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Review Article

Fermented Soybean Foods: Significance of Biogenic Amines

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Abstract

Microbial fermentation of soybean leads to the formation of biogenic amines that may cause intoxication symptoms in human. However, the safety issues of fermented soybean foods have been overlooked because human ancestors have taken these foods for centuries. Even though fermented soybean foods are believed to have health-promoting and -protective effects, it is important to monitor and reduce biogenic amine levels in the fermented foods because they contain not only abundant dietary amino acid precursors of biogenic amines, but also various biogenic amine-producing microorganisms. According to reports on biogenic amines, the amounts of biogenic amines in most fermented soybean foods are within the safe levels for human consumption. However, several types or samples of these fermented foods have the contents of vasoactive biogenic amines greater than a toxic dose of each amine. Therefore, it is also important to understand why there are differences in the contents and diversity of biogenic amines between types or batches of fermented soybean foods. Meanwhile, several biocontrol strategies have been developed for reducing biogenic amine formation in fermented foods, mainly focusing on microbial intervention, i.e., the use of starter and protective cultures that have the ability to degrade biogenic amines and inability to produce biogenic amines. However, little attention has been given to both starter and protective cultures for fermented soybean foods. In addition, when screening starter and protective cultures, genetically designed cultures needs to be considered to ensure the safety of fermented foods in the future.

Keywords: Biogenic amines; Fermented soybean foods; Safety; Starter culture; Protective culture

Introduction and Background

Biogenic amines

Microbial fermentation is one of the oldest and practical technologies in food processing and preservation. However, fermentation of protein-rich raw materials such as fish, meat, milk and soybean commonly leads to the formation of various vasoactive and/or putrefactive biogenic amines, including histamine, tyramine, β-phenylethylamine, tryptamine, putrescine and cadaverine, which, in turn, may cause various intoxication symptoms in human, i.e., nausea, respiratory distress, hot flushes, sweating, heart palpitation, headache, a bright red rash, oral burning, and hypo- or hypertension or enhance the toxicity of biogenic amines themselves [1-4]. Furthermore, biogenic polyamines, such as spermidine and spermine, are considered to generate carcinogenic nitrosamines in the presence of nitrites [5]. Fortunately, oral intake of biogenic amines generally results in no adverse reactions because human intestinal amine oxidases, such as monoamine oxidase (MAO), diamine oxidase (DAO) and polyamine oxidase (PAO), quickly metabolize and detoxify the amine compounds. However, food intoxication may occur if the amine-metabolizing capacity is over-saturated, and/or the metabolic activity is impaired by specific inhibitors; for instance, phenelzine used in the treatment of depression [6,7]. It is noteworthy that depression affects over 10% of the population worldwide, but the number of depressed patients prescribed MAO inhibitors (MAOIs) are small (probably <0.1% of the population according to a survey from 1995 to 2007 in UK).

Fermented soybean foods

In Asian countries fermented soybean foods have not only been consumed as they are but also been utilized in a variety of processed foods, which have, in turn, become a necessity in the household in the Asian cultures. The most popular fermented soybean foods are Miso, Natto (Japanese traditional fermented soybean pastes), Doenjang, Cheonggukjang, Gochujang (Korean traditional fermented soybean pastes) Doubanjiang, Dajiang (Chinese traditional fermented soybean pastes) and Tempeh (an Indonesian traditional fermented soybean cake), and soy sauces as well, which are believed to have significant health-promoting and -protective effects such as anti-oxidative, anti-inflammatory, anti-obesity and anti-cancerous effects. Because of their healthy functions, these fermented foods have recently gained popularity even in western countries, and their exportation and importation to other countries and even continents continue to increase year after year. But then again, the safety issues of fermented soybean foods have heretofore been overlooked because human ancestors have taken these fermented foods for centuries. Even though fermented soybean foods and their compositions have been scientifically proven to be beneficial for improving health by decreasing blood pressure, reducing blood cholesterol levels, inhibiting osteoporosis and diminishing the risk of degenerative

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disease [8,9], it is critically important to monitor and reduce the levels of biogenic amines in the fermented foods because these foods contain not only abundant dietary amino acid precursors of biogenic amines, but also diverse fermenting and contaminating microorganisms that actively produce vasoactive and putrefactive biogenic amines [10,11].

