**Research Paper**

# Biogenic Amines Detection by Chromatography and Sensor Methods: A Comparative Review

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## Abstract

Biogenic amines (BA) are chemical compounds shaped by amino acids decarboxylation and exist in food and beverages that contain protein. They are categorised as very toxic and some countries have even prohibited their consumption at high level especially histamine. Two major methods have been used and developed well such as chromatography methods and sensors methods. The common method applied for chromatography are liquid chromatography (LC) and gas chromatography (GC) while for sensor methods are optical, chemical and bio-sensor. These methods have advantages and disadvantages. For chromatography methods, derivatization is required in order to improve sensitivity and selectivity, nevertheless these methods are very expensive and time-consuming. Derivatization step is time-consuming and facing the risk of partial detection due to an incomplete derivatization. Thus, sensor method is used to solve these issues, since they do not require derivatization step, generate a direct signal that can be interpreted by anyone, very fast and simple. However, they have disadvantages in several aspects such as sensitivity, accuracy and selectivity compared to chromatography methods. This review is based on studies conducted onto biogenic amines detection related to food and beverage samples. Although biogenic amines commonly found in protein-food for decades, new approaches and technical possibilities are still required in order to increase the sensitivity, selectivity and accuracy of the analytical methods to tackle the complexity by their matrices. The rationale of this study is also to provide data about the comparison of the analytical techniques between conventional and sensor methods. Furthermore, the various approaches of biogenic amines determination and the most applied analytical methods have been reviewed.

## Keywords

Biogenic amines, histamine, chromatography, electrochemical sensor, optical sensor

## 1. INTRODUCTION

The demand for food supply increases with human population. This will give impact to food security and become challenging to encounter especially prior to market distribution. Fish, meat, cheese and some other variety of foods that contain protein have been extensively studied to identify presence of biogenic amines at various concentration

The accumulation of biogenic amines is caused by several factors related to chemical, biological and physical processes, such as storage conditions of food, inappropriate transportation and processing conditions leading to microbial growth. Furthermore, food and beverages that contain protein have high possibility to biogenic amines accumulation. The biogenic amines concentration are strongly dependence on the food and beverages characteristics and type of bacteria present. The main biogenic amines generally found in food and beverages are histamine, spermidine, spermine, tyramine, putrescine and cadaverine (Liu

et al. (2020);Mohammed et al. (2016)). In this review paper, we described and elaborated about biogenic amines, their issues and the methods that have been applied by several researchers to detect biogenic amines in food and beverages that contain protein using chromatography methods such as liquid chromatography and gas chromatography or the application of sensor methods such as electrochemical and optical sensors.

## 2. Biogenic Amines, Histamine and Their Issues

Biogenic amines (BA) are organic compounds with aliphatic, aromatic and heterocyclic structures of basic nitrogenous and also shaped by amino acids decarboxylation. Biogenic amines present in protein food and beverages such as fish, meat, cheese, vegetables, milk, yoghurt and wines and causing several adverse reaction if excessively consumed (Alizadeh et al. (2017); Gama and Rocha (2020); Gardini et al. (2016)). Figure 1 shows several biogenic amines that can be found in food and beverages.

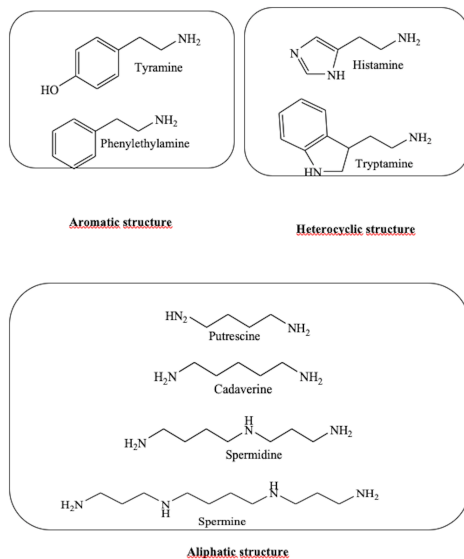The alpha-carboxyl group relocated from amino acid com-

**Figure 1.** The main biogenic amines chemical structures found in food and beverages (Mohammed et al. (2016) with modifications).



**Figure 2.** The biogenic amines formation by decarboxylation of the amino-acid through microbial or enzymatic processes (Francisco et al. (2019) with mofications).

pound causing biogenic amines production. For instance, histidine will generate histamine, lysine generates cadaverine, tyrosine generates tyramine and so on (Hidalgo et al., 2016). Biogenic amines limitation upon consumption by human is linked to the efficiency of detoxification mechanism in individuals (Plakidi et al., 2020). Since biogenic amines can be found easily in food and beverages at various concentrations, the highest concentration of biogenic amines in human body must be maintained at 750 – 900 mg/kg. However, for single amines such as tyramine and phenylethylamine, they should not be consumed more than 100 and 30 mg/kg, respectively, whereas for histamine, it should not be consumed more than 50 mg/kg in foods and 2 mg/L in beverages (Jain et al., 2015). Histamine is the most common biogenic amine exists in protein food or beverages. It has been receiving great attention by some authorities such as FDA and EFSA. Histamine [(2-1H-imidazole—yl)ethanamine] is an amine that can be acquired by decarboxylation of the amino-acid histidine through several factors such as microbial or enzymatic processes. Generally, cooking or heating process destroys some bacteria with the exception of food containing histidine where bacteria inside the foods and beverages causing histidine to be converted to histamine (Biji et al. (2016); Panula et al. (2015)). Histaminolytic bacteria found in food which is histamine oxidizing agent has the ability to exist in food and beverages during destruction process causing the formation of histamine (Naila et al. (2010); Phuvasate and Su (2010)). This occurs not only to histamine but also some other biogenic amines where their formations are influenced by decarboxylation process (Figure 2).

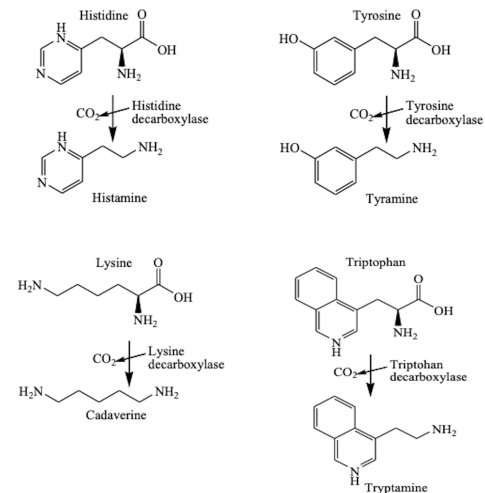However, the dose of toxicity is different from one individual to another owing to every human beings having different endurance. Histamine intolerance may develop some discomfort symptoms such as burning sensation, sweating, dizziness, nausea, tachycardia, headache and some serious cases can cause death (Wang et al., 2017)). Although many studies have shown the toxicity of histamine, its presence in human body is imperative due to the usability of histamine as a parameter for body temperature, influence appetite and even having physiological functions in nervous system as a neurotransmitter. It also causes increasing permeability in blood capillaries as response to inflammatory. Therefore, existence of histamine in human body is possible to causing immune system disorders and allergies (WHO, 2013). Histamine also plays an important role in human metabolism for the release of hydrochloric acid also known as gastric acid. Zero case was reported if the amount of histamine is in small quantity since low level of histamine has no toxic effect. Humans cannot absorb histamine from gastrointestinal tract but it can be dangerous upon intake of larger quantity of histamine. Human body has a system that can turn histamine into harmless compound by releasing enzymes such as diamine oxidase (DAO) and histamine-N-methyl transferase (HMT) to detoxify histamine. But, cadaverine and putrescine have the ability to inhibit these enzymes and eventually are having potential to increase histamine toxicity (Taylor and Eitenmiller, 1986). Some studies also reported histamine is not toxic at a low level, but with the presence of cadaverine and putrescine at higher level, an increase in toxicity of histamine was observed (Plakidi et al., 2020). According to some studies, putrescine and spermidine can be found in vegetables, whereas cadaverine and putrescine exist in vinegars (Křížek et al. (2014); Qiao et al. (2020)). They also can be found in infant milk products. Although there is no case of poisoning caused by putrescine and cadaverine being reported, yet some studies discovered that they could interact with amine oxidases and increase the toxicity of tyramine and histamine (Alavarez and Moreno – Arribas, 2014; Pereira et al.

