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REVIEW ARTICLE

Enzymatic biosensors for the quantification of biogenic amines: a literature update

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ABSTRACT

The present review emphasizes on the quantification of biogenic amines (BAs) which are regarded as a quality indicator of food freshness or spoilage and for evaluating microbial action while food processing. BAs have various potential adverse effects on human health and they are widely found in varying concentrations in different food stuffs. In the quest for a reliable method for their precise detection, BA biosensors have emerged as an efficient tool which enables rapid and accurate assessment in miniature form. Various combinations of amine oxidase enzymes have been used for the fabrication of biosensors in order to enhance specific biorecognition and signal transduction. This article also summarizes the widely employed components used in the construction of a pertinent biosensor and the research results conducted previously. The meticulous description regarding the choice of transducers and the significant role of mediators in a high response biosensor has been reviewed. Moreover, it also encompasses the utilization of highly attractive electrolytic characteristics of nanoparticles to enhance the specificity and accuracy of BA biosensors.

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Introduction

Biogenic amines are low molecular weight organic nitrogenous bases involved in a variety of biological processes. They are usually derived from the microbial decarboxylation of their precursor amino acids [1] or by the process of amination and transamination of the ketones and aldehydes in plants, animals and microorganisms [2]. These are small organic polycations having aliphatic structures such as Spermine (Spm), Spermidine (Spmd), Putrescine (Put) and Cadaverine (Cad); aromatic structures such as Phenylethylamine (PEA) and Tyramine (Tyr) as well as heterocyclic structures such as Tryptamine (Tryp) and Histamine (His) [3]. These are classified as Monoamines, Diamines and Polyamines based on the number of amino groups (Figure 1). The most important BAs related to food are: His, Put, Cad, Tyr, Trypt, PEA, Spm and Spd whereas Put, Cad, Spm and Spd are widely spread in the human body [4]. At low concentrations, these amines are not regarded as a serious risk for human beings. They have significant roles in physiological functions [5] and biological processes such as: cell growth, proliferation, integration and stabilization of proteins and lipids, development of the brain, inhibition of DNA damage, regulation of nucleotides, gene expression, renovation and preservation from external factors in all living organisms [6]. However, consumption of food containing high concentrations of BAs can possess several toxicological and pharmacological effects on human health. Fish, vegetables, fermented foods and beverages are the foods that contain high concentrations of BAs [7]. These are generally either psychoactive or vasoactive amines that act on the nervous system and the vascular system, respectively [8]. The most frequent intoxication reported includes histamine poisoning which causes a disease called 'scombroid fish poisoning'. This results in a variety of gastrointestinal, cutaneous, hemodynamic and neurological disorders [9,10]. Different varieties of cheese containing excessive amounts of tyramine that can cause the "cheese effect" or "cheese reaction" that results in hypertension with sensitive persons who can suffer from severe migraines and even brain hemorrhages [11,12]. Tyr, Tryp and PEA also increase blood pressure and cause migraines and hypertension [13]. Put and Cad increases His toxicity as they inhibit the metabolizing enzymes of His such as Monoamine Oxidase (MAO), Diamine Oxidase (DAO) and Histamine Methyl Transferase (HMT) resulting in food poisoning [14]. Moreover, certain types of cancer also produce high concentrations of Put and Cad and therefore they

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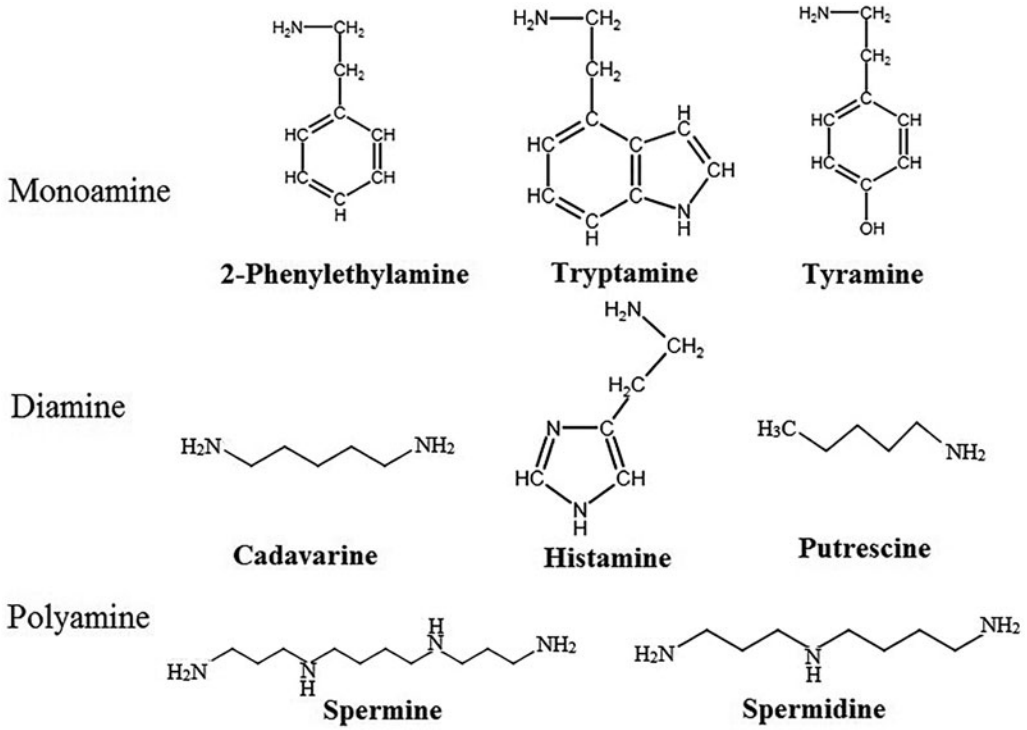

Figure 1. Structure of some common biogenic amines.

can be listed as tumor markers in clinical fields [15]. Put, Spm, Spd and Cad may react to nitrites and form carcinogenic nitrosamines [16,17]. This particular risk strongly relies upon their concentration and detoxification efficiency, which differs considerably between individuals and is affected by various factors [18]. Additionally, BAs are thermostable. This means once these compounds are formed, it becomes very difficult to destroy them. The final product will contain the same BA as is present in raw materials [19].

