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***Corresponding authors:** Jinhong Wu, Department of Food Science and Engineering, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai 200240, China, Tel: +86 -021-34206614; Fax: +86 -021-34205748; Email: wujinhong@sjtu.edu.cn

Sui Ni, Institute of Agricultural Product Processing Research, Ningbo Academy of Agricultural science, Zhejiang 315040, China, Email: nisui@nbu.edu.cn

ORCID: <https://orcid.org/0000-0002-1554-3599>

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Review Article

Review on biological degradation of biogenic amines in food

Jihao Zeng^{1,2}, Jinhong Wu^{2*}, Huiyun Chen¹ and Sui Ni^{1*}

¹Institute of Agricultural Product Processing Research, Ningbo Academy of Agricultural science, Zhejiang 315040, China

²Department of Food Science and Engineering, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai 200240, China

Abstract

In this paper, the application of biological methods to reduce biogenic amine content in foods was introduced. Biogenic amine oxidase, a special protein that can degrade biogenic amine into acetaldehyde, hydrogen peroxide and ammonia, has been introduced in this paper, and two major amine oxidases and their degradation effects on different biogenic amines were briefly reviewed. In addition, various microorganisms that could produce amine oxidase were summarized in this paper, and their application in the fermentation was shown. This short review summarizes the important biological methods currently used to degrade biogenic amines and provides new theoretical guidance for removing or reducing the biogenic amines in foods.

Abbreviations

PAO: The activity of Primary Amine Oxidase; DAO: Diamine Oxidase; MAO: Monoamine Oxidase

Introduction

Biogenic amines are a class of biologically active, low molecular mass compounds containing amino groups. These biogenic amines are found in most everyday foods and are mainly produced by the action of microbial amino acid decarboxylase enzymes to decarboxylate amino acids. Moderate amounts of biogenic amines can promote normal physiological activities in the human body, while excessive intake can produce adverse effects, such as heart rate disorders and hypertension [1]. Therefore, how to control and reduce the content of biogenic amines in food to make food safer has become an issue that must be considered during food processing and production.

Although controlling the content of free amino acids in raw materials can reduce the accumulation of biogenic amines to a certain extent, it also affects the flavor and nutritional value of food. At the same time, it is impossible to reduce the biogenic amines that have been generated and accumulated, therefore, it is necessary to find a better way to take into account the flavor and nutritional value of products while considering food safety issues in the actual production. The use of enzymes produced in the process of microbial fermentation can reduce the content of biogenic amines in food without affecting the quality of food, which has a wide range of application prospects and technical advantages, but there is a gap in the actual production use in this area. This paper introduces three commonly used biogenic amine degrading enzymes and their acquisition routes, and briefly introduces several examples of amine degrading enzyme producing strains applied to actual production, which provides a reference for the industrial production of seafood without biogenic amines.

Enzymatic degradation of biogenic amines by using amine oxidase

Amine oxidase exists widely in organisms, and the existence of biogenic amine oxidase can be detected in microbial metabolites (Table 1, Figure 1). Biogenic amine oxidase can split biogenic amines into aldehydes and ammonia, so as to reduce the harm of biogenic amines to human body. The amine oxidase existing in nature can be divided into copper amine oxidase and xanthamine oxidase. Most of these enzymes come from the oxidase produced by the growth of bacteria, and show different specificities for the substrate of biogenic amines and catalytic efficiency. Since copper-containing oxidases are widely distributed in bacteria, yeast, molds, plants and animals, and have multiple access channels, they can be combined with fermentation and seed flow to reduce biogenic amines in food after screening during food production. Moreover, histamine is present in large quantities in aquatic products, and histamine is harmful to humans, while diamine oxidase mainly acts on histamine, and one of the main sources of diamine oxidase is the metabolite of *Lactobacillus plantarum*, which is also one of the commonly used strains in food fermentation. It can be found in the metabolite of *Aspergillus niger*, which contains flavin oxidase. Therefore, considering the above reasons, combined with the factors of actual food production, this paper selects the above three biogenic amines for introduction.

