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Review

Antihypertensive effects of condiments prepared from fermented legumes: A review

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Abstract

The prevalence of hypertension has been increasing over the years. Thus, dietary guidelines focusing on the reduction of daily sodium intake are introduced. The association between the intake of condiments, one of the major sources of dietary sodium, and the prevalence of hypertension has been investigated. Regardless of high sodium content, condiments prepared from fermented legumes exert antihypertensive effects instead of increasing the risk of hypertension. Considering the hypotensive potency of legume-based condiments, modifications including reduction or removal of sodium content, incorporation of high protein fermentation substrate, changing of fermentation conditions, and selection of different microbial strains have been carried out to enhance their antihypertensive effects. The elevated antihypertensive activity of legume-based condiments is mainly associated with the increment of angiotensin-converting enzyme (ACE) inhibitory peptides formed during fermentation. The precise mechanisms of legume-based condiments in regulating blood pressure are complex and yet to be validated. Considering the antihypertensive potential of legume-based condiments, the present review paper aimed to summarise and elaborate their antihypertensive effects.

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Introduction

Hypertension is a health condition characterised by consistently elevated blood pressure in arteries compared to the normal range. Hypertension occurs when the systolic blood pressure (SBP) reaches 140 mmHg or higher, and/or diastolic blood pressure (DBP) reaches 90 mmHg or above (WHO, 2013). Hypertension is strongly associated with non-communicable diseases including cardiovascular diseases, stroke, and chronic kidney diseases which could lead to premature death (Wajngarten and Silva, 2019; Mills *et al*., 2020). The World Health Organization (WHO) estimates that 1.28 billion adults are experiencing hypertension and complications caused by hypertension, resulting in 9.4 million deaths annually (WHO, 2021). Meanwhile, according to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017, hypertension is the major risk factor causing premature death and disability-adjusted life years (GBD 2017 Risk Factor Collaborators, 2018).

Dietary sodium consumption is strongly related to blood pressure levels (Singh *et al*., 2017). Renin-angiotensin-aldosterone-system (RAAS) plays an important role in regulating blood pressure by maintaining body fluid homeostasis in response to the amount of sodium intake (Figure 1). In the event of reduced sodium intake, renin secreted from the kidney will convert angiotensinogen into angiotensin I. Angiotensin-converting enzyme (ACE) will convert angiotensin I to angiotensin II, a powerful vasoconstrictor that causes elevated blood pressure in organs such as the heart and kidney. In addition, the production of angiotensin II stimulates the release of aldosterone and antidiuretic hormone (ADH), which eventually increases blood pressure. Besides, angiotensin II elevates blood pressure through mechanisms such as reduced glomerular filtration rate and renal blood flow (Beevers *et al*., 2001; Yim

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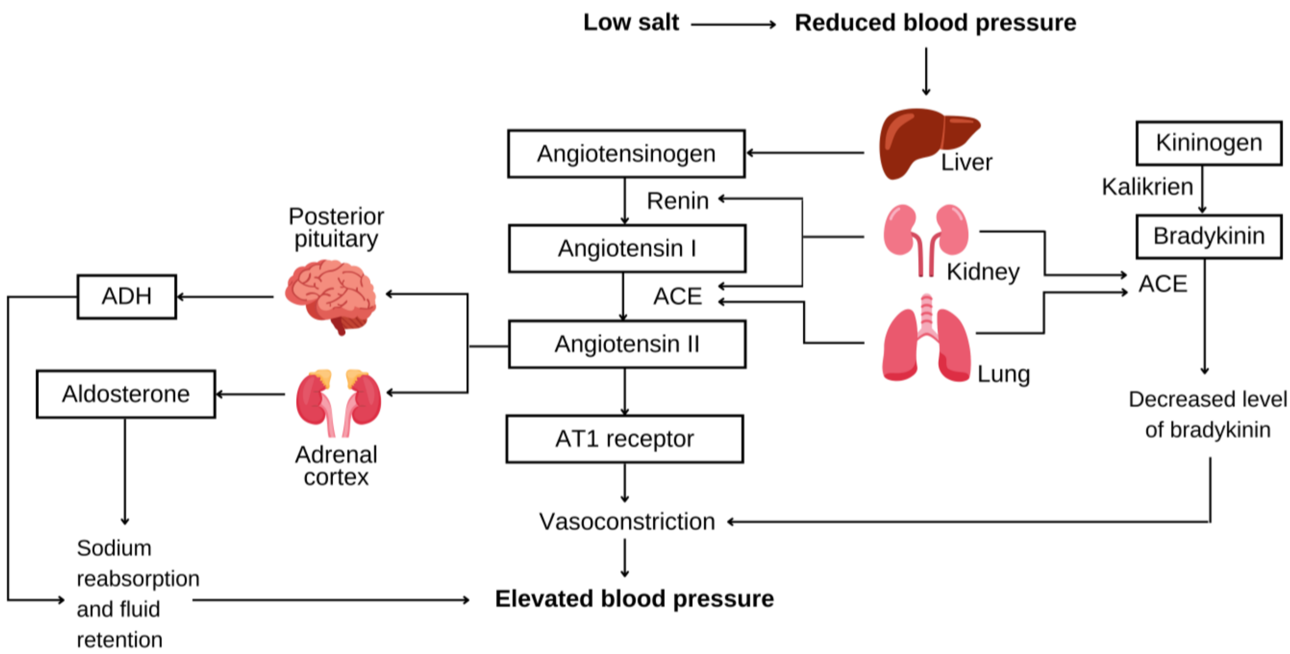