The BAs toxicological level is very difficult to demonstrate. It has been stated that the maximum acceptable level of His is 50–100 mg/kg and of Tyr is 100–800 mg/kg in foods [7]. The USA Food and Drug Administration (FDA) have accepted 500 ppm as the hazardous extent for His [20]. High amounts of Put and Cad have been shown as potentiators of His or Tyr toxicity, but no suggestions about their levels have been recommended [13]. The cheese toxicity threshold of Tyr is 100–400 mg/kg but there is no legislation to limit its value here [21,22]. Nevertheless, a maximum total BAs (Put, Tyr, Cad and His) amount of 750–900 mg/kg has been established as a safety range [23]. For such causes, examining BAs levels in food and beverages are progressively entailed by regulatory commissions such as the EU Commission Regulation (EC 2073/2005) [24]. The estimation of their levels is directly related to their impact on health conditions and the quality of food products [25] by serving as potential cancer markers [26] and for evaluating the freshness and quality of an extensive variety of foodstuffs [27–30]. Formation of quantity and the kind of BAs is firmly influenced by the composition of food, microbial fauna & flora and several other variables related to bacterial growth through food storage and processing [31]. Various conditions can also accelerate the growth of BAs such as increases in temperature and longer time periods will lead to more microbial growth and BA formation [32]. Therefore, their content is considered to be freshness and quality markers and these are used as indicators of the degree of microbial spoilage [33,34]. Major problems in BAs analysis are their low levels in a complex matrix [27]. Hence, it is of paramount importance to develop new health diagnostic techniques for selective and sensitive detection of BAs.

Various analytical approaches have been elaborated for the quantitative analysis of BAs in many food samples including: capillary electrophoresis (CE) [35,36], chromatographic methods such as TLC [37,38], GC [38–40], ion exchange chromatography (IEC) [41], HPLC [42,43], cation-exchange chromatography (CEC) [14,44,45] and matrix-assisted laser desorption/ionization mass spectrometry [46]. Alternative detection methods employed are: fluorimetry [47,48], conductimetry [44,45] and amperometry [49,50]. The standard spectrophotometric detectors cannot be used because aliphatic amines neither show distinct UV-VIS optical absorbance nor fluorescence [3,51,52]. Although these

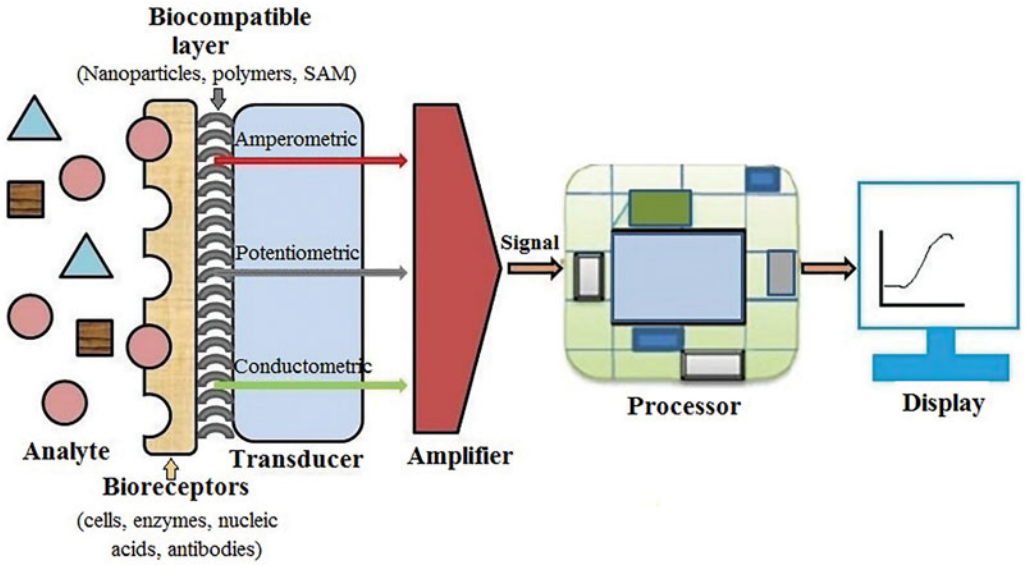

Figure 2. Schematic diagram showing basic principles of the electrochemical biosensor.

traditional methods show few helpful results, they are deprived by certain aspects such as: poor sensitivity, low specificity, complex and expensive instrumentation, skilled personnel required to operate, long analysis period, high potential etc. Additionally, tedious sample pretreatment and derivatization steps are also required which are complicated for small sample volumes. Contrary to all these listed methods, biosensors are: innovative, robust, sensitive and automated devices that offer simple, rapid and cost-effective solutions for the detection of BAs [53].

Basic concept of a BAs biosensor

Biosensors are a simple, robust and economical analytical devices based on the principle of the interaction of biological elements to a certain analyte (substance to be detected in the sample) and the generation of physicochemical changes (such as transfer of electrons or heat, change in pH and mass, absorption or release of particular ions or gases). Basically, biosensors consist of biorecognition layers (formed by antibodies, nucleic acids or enzymes), physical transducers and processors. Biological components recognize specific target analytes and the transduced signal becomes amplified, processed and converted into a digital format for the observations as shown in Figure 2. The transducer, being an important element in the biosensor device, transforms the resulting biochemical signal into a quantifiable electronic signal [54]. The signal produced is proportional to the concentration of the target analyte present in its proximity.