(2016)). Spermidine and spermine have some potentials to cause carcinogens after reacting with nitrite forming N-nitrosamines (Mey et al., 2014).

Histamine poisoning is considered one of the most general food poisoning caused by sea food consumption(Smiljkovic et al., 2017). According to some studies high concentration of histamine was detected in fish species coming from the Scombroidae family such as mackerel and tuna. However, non-scombroid fish species can also cause histamine poisoning such as bluefish, mahi-mahi, herring and sardine (Qiao et al., 2020). The toxicity causes by histamine consumption is currently popular as Scombroid poisoning. Histamine poisoning usually connected to fish samples despite some food and beverages can cause histamine poisoning. Nevertheless, based on some studies almost 80% cases of food poisoning in Europe is caused by fish consumption. Food allergy symptoms caused by histamine consumption can be hives, itching and diarrhea to life-threatening anaphylaxis (Akdis and Akdis (2015); Jones et al. (2014); Wood (2016); Yu et al. (2016)). These studies also reported several bacteria such as P. damselae subsp. Damselae (Pdd), Photobacterium, i.e. and P. Phosphoreum detected in fish flesh which can impulse the activity of histidine decarboxylase encountered in tuna, mackerel and bonito (Trevisani et al., 2017). These bacteria are very strong that they can produce histamine and Photobacterium damselae subsp. Damselae is considered a strong pathogen for Scombroid family amongst all of them (Terceti et al., 2016).

Several authorized bodies have different perspective about histamine consumption. Food and Drug Administration (FDA) has made a regulation for histamine consumption where the allowable intake is 5 mg/100 g of food (FDA 2011). Meanwhile, the European Union has guided that histamine content in food and beverages must be lower than 10 mg/100 g of food. However, it is interesting to discover that findings from several studies showed that histamine at 67 to 180 mg/100 g food orally taken by a sampling population showed no sign of toxicity(Wang et al., 2017). It was suggested that this is due to the endurance of human itself during the histamine consumption or the presence of DAO and HMT enzymes inside human body that change histamine into harmless compound determined through the absence of cadaverine and putrescine. Nonetheless, the consumption of histamine should be limited because several cases of histamine poisoning showed anaphylactoid reaction which is very dangerous for humans and even causing death (Feng et al., 2015). Therefore, due to these issues, monitoring and measuring of biogenic amines particularly histamine is an imperative task for the food industry and food safety, especially us as researchers to controlling and finding the best method to detect biogenic amines in food and beverages before being distributed to market.

## 3. Biogenic Amines Detection Using Chromatography Methods

Biogenic amines detection in food and beverages have some objectives such as to modify the current technique or developing new techniques so they can be applied by analyst, to identify biogenic amines concentration in various products from countries

that consume food protein and beverages regularly with high concentration. In addition, the relation between biogenic amines accumulation in food and beverages and the growth of bacteria inside the food and beverages as well as their potential toxicity require intensive investigation (Angulo et al., 2020). Biogenic amines analysis in food and beverages are not straightforward due to biogenic amines structures are very complex and some of them exist in food and beverages but at very low level (below 1 ppm). Appropriate extraction and purification methods must be selected accordingly (Jain et al., 2015). Thus, food and beverages should be treated to ensure the isolation of biogenic amines can be carried out. Sample clean-up plays an important role for biogenic amines extraction before further analysis using chromatography techniques. Common clean-up techniques applied are presented in Table 1 such as solid phase microextraction (SPME), hollow fibre liquid phase microextraction (HF-LPME), liquid-liquid extraction (LLE) and solid phase extraction (SPE). Upon completion of the clean-up techniques, analysis using instrument can be performed. The use of solvents is also important to ensure complete recovery of biogenic amines. Some studies applied water and methanol to extract histamine but some others suggested for acidic solvents such as perchloric acid, hydrochloric acid (HCl) or trichloroacetic acid (TCA) because they gave satisfactory accuracy and recovery (Sirocchi et al. (2014); Vieira et al. (2020)). QuEChERS method has also been applied in order to purify biogenic amines from complex samples since QuEChERS has some advantages such as fast, simple, effective, rugged and inexpensive (Guo et al. (2016); Xian et al. (2016)).

Several analytical techniques for biogenic amines detection in food samples have been thoroughly used such as capillary zone electrophoresis (CZE), thin-layer chromatography (TLC), high performance liquid chromatography (LC) and gas chromatography (GC). Various samples such as seafood, fish and fish products, juice, milk, dairy products, meat and meat products and wine (Çiçek and Tokatli (2018); Silva et al. (2020); Vieira et al. (2020)) have been analysed. These studies did not only focus on the biogenic amines detection in food but also on the detection of microorganisms that cause biogenic amines accumulation in food and beverages (Hao and Sun (2020); Jia et al. (2020)). The common chromatography techniques used are high performance liquid chromatography (HPLC) (Sagratini et al. (2012); Sentellas et al. (2016)) and gas chromatography (GC) accompanied by mass spectrometry (MS) (Munir et al. (2017); Zhang et al. (2019)).

Beside extraction methods and chromatography, the use of derivatizing reagents prior to chromatography methods are compulsory and have important role during chromatography analysis. These reagents improve the polarity and volatility of biogenic amines so they can be detected by chromatography instruments. Several biogenic amines such as cadaverine, putrescine and spermidine cannot be detected using UV detector whereas histamine and tyramine can be detected yet at lower wavelength region. Furthermore, almost all biogenic amines are impossible to be detected using fluorescence detector and gas chromatography. Moreover, the use of derivatizing reagents help in the analysis of biogenic amines using HPLC equipped by UV and fluorescence

**Table 1.** Various studies started from HPLC techniques for biogenic amines detection in food and beverages.

| Food Sample | Analyte | Extraction | Derivatizing / detector | LOD (µg/kg) | Ref. |
|---|---|---|---|---|---|
| Canned tuna, canned sardines, chicken sausage and beef | Met, Dim, Put, Cad, His, Tyr, Spd, Spr | SALLE | Dns-Cl / UV and FLD | 7.5-1600 | (Francisco et al., 2019) |
| Fish | His, Put, Cad, Spd, Spr | HClO$_4$ | PSCI/ UV and FLD | 100-1400 | (Plakidi et al., 2020) |
| Fish and fishery products, meat and meat products and cheese | His, Tyr, Cad, Put, Tryp | 5% TCA | DAD | Not defined | (Bogdanović et al., 2020) |
| Chub mackerel | His, Tyr, Cad, Put, Tryp | 5% TCA | Dns-Cl / FLD | 20-240 | (He et al., 2020) |
| Honey | His | 0.1 M HCl | MS/MS | 90 – 590 | (Zhang et al., 2020) |
| Cheese | His, Tyr, Cad, Put, Tryp | 0.1 M HCl | Dns-Cl/ UV | Not defined | (El-Salam, 2020) |
| Sausage products | His, Put, Spd, Tryp | 95% Ethanol | QO-MS | 0.9-1.5 | (Jiang et al., 2015) |
| Soy sauce | His, Put, Spd, Tyr | 5% TCA | Dns – Cl/ UV | 20-60 | (Hao and Sun, 2020) |
| Probiotic yogurts | Cad, Tyr, Put, Spd, Spr | 0.6 M HClO$_4$ | Bnz-Cl/ DAD | 180-4000 | (Vieira et al., 2020) |
| Chinese herbal | His, Tyr, Cad, Put, Tryp, Spd, Phm | 0.4 M HClO$_4$ | Dns-Cl / DAD | 1 x 104 | (Sánchez-López et al., 2017) |
| Wines and beers | His, Cad, Put, Spd, Spr | - | Dns-Cl/ UV and FLD | 30-180 | (Angulo et al., 2020) |
| Fish dried bonito flakes | His, Tyr, Spd, Put, Cad, Spr, Phe, Tryp | 5% TCA | Dns-Cl / UV | 0.1-0.7 | (Qiao et al., 2020) |
| Wine | His, Cad, Put, Try, Tryp | LLE | Dns-Cl / FLD | 1-50 | (Liu et al., 2020) |
| Cheese | His, Try, Tryp | TCA | UV | 50 – 100 | (Gama and Rocha, 2020) |
| Canned tuna fish | His, Cad, Put | LLME | DAD | 0.2-1.7 | (Nemati et al., 2020) |
| Cheese | His, Put, Dmet | SALLE | Dns-Cl / FLD | 1.5-1770 | (Ramos et al., 2020) |

