, the real-time analysis of various analytes is possible with the help of portable and simple operated design equipment (Veloso et al., 2012).

Sensors detect a given input signal and convert it into different combinations of output readings. These sensors are typically operated with specified analytes and certain sample types with other environmental conditions (Worsfold, 1995) Electrochemical sensors have been widely used in various applications, for example in the quality control of industrial products, human health activity monitoring, predicting emissions, medical diagnostics, home safety alarms, and many other applications. The design of electrochemical sensors is based on the parametric nature of sensor devices. Typically, the parameters are electronic, either current, voltage, or reactance change affected

FIGURE 1 | Schematic of sensing by biosensors.
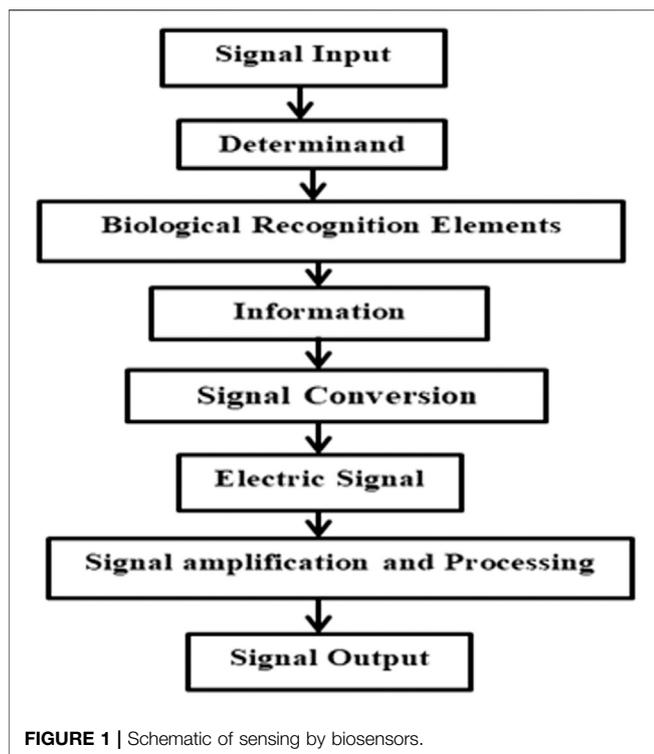
by varying analyte configuration. Electrochemical sensors can be extensively used for any form of solid, liquid, and gaseous analytes. The information captured from electrochemical sensors which are generally due to an interaction between analyte and electrode elements is converted into a qualitative or quantitative electrical signal (Vinay et al., 2020).

Electrochemical biosensors also play a vital role in many applications such as in medical diagnostics, monitoring environmental gases, and improving oxygen levels. They are also extensively used to monitor bioactivity in various compounds and organic materials. The working principle of bio-sensors is based on the use of a biomolecule to detect the concentration of a target bio-molecule. Biosensors are generally considered a subcategory of chemical sensors due to the transduction methods they employ (Joseph et al., 2003). A combination of electrochemical transducers, an electrode is attached, and a biomolecule is identified by the electrochemical biosensors. The dual nature of electrochemical biosensors can be used for applications such as real-time monitoring of the environment or subjects or targets in the form of selectivity and sensitivity. The major advantages of electrochemical biosensors over traditional analytical methods are that these materials could lead to various new features in chemical and biomedical applications in the future (Ruano, 2016). In General, biosensors are devices which convert a biological event or reaction into a readable output signal for analysis purpose (Hernandez-Vargas et al., 2018).

The biosensor's basic principle can be described as follows; it is sensitive to nucleic acids, cells, antibodies, enzymes, and other

biological activities. The working principle is based on acquiring the target reaction between base elements and exhibiting sensitivity through a physical or chemical transducer. The range of reactive conditions acquired by the discrete or continuous nature of the signals is the basic information for the biosensor device's analysis purpose. Electrochemical biosensors are composed of sensitive filament and electrochemical signal converter. The sensitive film is mainly used to identify the analytes and the electrochemical signal converter is to convert biomass activity to electrical signals. The basic working principle of biosensors is described in **Figure 1**.