Amongst the presently available biosensor systems for BA analysis, electrochemical biosensors hold leading positions for their high performance, simple design, rapid screening methods, low cost, low detection limits and the possibility of miniaturization [7]. In particular, enzymatic amperometric biosensors have attracted enormous attention in electroanalysis during the last decade [55]. These devices unite the enzyme selectivity for the identification of a specific target analyte with the direct transduction of the rate of the biocatalytic reaction into a current signal, enabling rapid, sensitive and accurate detection [56]. Thus, biosensors have gained huge attention in the electroanalysis of BAs during recent years as can be seen in Table 1. Biosensors have now proceeded to field testing from laboratory levels and many have been commercialized [89]. The current review provides comprehensive data about BAs biosensors with versatile fabrication procedures and materials embraced.

Mechanism involved in enzymatic detection of BAs

The enzymatic BAs biosensors based on the incorporation of an enzyme in close proximity with the biosensing electrode. The enzyme either devours an electroactive reactant or produces electroactive species during catalysis and the analyte can be measured directly by the generation or depletion of reactants. Amine oxidases (AOx) are a class of enzymes that play the chief role in quantifying BAs. They catalyze the oxidation deamination of amines in corresponding aldehydes, in the presence of molecular oxygen (as electron acceptor)

Table 1. Various electrochemical biosensors for biogenic amines determination.

Biogenic Amine	Enzyme	Working electrode	Mediator	Immobilization	Potential	pH	Detection Limit	Linear Range	Sensitivity	Ref.
His	DAO	SPCE	–	Crosslinking with GA and BSA	-o.3V	7.2	0.94 mg L^{-1}	1–75 mg L^{-1}	0.33 nA L mg^{-1}	[57]
Tyr	–	AuNP-PANSA modified Au electrode	–	–	+0.6V	7.0	0.04 μM	0.8–80 μM	–	[58]
His	DAO	LSG-nCu-CNC/DAO electroe (analytical grade materials) LSG-Cu-MFC/DAO electrode (locally sourced materials)	–	Crosslinking	+500 mV		7.7 ± 2.8 μM 11.6 ± 2.6 μM	50–1.6 mM	58.7 ± 5.9 μAmM^{-1} 23.3 ± 1.9 μAmM^{-1}	[59]
His	–	Cu-Pt electrode	–	–	200mV	10.0	0.33 μM	1 to 750 μM	15 nA μM^{-1}	[60]
Spdm	PAO	CS/zeolites-AuNPs modified Au electrode	–	Adsorption & cross linking	+0.2 V	7.0	0.1 μM	0.2–200 μM	0.693 μA $\mu M^{-1}cm^{-2}$	[61]
Spm, spmd & –seput	PAO & DAO	CS/CF/nZnO/PAO/DAO strip	–	Coimmobilisation with GA	–	7.0	.01 mM	0.01–5.0 mM	–	[62]
Spm, Spmd	PAO SMO	PB/GP-SPE	PB(Prussian Blue)	Photopolymerization	−100mV		0.16U 0.05U	–	–	[63]
Tyr	Polyphenol oxidase (PPO)	Glassy Carbon electrode	–	Crosslinking with GA	−0.1 V	6.0	4.85×10^{-8} M	5.8×10^{-7} -1.6×10^{-5} M	1.50×10^{3} mA $M^{-1}cm^{-2}$	[7]
Put	PUO-HRP	Ketjen Black (KB)-based mesoporous electrode	–	Crosslinking with GA	0.60 V	7.0	5 μM	17 μM–500 μM	0.33 ± 0.01 μA μM^{-1} cm^{-2}	[64]
His	DAO	nPt/GPH/chitosan/SPCE	–	Surface adsorption	+0.4 V	7.4	2.54×10^{-8} M	0.1–300 μM	0.0631 μA μM^{-1}	[65]
His	HMD	HMD/TTF/SPCEs	Tetrathiafulvalene-TTF	Crosslinking with GA and BSA	+130 mV	6.8	8.1 ± 0.7 μM	8–60 μM	–	[66]
Put	PUO	PUO/TTF/SPE			+300 mV	8.0	10 ± 0.6 μM	10–200 μM		
Spm Spmd Put	–	dsDNA/MWCNT modified Glassy Carbon electrode	–	DNA- Polyamine interaction	–	–	Few nM	0.04–100 μM 0.01–24 μM 0.08–100 μM	–	[67]
Spm	BSAO	SAMN@Cr^{vi}	–	Self-assembled membrane	−0.35V	7.0	2.47 μM	5–500 μM	−130.25 nA $\mu M^{-1}cm^{-2}$	[68]
Spm Spmd Spm	PAO SMO	Graphite-SPE PB-modified Graphite-SPE	Prussian blue(PB)	Entrapment	+700 mV −100 mV	5.8 8.0	0.001 mM 0.005 mM 0.002 mM	0.003–0.3 mM 0.01–0.4 mM 0.004–0.5 mM	–	[69]
Put Cad	MAO	SPCE	Tetrathiafulvalene - TTF	Crosslinking with GA and BSA	+250 mV	11	9.9 μM 19.9 ± 0.9 μM	9.9–74.1 μM 19.6–107.1 μM	1.16 nA μM^{-1} 1.05 nA μM^{-1}	[70]
His	DAO-HRP	PS/MWCNTs/Fc-SPE	Ferrocene- Fc	Phase inversion technique	−50 mV	7.5	1.7×10^{-7} M	3×10^{-7}–2×10^{-5} M	1.9×10^{7} nA^{-1}	[1]
Tyr	Plasma amine oxidase	SPCEs	Hydroxymethyl ferrocene	crosslinking	+260 mV	6.65	2.0 ± 0.18 μM	2–164 μM	100% (Cad), 87% (Put), 84% (Tyr)	[1]
Put	DAO	DAO/nano-Fe3O4/GC electrode	–	Covalent immobilization	+0.4V	7.2	0.65 nM	2–8 nM	–	[71]
Spmd Spm Put Cad	–	Cu plated Platinum electrode	–	–	0.25 V	10	0.05 μM 0.06 μM 0.11 μM 0.27 μM	0.2–15 μM 0.2–15 μM 0.5–20 μM 1–30 μM	–	[72]

(*continued*)

Table 1. Continued.