**Table 2.** Various studies started from HPLC techniques for biogenic amines detection in food and beverages.

| Food Sample | Analyte | Extraction | Derivatizing / detector | LOD (µg/kg) | Ref. |
|---|---|---|---|---|---|
| Milk | His, Phe, Spm, Spd, Trp, Try | DLLME | Dns-Cl / UV | 0.51-1.49 | (Cao et al., 2019) |
| Wina | His, Phe, Spm, Spd, Cad, Tyr | LLE | DAD | Not defined | (Rodríguez-Nogales et al., 2020) |
| Plant herbal | Phe, Tyr, Hep | ACN | Dns – Cl, OPA, FMOC – Cl / UV, FLD, MS/MS | Not defined | (Lkhagva et al., 2020) |
| Beer | His, Phe, Spm, Spd, Cad, Tyr | - | Dns-Cl / UV | 130-520 | (Lorencová et al., 2020) |
| Fish | His, Tyr, Tryp, Put, Cad, Phe | 0.1% TCA | MS | 0.064-1.00 | (Zhang et al., 2020) |
| Cheese | His, Cad, Put, Try, Tryp | HClO$_4$ | AQC/UV | 1000-3300 | (Mayer and Fiechter, 2018) |
| Fish meat and fermented fish | His, Cad, Put, Try, Tryp | HClO$_4$ | Dns-Cl / FLD | 10-210 | (Ishimaru et al., 2018) |
| Salted mackerel fillet | His, Cad, Put, Spd, Spr | 5% TCA | MS/MS | 10-20 | (Ochi, 2019) |
| Fermented meat sausages | His, Put, Cad, Spe | 5% TCA | Dns-Cl / UV | 150-280 | (Alves et al., 2017) |
| Turkish fermented dry sausages | Tyr, His, Cad, Phe, Tryp | 0.4 M HClO$_4$ | Dns-Cl / UV-Vis | Not defined | (Çiçek and Tokatli, 2018) |
| Fermented deer meat sausages | His, Tyr | Peptone water | DAD | | (Maksimovic et al., 2018) |
| Fermented pork product | Tyr | 0.5 N HClO$_4$ | Dns-Cl / DAD | Not defined | (Santiyanont et al., 2019) |
| Tuna and mahi – mahi | His, Cad, Put, Det | 5% TCA | Dns-Cl / UV | 10-20 | (Bai et al., 2019) |
| Plant milks | His, Spm, Put, Spd, Cad, Tyr, Phe | HClO$_4$ | Dns-Cl / FLD | Not defined | (Gobbi et al., 2019) |
| Cocoa beans | His, Spd, Cad, Tyr, Phe, Put, Spm | Ethanol | DAD and FLD | Not defined | (Spizzirri et al., 2019b) |
| Fish, Fish products and meats | Cad, His, Put, Tyr, Spd & Spr | Methanol: ACN: H$_2$O (45:45:10) | MS equipped with ESI and MRM mode. | 10-20 mg/kg | (Molognoni et al., 2018) |
| Fish samples & Wine | His, Phe, Spm, Spd, Trp, Try | DLLME | Dns-Cl / UV | 1.3-9.9 µg/kg | (Cao et al., 2020) |

**Table 3.** Various studies started from HPLC techniques for biogenic amines detection in food and beverages.

| Food Sample | Analyte | Extraction | Derivatizing / detector | LOD (µg/kg) | Ref. |
|---|---|---|---|---|---|
| Sausage & Kielbasa | His, Put, Cad, Spd, Trp | 1% TFA | Dbs-Cl / UV-Vis | 3.0–8.0 µg/kg | (Zarghampour et al., 2018) |
| Cheese | Et, His, Cad, Put, But, Phe, Trp | 0.1 M HCl | Dns-Cl / DAD (245 nm) | 0.25-50 mg/kg | (Shan-Shan et al., 2016) |
| Cheese and sausage | Cad, His, Phm, Put, Tyr & Tryp | 0.1M HCl | Dns-Cl / UV | 0.03-0.36 mg/kg | (Liu et al., 2020) |
| | | | Bnz-Cl / UV | 0.09-0.38 mg/kg | |
| Fresh milk fish and Indian whiting | His | 6% TCA | Dns-Cl / UV-Vis | Not defined | (Arulkumar et al., 2016) |
| Soy sauce | His, Spd, Put, Tyr, Trp, Spr | Acetonitrile | UHPLC-MS/MS | 4-8 µg/kg | (Dong and Xiao, 2017) |
| Wine | His, Tyr, Put, Cad, Spr, Det, Dmet, Prop, Agm, Spd | Dilution with water | p-toluenesulfonyl chloride / MS / MS | 0.023-83 µg/kg | (Nalazek-Rudnicka and Wasik, 2017) |
| Milk | His, Put, Spd, Spr, Cad, Tyr,Phm | SPE | Dns-Cl / UV | 0.03-0.05 mg/kg | (Spizzirri et al., 2019a) |
| Poultry meals | Cad, His, Put, Spd, Spr, Tyr & Tryp | 0.1 M HCl | No derivatizing reagents used/ DAD & FLD | 0.11-2.27 mg/kg | (Spizzirri et al., 2019b) |
| | | | Dns-Cl / DAD & FLD | 0.04-0.20 mg/kg | |

**Biogenic amine**: agmatine (Agm), amylamine (Am), butylamine (But), cadaverine (Cad), diethylamine (Det), dimethylamine (Dmet), dopamine (Dop), ethylamine (Et), ethanolamine (Eth), heptylamine (Hep), 1,6-hexamethylenediamine (Hex), histamine (His), isoamylamine (Iam), isobutyamine (Ibut), methylamine (Met), nitrosamine (Ntr), 2-phenylethylamine (Phm/2-PE), propylamine (Prop), putrescine (Put), spermine (Spr), spermidine (Spd), tryptamine (Trm/Tryp), tyramine (Tyr). **Extraction**: acetonitrile (ACN), direct immersion solid phase microextraction (DI-SPME), dispersive liquid liquid microextraction (DLLME), matrix solid-phase dispersion (MPSD), methanesulfonic acid (MSA), perchloric acid (HClO4), liquid- liquid extraction (LLE), salting – out assisted liquid - liquid extraction (SALLE), sulphosalycilic acid (SSA), solid-phase extraction (SPE), trichloroacetic acid (TCA), trifloroacetic acid (TFA), ultrasound-assisted dispersive liquid-liquid microextraction (UA-DLLME), ultrasound-assisted liquid-liquid microextraction (UA-LLE). **Derivatizing agent**: benzoyl chloride (Bnz-Cl), (N, O-bis (trimethylsilyl) acetamide & trimethlchlorosilane) (BSA+TMCS), 2-(11H-benzo[a]carbazol-11-yl) ethyl carbonochloridate (BCEC-Cl), dabsyl chloride (Dbs-Cl), dansyl chloride (Dns-Cl), heptafluorobutyric anhydride (HFBA), isobutyl chloroformate (IBCF), o-orthophthalaldeyde (OPA), sodium dodecylbenzenesulfonate (SDBS). **Chromatography/detectors**: Atmospheric-pressure chemical ionization (APCI), Diode-Array Detection (DAD), Electrospray ionization (ESI), Evaporate light scattering detector (ELSD), fluorescence detector (FLD), mass spectrometry (MS), multiple – reaction monitoring (MRM), Quadrupole time-of-flight (QToF), quadrupole orbitrap (QO), ultraviolet detector (UV).
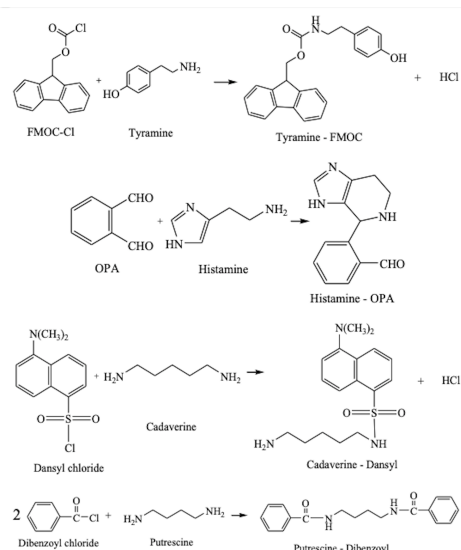
**Figure 3.** Reaction of derivative reagents such as dansyl chloride and OPA with amines. Adopted from (Mantoanelli et al., 2020).

detectors and GC equipped by FID and MS detector (Dong and Xiao (2017); Parchami et al. (2017); Sajid and Płotka-Wasylka (2018)).