The electrochemical biosensors are classified based on the nature of the transducer into potentiometric, amperometric, and impedimetric transducers. These individual transducers convert the chemical information into measurable resistive, amperometric, and reactive signals, respectively. Electrochemical biosensors have been used in extensive ways, with various applications, for over fifty years. Generally, the materials used for electrochemical sensors are categorized into the electrode and supporting substrates for electroanalytical performances and the recognition of the biological elements. **Figure 2** shows the scheme of an electrochemical biosensor. Here biological sensing elements are coupled to the electrodes. Transducers used in the electrode elements convert the electric signal into a readable output to the processing circuit for monitoring purposes (Hernandez-Vargas et al., 2018). The advancement and adaptation of electrochemical biosensors seem to possess great potential for the future. The technological gains in electrochemical biosensors with a range of practical uses, through a combination of selective biochemical detection methods, have led to a new era in the field of chemistry (Pohanka and Skladal, 2008).

ADVANCED CERAMICS

The design strategies that have driven biosensor development include detecting and measuring the parameters, transducer working mechanism, the technology, materials used for sensor fabrication, and finally, applications (Hernandez-Vargas et al., 2018). Various materials have been explored in recent years for their electrochemical sensing and biosensing applications in various fields. Advanced ceramic materials are one such material used for the fabrication of electrochemical and biosensors. Researchers have emphasized the utilization of advanced ceramic materials for selecting, sensing, and detecting certain materials. These are summarized in **Table 1** below.

Advanced ceramics are becoming a more attractive option in modern technological applications with maximum focus on material properties. This focus on material properties has led to a significant expansion in research and development, and in optimizing the properties of ceramics and their matrix composites. Traditionally ceramics either inorganic or non-metallic solids are prepared from powdered materials by applying heat and possess characteristic properties, including hardness, strength, low electrical conductivity, and brittleness.
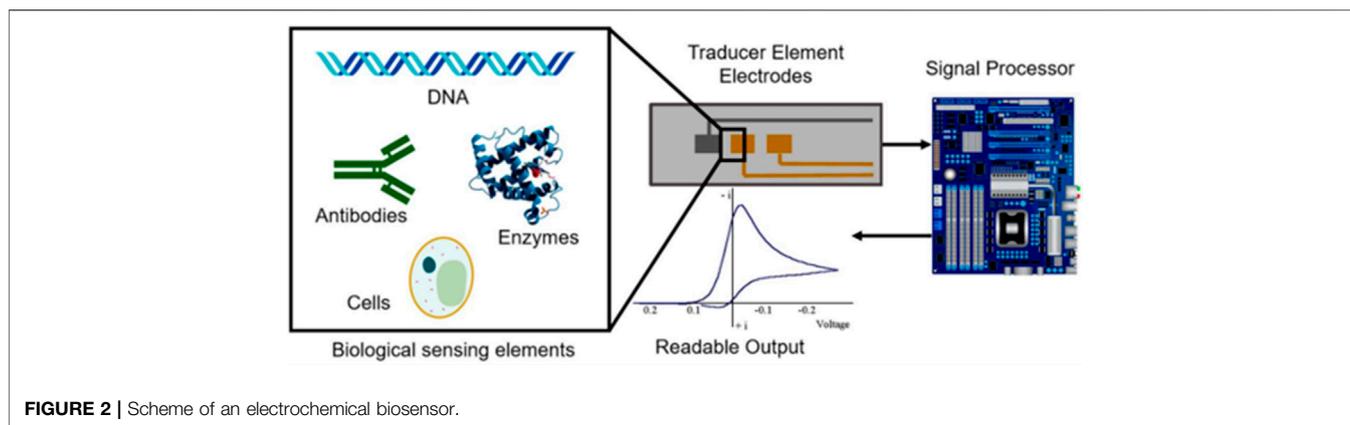
FIGURE 2 | Scheme of an electrochemical biosensor.