Biogenic Amine	Enzyme	Working electrode	Mediator	Immobilization	Potential	pH	Detection Limit	Linear Range	Sensitivity	Ref.
His	DAO	Graphite electrode	Os (osmium) redox polymer	Crosslinking	−50 mV	7.0	5 μM	0.01–0.5 mM	867% (Cad), 100% (His)	[73]
Put	PUO-HRP				+50 mV	8.0	5 μM	0.01–0.05 mM		
Tyr	MAO				−50 mV	8.0	2 μM.	0.01–0.05 mM	100% (Put) 100% (Tyr), 90% (Pea)	
His	MAO	MAO/HRP/SPCE	Hydroxymethyl ferrocene	Covalent binding	250 mV	9.3	0.40 ± 0.04μM	0.4–2.4 μM	19.68 μA μM^{-1}	[74]
	DAO	DAO/HRP/SPCE					0.18 ± 0.01 μM	0.2–1.6 μM	32.77 μA μM^{-1}	
Put	DAO	PB modified SPE	–	Crosslinking with GA and BSA	−0.05 V	7.4	1×10^5 M	2×10^{-5}–3×10^{-4} M	–	[75]
Spmd	–	dsDNA-modified gold electrode	–	Self-assembled membrane	0.2V	7.4	0.72 μM	1.6–70.4 μM	–	[76]
	Amine Oxidase	Graphite electrode	Osmium redox polymer	Phase inversion technique	−50 mV	7.2	–	Up to 5 nm	–	[27]
His	DAO	Pt/CSPE	–	Physical entrapment	0.35 V	7.4	0.65 ppm	0–60 ppm	5.56 nA ppm^{-1}	[77]
Serotonin	HRP	Graphite electrode	–	Crosslinking with BSA and GA	−50 mV	7.0	17 ng ml^{-1}	40–470 ng ml^{-1}	0.95 ± 0.02 nA ml ng^{-1} cm^{-1}	[26]
Put	Amine oxidase	Nine carbon atom spacer	–	Protein coupling	–	–	0.5 nmol	0.9 ± 70 nmol	–	[78]
His							4.4 nmol	7.0 ± 90 nmol		
His	DAO	platinum electrode	–	Covalent immobilization	600 mV	7.0	0.5 μM	0–60 μM	–	[79]
Put	PUO						0.07μM	0.07–500 μM		
Put	Amine oxidase	Carbon paste electrode	–	Via affinity carrier BAT- Silasorb	0.0V	7.0	10 nmol l^{-1}	0.01–100 $nmoll^{-1}$	636.9 ± 2.03 mA mol^{-1} cm^{-2}	[80]
His.+45	DAO	Pt electrode	ferrocene monocarboxylic acid-FcA	Crosslinking with GA	+700mV	7.4	0.6 μM	1 ± 100 μM	0.025 nA μM^{-1}	[81]
	DAO-HRP						0.1μM	1 ± 100 μM	1.95 nA μM^{-1}	
Put , cad	DAO	platinum electrode	–	Cross linking with GA on nylon-net membrane	+650mV	8.0	5× $l0^{-7}$mol $litre^{-1}$	1×10^{-6} to 5×10^{-5}mol $litre^{-1}$	–	[25]
Put	PUO	platinum microdisk working electrode	–	Photolitographically	600 mV	8.0	0.01 Uml^{-1}	3–6 μl	–	[82]
Put	PUO	Platinum plated gold electrode	–	Crosslinking with GA and BSA	0.5V	8.5	0.5 μM	0.5–300 μM	2.2 nA μM^{-1}	[83]
His	MAO	Screen printed-Platinum electrodes	–	Crosslinking with GA and BSA	+ 600 mV	8.5	–	0.17–20 uM	0.93 nA μM^{-1}	[84]
put	PUO							0.06–200 uM	2.4 nA μM^{-1}	
His	MADH	MADH-TCNQ carbon electrode	TCNQ	Adsorption	+200 mV	7.5	4.8 μM	0–200 μM	5.35 nA μM^{-1}	[85]
Put	DAO	H2O2 selective membrane	–	Physical	–	6.6	0.25μmol/l	0.5–320 μmol/l	–	[86]
Cad				Adsorption			0.1 μmol/l	0.25–200 μmol/l		
Put	PUO	Micro planar hydrogen peroxide electrode	–	GA-albumin crosslinking	+10V	8.0	0.03 μM	0.l-l mM	25.3 nA mM^{-1}	[87]
spmd								0.1–0.8 mM	8.4 nA mM^{-1}	
cad								0.1–0.9 mM	8.5 nA mM^{-1}	
Cad, put	Amino oxidase	Platinum electrode	–	Crosslinking with GA and BSA	+ 500 mV	7.0	0.2 μM	0.5–10 μM	5.1 μA cm^{-2}	[88]

PUO: Putrescine oxide, HRP: Horseradish Peroxide, GA: Glutaraldehyde, BSA: Bovine serum albumin, DAO: Diamine Oxidase, GPH: Graphene, nPt: Platinum nanoparticles, SPCE: Screen printed Carbon electrode, MAO: Monoamine Oxidase, HMD: Histamine dehydrogenase, PAO: Polyamine oxidase, CF: coconut fiber, CS: Chitosan, nZnO: zinc oxide nanoparticles, TCNQ: tetracyanoquinodimethane, MADH: Methylamine dehydrogenase, BSAO: bovine serum Amine Oxidase, SAMN@CrVI: stable core–shell nanostructures, GC:Glassy Carbon, MWCNTs: Multiwalled Carbon Nanotubes, PS: polysulfone, AuNP-PANSA AuE: gold nanoparticle-poly-(8-anilino-1-napthalene sulfonic acid modified gold electrode, LSG: laser scribed graphene, MFC: microfibrilated cellulose, CNC: nanocrystalline cellulose hydrogel, nano-Fe_3O_4: ironoxide nanoparticles, BAT: 2-[4,6-bis (aminoethylamine)-1,3,5-triazine].