### 3.1 High Performance Liquid Chromatography

Compared to other chromatography methods, HPLC becomes the common method used by researchers. Nevertheless, due to the characteristic of biogenic amines such as low volatility and lack of chromophores, almost all biogenic amines require derivatization step during their analysis in order to modify their characteristic. The derivatization steps are divided into two such as pre- and post-column. Various chemical reagents were used to perform the derivatization step and their usages rely on the HPLC detector used. O-phthaldialdehyde (OPA), dansyl-, benzoyl- and dabsyl- chloride, fluoresceine, 9-fluorenylmethyl chloroformate (FMOC), 6-aminoquinolyl-N-hydroxysuccinimidy (AQC) (Angulo et al. (2020); Fu et al. (2016); Sánchez-López et al. (2017)) are examples of the reagents and as shown in Figure 3 with their reaction with amines. These are common derivatizing reagents used by researchers where some of them are suitable in ultraviolet (UV) detector and some others are more suitable in fluorescence detector. The common derivatizing reagent used are OPA, benzoyl and dansyl chloride. The use of OPA applied by some researchers because it is fast. The derivatization can be completed below 2 min with a mixture of borate buffer (pH 6-8) and methanol at ambient temperature. It can also react with primary amines easily below 1 min upon addition of reducing reagent, such as 2-mercaptoethanol or N-acetylcysteine to modify the characteristics of polyamines such as putrescine, cadaverine, spermidine and spermine. Nevertheless, some studies reported that OPA has poor stability and experienced short life ((Liu et al., 2020)).

During HPLC analysis, the sensitivity of amine derivatized by OPA can decrease owing to its characteristics. Thus, in order to improve the stability, dansyl or benzoyl chloride become a better choice for researcher as they are more stable than OPA. The use of dansyl chloride is suggested for derivatization step due to the stability given for di and polyamines. Some researches also showed satisfactory results when dansyl chloride was used to detect histamine using HPLC method with C18 column equipped with UV detector at 254 nm wavelength (El – Salam et al., 2020; Francisco et al. (2019); Plakidi et al. (2020); Vieira et al. (2020); Wu et al. (2020)). Benzoyl chloride is also an advantage as it has long elution time in dansyl derivatives. A procedure of derivatization using benzoyl chloride was described by (Vieira et al., 2020). Several studies reported the comparison of OPA and benzoyl chloride for histamine determination in tuna fish and found that the derivatization using benzoyl chloride was longer and more complex but the histamine derivative was more stable than OPA (Bani et al. (2019); Mantoanelli et al. (2020); Weremfo et al. (2020)).

The off-line pre-column derivatization technique is the best choice for the detection of biogenic amines using HPLC because it does not need the addition of derivatizing reagents (Mohammed et al. (2016)), thus, this method can decrease the use of derivatizing reagents and disposal of the used reagents. This method also showed an excellence stability of the derivatives (Preti et al., 2015).

The use of detectors is also an important factor in determining biogenic amines in food samples. UV and fluorescene detectors are generally applied, whilst it is very common to use HPLC coupled to mass spectrometer (MS). However, the use of MS to analyse biogenic amines in food and beverages is not usually considered since UV and fluorescene detectors are less expensive, less time consuming and are sufficient for biogenic amines detection (Dai et al. (2014); Zhang et al. (2019)). The most popular method for the biogenic amines detection in food and beverages is the HPLC with Reversed-Phase separation using C8 and C18 columns. Table 1 summarizes the HPLC methods used to determine biogenic amines in food and beverages in the last decades.

Biogenic amines can be found in solid and liquid samples. HPLC method gave satisfactory results. C18 column was a preference. The choice of derivatizing agent also influenced the choice of detector. The use of OPA should be followed by fluorescence detector whereas the use of dansyl, dabsyl and benzoyl chloride were suitable for UV detector (Herrero et al., 2016). The selection of wavelength is crucial and normally is influenced by the column, derivatization reagent and detector. For liquid samples, the extraction solvents are not seemingly necessary but the use of derivatizing reagent is important.

Dong and Xiao (2017) reported that HPLC technique applied for biogenic amines determination in food samples and gave satisfactory results if ultra-HPLC is equipped with MS/MS to gain its selectivity and anti-jamming capability as compared to other detectors. The study used acetonitrile, ethyl acetate and trichloromethane in deciding the best extracting solvent for

biogenic amines. Acetonitrile gave satisfactory recovery and accuracy of more than 100% for extracting biogenic amines from soy sauce. No derivatization procedure was applied for this study even though some studies require derivatization step to modify the characteristic of biogenic amines prior to analysis using HPLC. Application of QuEChERS Dong and Xiao (2017) in purifying target analytes in solution samples disregarded usage of derivatization procedure on food samples. Furthermore, QuEChERS technology was meant to eliminate the matrix interference in order to isolate biogenic amines from food samples.

According to Table 1, several researchers reported on the value of detection limit (LOD) after biogenic amines has been derivatized using several reagents and later analysed using HPLC with different detectors such as UV and fluorescence. Liu et al. (2020) reported the detection of biogenic amines using UV detector and derivatized with benzoyl and dansyl chloride in sausage and cheese. LOD of dansyl chloride is lower than benzoyl chloride. Dansyl chloride, as a popular reagent is more sensitive than benzoyl chloride. It can react with primary and secondary amines and show stability at high temperature Angulo et al. (2020) while benzoyl chloride, though it is a fast reagent but it has some drawbacks such as unstable at high temperature and easily degraded even when stored at -20$^o$C (Liu et al., 2020).

Analysis of biogenic amines using HPLC without derivatizing reagent has been studied by Mologni et al. (2018) but using MS detector because it is more powerful than UV and fluorescence detectors. HPLC-MS can detect biogenic amines by using selected ion monitoring (SIM) or multiple reactions monitoring (MRM) modes. But, in order to tackle the polarity issue of biogenic amines, a particular column should be used such as hydrophilic interaction liquid chromatography (HILIC) and pentafluorophenylpropyl (PFP) (Konieczna et al. (2016); Pawar et al. (2014)). However, some studies reported the use of LC/MS with derivatization step is more sensitive (Sagratini et al., 2012).

### 3.2 Gas Chromatography
Gas chromatography becomes the general method applied by researchers beside HPLC. It has several advantages such as high accuracy, sensitivity, selectivity and having higher resolution compared to HPLC. Nevertheless, similar like HPLC where during GC analysis derivatization step is required since biogenic amines have high polarity and not easily vaporize. Derivatizing agents used for HPLC in running the alkylation, acylation and silylation are also considered and suitable for biogenic amines in order to increase the sensitivity of biogenic amines so they can be easily detected using GC (Płotka-Wasylka et al., 2015). Several studies using GC for biogenic amines determination in solid and liquid samples are presented in Table 4.

The isolation of biogenic amines from food and beverages samples are very important to ensure the accuracy in determining the content of biogenic amines prior to analysis using chromatography techniques. Distilled water is commonly used to extract biogenic amines from fish sample due to the solubility properties of biogenic amines where they are soluble in water. Nevertheless, according to some studies the use of acidic solvent
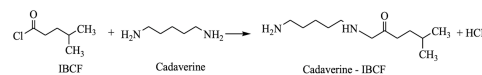


**Figure 4.** Reaction process for biogenic amines derivatized by isobutyl chloroformate.

such as hydrochloric acid and trichloroacetic acid giving the better results. GC analyses using 5MS column has also become the common column used by many studies (Munir and Badri, 2020). MS detector is applied in order to identify the structure of biogenic amines while FID is used as the detector. In general, the derivatizing step is reported as the utmost important procedure and if without this step is a must, the use of double detector namely MS/MS is required in order to analyse the structure of biogenic amines in food samples. Derivatization procedure alters the properties of analyte to decrease polarity but to increase volatility of biogenic amines and also to improve the selectivity, sensitivity and resolution of GC analysis. On the other hand, the use of MS/MS is expensive and time consuming in sample preparation prior to analysis using MS/MS (Płotka-Wasylka et al., 2015). Nevertheless, the use of derivatization reagents have some issues due to they may cause the loss of the analytes, presence of by-products, extra steps in sample preparation and sometimes required more time when derivatize reagent is used (Papageorgiou et al., 2018). The derivatization reagents for acylation and silylation are heptafluorobutyric anhydride (HFBA) and N, O-bis(trimethysilyl)acetamide + (trimethylchlorosilane) (BIS+TMCS) respectively, applied before analysis using GC (Munir et al. (2017); Petrarca et al. (2017)). These derivatizing agent has given satisfactory results since the derivatized biogenic amines were able to be detected using GC with FID and MS detectors. They also gave high accuracy and recovery (above 100%). Successful biogenic amines analysis has also been achieved using GC coupled to mass spectrometry (GC-MS) (Cunha et al. (2017); Płotka-Wasylka et al. (2016)). Other than these derivatizing reagents, Papageorgiou et al. (2018) has successfully used isobutyl chloroformate (IBCF) as the derivatization agent and the structure of amine after derivatization is shown in Figure 4.

