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A study of the tyramine/glucose Maillard reaction: Variables, characterization, cytotoxicity and preliminary application

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ABSTRACT

The tyramine/glucose Maillard reaction was proposed as an emerging tool for tyramine reduction in a model system and two commercial soy sauce samples. The model system was composed of tyramine and glucose in buffer solutions with or without NaCl. The results showed that tyramine was reduced in the model system, and the reduction rate was affected by temperature, heating time, initial pH value, NaCl concentration, initial glucose concentration and initial tyramine concentration. Changes in fluorescence intensity and ultraviolet–visible (UV–vis) absorption spectra showed three stages of the Maillard reaction between tyramine and glucose. Cytotoxicity assay demonstrated that tyramine/glucose Maillard reaction products (MRPs) were significantly less toxic than that of tyramine ($p < 0.05$). Moreover, tyramine concentration in soy sauce samples was significantly reduced when heated with the addition of glucose ($p < 0.05$). Experimental results showed that the tyramine/glucose Maillard reaction is a promising method for tyramine reduction in foods.

1. Introduction

Tyramine, (4-(2-aminoethyl) phenol), is a biogenic amine derived from the decarboxylation of amino acid tyrosine by bacteria. As shown in Fig. 1, tyramine is an aromatic monoamine compound. Tyramine can accumulate in a wide range of foods, especially fermented foods, such as cheese, fish sauce and soy sauce (Guidi & Gloria, 2012; Jiang, Xu, Li, Dong, & Wang, 2014; Linares, Martín, Ladero, Alvarez, & Fernández, 2011). A low level of tyramine does not cause harmful effects in normal individuals due to the presence of amine oxidases in the human intestine. Nevertheless, consumption of foods containing high level of tyramine causes migraine, neurological disorders, headaches, respiratory disorders and hypertension, which are together known as the "cheese effect" (Finberg & Gillman, 2011). These symptoms can be much more severe in people taking antidepressant monoamine oxidase inhibitor medication (Ladero, Calles-Enriquez, Fernandez, & Alvarez, 2010). Besides, tyramine can react with nitrite to form *C*-nitroso compounds, which are known carcinogenic agents (González-Jiménez, Arenas-Valgañón, García-Santos, Calle, & Casado, 2017). Recent studies suggest that tyramine exhibits a stronger and more rapid cytotoxic effect than histamine (Linares et al., 2016). Therefore, the prevention of tyramine formation in foods or reduction of its level once it has formed should be studied.

In the past few decades, high hydrostatic pressure (Matějková, Křížek, Vácha, & Dadáková, 2013), irradiation (Zhang, Wang,

Abbreviations: UV–vis, ultraviolet–visible; MRPs, Maillard reaction products; RPMI, Roswell Park Memorial Institute; FBS, fetal bovine serum; DMSO, dimethyl sulfoxide; 5-HMF, 5-hydroxymethlofurfural; AGEs, advanced glycation end products; Has, heterocyclic amines; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenylte trazolium bromide.

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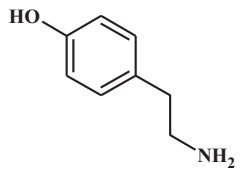

Fig. 1. Structure of tyramine.

Zhang, Wang, & Ye, 2016), modified atmosphere packing (Yassoralipour, Bakar, Rahman, & Abu Bakar, 2012) and low storage temperature (Fan et al., 2016) have been employed to prevent the formation of tyramine by inhibiting the growth of microorganisms. Nevertheless, microbial inhibition by these methods is random, not only aiming at tyramine producing bacteria. Thus, they are not suitable for fermented foods where the growth of microorganisms is very important. Moreover, the above techniques cannot decrease the level of tyramine that already exists. Tyramine degrading bacteria can be used as functional starter cultures to reduce already existing tyramine (Xu, Liu, Xu, Wang, & Jiang, 2016), but more effective tyramine degrading strains and professional equipment/staff are required. Therefore, high efficiency, lower cost and more convenient methods are desired for tyramine reduction.

The Maillard reaction occurs between the amino group of amino acids, peptides, proteins or other nitrogen containing compounds and carbonyl groups of reducing sugars, during the processing and storing of foods. This reaction is a series of successive and parallel reactions, which can be influenced by many factors such as temperature, heating time, pH, substrate type, substrate concentration and water activity (Caballero, Finglas, & Toldrá, 2016). To reduce the complexity of the Maillard reaction, the reaction process is divided into three stages (namely initial stage, intermediate stage and final stage) according to the generation of different compounds, which can be characterized by fluorescence intensity and ultraviolet–visible (UV–vis) absorption (Nursten, 2005). Although the Maillard reaction can result in the loss of essential amino acids, production of undesired pigment and generation of toxicants (Zhang, Tao, Wang, Chen, & Wang, 2015), it can also enhance the emulsifying property, solubility, antioxidant activity and metal chelating activity of food ingredients (Dong et al., 2012; Oliveira, Coimbra, Oliveira, Zuñiga, & Rojas, 2016). The Maillard reaction has also been used to reduce fumonisin B_1 in corn grits (Bullerman et al., 2008), which expands the application area of Maillard reaction to the reduction of toxic substances. As shown in Fig. 1, tyramine has a free amino group, suggesting that it may be reduced by Maillard reaction. However, the Maillard reaction between tyramine and sugars has not been studied previously.

