Biosensors and Bioelectronics 107 (2018) 76–93

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

A review on electrochemical detection of serotonin based on surface modified electrodes

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ARTICLE INFO

Keywords:
Serotonin
Surface modified electrodes
Electrochemical detection
Electrocatalysis

ABSTRACT

Serotonin is one of the important neurotransmitters of our body. It's abnormal concentration is associated with multiple disorders and diseases. Sensitive and precise electrochemical determination of serotonin is not possible with bare working electrodes due to various reasons *viz.* electro-chemical fouling, presence of other biological molecules having similar oxidation potential, and lower concentration of serotonin in biological samples. Surface modification of working electrode is required for fast, precise, selective, and sensitive detection of serotonin. We have extensively reviewed the research approaches where serotonin has been sensitively detected using surface modified electrodes in the presence of other interfering agents. This review aims at presenting the electrochemical detection of serotonin using various surface modified electrodes such as glassy carbon, graphite, carbon fiber, diamond, screen printed, ITO, and metal electrodes modified with conducting polymers and polyelectrolytes, carbon nanomaterials, metal or metal oxide nanoparticles, biological compounds, and other conducting materials. The analytical figures of merits of various research approaches for detection of serotonin have been compared in the article. The properties of material used for surface modification, chemical interactions at the interfaces, and electrocatalytic effects of modified surfaces on sensing of serotonin have been thoroughly discussed in this review.

1. Introduction

Serotonin or 5-hydroxytryptamine (ST or 5-HT), is one of the monoamine neurotransmitters widely distributed in our body and synthesized in brain, intestine, and spinal cord (Purves et al., 2001; Sirek and Sirek, 1970) (Fig. 1). It plays a vital role in the regulation of numerous behavioral and physiological functions such as mood, sleep, emesis, sexuality, and appetite (Young and Leyton, 2002). Low level of ST is associated with several diseases and disorders, including depression, anxiety, migraines, unregulated hemostasis, blood clotting, sudden infant death syndrome (SIDS), and carcinoid syndrome (Jones and Blackburn, 2002; Lin et al., 2014; Maximino, 2012) etc. On the

Abbreviations: AA, ascorbic acid; ACh, acetylcholine; ADR, adrenaline; ADSV, adsorptive differential pulse stripping voltammetry; AFM, atomic force microscopy; Ala, alanine; Amp, amperometry; ASDPV, anodic stripping differential pulse voltammetry; Asp, aspartate; AuNPs, gold nanoparticles; BAM, bovine assayed multi-sera; BDD, boron doped diamond; CA, chronoamperometry; CC, chronocoulometry; β-CD, β-cyclodextrin; CFM, carbon fiber microelectrode; CGSPE, colloidal gold screen printed electrode; Ch, choline; CHT, chitosan; CILE, carbon ionic liquid electrode; CNT, carbon nano tube; CNTN, carbon nano tube network; CPE, carbon paste electrode; CT-DNA, calf thymus-DNA; CUCR, C-undecylcalix[4]resorcinarene; CV, cyclic voltammetry; Cys, cysteine; DA, dopamine; DNA, deoxyribo nucleic acid; DOPAC, 3,4-Dihydroxyphenylacetic acid; DPV, differential pulse voltammetry; DTDB, 5,5-ditetradecyl-2-(2-trimethylammonioethyl)-1,3-dioxane bromide; EC, enterochromaffin cells; ECR, eriochrome cyanine R; EIS, electrochemical impedance spectroscopy; ELISA, enzyme-linked immunosorbent assay; Ep, epinephrine; EPPGE, edge plane pyrolytic graphite electrode; FA, folic acid; f-AuNP, functionalised gold nanoparticles; FEG-SEM, field emission gun scanning electron microscopy; FePc, iron(II)phthalocyanine; $[FeTSPc]_4$, iron(II)tetrasulfophthalocyanine; FSCV, fast scan cyclic voltammetry; GA, glutamic acid; GCE, glassy carbon electrode; G-g-PLA-Pd, graphene oxide grafted poly(lactic acid) with palladium; GI, gamma ray irradiated; Gly, glycine; GO, graphene oxide; GR, graphene; HIAA, 5-hydroxyindoleacetic acid; His, histidine; HPLC-ECD, high precision liquid chromatography electrochemical detection; 5-HT, 5-hydroxytryptamine; 5-HTP, 5-hydroxytryptophan; IL, ionic liquid; 3IP, 3-iodopropionate; ITO, indium tin oxide; L-Dopa, L-3,4-dihydroxyphenylalanine (Levadopa); LOD, limit of detection; MEL, melatonin; MIP, molecularly imprinted polymer; MWCNT, multi wall carbon nano tube; NE, norepinephrine; [Ni(TSPc)], Ni(II)phthalocyanine; nor-ADR, nor-adrenaline; NP's, nano particles; [OMIM] PF_6, 1-butyl-3-methylimidazolium hexafluorophosphate; OSWV, Osteryoung square wave voltammetry; PANI, polyaniline; PAMT, poly(2-amino-5-mercapto-thiadiazole); p-AMTa, poly 3-amino-5-mercapto-1,2,4-triazole; pBDD, polycrystalline boron-doped diamond; P3CA, Pyrrole-3-carboxylic acid; PNAANI, poly(N-acetylaniline); Poly(BCG), Poly(bromocresol green); poly(N, ,N-dimethylaniline); PEDOT, Poly (3, 4-ethylene dioxythiophene); PGE, pencil graphite electrode; Poly(p-ABSA), poly(p-aminobenzenesulfonic acid); PPD, poly(o-phenylenediamine); Poly(SFO), poly(safranin O); PPS, poly (phenosafranine); PPyox, overoxidised-polypyrrole; PSS, poly(sodium 4-styrenesulfonate); RGO, reduced graphene oxide; SAM, self assembled monolayer; SERT, serotonin transporter; SME, surface modified electrode; SPE, screen printed electrode; ST, serotonin; SWASV, square wave adsorptive stripping voltammetry; SWCNT, single wall carbon nano tube; SWV, square wave voltammetry; TA, tartaric acid; TOC, tocopherol; TP, thiophenol; TPyP, 5,10,15,20-tetrakis(4-pyridyl)-21H,23H-porphyrin; Trp, tryptophan; Tyr, tyrosine; UA, uric acid