Figure 1. Role of RAAS in blood pressure. ACE: angiotensin-converting enzyme; AT1 receptor: angiotensin II type 1 receptor; and ADH: antidiuretic hormone

and Yoo, 2008). Additionally, bradykinin acts as a vasodilator that can be degraded by ACE, resulting in elevated blood pressure. On the contrary, high sodium intake leads to water retention in the body, causing blood pressure to increase due to the high flow rate of circulating volumes. Persistent high blood pressure may lead to vascular dysfunction, leading to various cardiovascular diseases (Grillo *et al*., 2019).

In the treatment of hypertension, antihypertensive drugs including diuretics, calcium channel blockers, renin inhibitors, and ACE inhibitors are often prescribed to the patients. However, some patients experience side effects including frequent urination, hyperkalaemia, headache, dry cough, and loss of libido (Khalil and Zeltser, 2022). This leads to the discovery and development of food products and naturally occurring bioactive compounds as alternatives to antihypertensive drugs for preventing and managing hypertension (Ortega and Campos, 2019).

Considering the strong association between high sodium consumption and the development of hypertension, WHO has suggested limiting daily salt intake to less than 5 grams per day for an adult. National salt reduction strategies have been implemented in many countries, boosting the trends of low-sodium food products in food industries. Focus has been given to the food that has been categorised as the major dietary sodium intake (Cashman *et al*., 2019). For instance, processed meats and bakery products are the major contributors to sodium intake in the United Kingdom (Ni Mhurchu *et al*., 2011). By gradually lowering the salt content in processed meats and bakery products, the United Kingdom successfully reduced the salt intake among the population (He *et al*., 2014). Thus, it is crucial to determine the food preferences of the general population before executing the strategies to reduce salt content in food products. Meanwhile, in Asian countries, the major sources of sodium intake are the salt and condiments added during the preparation of food. Besides table salt, soy sauce is the highest contributor of dietary sodium in countries including China, Japan, and Korea (Elliott and Brown, 2007; Brown *et al*., 2009; Lee *et al*., 2013; Ghimire *et al*., 2021). Consequently, condiments with reduced sodium content have been developed and introduced into the market in recent years (Sassi *et al*., 2021). The making of condiments lacks a standardised recipe as it differs greatly in terms of ingredient ratio, fermentation time, and temperature. Thus, the salt content in condiments varies based on the formulation adopted by individual manufacturers. In general, liquid condiments have relatively high salt content ranging from 18 to 25% (Diez-Simon *et al*., 2020; Hao *et al*., 2022; Byeon *et al*., 2023). Meanwhile, paste-form condiments have relatively low salt content ranging from 6 to 13% (Chun *et al*., 2020; Allwood *et al*., 2021). Manufacturers are required to adhere to the regulations and guidelines set by the local government when it comes to the making of salt-reduced condiments, as the minimum salt content required in condiments may vary depending on the country or region. Particularly in soy sauce, the salt content is typically maintained between 8 and 11% to ensure its taste quality (Sassi *et al*., 2021).