Copper-containing amine oxidase

Copper oxidase is a copper-containing amine oxidase that includes primary amine oxidase and diamine oxidase. Taking Cu^{2+} as a prosthetic group, it can catalyze the oxidation of a series of biogenic amines, including histamine, alkylamine and other neurotransmitters, which are isodimers linked by disulphide bonds to the aldehydes of oxidize primary amines,

Table 1: The major amine oxidase-producing microorganisms.

Amine oxidase species	Amine producing microorganism	Reference
POA	<i>Yeast, Escherichia coli, Aspergillus niger, Candida boidinii.</i>	HAYWOOD G W [5]
DOA	<i>Kocuria varians, Micrococcus rubens, Pedopococcus acidilactici, Lactobacillus plantarum</i>	CALLEJON S
MAO	<i>Aspergillus niger, Micrococcus varians, Staphylococcus carnosus, Bacillus amyloliquefaciens, Enterobacteriaceae</i>	YAMADA H [15]

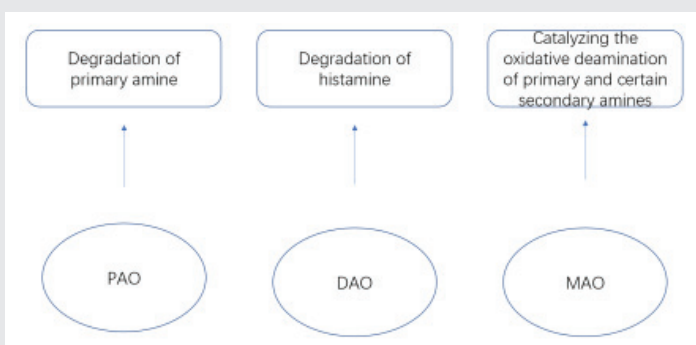


Figure 1: Target of amine degradation enzymes.

while reducing dioxygen to hydrogen peroxide. Cu^{2+} plays an important role in the activity of copper amine oxidase. By substituting Cu^{2+} with other divalent cations (Co^{2+} and Ni^{2+}), it was found that the activity of copper amine oxidase in *Arthrobacter Globiformis* and the Mie constants of the substrate were only 2.2% and 0.9% for the proenzyme [2].

The activity of primary amine oxidase (PAO) was inhibited by carbonyl-containing reagents such as aminourea, but common inhibitors such as dithiothreitol, ethylenediamine tetraacetic acid, and sodium azide had no inhibitory effect on the primary amine oxidase [3]. An amine oxidase from *A. niger SPFJ05* is capable of degrading eight biogenic amines which commonly found in the fermented foods, with an optimal reaction pH and temperature of 7.0 and 35°C, respectively, and an optimal substrate of hexylamine. Although the type of *A. niger SPFJ05* amine oxidase is not known yet, 1.0 mmol/L Cu^{2+} was found to have an activating effect on the enzyme [4]. Many microorganisms can utilize the oxidation pathway to decompose primary amines, which also promote their own growth. Currently, yeast, *Escherichia coli* and *Aspergillus Niger* are known to produce primary amine oxidase. Haywood, et al. [5] isolated and purified two kinds of primary amine oxidase from *Candida Boidinii*, which are benzylamine oxidase and methylamine oxidase. The optimum pH of the two enzymes is about 7.0, and the specificity of the two enzymes to the substrate is similar. In terms of inhibitors, both of them are sensitive to carbonyl reagents, copper chelating agents and some typical diamine oxidase inhibitor. The molecular weight of both is about 80 kDa. However, benzylamine oxidase is more stable than methylamine oxidase at 45°C and 50°C.

Diamine Oxidase (DAO) mainly acts on histamine, and can also oxidize putrescine and cadresine. It can also act on some monoamines, but it has little or no catalytic activity for secondary and tertiary amines. Similar to primary amine oxidase, it is a cuprous quinone protein whose activity can be inhibited by carbonyl reagents such as carbamide. Common inhibitors also include 1, 4-cyclohexandiamine and o-diazphenanthrene. 5 mmol/L cyclohexandiamine can reach 69% of the inhibition rate, and 1 mmol/L o-diazphenanthrene has 71% of the inhibition rate [6,7]. The DAO in *Arthrobacter spheroides* mainly oxidized histamine, and the DAO in *Arthrobacter spheroides* could degrade histamine, putrescine and spermidine with histamine as substrate, and its Km value was 0.274 mmol/L. The enzyme had poor thermal stability, and the maximum temperature at which it could show activity was 37°C, and its activity decreased by 50% when incubated at 35°C for 50 min [8]. 2534 U/L of DAO was added to tuna soup containing 500 mg/L histamine (pH 6.0, 1% NaCl) and incubated at 37°C at 100 r/min for 10 h. Results show it can reduce histamine concentration to undetectable levels (<0.5 mg/L) [9]. The diamine oxidase, represented by histamine oxidase, has highly specific substrates and usually it only degrade certain biogenic amines, such as histamine, tyramine, cadaverine and putrescine [10]. In addition, histamine oxidase exhibits optimal enzymatic activity at a pH>7.0, so it is almost impossible to be used in acidic fermented foods whose pH is lower than 4.5 [11].