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https://doi.org/10.1016/j.bios.2018.02.013
Received 4 November 2017; Received in revised form 2 February 2018; Accepted 2 February 2018
Available online 06 February 2018
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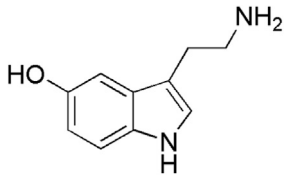


Fig. 1. Structure of serotonin.

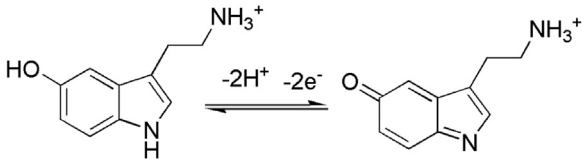
other hand, high levels of ST can cause noticeable toxicity and potentially fatal effects known as serotonin syndrome (Birmes et al., 2003; Buckley et al., 2014; Volpi-Abadie et al., 2013). For all the above reasons, detection of ST is of great significance in the diagnosis of various diseases and in understanding the role of serotonin in some neurological disorders. As the low level of serotonin in the brain can be a sign of depression, serotonin in the blood, serum, plasma, and platelet may be considered as peripheral biochemical marker for depression. Thus, there is a crucial requirement of simple, highly sensitive, economic, and fast detection of serotonin.

A range of analytical methods have been used for detection of ST *viz.* fluorimetry, HPLC-ECD, capillary electrophoresis, enzyme immunoassay, chemiluminescence, ELISA, and mass spectrometry (Chauveau et al., 1991; Danaceau et al., 2003; Panholzer et al., 1999; Tsunoda et al., 1999; Zinellu et al., 2012). These conventional methods are cumbersome, time-consuming, and often require sample pretreatment which makes them unsuitable for rapid detection and inconvenient for everyday test. Moreover, due to the electroactive properties of ST, it can be determined by electrochemical methods. Electroanalysis of ST is based on electro-oxidation of serotonin on the electrode surface (Scheme 1). Electrochemical sensors offer advantages of high sensitivity, wide linear response, good stability, and reproducibility. Additionally, Low cost associated with electrochemical measurements supports a major advantage. Consequently, the development of electrochemical sensors for the detection of ST has received large interest during the last few decades.