TABLE 1 | Examples of advanced ceramic materials and their various applications.

Sl.No	Ceramic materials	Applications	Reference
1	Alumina	Identification of environmental gas	Joseph et al. (2003)
2	Pyro electric	Vapors identification	Joseph et al. (2003)
3	Alpha sense oxidative gas	NO_2 and O_3 Concentration identification	Gorska et al. (2020)

Advanced ceramics represent a modern class of materials which are generally new materials or a combination of traditional ceramic materials designed to exhibit surprising variations in the properties traditionally ascribed to ceramics. As a result of these modern synthetic approaches to advanced ceramics, we now have new ceramic products that are as tough and electrically conductive as some metals. This is a very important characteristic property for any material used in electrochemical biosensors. Developments in advanced ceramics continue at a rapid pace constituting what can be considered a revolution in the kind of materials and properties obtained.

In 1993, the Versailles Project on Advanced Materials and Standards (VAMAS), described advanced ceramics as "an inorganic, non-metallic (ceramic), basically crystalline material of rigorously controlled composition and manufactured with detailed regulation from highly refined and/or characterized raw materials giving precisely specified attributes." The distinguishing features of advanced ceramics from the above definition is that they lack a glassy component, i.e., they are "basically crystalline." and their microstructures such as grain sizes, grain shapes, porosity, and phase distributions are carefully planned, engineered and controlled. This planning requires detailed monitoring of composition and processing with "clean-room" processing being the norm. Pure synthetic compounds, rather than naturally occurring raw materials, are used as precursors in manufacturing. As a result of these manufacturing conditions, the final advanced ceramics tend to exhibit unique or superior functional attributes. Examples include unique electrical properties such as superconductivity or superior mechanical properties such as enhanced toughness or high-temperature strength.

ALUMINUM OXIDE BASED BIOSENSORS

The search for metal oxides that can be used in electrochemical sensors to detect various analytes has recently started to focus on aluminum oxide, which has become a prominent candidate. Al_2O_3 has been widely used as a good gate dielectric for the future of nano electronic devices due to its high dielectric constant, remarkable hardness, thermal stability, uniform pore size, and high pore density together with the potential low cost and relatively simple preparation procedure. Among different phases of Al_2O_3 *viz.* γ, η, δ, θ, and χ phases, the α-Al_2O_3 possess thermodynamic stability. Each form of the Al_2O_3 has its specific band gap value, particularly, α, β, and γ Al_2O_3 phases have 8.8 eV, 7.0–8.7 eV, and 5.1–7.1 eV, respectively. Al_2O_3 NPs have been prepared by various methods like laser ablation, sol-gel, hydrothermal reactions, pyrolysis, sputtering, and pyrolysis, etc.

During the past few years, Al_2O_3 NPs have been synthesized and there has been increasing attention on applications in several fields such as photocatalysts, sensors, capacitors, and semiconductors. An electrochemical biosensor was fabricated (Mekawy et al., 2018) for the detection of NADH using a nanocomposite of alumina with GO. In another work, PANI with γ-Al_2O_3 nanocomposite was synthesized (Parvin et al., 2018) *via in situ* electro polymerization method on gold electrodes for detection of vitamin-E which exhibited good lowest detection limit (LOD) of 0.06 μM. A ternary ZnO/NiO/Al_2O_3 nanoparticles were prepared by Alam et al. (2020) for the detection of L-Glutamic acid using a glassy carbon electrode as a non-enzymatic electrode. Sivasankar et al. (2018) introduced a new hierarchical mesoporous graphite oxide (HMGO) with Al_2O_3 for the identification of caffeic acid in red wine samples using a modified GCE. For the detection of glycine, Alam et al.

TABLE 2 | Al_2O_3 nanoparticles as ceramic sensors for detection of biomolecules.