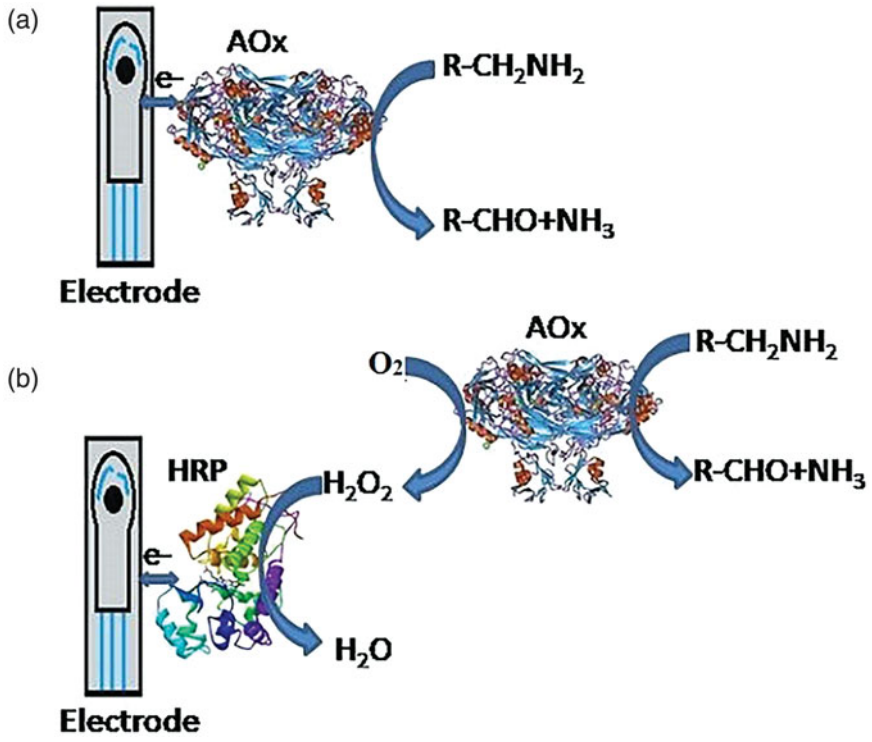

Figure 3. Sensing mechanism between electrode and enzyme (a) monoenzymatic (b) bienzymatic.

with the production of ammonia and hydrogen peroxide [24]. Formerly they were categorized into monoamine oxidase, diamine oxidase and polyamine oxidase. However, the substrate specificity of these enzymes is quite broad [90]. Diamine oxidase is a copper containing diamine: oxygen oxidoreductase (EC 1.4.3.6) that transforms toxic BA into non toxic H_2O_2 [91]. The enzyme is a homodimer of 60–105 kDa containing tightly bound copper and 6-hydroxy dopa (TOPA), a carbonyl cofactor.

$$R - CH_2NH_3^+ + O_2 + H_2O \xrightarrow{AOx} NH_4^+ + R - CHO + H_2O_2$$

$$Putrescine + O_2 + H_2O \xrightarrow{DAO} NH_3 + \Delta' - Pyrroline + H_2O_2$$

$$Cadaverine + O_2 + H_2O \xrightarrow{DAO} NH_3 + \Delta' - Piperideine + H_2O_2$$

DAO exhibits high affinity towards diamines like Put and Cad but also oxidatively deaminates His and Spdm efficiently [92]. DAO can measure the total BA content; MAO can determine tyramine, tryptamine and phenylethylamine content while Putrescine is selectively detected with putrescine oxidase (PUO) [51]. Flavin-containing polyamine oxidases (PAOs, EC 1.5.3.) are also used for the catalysis of the secondary amino group of polyamines (namely triamine spermidine and tetraamine spermine) and oxidizes them to form aldehyde and hydrogen peroxide but not ammonia [93].

In amperometric biosensors, electric potential is applied for the electrochemical oxidation of H_2O_2 to produce electrons that further produce a current [24]. The current produced depicts the analyte content and is measured by a potentiometric biosensor.

$$Biogenic\ \ amine + O_2 + H_2O \xrightarrow{AOx} ammonia + aldehyde + H_2O_2$$

$$H_2O_2 \xrightarrow{Electric\ \ Potential} 2H^+ + O_2 + \ \ electrons$$

BAs can be quantified either by the oxygen consumption or the hydrogen peroxide production. But the later reaction implies the application of high operational potentials that increase the possibility of interferences in the measurement and non selectivity of electrodes. Interferences can be reduced by a new approach of using mediators that decrease the potential [1]. Horse radish peroxidase (HRP) has been also used to overcome this lack of sensitivity. HRP has a heme group that promotes direct electron transfer from the redox center to the conduction sites available on transducers. This ingenuous combination of enzymes with HRP can be seen with amine oxidase, diamine oxidase and putrescine oxidase [26]. This dual system makes suitable the developed methods for routine analysis for food safety and control [66]. Sensing mechanisms between the enzyme and electrode has been shown in Figure 3.