However, electrochemical determination of ST levels is usually complicated by the following factors:

- Often the presence of other electroactive biomolecules in biological samples such as dopamine (DA) interfere with the signal of ST since the oxidation potential of ST is close to that of DA. The other interfering biological compounds are ascorbic acid (AA) and uric acid (UA) which have high concentrations and similar oxidation potentials to ST at bare conventional electrodes (Kim et al., 2012; Robinson et al., 2008).
- The concentration of ST in human samples is too low to detect.
- Reusability and reproducibility of the electrode gets reduced by the oxidation products of serotonin which gets absorb on the surface of bare electrode.

Use of bare electrode for determination of serotonin results in low sensitivity and selectivity due to above defined reasons. To resolve these problems, the most effective approach is to choose conductive, and selective materials for modification of working electrode, to improve the measuring sensitivity and selectivity for ST. Chemically modified electrodes offer sensitive detection of ST, even in presence of DA, UA, and AA with very low detection limits. Such detections are not possible with bare electrodes. Materials used for modification of electrode surface for detection of serotonin include a wide variety *viz.* conducting polymers & polyelectrolytes, carbon nanomaterials, metal nanoparticles (NPs) & nanocomposites, ionic liquids etc.



Scheme 1. Electro-oxidation of serotonin.

There are a number of research articles available in literature where the chemically modified electrodes have been used for detection of serotonin. To compile these reports in a review article is not easy because a critical comparison with the published work has not been given in most of the research articles.

We have extensively illustrated the most successful and promising electrochemical approaches for detection of serotonin using surface modified electrodes from its origin to present status. To the best of our knowledge, there is no such review article published earlier to summarize the electrochemical determination approaches for serotonin. Various research articles for detection of serotonin with SME based on conducting polymers & polyelectrolytes, carbon nanomaterials, metal nanoparticles, nanocomposites and ionic liquids have been collated and analytical results of these approaches have been compared in this review article. Detection of serotonin in presence of other interfering agents *viz.* DA, AA, UA etc has been focused. We have thoroughly discussed the properties of the modified electrode surfaces that enhance their electrocatalytic activity towards serotonin. Specific interactions of modified surface layer with ST have been explained at appropriate places. The best serotonin detection approaches are preferred on the basis of sensitivity, selectivity, linear working concentration range, lower limit of detections (LODs), simplicity of the sample pretreatment, stability of the modified electrode surface, enhancement of signal compared to bare electrodes, and separation between oxidation peak potentials.

2. Electrochemical sensing with surface modified electrodes

Modified carbon based electrodes (glassy carbon electrode, graphite electrode, carbon fiber electrode, boron doped diamond electrode, screen printed carbon electrode) and metal based electrodes (Pt electrode, gold electrode, tin-oxide electrode, Cu electrode) are frequently used as a working electrode for electrochemical detection of bio-molecules (Khan, 2017; Lydon et al., 2016; Uslu and Ozkan, 2007). Surface modification of working electrode generates a sensor with new and interesting properties. Modification material exists in the form of electroactive thin films, monolayers, or thick coatings on the electrode surface. The fabrication of surface modified electrodes is an advance approach that can figure conductive materials into practical electrodes suitable for biological environments. Modification of electrode surface improves the performance of an electrode as a sensor device by many ways.

- Chemical modification limits the access of interference and provides better selectivity towards target molecule as a result of specific interactions of modification material with the target molecule.
- Modification material acts as a fast electron transfer mediator between the target molecule and electrode that induce the fast oxidation or reduction of target. This results in negative shift of peak potential that in turn allows better peak separation between different analytes.
- Better sensitivity is observed with the coating materials having large surface area due to enhanced electrocatalytic activities.
- Leads to fast diffusion and preconcentration of target molecule at the electrode surface.
- Reduces the fouling effect.

It is pertinent to mention here that there are very few reports available in literature, where the bare or unmodified electrode has been used for determination of serotonin (Guell et al., 2010; Kachoosangi and Compton, 2007; Miyazaki et al., 1999; Patel et al., 2007; Patel, 2008; Rand et al., 2013; Sarada et al., 2000; Zhao et al., 2010). Though,