Sl. No	Nanomaterial/Composite	Analyte	LOD	Sensitivity	References
1	Al_2O_3-GO	NADH	4.5 µM	–	Mekawy et al. (2018)
2	PANI with γ-Al_2O_3	Vitamin E	0.06 µM	–	Parvin et al. (2018)
3	Ternary $ZnO/NiO/Al_2O_3$	L-Glutamic acid	95.35 pM	–	Alam et al. (2020)
4	Hierarchical mesoporous graphite oxide/Al_2O_3	Caffeic acid	0.004 µM	429 µA $mM^{-1} cm^{-2}$	Sivasankar et al. (2018)
5	$ZnO/Al_2O_3/Cr_2O_3$	Glycine	82.25 pM	2.09×10^2	Alam et al. (2018a)
6	TPhPFe(III)/Al_2O_3/Pb and TPhPFe(III)/Al_2O_3/Si	H_2O_2	–	–	Malikova et al. (2015)
7	Pt–γ– Al_2O_3 composite	Guaiacol	17.9 nM	–	Sun et al. (2015a)
8	Cu– Al_2O_3-g–C_3N_4–Pd	Amyloid β-Protein	3.3 fg ml^{-1}	–	Miao et al. (2019)
9	Graphite-SiO_2/Al_2O_3/Nb_2O_5-methylene blue	Dopamine	1.49 µmol L^{-1}	–	Giarola et al., 2017
10	ZnO/Al_2O_3 Nanocomposite	Dopamine	2.0×10^{-6} M	–	Ganjali et al. (2018)
11	ZnO/Al_2O_3 nanocomposite	Salicylic acid	0.25 µM	–	Ganjali et al. (2017a)
12	ZnO/Al_2O_3 nanocomposite	Ascorbic acid	0.6 µM	–	Ganjali et al. (2017b)
13	MWNTs/Al_2O_3/chitosan	Serotonin	0.005 µM	–	Wu et al. (2018)
14	MWNTs/Al_2O_3/Poly-L-Lysine Composite	Salicylic acid	0.25 µM	–	Wang et al. (2018)
15	$ZnO/Al_2O_3/Cr_2O_3$	Xanthine	1.34 pM	70.8861 mA $µM^{-1} cm^{-2}$	Alam et al. (2018b)
16	TiO_2-Al_2O_3Nanocomposite	3,4-diaminotoluene	0.19 pM	0.5024×10^3 µA $µM^{-1} cm^{-2}$	Rakib et al. (2019)

(2018a) developed a non-enzymatic electrochemical sensor of modified GCE using low dimensional ternary $ZnO/Al_2O_3/Cr_2O_3$ nanoparticles, where it exhibited a good limit of detection of 82.25 pM. Interestingly Malikova et al. (2015) developed a biomimetic electrode using catalase on TPhPFe(III)/Al_2O_3/Pb and TPhPFe(III)/Al_2O_3/Si for the detection of low amounts of H_2O_2.

To find out a polyphenol analyte of guaiacol in food samples, the research group of Sun et al. (2015a developed an electrochemical sensor using Pt–γ–Al_2O_3 modified GCE that exhibits good results. An electrochemical immunosensor was developed by Miao et al. (2019) taking Cu doped Al_2O_3 with graphite carbon nitride (g-C_3N_4) to generate CueAl_2O_3-g-C_3N_4 for the detection of amyloid β-protein (Aβ). Giarola et al. (2017) identified that graphite-SiO_2/Al_2O_3/Nb_2O_5-methylene blue (GRP-SiAlNb-MB) composite was suitable for the detection of dopamine, DA, in real and pharmaceutical samples with good detection limit. Other works by (Ganjali et al., 2017a; Ganjali et al., 2017b; Ganjali et al., 2018) have also reported the detection of DA by modifying a glassy carbon electrode (GCE) using ZnO/Al_2O_3 nanocomposite. The same group of workers suggested that ZnO/Al_2O_3 nanocomposite can also be used for the determination of salicylic acid and ascorbic acid in pharmaceutical samples. In another study by Zheng et al. (2018) brain serotonin 5-hydroxy tryptamine was detected using a modified screen-printed electrode (SPE) based on MWCNTs/Al_2O_3/Chitson composite. In addition to the above electrochemical studies, Wang et al. (2018) developed a novel disposable sensor modified with MWNTs/Al_2O_3/poly-l-lysine film for the detection of clinical 17β-estradiol (17β-E2) urine samples. Alam et al. (2018b) have studied a chemical sensor based on $ZnO/Al_2O_3/Cr_2O_3$ nanocomposite, which is used for modification of GCE for sensing xanthine with good sensitivity and limit of detection. A TiO_2-Al_2O_3 nanocomposite was synthesized by Rakib et al. (2019) and was used for the modification of GCE as a chemical sensor for sensing hazardous chemical 3,4-diaminotoluene. It is clearly understood from the above findings and developments that the dominant