$$H_2O_2 + 2H^+ + HRP(Red) \rightarrow 2H_2O + HRP(Oxd)$$

$$HRP(Oxd) + 2e^- \leftrightarrow HRP(Red)$$

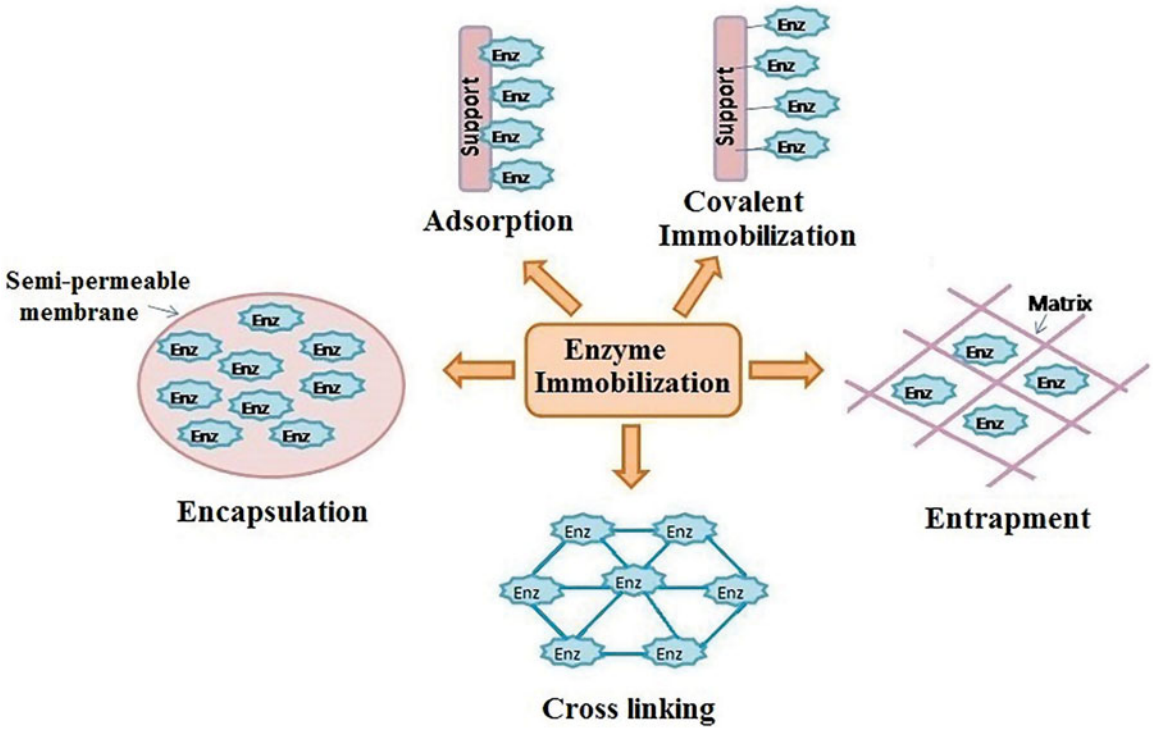

Figure 4. Different methods of enzyme immobilization.

Methods of enzyme immobilization

In order to make a viable enzymatic biosensor, the enzyme should be compactly attached onto the working electrode without denaturation. This significant step of enzyme immobilization decides the level of sensitivity, stability and performance of the biosensor. Various physical and chemical interactions have been described for immobilization of enzymes on different supports as depicted in Figure 4.

Physical adsorption

This is the simplest way for immobilization in which enzymes become physically adsorbed onto the inert support by the involvement of weak forces of attraction mainly Van der Waals forces, ionic and hydrophobic interactions, salt linkages and hydrogen bonding for the stabilization of the enzyme with no complications. It provides reversible enzyme immobilization where enzymes are placed on the specific membrane surface of a transducer [86]. Their interaction relies upon physicochemical parameters such as pH, temperature, polarity etc. Therefore, after the decay of enzymatic properties, interaction can be reversed by controlling these parameters of the solvents.

Pros- simple, economical and manageable, effortless binding, maintain high enzymatic properties.

Cons- desorption due to weak interactions, response time is less, poor operational stability [7].

Covalent bonding

This is the widely used technique for immobilization. It provides irreversible immobilization where a covalent bond is created between the enzyme functional group and chemical groups of the transducer establishing a stable covalent linkage between them. Covalent association is implicit by two ways- either by activation of the support by providing some reactive functional groups or by producing an activated group as a result of polymer modification. This method provides a wide range of options to select a carrier material due to its diverse functional groups. Some parameters like low ionic strength, shallow temperature and a physiological pH is needed for covalent bonding. Thermal stability and half life of enzymes can be enhanced by linking other supports (like chitosan, silica, etc.) with covalent coupling.

Pros- provide stability, quick response, no enzyme leakage, reduced diffusion barriers; various supports are available with different functional groups.

Cons- chemical modifications may result in enzyme denaturation [25,74].

Cross linking (Co-Polymerization)

This is the method of enzyme immobilization where no support or matrix is needed and irreversible

immobilization is acquired by direct cross linking between enzyme and the transducer with the aid of polyfunctional reagents. Glutaraldehyde with BSA is the most widely used linkage among various cross linking agents as it is economically favorable and easily accessible [26,70,75,84,87,88,92]. The absence of support provides preventions of all the hindrances associated with it making it a major characteristic of this method.

Pros- simple and cost effective, very less desorption.

Cons- agents used may denature the enzyme, requires a pure form of the enzyme with high activity.