Shin et al. (2017) reported that amines can also be found in human urine beside food and beverages. The amines found in human urine were dopamine, tyramine and octopamine. In order to extract amines from urine samples, it was extracted using 0.1 M HCl and the derivatization step used N-methyl-N-hexamethyldisilazane (HMDS) and N-methyl-bis(heptafluorobutyramide) (MBHFBA) in order to modify the amine structures in human urine samples. The GC analysis using MS/MS detector was applied and equipped with DB-5MS capillary column. Almost all solid and liquid samples composed of biogenic amines and half of them contained histamine. It was reported that none of them contained histamine more than 200 ppm. The histamine concentration in the samples were below the FDA regulated level (50 ppm), and zero cases of histamine poisoning has been reported in their study.

**Table 4.** Various studies based on GC techniques for biogenic amines detection in food and beverages.

| Food Sample | Analyte | Extraction | Derivatizing / detector | LOD | Ref. |
|---|---|---|---|---|---|
| Fish & Fish products | His, Tyr, Cad, Put, Spd | Distilled water | BSA / FID & MS | 1.20-2.90 mg/kg | (Munir et al., 2017) |
| Sausage products | His, Put, Spd, Tryp | Ethanol | MS | 0.1-50 $\mu$g/g | (Jia et al., 2020) |
| Bonito, mackerel and sardine | His, Tyr, Cad, Put, Spd | - | IMS | Not defined | (Espalha et al., 2019) |
| Canned fish | His, Cad, Tyr, Put | DLLME | MS | 0.03-0.29 $\mu$g/g | (Kamankesh et al., 2019) |
| Poultry, Beef and Meat products | His, Hex, Cad, Det, Put, Spd, Try, Tyr | DLLME | IBCF / MS | 0.009-0.029 $\mu$g/g | (Wojnowski et al., 2019) |
| Meat | His, Tyr, Put, Cad | SPE | HMDS / MS - MS MBHFBA / MS-MS | 0.24-1.23 ng/mL | (Wood, 2016) |
| Baby food products | Spd, Spm | 1M HCl | HFBA / MS | 5 $\mu$g/kg | (Petrarca et al., 2017) |
| Canned fish | His, Tyr | 5% TCA | SDBS / MS | 3 and 4 ng/g | (Alizadeh et al., 2017) |
| Fish and canned fish | His, Tyr, Put, Cad | DI-SPME | IBCF / MS | 2.98-45.3 $\mu$g/kg | (Huang et al., 2016) |
| Salted fish | Ntr | Solvent extraction | No derivatizing / MS-MS | 0.03-0.33 $\mu$g/kg | (Qiu et al., 2017) |
| Cheese | His, Tyr, Put, Cad | DLLME | IBCF / MS | 5.9-14.0 ng/g | (Mohammadi et al., 2017) |
| Grape juice & wine | His, Tyr, Put, Cad, Hex, Am, Prop, But | DLLME | IBCF / MS | 1.8-36.8 $\mu$g/kg | (Cunha et al., 2017) |
| Wine | His, Hex, Cad, But, Det, Put, Try, Tyr, Ibut | DI-SPME | IBCF / MS | 0.009-0.859 $\mu$g/kg | (Papageorgiou et al., 2018) |
| | His, Cad, Det, Tryp, Tyr, Put, Spr, Met, Et | DLLME | IBCF / MS | Below 4.1 $\mu$g/kg | (Phuvasate and Su, 2010) |
| Beer | His, Cad, Put, Tyr, Met, Et, Dmet, Ibut | DLLME | IBCF / MS | Below 2.9 $\mu$g/kg | (Plakidi et al., 2020) |

Biogenic amine: amylamine (Am), butylamine (But), cadaverine (Cad), diethylamine (Det), dimethylamine (Dmet), ethylamine (Et), ethanolamine (Eth), heptylamine (Hep), 1,6-hexamethylenediamine (Hex), histamine (His), isoamylamine (Iam), isobutyamine (Ibut), methylamine (Met), nitrosamine (Ntr), 2-phenylethylamine (Phm/2-PE), piperidine (Pip), propylamine (Prop), putrescine (Put), spermine (Spr), spermidine (Spd), tryptamine (Trm/Tryp), tyramine (Tyr).

Extraction: direct immersion solid phase microextraction (DI-SPME), dispersive liquid liquid microextraction (DLLME), hydrochloric acid (HCl), trichloroacetic acid (TCA).

Derivatize agent: (N, O-bis (trimethylsilyl) acetamide & trimethlchlorosilane) (BSA+TMCS), heptafluorobutyric anhydride (HFBA), hexamethyldisilazane (HMDS), isobutyl chloroformate (IBCF), *N*-methyl-bis-heptafluorobutyramide (MBHFBA), sodium dodecylbenzenesulfonate (SDBS).

Chromatography/detectors: Flame ionization detector (FID), mass spectrometry (MS), ion mobility spectrometry (IMS)

Based on Table 4, it can be concluded that addition of derivatizing reagent prior to GC analysis is crucial in order to improve the properties of analytes and improve the sensitivity and selectivity of GC analysis. The use of GC with column ZB-5MS) and column HP-5MS are suitable to detect biogenic amines in food or beverages. These methods are well accepted. Nevertheless, the use of derivatization agents and conventional methods such as HPLC and GC have some disadvantages for analytical techniques. They are not only time consuming but also bear the risk of having only partial detection due to an incomplete derivatization. They are also very expensive and need to be analysed by experts. The determination of biogenic amines cannot be a concern to researchers only but also to distributors, sellers and farmers in monitoring the biogenic amines concentration in markets. Simplified instrument is needed for direct and rapid detection of biogenic amines from foods and beverages.

## 4. Biogenic Amines Detection Using Sensor Methods

Sensor methods show some advantages compared to chromatography methods such as HPLC and GC. They do not require sample derivatization and also generate a direct signal that can be interpreted by analyst expert and non-expert. Furthermore, they are much more economic than HPLC and GC. By choosing the right chemical/bio–component the electrochemical sensor can be applied to detect biogenic amines in food and beverages. It is also more appropriate to use electrochemical sensor since the selectivity and sensitivity are adequate (Telsnig et al. (2012); Turner (2013)). Sensor methods are attractive because of their remarkable detectability and experimental simplicity. They have a great position among the current analytical techniques that have reached the commercial stage and which have found a vast range of important applications in the fields of environmental, industrial, agricultural and even clinical analyses.

Based on some studies that is presented in Table ??. Sensor methods provide accurate, reproducible, fast and often selective determination of various biogenic amines found in food and beverages. They are also user friendly because they do not use a large amount of organic solvents. Other advantages of sensors are they are non-destructive, adaptable to small sample volumes, the instruments are small and skilled chemistry analyst is not required to operate this sensor (Degefu et al. (2014); El-Nour et al. (2017); Roales et al. (2015)). Sensors based on electrochemical or optical sensors have been studied over the last decades with satisfactory results.