properties of alumina particles can be unraveled in the form of nanocomposite with various other metal oxides, metals, polymers, and carbon materials like graphene, graphene oxide. **Table 2** provides a summary of the electrochemical biosensor properties of Al_2O_3 based sensors for the detection of various biomolecules.

ZIRCONIUM OXIDE BASED BIOSENSORS

The ZrO_2 exists in various structures including monoclinic, tetragonal, cubic lattice imbibe with unique thermal, structural, electronic properties. It has a fine natural color, high stability, high toughness, high chemical strength, desirable resistance to corrosion, chemical, and microbial action that have made it a highly significant advanced ceramic in terms of its technological aspects (Sagadevan et al., 2016).

For the past 2 decades, a large amount of attention has been focused on zirconium oxide nanoparticles due to their particle size-dependent properties. Outstanding properties like a high surface area to volume ratio, surface activity, catalytic efficiency, strong adsorption affinity, biocompatibility, facile electron transfer rate, and chemical inertness make the nanostructured zirconium oxide particles an interesting material in the field of electrochemical sensors. This has led to many researchers exploring its applications. It also offers a great affinity for proteins like enzymes, which lead to immobilization of enzyme activity, the finest feature of bio-sensing applications as well as non-toxicity, low thermal conductivity, and high isoelectric point. Due to the availability of plenty of oxygen vacancies on its surface and a wide band gap for that p-type semiconductor, it is also used as an insulator in transistors and as a dielectric material. The high ion exchangeability and redox movement make it useful in many catalytic processes as a catalyst. Different approaches have been used to synthesize the ultrafine ceramic powders of ZrO_2, such as sol-gel, hydrothermal, spray pyrolysis, salt-assisted aerosol decompositions, carbon nanotube templated technique, and reflux and emulsion precipitation, etc.

TABLE 3 | Properties of metal carbide and nitride materials through carbothermic reduction approach.

Precursor	Product	Shape	Particle size	Surface area (m^2/g)	Reference
$Fe_2(C_2O_4)_3$ $Fe(C_6H_5O_7)$ $Fe(C_2H_3O_2)_2)$	C-Fe	Sphere	20–50 nm	38–95	Hoch et al. (2008)
F_3O_4	Fe_3C	Sphere	20 nm	–	Schnepp et al. (2010)
Fe $(CO)_5$	Fe-Fe_3C	Core-shell	30–50 nm	–	Wang et al. (2007)
Ferrocene	Fe_3C	–	18–23 nm	–	Huo et al. (2006)
Ferrocene	Fe_3C	Sphere	50–100 nm	15–39.8	Sajitha et al. (2007)
SiO_2	SiC	Sphere	–	–	Weimer et al. (1993)
$TiCl_4$	TiC	Whiskers	150 μm	–	Kim and Kumta (2003)
$TiCl_4$, $ZrCl_4$	TiN, ZrN	Whiskers	–	–	Kato et al. (1980)
TiO_2	TiC	Whiskers	1–10 μm	–	Wokulski (1987)
TiO_2	TiC	Whiskers	–	–	Krishnarao et al. (2001)
Nb_2O_5	NbC	Whiskers	0.1–0.5 μm	–	Johnsson (2000)
$TiCl_4$	TiN	Whiskers	30 μm	–	Bojarski et al. (1981)
Ta_2O_5	TaC	Whiskers	0.5–1 μm	–	Johnsson (2004)
TiO_2	TiC	Nanowire	20–50 μm	–	Huo et al. (2007)

TABLE 4 | Metal carbide, Metal Nitride based electrochemical sensors for detection of various species.

