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REVIEW

Functional Effects of Japanese Style Fermented Soy Sauce (Shoyu) and Its Components

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The functional effects of Japanese style fermented soy sauce (shoyu) have been studied. Soy sauce promotes digestion, because the consumption of a cup of clear soup containing soy sauce enhances gastric juice secretion in humans. Soy sauce possesses antimicrobial activity against bacteria such as *Staphylococcus aureus*, *Shigella flexneri*, *Vibrio cholera*, *Salmonella enteritidis*, nonpathogenic *Escherichia coli* and pathogenic *E. coli* O157:H7. Soy sauce also contains an antihypertensive component. An angiotensin I-converting enzyme inhibitor having antihypertensive effects was found in soy sauce. The active compound was identified as nicotianamine, which comes from soybeans. Soy sauce exhibits anticarcinogenic effects. Giving diets containing soy sauce to mice inhibit benzo[a]pyrene (BP)-induced forestomach neoplasia. The anticarcinogenic compounds in soy sauce were identified. The flavor components of Japanese style fermented soy sauce, such as 4-hydroxy-2(or 5)-ethyl-5(or 2)-methyl-3(2*H*)-furanone (HEMF), which is a characteristic flavor component of Japanese style fermented soy sauce and 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone (HDMF) and 4-hydroxy-5-methyl-3(2*H*)-furanone (HMF) exhibit antioxidant activities and anticarcinogenic effects on BP-induced mice forestomach neoplasia when fed following carcinogen exposure. The feeding of a diet containing 10% soy sauce to male C3H mice for 13 months also reduces the frequency and multiplicity of spontaneous liver tumors. HDMF and HEMF also exhibit anticataract effects in the spontaneous cataract rat (ICR/f rat). Fermented soy sauce contains three tartaric isoflavone derivatives called shoyuflavones. These shoyuflavones were shown to have inhibitory activities against histidine decarboxylase, which produces histamine, a mediator of inflammation, allergy and gastric acid secretion. Soy sauce also exhibits antiplatelet activity. β-Carbolines were isolated from soy sauce as the active compounds. Soybeans and wheat, which are the main raw materials of soy sauce, are allergenic foods. However, recent studies by enzyme-linked immunosorbent assay showed the absence of soybean and wheat allergens in soy sauce.

[**Key words:** fermented food, shoyu (soy sauce), 4-hydroxy-2(or 5)-ethyl-5(or 2)-methyl-3(2*H*)-furanone (HEMF), antioxidant, anticarcinogen, antimicrobial activity, allergy]

Japanese style fermented soy sauce (shoyu) is a typical traditional Japanese fermented food. Shoyu is the Japanese name for soy sauce and the most popular liquid condiment used in Japanese cuisine as well as in cuisine of other oriental countries. Soy sauce increases the appetite, imparts a delicious flavor and promotes digestion.

Generally, soy sauce is divided into two categories: fermented soy sauce and chemical soy sauce, which is produced by the acid hydrolysis of raw materials. Chemical soy sauce is not recognized as soy sauce by the Japanese government. Chemical soy sauce is used only as an extender of fermented soy sauce in Japan. Fermented soy sauce, semi-chemical soy sauce, in which the acid hydrolysis-derived product is subjected to fermentation, and blended soy sauce, which is produced by mixing fermented soy sauce with chemical soy sauce and/or enzymatically hydrolyzed vegetable proteins, are produced in Japan. Fermented soy sauce is of high quality. About 83% of all soy sauce products consumed in Japan in 2002 was of this type.

Japanese style fermented soy sauce is prepared by digesting mold-cultured soybeans and wheat, called koji in Japan, at different ratios, usually about 50:50, in the presence of about 17% sodium chloride and concurrently fermenting the mash with lactobacilli and yeasts. After 6–8 months the well-aged mash is pressed and the liquid part obtained is pasteurized to make the final product.

Five varieties of soy sauce are available in Japan: (i) koikuchi (a dark-colored common soy sauce produced using soybeans and wheat in almost the same quantities as the raw

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materials of shoyu koji), (ii) usukuchi (a light-colored soy sauce produced using soybeans and wheat in almost the same quantities as the raw materials of shoyu koji, and using moromi prepared with or without steamed rice or rice saccharified by koji mold, which is subjected to control in the manufacturing process so that the color is not deepened), (iii) tamari (produced using soybeans alone or soybeans with a small quantity of wheat as the raw materials of shoyu koji), (iv) saishikomi (produced using soybeans and wheat in almost the same quantities as the raw materials of shoyu koji, and using moromi prepared with kiage instead of salt water; kiage is raw soy sauce that is not pasteurized) and (v) shiro (an extralight-colored soy sauce produced using wheat with a small quantity of soybeans as the raw materials of shoyu koji).

The annual production of soy sauce in Japan has been about 1 million kiloliters in recent years. Soy sauce is exported from Japan to more than 110 countries.