### 4.1 Electrochemical Sensors

Electrochemical sensors have recently found extensive applications in diverse industries. Nowadays, many analytical instruments used in environmental, food, pharmaceutical or clinical laboratories. For an instance, where glucose biosensors use widely in order to monitor the level of glucose in human blood while pH electrodes are used to identify the acidity of sample. Electrochemical sensors are analytical methods using chemical and bio-sensors as a whole or a basic part. Both of them work as a receptor to capture the analyte required. The receptor is divided into two namely biological and chemical. Electrochemical sensors are divided into two such as biosensor and chemical sensor. Electrochemical sensor produces electronic signals from a single analyte or group of analytes that can be interpreted easily. Electrochemical sensors are using either chemical receptors or have undergone chemical modification (Degefu et al. (2014); Geto et al. (2014); Stojanović et al. (2016)) or even using biology receptors such as immobilized amine oxidases and dehydrogenases (Apetrei and Apetrei (2016); Keow et al. (2007); Pérez et al. (2013); Telsnig et al. (2012)). All these have been described and studied in biogenic amines determination in food and beverages. The modification of receptor chemically or biologically to obtain electrical signal can be performed by using amperometry, voltammetry, potentiometry or conductometry methods (Justino et al., 2015). Amperometry method is a method that can measure the current generated by analyte, while potentiometry method is a method to measure the potential charge in order to analyse the alteration of a medium between electrodes which is also called conductometry method. Beside these methods, a study has reported the use of impedimetric method where measurement of impedance which is resistance and reactance from analyte was determined (Ho et al. (2020); Kaçar et al. (2020)).

Electrodes also play crucial role for electrochemical sensors performance because reaction between analyte and receptor occur at the electrode surface and the result of their reaction is read by an instrument. Electrochemical sensors usually need three electrodes such as a reference electrode, a counter or auxiliary electrode and a working electrode, also known as the sensing or redox electrode. The reference electrode, commonly made from Ag/AgCl because it has the ability to maintain a distance from the reaction site in order to achieve a stable measurement. The working electrode serves as the transduction element in the biochemical reaction, while the counter electrode establishes a connection to the electrolytic solution so that a current can be applied to the working electrode (Ali et al., 2006). These review papers have elaborated the use of electrochemical sensors for biogenic amines determination in various food samples until now.

### 4.2 Biosensors

The biogenic amines determination using biosensors is a general method applied by some researchers compared to chromatography methods. They have several solutions to handle chromatography problems such as short time analysis time, simplicity and can be used easily anywhere and anytime by everyone. In order to acquire reliable biosensor for biogenic amines determination, enzymes become the most important part as a receptor. Enzymatic reactions catalysed by amine-selective enzymes such as monoamine and diamine oxidase, putrescine oxidase and methylamine dehydrogenase are applied by some studies to react with biogenic amines (Verma et al., 2020). Table ?? summarizes the electrochemical techniques used to determine biogenic amines in food and beverages by bio-sensors, in the past years. These methods were using various approaches in order to detect biogenic amines in food samples and also show various detection

**Table 5.** Various electrochemical methods based on biological and chemical sensor to detect biogenic amine in food samples.

| Food Sample | Analyte | Technique | LOD (mol $L^{-1}$) | Ref. |
|---|---|---|---|---|
| Tuna fish | His | Chemical sensor using aerosol – jet – printed graphene | $3.1 \times 10^{-5}$ | (Parate et al., 2020) |
| Marine fish | His | Amperometric biosensor using diamine oxidase and peroxidase as molecular recognition element | Not defined | (Trevisani et al., 2017) |
| Food products | | Voltammetric sensor based on molecularly imprinted polymer (MIP) | $7.4 \times 10^{-11}$ | (Akhoundian et al., 2017) |
| Chicken meat | Put, Cad, Tyr | Amperometric biosensor using pea seedling amine oxidase (PSAO) as molecular recognition element | $1.2\text{-}4.5 \times 10^{-5}$ | Telsnig et al. (2012) |
| Beef, chicken, turkey and fish meat | Put | Chemiluminescene biosensor using putrescine oxidase and diamine oxidase as molecular recognition element | $1.4 \times 10^{-5}$ | (Miklicanin and Valzacchi, 2017) |
| Octopus and red wine | His, Put, Tyr, Cad | Amperometric biosensor using diamine oxidase attached to screen printed electrode (SPE) | $8.1 \times 10^{-6}$ | (Henao-Escobar et al., 2016) |
| Fish | His | Amperometric biosensor using diamine oxidase as molecular recognition element | $2.54 \times 10^{-8}$ | (Apetrei and Apetrei, 2016) |
| | | Amperometric biosensor using diamine oxidase and horseradish peroxidase as molecular recognition element | $1.7 \times 10^{-7}$ | (Pérez et al., 2013) |
| | | Chemical sensor using square wave stripping voltammetric (SWSV) | $3 \times 10^{-7}$ $1 \times 10^{-5}$ | (Yilmaz and Inan, 2015) |
| | | Chemical sensor using differential pulse voltammetric (DPV) | $7.62 \times 10^{-8}$ | (Geto et al., 2014) |
| | His | Amperometric immunosensor | $1.12 \times 10^{-11}$ | (Dong et al., 2017) |
| | | Surface plasmon resonance (SRP) based on a molecularly imprinted polymer (MIP) film as a biosensor | $2.25 \times 10^{-7}$ | (Jiang et al., 2015) |
| | His, Tyr, Phm | Quartz crystal microbalance (QCM) based on a molecularly imprinted polymer (MIP) | $6.74 \times 10^{-9}$ | (Dai et al., 2014) |

**Table 6.** Various electrochemical methods based on biological and chemical sensor to detect biogenic amine in food samples.

| Food Sample | Analyte | Technique | LOD (mol $L^{-1}$) | Ref. |
|---|---|---|---|---|
| Fish sauce | His | Amperometric biosensor using rhenium dioxide as molecular recognition element | $1.8 \times 10^{-6}$ | (Veseli et al., 2016) |
| Tiger prawn | | Amperometric biosensor using di-amine oxidase as molecular recognition element | $5.85 \times 10^{-6}$ | (Keow et al., 2007) |
| Alcoholic beverages | His | Chemical sensor using differential pulse voltammetric (DPV) | $1.3 \times 10^{-6}$ | (Stojanović et al., 2016) |
| Wine | His | Chemical sensor using square wave voltammetry (SWV) | $0.3 \times 10^{-6}$ | (Degefu et al., 2014) |

Biogenic amine: agmatine (Agm), amylamine (Am), butylamine (But), cadaverine (Cad), diethylamine (Det), dimethylamine (Dmet), dopamine (Dop), ethylamine (Et), ethanolamine (Eth), heptylamine (Hep), 1,6-hexamethylenediamine (Hex), histamine (His), isoamylamine (Iam), isobutyamine (Ibut), methylamine (Met), nitrosamine (Ntr), 2-phenylethylamine (Phm/2-PE), piperidine (Pip), propylamine (Prop), putrescine (Put), spermine (Spr), spermidine (Spd), tryptamine (Trm/Tryp), tyramine (Tyr).

limits.

Antibody based immunoassays known as the enzyme-linked immunosorbent assay (ELISA) had been proven to be rapid, sensitive and low-cost screening tools for chemical analysis. Several ELISAs have been developed and reported for histamine detection in food samples or even blood samples. Although ELISA method offering speedy result during the analysis but it lacks selectivity and sensitivity. Jiang et al. (2015) reported that ELISA method is tedious and time-consuming. Thus, in order to solve this problem, some researchers found that usgae of diamine oxidase for biogenic amines determination is better than ELISA. Several biosensors have also been studied for biogenic amines determination using diamine oxidase (Dai et al. (2014); Jiang et al. (2015); Pérez et al. (2013); Veseli et al. (2016)). Furthermore, diamine oxidase is cheaper than ELISA but enzymes are also lack of stability. Immunosensors have superior characteristics compared to ELISA and diamine oxidase due to their high sensitivity, satisfactory specificity and higher stability (Apetrei and Apetrei (2016); Dong et al. (2017)).