Due to the nutritional and economical value of legumes, the majority of the condiments are made of vegetable protein derived from legumes. Apart from being a cheap meat alternative, legumes proved to benefit human health (Maphosa and Jideani, 2017; Semba *et al*., 2021). In addition, a study reported that fermented legumes exhibit antihypertensive properties (Maleki and Razavi, 2021). Besides reformulating salt content in legume-based condiments, studies have discovered and attempted to enhance the release of antihypertensive compounds in condiments. Considering the association between hypertension and legume-based condiments, the present review aimed to summarise the antihypertensive effects of condiments prepared using fermented legumes.

Fermentation of condiments prepared from legumes

Fermentation refers to a biological process that involves the action of microorganisms or enzymes, which converts substrates into the desired new substances with a modified food profile (Adebo *et al*., 2017; Bamforth and Cook, 2019; Garrido-Galand *et al*., 2021). Initially, fermentation was applied to extend the shelf life of food by inhibiting the growth of spoilage and pathogenic microorganisms (Adebo *et al*., 2017). As fermentation techniques developed over the years, studies have revealed that fermentation enhances the organoleptic properties and nutritional profile of food. Therefore, legumes have been subjected to fermentation, particularly in Asia and Africa, where they remain a staple food (Subuola *et al*., 2012). As the condiments made of fermented legumes grow in number, they become essential in food preparation nowadays.

During the fermentation of legumes, microorganisms consume different types of nutrients to carry out their metabolic activities, which involve the break-down of food matrices, and the production of metabolic by-products. These biochemical changes occur due to the action between the enzymes released by microorganisms, and the molecules in legumes. Consequently, fermentation results in the alteration of nutrients and the bioavailability of legumes. Depending on the stage of fermentation, microbial and enzymatic activities will cause the starch and carbohydrates to increase and decrease simultaneously. The decrease in starch content is associated with the conversion of starch into reducing sugars. Meanwhile, the decrease in carbohydrate content is often associated with the metabolic activities of microorganisms, which consume carbohydrate-related compounds as sources of energy for growth. In addition, lipase will hydrolyse fat in legumes into fatty acids and glycerol during fermentation as a result of the metabolic activity of fermenting microorganisms. During legume fermentation, proteases produced by the starter culture will hydrolyse the storage proteins into free amino acids or peptides. This conversion improves the digestibility of legumes for better nutrient absorption. Furthermore, the increased protein content during fermentation is associated with the release of protein bound to anti-nutritional factors. The breaking down of protein in legumes also leads to the generation of bioactive peptides which has become the subject of research interest in recent years (Kwon *et al*., 2019; Maleki and Razavi, 2021; Adebo *et al*., 2022).

Antihypertensive effects of soy sauce

Soy sauce has been widely used as a condiment worldwide due to its pleasant and distinctive flavour. Although soy sauce has a long history of development, there is no global standard in the making of soy sauce as it involves a complex mechanism to develop flavour. The mechanisms involved during soy sauce fermentation are primarily associated with two reactions: (1) the breaking down of starch and protein into sugars and amino acids; and (2) the formation of Maillard reaction products or volatile compounds. The reaction rates of these two reactions vary throughout fermentation, resulting in the formation of compounds contributing to the taste and odour of soy sauce. The production of reduced sugar is affected by the amount of carbohydrates, which is usually facilitated by the presence of wheat or rice. Apart from the enzymatic reaction, the Maillard reaction results in the formation of components that contribute to the unique organoleptic properties and colour of soy sauce (Shin and Jeong, 2015; Devanthi and Gkatzionis, 2019; Diez-Simon *et al*., 2020; Adebo *et al*., 2022). The generation of amino acids depends on the substrate used, *e.g.*, soybean and fermentation time. For instance, a higher content of soybean and longer fermentation time lead to the release of a higher amount of amino acid (Kwon *et al*., 2019; Diez-Simon *et al*., 2020). As an excellent source of protein, the fermented soybean is a promising source of peptides. Thus, the antihypertensive properties of soy sauce have often been associated with the generation of bioactive peptides during fermentation. The outcomes of the related studies were reviewed, and are summarised in Table 1.