Electrode	Analyte	Detection method	Detection limit	Detection range	Reference
Hb/Ti_3C_2-GO/gold foil electrode	H_2O_2	Amperometry	1.95 μM	2 μM–1 mM	Zheng et al. (2018)
LO/CNTs/Ti_3C_2Tx/Pb/CFMs	Lactase	Chronoamperometry	0.67 μM	10–22 μM	Lei et al. (2019)
Ti_3C_2-ATP-$Mn_3(PO_4)_2$/GCE	Superoxide anion	Amperometry	0.5 nM	2.5 nm–14 μM	Zheng et al. (2019)
Ti_3C_2Tx/Pt NP/GCE	ACOP, AA, UA, DA	DPV	0.048 μM	0.25–2000 μM	Lorencova et al. (2018)
Nafion/Ti_3C_2Tx/GCE	Bromate	DPV	41 nM	50 nm–5 μM	Rasheed et al. (2018)
Alk-Ti_3C_2/GCE	Cd(II), Pb(II) Cu(II), Hg(II)	SWASV	0.098 μm, 0.041 μm	0.1–1.5 μM	Zhu et al. (2017)
Ti_3C_2Tx-MXene	Carbendazim	DPV	10.3 nM	50 nM–100 μM	Wu et al. (2019)
TiN/GCE	UA, AA	DPV	1.52 and 0.28 μM	10–300 μM 50–1500 μM	Liqin et al. (2017)
Ni_3NNS/Ti	Glucose	Amperometry	0.06 μM	0.2 μM	Fengyu et al. (2018)
(rGO)/(g-C_3N_4) (GCN)	Cd^{2+}	DPASV	0.337 nM	1 nM to 1 μM and from 1 μM to 1 mM	Wang et al. (2018)

Malhotra et al. (2016a) have developed a non-invasive biosensor of serine/nZrO$_2$ to detect the oral cancer biomarker (CYFRA-21–1) that is highly efficient, with a sensitivity of 0.295 mA mL ng^{-1}. The same group of researchers, Malhotra et al. (2015) have continued with bovine serum albumin (BSA)/anti-CYFRA-21-1/3-aminopropyl triethoxy silane (APTES)/ZrO$_2$/ITO immunoelectrode for the detection of CYFRA-21-1 biomarker for oral cancer. An electrochemical immunosensor, BSA/anti-cTnI/APTES/nZrO2/ITO, was developed by an earlier research group Malhotra et al. (2017), for the identification of cardiac troponin I biomarker (acute myocardial infarction) detection, which exhibits a good sensitivity of 3.9 μA ml/(ng cm^2). Uzungolu (2018) worked on the development of CeO$_2$-ZrO$_2$ nanoparticle modified lactate oxidase enzyme, an enzymatic sensor in an oxygen-depleted environment. The fabrication of Au electrodes functionalized with ZrO$_2$ thin film has been developed by Raileanu et al. (2018) for the determination of enzymatically produced thiocoline (Tch). Triglyceride tributyrin was detected using a bi-enzymatic biosensor of Chit-nano-ZrO$_2$/ITO electrode and was developed by Solanki et al. (2016), with a good LOD of 155 μg mL^{-1}. A novel Ga$_2$O$_3$/lignin and ZrO$_2$/lignin hybrid materials have been developed by Jędrzak et al. (2019) for the immobilization of glucose oxidase

which acts as a biosensor for the detection of glucose. An amperometric choline biosensor was introduced by Ouiram et al. (2020) based on zirconium dioxide decorated gold nanoparticles (ZrO$_2$@AuNPs), copper (I) oxide at manganese (IV) oxide (Cu$_2$O@MnO$_2$), and immobilized choline oxidase (ChO$_x$) onto a glassy carbon electrode (GCE) (ChO$_x$/Cu$_2$O@MnO$_2$-ZrO$_2$@AuNPs/GCE) for the detection of choline in blood samples.