Significance and Biocontrol of Biogenic Amines in Fermented Soybean Foods

Presence and toxic levels of biogenic amines

According to reports on biogenic amines, the amounts of biogenic amines in most fermented soybean foods are within the safe levels for human consumption. It is noteworthy, however, that several types or samples of these fermented foods have the contents of vasoactive biogenic amines, including β-phenylethylamine, tyramine and histamine, greater than a toxic dose of each amine proposed for human exposure through the consumption of common foods [11-18]. For instance, the maximum reported levels in the literature reviewed are 185.6 mg/kg of β-phenylethylamine in Doubanjiang [13], 1190.7 mg/kg of tyramine in Doenjang [16] and 457.0 mg/kg of histamine in Natto [18], respectively. Regarding the toxicity of biogenic amines, it has been proposed that 100-800 mg/kg of tyramine and 30 mg/kg of β-phenylethylamine in foods are toxic doses, respectively, and 100 mg/kg of histamine in foods is suggested as an upper limit for human consumption [1]. Therefore, it is apparent that the levels of biogenic amines in fermented soybean foods sometimes exceed such limits depending on types, batches or samples. However, it is not known how often this occurs due to the absence of epidemiological data on the frequency and/or prevalence of excessive accumulation of biogenic amines in fermented soybean foods. Apart from scientific literature, histamine is the only biogenic amine for which a national guidance is set in the countries and organizations over the world; for instance, 50 mg/kg and 100 mg/kg of histamine are the guidance levels set in US and EU legislations, respectively, for fish [19,20]. On the other hand, there are no government's regulations on maximum allowable levels of individual or overall biogenic amines in fermented soybean foods.

Occurrence and biocontrol of biogenic amines

Considering the amounts and diversity of biogenic amines detected in fermented soybean foods, it is important to understand why there are differences in the contents and diversity of biogenic amines between types or individual batches of these fermented foods. Possible reasons explaining these differences are divided into three aspects: (i) the ratio of ingredients used in raw material, (ii) microbial and/or physicochemical contribution, and (iii) conditions and periods of the entire food supply chain, each of which would probably provide direction and framework for developing strategies to reduce biogenic amine formation chemically, biologically and physically. Among them, biocontrol strategies have been vigorously developed for reducing biogenic amine formation in common fermented foods, mainly focusing on microbial intervention; for instance, the use of starter and/or protective cultures would be a successful way to achieve this goal, causing less adverse organoleptic and unhealthy alterations than that of additives [21-23]. As one of the intervention approaches for fermented foods (mainly fermented sausage and cheese), indeed, a variety of microorganisms have been compared and screened for their ability to degrade biogenic amines and inability to produce biogenic amines not only at the level of genus, species or both, but also at the level of individual strain [24-28]. However, little attention has been given to both starter and protective cultures effective in preventing or reducing biogenic amine formation in fermented soybean foods.

Molecular genetic characteristics of biogenic amine producers

Most fermented soybean foods are fermented or contaminated by *Bacillus* spp., particularly *B. subtilis*, some strains of which are strongly capable of decarboxylating amino acids and thereby of producing biogenic amines [12-15]. Therefore, molecular genetic studies would be necessary to fully characterize genes and quickly detect these microorganisms (or genes) responsible for biogenic amine formation in the fermented foods. It is not surprising that the homologues of Odc (ornithine decarboxylase) and Ldc (lysine decarboxylase) proteins responsible for putrescine and cadaverine production, respectively, are present in *B. subtilis*, mainly fermenting or contaminating fermented soybean foods. In the same species, however, Hdc (histidine decarboxylase) and Tdc (tyrosine decarboxylase) homologues responsible for histamine and tyramine formation, respectively, are not found by searching the GenBank database with the Basic Local Alignment Search Tool (BLAST) provided by the National Center for Biotechnology Information (NCBI) [29]. This fact indicates that the genes encoding Hdc and Tdc homologues are absent or not well conserved with other species. Therefore, it will be a great challenge and interesting topic for researchers to unveil the mechanism(s) by which *B. subtilis* produces histamine and tyramine in fermented soybean foods. Moreover, it will be possible to develop rapid detection methods for biogenic amine producers in the fermented foods using polymerase chain reaction (PCR) or real-time PCR on the basis of this genetic information.

Future strategy to biocontrol biogenic amines

Starter cultures for indigenous fermented foods are commonly isolated from the same or similar natural food sources [30]. Nonetheless, it is worth mentioning that when screening the aforementioned starter and protective cultures, for instance probiotic *B. subtilis*, genetically designed cultures needs to be considered to ensure the healthy functions as well as safety of fermented foods in the future [31]; for instance, the construction and application of the *odc* and *ldc* knockout or loss-of-function *B. subtilis* mutants in fermented soybean foods may lead to the prevention or at least reduction of the formation of the related biogenic amines in the fermented foods. However, due to the remaining scientific uncertainty and consumers' concerns about unpredictable risk of genetically modified organisms [32], the genetically designed starter and protective cultures should be precisely engineered from the ground up, not to express unintended and undesired gene products, which, in turn, make this new technology require long-term elaborate researches. In other words, food microbiologists may need to keep developing genetically designed cultures, carefully managing the balance between risk and benefit of this technology, for the purpose of future rather than immediate use.

Conclusion

Fermented soybean foods contain biogenic amines as a result of microbial fermentation as well as contamination. The amounts of vasoactive biogenic amines are occasionally greater than a toxic dose of each amine depending on types and batches of fermented soybean foods. Therefore, it is important not only to monitor and reduce levels of biogenic amines, but also to set regulations on maximum allowable levels in the fermented soybean foods. Due to this, this review proposes possible reasons explaining why there are differences in the contents and diversity of biogenic amines between types and batches of fermented soybean foods and suggests several ways to biocontrol biogenic amines in the fermented foods. Separately, an immediate clinical implication of this review is that individuals taking MAOIs need to modify their diet to reduce the risk of intoxication from orally ingested biogenic amines.

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