Amperometry method become a common method in biosensor studies since enzymes can easily react with the analyte in order to obtain the current. Enzymes are biologic polymers that catalyse the chemical reactions that make biological life possible. They have a wide variety of biochemical, biomedical, pharmaceutical and industrial applications. Furthermore, amperometry data or cyclic voltammetry (CV) measures the current during the reaction between bio-receptor and analyte on the electrode surface. CV is performed by cycling the potential of a working electrode, and measuring the resulting current. A cyclic voltammogram is obtained by measuring the current at the working electrode during the potential scans. Figure 5 shows a cyclic voltammogram resulting from a single electron reduction and oxidation. In Figure 5, the reduction process occurs from (a) the initial potential to (d) the switching potential. In this region the potential is scanned negatively to cause a reduction. The resulting current is called cathodic current ($i_{pc}$). The corresponding peak potential occurs at (c), and is called the cathodic peak potential ($E_{pc}$). The $E_{pc}$ is reached when all of the substrates at the surface of the electrode has been reduced. After the switching potential has been reached (d), the potential scans positively from (d) to (g). This results in anodic current ($I_{pa}$) and oxidation to occur. The peak potential at (f) is called the anodic peak potential ($E_{pa}$), and is reached when all of the substrate at the surface of the electrode has been oxidized.

Keow et al. (2007) studied the use of enzyme immobilization in biosensor to detect histamine in prawn. The histamine biosensor operated at a lower potential where to achieve it, the process underwent the electrochemical oxidization of the product imidazole acetaldehyde, which was produced from the enzymatic reaction of diamine oxidase on histamine Figure 6, where the biosensor utilized a photocuring technique for the immobilization of the diamine oxidase enzyme. It was directly entrapped in a photocured membrane and deposited onto a carbon paste screen-printed electrode (SPE).

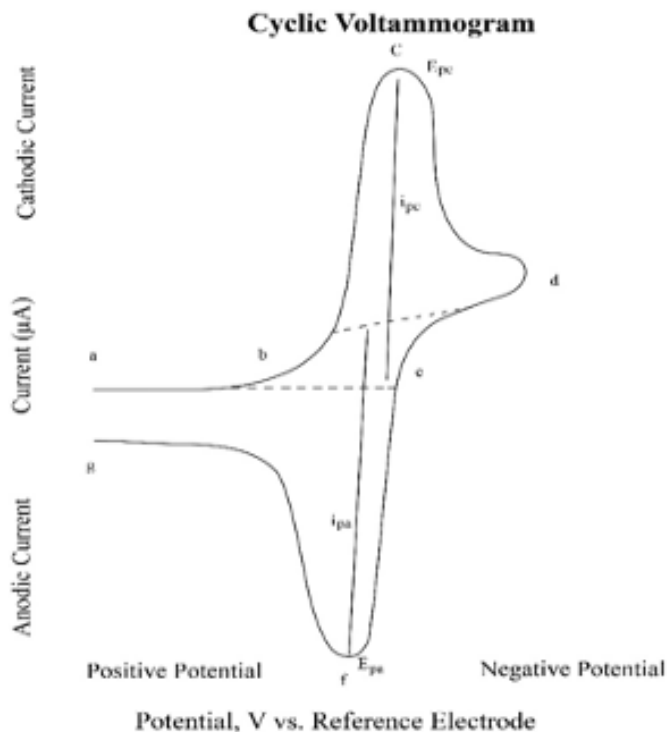However, there are some disadvantages of enzymes and one



**Figure 5.** Voltammogram of a single electron oxidation-reduction.

of the major problems is stability of the enzyme itself. They cannot be reused owing to the difficulty to separate enzyme from the reaction media (Romaškevič et al., 2006). A solution made to tackle this problem such as using an enzyme immobilization. This is a method of keeping the enzymes molecules confined or localized in a certain defined region of space with a retention of their catalytic activity (Verma et al., 2020). Pérez et al. (2013) used diamine oxidase (DOx) combined with horseradish peroxide (HRP) for the determination of histamine in fish samples where these enzymes need to be immobilized in order to modify the stability of enzymes. They co-immobilized into a polysulfone/carbon nanotubes/ferrocene membrane by means of phase inversion technique onto screen-printed electrodes. These enzymes were used in order to increase the possibility to detect $H_2O_2$ at lower applied potentials. This method was used to produce an amperometric biosensor. The electrochemical measurements have been carried out in phosphate buffer solution at pH 8.0 in batch mode and low applied potential (-50 mV vs. Ag/AgCl, KCl 0.1 M) in order to reduce the interferences.

Several techniques have been applied to immobilize enzymes on a solid support. They are based on chemical and physical methods. Both physical and chemical immobilization methods give advantages and disadvantages. During the chemical methods, the activity of enzyme was loss where the immobilization process can perturb the native structure of enzyme, nevertheless covalent bonding give a firm and stable enzyme attachment and in some cases can reduce the enzyme deactivation rates. The
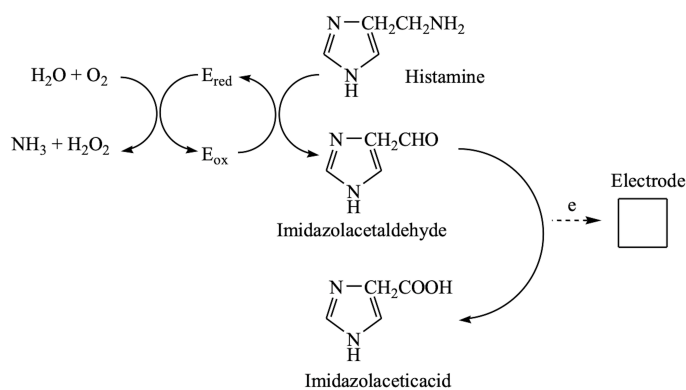
**Figure 6.** The mechanism of operation of the histamine biosensor, where the product imidazole acetaldehyde from the enzymic reaction (diamine oxidase, Ered and Eox) of histamine was electrochemically oxidazed at lower potential of 0.35V at the screen-printed electrode (Adapted from Keow et al. (2007)).

physical immobilization methods showed less perturbation but the enzyme can not bind firmly. For some studies, immobilization of enzymes can cause instability, expensive test kits and tend to overestimate histamine (Akhoundian et al., 2017). Furthermore, biological recognition elements such as antibodies or enzymes are expensive, difficult to prepare and not always available for the desired target. Furthermore, these elements are unstable in organic solvents, high temperature or changing pH. Thus, a synthetic recognition element is strongly needed so it can overcome the temperature and pH issues.

Nanomaterials are also applied to modify the sensitivity of biogenic amines biosensor by amplifying their conductivity, catalytic activity and biocompatibility signals (Ma et al. (2013); Song et al. (2016)). Prussian blue (PB) shows good electrocatalytic activity and generally used for the immobilization of enzymes to produce an enzymatic biosensor. Dong et al. (2017) developed a sensitive and selective electrochemical immunosensor which was constructed to analyse histamine by assembling a PB-CS-AuNP nanocomposite film on a screen-printed carbon electrode (SPCE) to capture histamine-antibody (HA-Ab) and histamine-antigen (HA-Ag). Its study acquired satisfactory sensitivity and selectivity to detect histamine in fish samples by the catalytic reaction between the signal tag (HRP) and $H_2O_2$ using hydrquinone (HQ) as an electron mediator. The PB-CS-AuNP nanocomposite film was electrodeposited on the SPCE. The blocking solution was coated on the electrode surface to block the possible remaining active sites to avoid nonspecific binding. Finally, the immunosensor was thoroughly washed with 0.01 M phosphate buffer solution (PBS) and stored at 4 $^oC$ until used.

Jiang et al. (2015) had also studied the use of surface plasmon resonance (SPR) based on molecularly imprinted polymers (MIPs) as a biosensor due to its selectivity and sensitivity in order to detect histamine. MIPs showed a satisfactory alternative during histamine detection. MIPs are synthetic receptors with imprinted nanocavities, which exhibit similar specificity and selectivity to the desired target molecules as their natural antibodies or enzymes. They are also suitable for detection of small molecules. Not only that, MIPs have several advantages such as it can be synthesised at a relatively low cost, robust and can withstand extreme temperature and pH. The MIPs can also be prepared using the noncovalent approach presenting the regeneration potential (Akhoundian et al., 2017). It shows that MIP has good ability to recognize histamine from food samples.

### 4.3 Chemical Sensors

These methods are only using electrode but the electrode need to be chemically modified. The electrode should be both conductive and chemically stable. Therefore, platinum, gold, carbon and silicon are commonly used by researchers to detect biogenic amines in food and beverages samples. Moreover, conducting polymer modified electrodes have attracted much attention due to their good stability, reproducibility, homogeneity in electrodeposition, strong adherence to electrode surfaces and their available active sites. Studies on carbon nanatubes (CNT) have been applied as a novel materials in electrochemical sensor applications owing to their unique properties including high chemical and thermal stability, high elasticity and high tensile strength make them suitable to be applied as electrode modifiers. The use of composite modified electrodes involving conducting polymers and carbon nanotubes for chemical sensor has also been reported to increase the catalytic role of both materials (Geto et al., 2014). CNT belongs to the group of rather new nano-sized materials and they have the ability to functionalize the electrode surface. CNT is divided into two types namely single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs). The structure of CNTs provides them unique electrical, chemical and physical properties (Stojanović et al., 2016).