ZRO$_2$-CARBON BASED BIOSENSORS

In the family of nanocarbon graphene oxide (GO), reduced graphene oxide (rGO), graphene, and carbon nanotubes are prominent new candidates in electrochemical sensors (Pumera, 2010). Graphene material has sp^2 hybridized carbon atoms that possess a high electron transfer rate, surface area, good electrical conductivity, and act as a functional material to modify the bare electrode surfaces (Unwin et al., 2016). For the synthesis of graphene materials, different methods are proposed. However, each method has its advantages and limitations. Graphene oxide is a layered material where the oxygen content is high in the form

of functional groups like hydroxyl, carboxyl, and epoxy groups for specific target molecules. On the reduction of graphene oxide through different methods, reduced graphene oxide (rGO) was obtained, which has good electrical conductivity and acts as a current enhancer in electrochemical sensors (Russo et al., 2011).

Devnani et al. (2017) synthesized ZrO2/graphene/chitosan nanocomposite coupled with carbon paste electrode for the detection of dopamine in the presence of ascorbic acid and uric acid. A nanocomposite of zirconia with graphene for the detection of label-free exon-19 mutations has been developed by Lin et al. (2019). A novel Au-ZrO2-graphene electrochemical sensor was fabricated by Tao et al. (2020) for the detection of methyl parathion. Earlier, Sun et al. (2015b) developed a nanocomposite of ZrO2 with graphene that was electrodeposited on the surface of a carbon ionic liquid electrode (CILE) to act as an electrochemical DNA sensor for the *Staphylococcus aureus* nuc gene sequence. In this succession, a novel biosensing electrode of ZrO2/rGO immobilized acetylcholinesterase (AChE) was developed by Mogha et al. (2016) for the detection of chlorpyrifos. Later, an efficient biosensing platform was designed by Malhotra et al. (2016b) using ZrO2/rGO for sensing the oral cancer biomarker (CYFRA-21-1). Chen et al. (2020) fabricated an electrochemical DNA sensor for the detection of nucleic acid using zirconia-reduced graphene oxide-thionine (ZrO2-rGO-Thi) nanocomposite for integral DNA recognition. An anticancer drug (regorafenib, REG) was detected selectively along with other analytes of ascorbic acid and uric acid, using an electrochemical sensor made with ZrO2/rGO nanocomposite by a group of researchers (Venu et al., 2018), where it exhibits a good limit of detection 17 nM.

In another work, an immune sensor was fabricated using ZrO2/rGO nanocomposite functionalized with L-Methionine as BSA/antiOTA/Meth/ZrO2-rGO/ITO was used for specific target detection of ochratoxin A (OTA) by (Gupta et al., 2017a). Puangjan et al. (2016) reported that ZrO2/Co3O4 reduced graphene oxide for the simultaneous detection of gallic acid (GA), caffeic acid (CA), and protocatechuic acid (PA). In other studies, reduced graphene oxide-zirconium dioxide-thionine (rGO-ZrO2-Thi) nanocomposite was synthesized by (Chen et al., 2018) for electrochemical assay of protein kinase activity. The other carbon materials like amorphous carbon along with zirconia as an immune-sensor for ochratoxin A (OTA) by (Solanki et al., 2016) and graphitic carbon nitride with zirconia, ZrO2/g-C3N4, nanocomposite were developed by Zarei (2020) as an aptasensor for the detection of tetracycline.