Xanthamine oxidase

Monoamine oxidases catalyze the oxidative deamination of primary and some secondary amines and are located mainly on the outer membrane of mammalian mitochondria [12]. Monoamine Oxidase (MAO) is one kind of xanthamine oxidase, and it can catalyze the oxidative deamination of primary amines and some secondary amines. According to substrate selectivity and sensitivity to inhibitors, monoamine oxidase is divided into two types: monoamine oxidase A (MAO-A) and B (MAO-B), and they contain different genetic codes. MAO-A had a high affinity for chlorylamine, while MAO-B showed high affinity for phenylethylamine, benzylamine and selegiline. Common tyramine and tryptamine can be used as the substrate of monoamine oxidase [13]. Study shows that the activity of monoamine oxidase was significantly negatively correlated with the biogenic amine accumulation during fermented bean curd [14]. When the mass fraction of salt in the soup was 3%-7%, the volume fraction of alcohol was 15%-25%, and the pH value was 4.5-5.5, the activity of monoamine oxidase in the fermented bean curd was decreased after 30 days fermentation. Meanwhile the total biogenic amine accumulation peaked from 20 to 45 days after fermentation, which basically maintained below 6.5 mg/g, and then gradually decreased.

Application of microorganisms in the degradation of biogenic amines

Using microbial methods to reduce or prevent the accumulation of biogenic amines in fermented foods has become a hot research trend, and some of them have been used in practical production.

Wang Qiang has screened five lactic acid bacteria strains with high biogenic amine degradation efficiency, among which *Lactobacillus plantarum* 30 had the best biogenic amine degradation ability [15]. The degradation rate of *Lactobacillus plantarum* 30 for painamine, histamine and tyramine was up to 62.42%, 74.32% and 89.97%, respectively. This strain can grow and multiply well in the environment of 0-9% salt content and pH 4.5-8.5. The strain has no amine-producing activity, but has the degradation ability of biogenic amine, and can be used as the starter of protein fermented food to reduce biogenic amine toxicity.

Studies have also shown that the histamine levels are significantly reduced when a mixture of starter cultures (*Lactobacillus casei* and *Staphylococcus xylostella*) is added to sausage products. *Lactobacillus* using as starter cultures can induce fast acidification, inhibit the decarboxylation of microbial growth, and damage the cell membrane, which results in the decrease of microbial decarboxylation activity, thereby reducing the formation of biogenic amines. *Lactobacillus farciminis* has been found that it could degrade histamine, tyramine and putrescine in red wine [16]. Li, et al. used *Staphylococcus xylosus* and *Lactobacillus plantarum* to ferment the red sausage, and results show that they can significantly improve the safety and quality of red sausage [17].

Conclusion

The sources of biogenic amines in foods are complex and the influencing factors are numerous, so it is easy to produce a large amount of biogenic amines accumulation in the products. Amine oxidase is an important enzyme that can be used to degrade the biogenic amines in food, and it has different types based on its structure and enzyme specificity. Some certain microorganisms, such as lactic acid bacteria, could produce enzymes, and through the selection and application of suitable microorganism it can reduce the content of biogenic amines in fermented foods.

At present, most researches on the use of amine oxidase or microorganisms whose metabolites can degrade the biogenic amines are not deep enough. There are still some problems to be solved up to now, such as the symbiotic relationship between amine-producing bacteria and amine-reducing bacteria in fermented food, and how to developing a plurality of starter strains which do not produce amine and have specificity to degrade various biogenic amines, needs to be further studied.

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