Many substances are formed during the fermentation and production processes, such as the heat treatment of raw materials and the pasteurization of the liquid part of the mash. The functional effects of fermented foods have been focused on in recent years (1–4). Some 83% of all soy sauce products consumed in Japan is koikuchi shoyu, which has a dark reddish-brown color and a strong flavor. In this paper, I review the functional effects of Japanese style fermented soy sauce (the common soy sauce koikuchi shoyu) and its components.

I. PROMOTION OF GASTRIC JUICE SECRETION

It was reported that soy sauce promotes gastric juice secretion in humans (5). A clear soup containing 25 ml of soy sauce in 300 ml of hot water was given to each of 15 people and the amount of gastric juice secreted was measured. The average amount of secreted gastric juice was 46.8 ml, which was almost the same as that (44.0 ml) in the positive control given Katsch–Kalk's caffeine solution (0.07% caffeine solution), which is a commonly used in inducing gastric juice secretion. In chemical soy sauce, the average secretion amount was 33.4 ml in the same people. Therefore, it seems that Japanese style fermented soy sauce promotes digestion to a greater extent than chemical soy sauce.

II. HYPOTENSIVE EFFECT

I reviewed two reports on the effects of soy sauce on blood pressure. Kajimoto (6) reported that soy sauce decreases blood pressure. When 25 to 30 ml of soy sauce was administered to dogs, whose body weights were 6–10 kg, their blood pressures decreased 1 min after the administration and returned to the baseline level within 1 h. Kajimoto suggested that soy sauce contains a substance that promotes histamine absorption as the causative agent of the blood pressure decrease effect.

Kinoshita *et al*. (7) found an inhibitory compound of the angiotensin I-converting enzyme (ACE) in soy sauce. ACE catalyzes the hydrolysis of angiotensin I resulting in the generation of the potent vasoconstrictor angiotensin II, which regulates arterial blood pressure (8, 9). ACE inhibitory activity in soy sauce was fractionated into two major fractions of high molecular weight (Hw) and low molecular weight (Lw) by gel filtration chromatography after treating with ethanol. The Hw fraction decreased blood pressure in hypertensive rats after oral administration, while the Lw fraction did not (Table 1). Blood pressure decreased 1–8 h after the administration of the Hw fraction and returned to the baseline level within 24 h in spontaneously hypertensive rats (SHR) and two-kidney Goldblantt hypertensive rats (2KGH rats). The Lw fraction had no effect on blood pressure in either type of rat. The main ACE inhibitor in the Hw fraction was purified by high-performance liquid chromatography and was identified as nicotianamine (*N*-[*N*-(3-amino-3-carboxypropyl)-3-amino-3-carboxypropyl]-azetidine-2-carboxylic acid) (Fig. 1). The IC_{50} of nicotianamine for ACE was 0.26 μM. It was one-tenth of that of the widely used antihypertensive drug Captopril.

Blood pressure decreased to 24, 20 and 19 mmHg at 1 h, 4 h and 8 h respectively, after a single administration of 20 mg/kg body weight of the purified inhibitor (nicotianamine) to SHR. Kinoshita *et al*. (7) found that soybeans contain a large quantity of nicotianamine. They suggested that the

TABLE 1. Relationship between oral administration of Hw or Lw fraction and blood pressure decrease in SHR[a] and 2KGH rats[b]

Group	No. of rats	Blood pressure decrease after administration[c] (mmHg)			
		1 h	4 h	8 h	24 h
SHR					
Captopril, 10 mg/kg	4	39.3±16.7	31.0±28.8	22.0±9.7	10.3±18.6
Hw, 3.6 g/kg	5	22.3±6.6	24.7±6.4	23.6±5.8	0.9±0.9
Lw, 6.0 g/kg	5	1.1±2.4	0.2±0.5	0.1±0.3	1.1±1.5
Distilled water	4	1.8±1.9	0.8±0.9	1.3±2.1	–4.6±1.8
2KGH rats					
Captopril, 10 mg/kg	4	54.8±15.8	48.0±20.4	29.8±8.8	12.8±18.4
Hw, 3.6 g/kg	3	22.1±16.8	24.8±11.3	38.8±5.8	4.4±4.5
Lw, 6.0 g/kg	4	1.1±2.4	0.2±0.5	0.1±0.3	0.3±0.5
Distilled water	4	0.8±0.9	0.7±0.8	1.5±2.6	2.2±2.9

A single oral administration of the test substances dissolved in distilled water was given, and the control rats were given the same amount of distilled water. Tail systolic blood pressure was measured by the tail cuff method (10).

[a] Spontaneously hypertensive rats (SHR).

[b] Two-kidney Goldblantt hypertensive rats (2KGH rats).

[c] Blood pressure decrease in each group is given by (blood pressure before administration) − (blood pressure after administration). Values are shown as mean±SD. Adopted from Ref. 7.