Physical entrapment

This method involves the irreversible location of enzymes within interstitial spaces of cross linked and water insoluble polymer matrix so that the low molecular substrate and products pass through it and the enzyme are retained. Enzymes are not directly attached to the support here. The matrix should be tight enough to prevent leakage of the biocatalyst and permeable enough for the substrate and products to diffuse into or out of the reaction medium. Covalent and non covalent binding may be involved for the enzyme stabilization to the matrix PVA-Sbq and photoHEMA has been successfully used as matrices for enzyme entrapment. The photopolymerization process is followed to allow the entrapment after initiation of change in parameters (e.g. temperature) or by some chemical changes and is conducted under UV exposure [69,77].

Pros - simple and fast, cost effective, one step process, no loss of enzyme activity and support.

Cons- leakage of enzymes, contamination chances, not applicable for industrial processes, pore size related problems.

Self assembled monolayer

Self-assembled monolayer (SAM) is a nanostructured layer of molecular thickness 1–3 nm formed by chemisorption of selected organic molecules on solid metal surfaces [76]. The organic molecules used to assemble SAMs usually have different terminal functional groups (sulfides, thiols, amines, etc.) and can be modulated by using various strategies making them compatible according to the desired applications. Functional SAMs gives a reproducible and robust technique of immobilizing desired biomolecules in the near proximity of the electrode. Although its nanometer size and other advantages have increased its value, it also has some disadvantages. It can decrease electron transfer rates. It can accumulate several contaminants due to their high surface energy, thus unwanted impurities can absorb and block the analyte recognition sites.

Pros- provides high molecular recognition.

Cons- complex process and easily accessible to electrode fouling [68].

Role of nanoparticles in BAs detection

Nanotechnological applications have achieved significant milestones in the detection of BAs. Performance of biosensors can be enhanced by the unique and fascinating physicochemical properties [94] of nanoparticles such as high catalytic efficiency and improved response times [95]. They also enhance electron transfer kinetics, provide more sensitivity and high surface-volume ratio for better adsorption of enzymes. They can also act as redox enzymes by conjugating with biomolecules for biorecognition [96,97]. Nanozymes are enzymes processed with nanoparticles and can be used to overcome the inherent drawbacks of enzymes [94]. In the medical field, these particles can also act as theranostic agents where they reduce systemic toxicities and upgrade the retention and efficacy of drugs [98]. In particular, metal nanoparticles and carbon nanomaterials have been used in high number for the preparation of efficacious biosensors [94]. Also, AuNPs and zeolites are increasingly used to develop amperometric biosensors [61]. As their good electrical conductivity provides eminent electrical wiring of enzymes to the electrode [61] and it imposes minimal diffusion limitations [99]. Core-shell nanostructures are also gaining attention because of their versatile composition and structure that can be employed for distinct functions [100]. Recently, polyamines sensing strips were developed by co-immobilizing PAO and DAO on chitosan/coconut fiber/zinc oxide nanoparticle (CS/CF/nZnO) supports [62]. Here, ZnO NPs, annexed on a CS/CF matrix, improved performance and the handling of immobilizated enzymes and provided more interfacial space to enhance enzyme loading. This biosensor exhibited excellent linearity of 5.0 mM as well as a very low detection limit of 0.01 mM. Chauhan et al. [61] developed a sensitive and stable biosensing modified gold electrode with AuNPs and zeolite nanocrystals. This zeolites-AuNPs combination provided large surface areas for retainment of enzyme and desirable electron transport characteristics. The linear response was between 0.2 and 200 μM and the minimum detection limit was 0.1 μM that was certainly lower than previously reported methods. Initially, Shanmugam et al. [71] fabricated a highly selective DAO/nano-Fe_3O_4/GC electrode to detect putrescine. Use of iron oxide nanoparticles enabled an improved

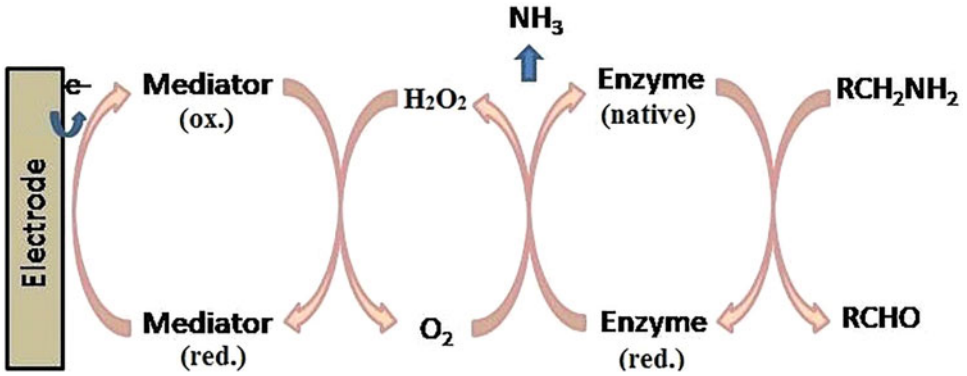

Figure 5. Role of the mediator in electron transfer.

sensitivity. The electrode showed linear range between 2 and 8 nM, a limited of detection of 0.65 nM and a rapid response time of 0.3 s.

During the recent period, Henaoescobar et al. [70] developed a selective screen-printed carbon electrode (SPCE) using gold nanoparticles for the simultaneous detection of Put and Cad. For putrescine, a linear response range from 9.9 to 74.1 μM with capability of detection equal to 9.9 mM and for cadaverine, linear response from 19.6 to 107.1 mM with capability of detection of 19.9 mM was observed at the MAO/AuNPs/TTF/SPCE biosensor. Spehar-Délèze et al. [101] reported a solid state ECL sensor based on tris(2,2'bipyridyl)ruthenium(II) sheated silica nanoparticles (RuNP) onto SPCEs for biogenic polyamines detection. The device showed stability with multiple measurements and a limit of detection was found to be 5 nM for spm and spmd, 120 nM for cad and 90 nM for Put. Rawat et al. [95] fabricated tyrosine-protected gold nanoparticles (Tyr-Au Nps) using microwave irradiation and used them as efficient probe (colorimetric and fluorescence assays) for spm and spmd detection in biotic samples. Their notable optical properties and eminent surface recognition property enabled highly sensitive and selective detection during real biological applications. Surface-active maghemite nanoparticles (SAMNs) were used to fabricate a polyamine biosensor to discriminate tumorous tissues from healthy tissues in human crude liver extracts. Core–shell nanostructures (dichromate binded SAMNs) acted as a prominent electrocatalyst for reduction of H_2O_2. The device showed remarkable results due to its amazing colloidal stability, and the unique spectroscopic properties of SAMNs without need for any other coating modifications [68].