In this study, effects of temperature, heating time, initial pH value, NaCl concentration, initial glucose concentration and initial tyramine concentration on tyramine reduction in the tyramine/glucose Maillard reaction model system were investigated. Three stages of the tyramine/glucose Maillard reaction were characterized by fluorescence intensity and UV–vis spectroscopy. Cytotoxicity of tyramine, glucose, tyramine-glucose mixture, and tyramine/glucose Maillard reaction products (MRPs) was assayed. Furthermore, the reduction of tyramine by Maillard reaction in commercial soy sauce samples was preliminarily evaluated. The aim was to reveal the possibility of using tyramine/glucose Maillard reaction for tyramine reduction in foods.

2. Materials and methods

2.1. Chemicals

Tyramine, dansyl chloride and dimethyl sulfoxide (DMSO) were obtained from Sigma-Aldrich, Inc. (St. Louis, MO, USA). Roswell Park Memorial Institute (RPMI) 1640 medium, fetal bovine serum (FBS), streptomycin sulphate, ampicillin, trypsin and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were obtained from Gibco Invitrogen Co., (Burlington, ON, Canada). Glucose was obtained from Solarbio Inc. (Beijing, China). Methanol (HPLC grade) was supplied by Merck (Darmstadt, Germany). Ultrapure water was prepared by Milli-Q (Millipore, Billerica, MA, USA). The other chemicals used were of analytical grade and obtained from Sinopharm Chemical Regent Co. Ltd (Shanghai, China).

2.2. Tyramine/glucose Maillard reaction model system

Tyramine was incubated with glucose in 16 mm × 155 mm glass screw tubes capped with a tight screw-cap. Unless otherwise stated, the incubations contained 50 mM potassium phosphate, pH 8.0, 2.5 mM tyramine and 40 mM glucose in a total volume of 5.0 ml. The tubes were incubated at designed temperature in a Digital Dry Bath (Jinxin, JX100-4, Shanghai, China). To ensure the reaction was stopped at appropriate time points, the tubes were cooled in a mixture of ice and water for 30 min.

2.3. Variables of the tyramine/glucose Maillard reaction model system

2.3.1. Temperature

To evaluate the effect of temperature on the tyramine reduction rate, 2.5 mM tyramine and 40 mM glucose were incubated at pH 8.0 and 60, 70, 80, 90, 100 or 110 °C for 12 h without the addition of NaCl. Samples were taken at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10 and 12 h.

2.3.2. Initial pH

To evaluate the effect of initial pH value on the tyramine reduction rate, 2.5 mM tyramine and 40 mM glucose were incubated at 100 °C and pH 5.0, 6.0, 7.0, 8.0, 9.0, 10.0, 11.0 or 12.0 for 5 h without the addition of NaCl. Samples were taken at 0.5, 1, 3 and 5 h.

2.3.3. NaCl concentration

To evaluate the effect of NaCl concentration on the tyramine reduction rate, 2.5 mM tyramine and 40 mM glucose were incubated at 100 °C and pH 8.0 with 0, 1, 3, 5, 8, 11, 14, 19, 24 or 29% (w/v) of NaCl for 5 h. Samples were taken at 0.5, 1, 3 and 5 h.

2.3.4. Initial glucose concentration

To evaluate the effect of initial glucose concentration on the tyramine reduction rate, different initial glucose concentrations of 5, 10, 20, 40, 60, 80, 160 or 320 mM glucose and 2.5 mM tyramine were incubated at 100 °C and pH 8.0 for 5 h without the addition of NaCl. Samples were taken at 0.5, 1, 3 and 5 h.

2.3.5. Initial tyramine concentration

To evaluate the effect of initial tyramine concentration on the tyramine reduction rate, different initial tyramine concentrations of 0.5, 1.0, 2.5, 5.0, 10.0 or 20.0 mM tyramine and 40 mM glucose were incubated at 100 °C and pH 8.0 for 5 h without the addition of NaCl. Samples were taken at 0.5, 1, 3 and 5 h.

2.4. Tyramine concentration determination

Tyramine concentration was determined by HPLC using pre-column derivatization with dansyl chloride (Jiang et al., 2014). The HPLC system consisted of a Waters 2695 series (Milford, USA) equipped with a degasser, quaternary pump, column oven, fluorescence detector and automatic sampler. A reversed-phase chromatographic column (Capcell PAK 5 μm C18 MG, 150 × 4.6 mm) was used. The derivatised tyramine was detected at 350 nm (excitation) and 520 nm (emission). Calibration curves