Determination of histamine using SWCNT-modified carbon paste electrode (CPE) was applied by Stojanović et al. (2016) where the electrochemical behaviour of histamine in beverages on SWCNT-CPE was investigated and a voltammetric method was elaborated by using differential pulse mode. The method was success and shown in Figure 7. This study showed the importance of CNT as a conducting polymer in order to modify the electrode behaviour. The SWCNT-CPE showed higher current response accompanied with better defined peak shapes in comparison to the unmodified CPE where the response of histamine on SWCNT-CPE was 15-fold higher than a plain CPE. After effect of pH and scan were optimized and validated their study continued for optimization of experimental parameters of differential pulse voltammetry (DPV).

The SWCNT-CPE gives satisfactory result but it is undeniable that the method is expensive and the complexity of the modification electrode will be faced. Geto et al. (2014) reported the use of MWCNT modified glassy carbon electrode (GCE) to detect histamine in fish muscle. However, a chemical method using cheap and material from biopolymer as electrode modifier should be developed. Several biopolymers reported having the ability as a conducting polymer such as lignin, polyurethane and
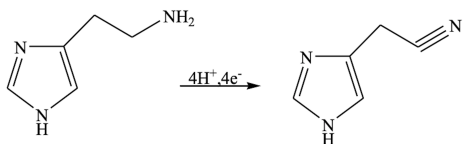
**Figure 7.** Schematic illustration of proposed reaction for the oxidation of histamine on SWCNT-CPE.

chitosan (Degefu et al. (2014); Nezakati et al. (2018)).

The use of lignin modified glassy carbon electrode (GCE) as a chemical sensor in human urine and wine was studied by (Degefu et al., 2014). Cyclic voltammetry was used to investigate the electrochemical behaviour of histamine at the surface of lignin modified GCE and unmodified GCE. This study showed that GCE modified by lignin has higher sensitivity to analyse histamine due to the properties of lignin as a conducting polymer. Furthermore, this study also used square wave voltammetry (SWV) for the quantitative analyses of histamine since this method was more sensitive than cyclic voltammetry (CV) and differential pulse voltammetry (DPV).

### 4.4 Optical Sensors

Optical sensors for amines detection equipped with UV-Visible or fluorescence spectroscopic methods have been developed. In addition, they do not consume much of the analyte and less diffusion-limited. Furthermore, they have better selectivity and need no elevated temperatures and are compatible with telecommunication fibres and microfluidic systems. Optical sensors for amines usually are applied in food technology and biotechnological processes. Two approaches used for the optical determination of amines. First is by embedding a pH indicator dye into a hydrophobic matrix and measuring the basicity of the amine through its deprotonation of the indicator dye whereas the second approach uses a more selective method of interaction between the indicator and the amine by employing trifluoroacetyl or aldehyde (Schaude et al., 2017). Table 7 below shows the comparison data for the optical determination of the biogenic amines in various samples.

Optical sensors have been applied to determine biogenic amines in various food and beverages such as histamine, tyramine, ethylamine, putrescine, agmatine, isopentylamine, methylamine and propylamine by using specific indicator dyes that exhibit different spectral characteristics when exposed to these analytes (Kumpf et al. (2015); (Mastnak et al., 2018); Nedeljko et al. (2017); Rawat et al. (2017)). Malik et al. (2016) reported the biogenic amines determination in liquid samples where this study synthesized the water-soluble cationic conjugated polymer using [9,9-bis(6'-methylimidazoliumbromide)hexyl)-fluorene-co-4,7-(2,1,3-benzothiadiazole)](PFBT-MI) and combined it with a surfactant in order to acquire aggregates, which enabled the spermine detection. Rawat et al. (2017) on the other hand, used tyrosine-protected gold nanoparticles (Tyr-Au-NPs) as a dual probe for colorimetric and fluorescene turn-on assays of spermine and spermidine in biological samples. Determination of

biogenic amines in meat and cheese has also been reported by Khairy et al. (2016) using optical sensor based on fluorescence sensor microtiterplate against GC-MS. The data obtained from this study was comparable with data obtained from GC-MS. It can be concluded that the sensor microtiterplate can be used for cheap pre-screening of the biogenic amines content in food samples.

### 5. CONCLUSIONS

The presence of biogenic amines in food and beverages that contain protein are inevitable especially when several factors can also increase the biogenic amines levels in food and beverages. Two major reasons for the determination of biogenic amines are because of their potential toxicity and also possibility of developing food quality markers. Thus, in order to protect the health of consumers, there is a necessity and compulsion to monitor food and beverages. Among the methods reported in this review paper are chromatographic techniques such as HPLC and GC as popular methods for biogenic amines analysis. Nevertheless, these techniques are often time-consuming as well as they require considerable skill to use them. They are also tedious owing to need time for sampling pre-treatment and even need to be derivatize in order to change the analytes properties and sensitivity of the instruments. Another drawback of these methods is the requirement of organic solvents of HPLC grade quality, whereby the cost for their purchase and disposal has to be taken into consideration. Additional problem in biogenic amines quantification is they occur at very low level which means a highly sensitive method is needed to analyse the biogenic amines level. Electrochemical sensors show low detection limit, wide linear working range and comparable sensitivity and selectivity to the advanced instrumentation. Sensor methods such as electrochemical and optical sensors are promising techniques being low cost, fast response and easy to use and also good sensitivity, selectivity, accuracy and precision. The advantages and limitations of each technique has been reviewed. Consequently, none of these techniques has become a routine method in daily practice due to the fact that each method has its particular advantages and disadvantages. Therefore, the use of chromatography methods and more innovative methods, including spectroscopic and other emerging techniques in combination with sensor approaches could be powerful instruments for the detection of biogenic amines.

### 6. ACKNOWLEDGEMENT

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**Table 7.** Biogenic amines determination using optical sensors.

| Indicator | Analyte | Remark | LOD (mol L-1) | Ref. |
|---|---|---|---|---|
| CR-528 & CR-555 | Spermine, spermidine & ethanolamine | Absorbance-based assay & ethanol solution | 1.46-2.03 x 10-5 | (Mastnak et al., 2018) |
| Tyrosine-protected gold nanoparticles (Tyr-Au-NPs) | Spermine & spermidine | Absorbance-based assay, fluorescence-based assay; PBS buffer at pH 6.0 | $5.3 \times 10^{-9}$ & $6.2 \times 10^{-9}$ | (Rawat et al., 2017) |
| Aggregates from [9,9-bis(6'-methylimidazoliumbromide)hexyl)-fluorene-co-4,7-(2,1,3-benzothiadiazole)](PFBT-MI) and surfactant | Spermine | Fluorescence-based assay; aqueous solution | $1.2-3.3 \times 10^{-7}$ | (Malik et al., 2016) |
| Cu(II) complex of Schiff-base receptor organic nanoaggregates | Spermine | Absorbance-based assay, DMF/water (1/99, v/v) solvent system | $7.62 \times 10^{-9}$ | (Keow et al., 2007) |
| Chameleon dye (Py-1) embedded in a polymeric (sensor microtiterplate) | Histamine | Fluorescence-based assay; methanol solution | $1.48 \times 10^{-6}$ | (Khairy et al., 2016) |
| (Trifluoroacetyl)azobenzene dye added in carbon nanotube-Nafion® composites | Ethylamine, Cadaverine & putrescine | Ethanol/deionized water solution | Not defined | (Lin et al., 2015) |
| ZnTriad poryphyrin thin films | Butylamine, propylamine& heylamine | Optical fiber spectrophotometer to record UV-Vis spectrum | Not defined | (Roales et al., 2015) |
| 4-(Dioctylamino)-4'(trifluoroacetyl)azobenzene (ETH4001) | Isopentylamine, propylamine & putrescine | The indicator dye Chromoionophore XV (ETH 4001), ethanol solution | $1.2-7.8 \times 10^{-3}$ | (Nedeljko et al., 2017) |

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