CNTs permit direct electron transfer with enzymes because of their flexibility and electrical conductivity [102] Moreover, MWCNTs enable a more current response, large chemical stability and a high surface to volume ratio. These properties led Rochette et al. [103] to construct a mediatorless biosensor for putrescine determination using MWCNTs onto a glassy carbon electrode. The test was carried out on mammalian plasma without preceding purification. Detection limits of more than 5 mM were reported as compared to most common interfering species (spd, spdm, cad, histamine). Bagheryan et al. [67] also developed electrochemical biosensors using MWCNTs that gave a broad dynamic range of 0.04–100 μM, 0.01–24 μM, and 0.08–100 μM for SPM, SPD and PUT respectively and very low detection limits of few nM. Pérez et al. [1] fabricated a bienzymatic biosensor by co-immobilizing diamine oxidase (DOx) and horseradish peroxidase (HRP) into polysulfone/carbon nanotubes/ferrocene membranes onto screen-printed electrodes. The developed biosensor using carbon nanotubes offered excellent sensitivity of 1.9×10^7 nA^{-1} with the minimum detection limit of 1.7×10^{-7} M and a broad linear range from 3×10^{-7} to 2×10^{-5} M.

Role of mediators in BAs biosensor

There are two groups of biosensors that differ in electrical transfer between the transducer and the immobilized enzymes – Direct electron transfer (DET) and Mediated electron transfer (MET). The first group is related to the third generation of biosensors that operates without mediator and provides a direct exchange of electrons between enzyme active sites and the electrode surface that accredits action near to the redox potential of enzymes. Seven BAs have been detected by DET between the enzyme amine oxidase (AO) and solid graphite electrode [104]. CNTs can also be combined to DET that facilitates the transfer mechanism by their flexibility and high electrical conductivity and has been used to fabricate a highly efficient non mediated putrescine biosensor [103]. Aside from these benefits, it may also have hindrances also. Electron transfer can be slow in DET due to their low selectivity and multiple

orientations. The need for high working potentials enhances the possibility of oxidation of other electroactive species that interfere with the produced current. To overcome all these hindrances and develop high efficiency in the DET, the concept of mediators is introduced. In later group mediated electron transport, MET, a redox mediator is used that decreases the distance between the enzyme redox center and electrode surface, this facilitates the rate of electron transfer as shown in Figure 5. Mediators are electron exchange agents that act as a shuttle between the enzyme active site and the electrode surface. They are low molecular weight artificial electroactive species and become reduced at low potential, thereby preventing oxidation of other substances. Screenprinted TTF has been used as a mediator in the biosensor for detection of Put and Cad that allowed measurement at low working potentials and reducing possible interferences [70]. Another different approach was used by Calvo-Perez in which hydrogen peroxide was detected [1]. H_2O_2 normally requires a high working potential at which many electroactive substances may be oxidized to create interferences. Here the biosensor was made by using a mediator ferrocene that allowed detection at lower operational potentials [1]. Prussian blue (PB) is also used for H_2O_2 measurement at low potential to decrease interferences. In oxidase based biosensors, the redox mediator cannot be able to shuttle electrons then the mediator, that catalyzes oxidation or reduction, is used for fabrication [69]. The osmium redox polymer has been used in the development of amperometric biosensors for determination of different BAs [27,73]. Various mediators used in the detection of different BAs are hydroxymethylferrocene (HOMeFc) (with MAO and HRP) and Prussian blue (using diamino oxidase) [1]. Sometimes, oxidized forms of the mediator is regarded to recycle the reduced enzyme to its active and initial state and then it allows electron transfer. These have been found to exchange electrons very efficiently from reduced enzymes. Some of the mediators include: 1,l-dimethylferrocene-2-hydroxypropyl-P_cyclodexrin (HPBC) complex; tetrathiafulvalene-HPBC inclusion complex; 4-aminodiphenylamine-HCl; ferrocene carboxylic acid HPBC complex; 2,6-dichlorophenolindophenol; and potassium ferricyanide [92].

Conclusion and future prospectives

Taking into account the quality control of food, a more precise, sensitive, rapid, economical and easily adopted method, which can detect even slight changes in BAs profile, is required. Biosensors are preferred over other analytical methods as these are cost effective and provide rapid on-site analysis of BAs. It is anticipated that the utilization of enzymes such as DAO and PAO along with several nanomaterials (CNTs, AuNPs, ZnONPs and PtNPs) in the fabrication of BA biosensors have exposed new prospects to enhance their electrochemical performance and catalytic efficiency. Mediators are also used to facilitate the rate of electron transfer between the enzyme redox center and the working electrode surface. Many appealing prospects of biosensors such as the utilization of multifunctional nanocomposites, nanoelectrodes and nanofilms are still being researched. Continuous monitoring of reliable biosensors would certainly led researchers to better understand and reveal the impacts of BAs in our food. An intriguing possibility for the future is to soon clear how these compounds can be controlled and the food can be ensured regarding its safety and quality standards.

Disclosure statement

The authors report no potential conflict of interest.

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