ZRO2-METALS/MO-BASED BIOSENSORS

A nanocomposite of ZrO2-ChCl-AuNPs/CPE was used to construct a carbon paste electrode as an electrochemical sensor by Shahamirifard et al. (2018) for simultaneous determination of gallic acid (GA) and uric acid (UA). Solanki et al. (2016) prepared aluminum-doped zirconium oxide nanoparticles for sensing ochratoxin A with a good limit of detection of 0.14 ng ml^{-1}. For the detection of glucose in raw citrus aurantium *var.* Sinensis, a ZrO2-Cu (I) material was used by (Parashuram et al., 2019) and exhibits a very low limit of detection 0.25 mM (Gu et al., 2016). conducted studies on a ternary and oxide NiO-TiO2-ZrO2/SO4^{-2}

which is a solid superacid catalyst for glucose oxidation. Furthermore, ZrO2/ZnO nanocomposites act as sensing material fabricated by (Wang et al., 2020) for the simultaneous detection of epinephrine (EA), uric acid (UA), and folic acid (FA) (Parthasarathy et al., 2019). introduced a method of detection of uric acid using Urs-GLDH/TiO2-ZrO2/ITO electrode.

METAL CARBIDE AND NITRIDE BASED BIOSENSORS

Metal carbides and nitride usage has increased in recent years could potentially replace the conventional materials used in gas sensing, environmental remediation, photocatalysis, medicine, and ceramics. Moreover, a number of composites are made using transition metal carbide and nitrides especially the nanoform of various morphologies such as spheres, particles, plates, fibers, whiskers possessing significant properties including large surface area, high toughness, flexibility, low density, and thin walls with enhanced conductivity with good electrical properties (Donath et al., 2002; Cheng et al., 2006; Guo et al., 2008; Zhao et al., 2008; Karan et al., 2009; Li et al., 2009; Ni et al., 2009; Yu et al., 2009), which are summarized in **Table 3**. These materials are quite promising in making electrochemical sensors.

Titanium based carbides (Ti3C2) with graphene oxide based electrochemical sensors were synthesized and used as effective sensors for H2O2 as reported by (Zheng et al., 2018). Lei et al. reported wearable and stretchable biosensors for the quantification of biomarkers like glucose and lactose in sweat and efficiently act as monitors for non-invasive biomarkers (Lei et al., 2019). Mxene based nanocomposite based biomimmetic enzyme was used for the quantification of superoxide anion, which is considered to be a significant biomarker in the diagnosis of cancer by Zheng et al. (2019). In addition, Ti3C2TxePtNP composite derived from the Pt precursor by reduction process on Mxene surface are used as an effective electrochemical sensor for various biomolecules (Lorencova et al., 2018).

Nafion based titanium carbides are used for the detection of bromate in water resources (Rasheed et al., 2018). The detection of heavy metals such as Cd (II), Pb (II), Cu (II), and Hg (II) at trace level is essential due to the detrimental effects they have on humans and the environment. (Zhu et al., 2017). Delaminated Ti3C2TxeMXene was used as an electrode modifier for the detection of fungicide carbendazim (Wu et al., 2019). Titanium nitrite based electrochemical sensors were used for the detection of ascorbic acid and uric acid (Liqin et al., 2017). Metallic nickel nanosheets are efficiently used for selective selection of glucose molecule as a non enzymatic sensor (Fengyu et al., 2018). Wang et al. reported carbon nitide based graphene incorporated carbon nanocomposites as selective sensors for detecting cadmium ions (Wang et al., 2018).

CONCLUSION

The present study has reviewed the electrochemical biosensor applications of advanced ceramics, particularly metal and

metal oxide-based ceramics. The study discussed the working mechanisms and methods used to modify the base electrode with these advanced ceramics. $ZnO/Al_2O_3/Cr_2O_3$ were found to show the lowest detection limit of 82.25 pM with a sensitivity of 2.09×10^2 µAµM^{-1} cm^{-2} compared to all other ceramic based electrochemical biosensors. Similarly, among, metal carbides and nitrides, Ti_3C_2-ATP-$Mn_3(PO_4)_2$/GCE was found to show the lowest detection limit of 0.5 nm. **Table 4** gives a detailed summary of of the electrochemical bio-sensing properties of metal carbide and nitrides.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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