A recent study conducted using male Sprague-Dawley (SD) rats demonstrated that a daily consumption of Chinese traditional fermented soy sauce relieved hypertension-associated injury by preventing the occurrence of glomerular hypertrophy and hyaline degeneration. It was observed that the SBP of SD rats consuming soy sauce was significantly lower than rats consuming the same amount of salt from saline. The reduction of SBP was found to be associated with the downregulation of angiotensinogen and the expression level of RAAS-related genes in SD rats (Zhong *et al*., 2021). Another experiment was conducted using SD rats to evaluate the antihypertensive effects of a Korean traditional soy sauce, *ganjang*. Even though the SBP of SD rats consuming soy sauce was not significantly different from rats consuming saline, a decreasing trend was observed throughout the intervention. In addition, the mRNA expression level of rats consuming soy sauce was significantly lower, resulting in a decrease in serum renin and aldosterone. The excretion of sodium ions in rats consuming soy sauce also increased. These findings may reveal the underlying mechanisms attenuating the development of hypertension (Mun *et al*., 2017). In Japan, a cross-sectional study was carried out among 25,738 participants to investigate the relationship between the portion size of soy sauce and the occurrence of hypertension. Interestingly, the results demonstrated that the portion size of soy sauce did not correlate with the occurrence of hypertension (Okada *et al*., 2018).

In recent years, various attempts have been carried out to further enhance the antihypertensive properties of soy sauce. Various studies conducted have shown that the modified soy sauces exhibited antihypertensive effects that are beneficial for human health. The findings of these studies are summarised in Table 2. A salt-free soy sauce was developed by Zhu *et al*. (2008), and the peptides isolated from this soy sauce were identified. The analysis revealed that two ACE inhibitory dipeptides, Ala-Phe and Ile-Phe, were able to transport intact proteins through the intestinal membrane. This finding suggested that blood pressure was regulated through the inhibition of ACE under the influence of antihypertensive peptides. An *in-vivo* study was conducted to further elucidate the antihypertensive effects of salt-free soy sauce. Similarly, the salt-free soy sauce exhibited antihypertensive effects as observed in the significant drop in blood pressure of spontaneously hypertensive rat (SHR). It was suggested that a higher vascular constrictive response in SHRs fed with salt-free soy sauce may be the leading cause of antihypertensive effects found in salt-free soy sauce (Matsui *et al*., 2010). Gamma-aminobutyric acid (GABA) is a non-protein amino acid that is known as the main inhibitory neurotransmitter in vertebrates' central nervous system (Tarkowski *et al*., 2020). Apart from maintaining the neurologic function, GABA was found to exert an antihypertensive effect through the regulation of antidiuretic hormone and chloride ions (Ma *et al*., 2015). Thus, there has been a growing interest among researchers in studying the development of GABA-enriched functional food. Glutamate decarboxylase is an intracellular enzyme responsible for the conversion of L-glutamate into GABA during the fermentation of condiments. Therefore, antihypertensive effects of the sodium-reduced soy sauce containing GABA were assessed by Yamakoshi *et al*. (2007). Compared to regular soy sauce and potassium-enriched soy sauce, both single and chronic administration of GABA-rich soy sauce significantly lowered the SBP in SHRs. The results demonstrated that the intake of GABA-rich soy sauce in SHRs decreased renal sympathetic nerve activity (RSNA), leading to an increase in renal sodium excretion. Vascular hypertrophy, which has often been associated with hypertension, was reduced in SHRs administered with GABA-rich soy sauce. The findings also imply that natriuresis and reduced vascular hypertrophy are associated with antihypertensive effects of GABA-rich soy sauce. Nakahara *et al*. (2010) assessed the antihypertensive effects of a peptide-enriched soy sauce, fermented soybean seasoning (FSS). The concentration of ACE inhibitory peptides isolated from FSS was higher than that of regular soy sauce. This finding was supported by the outcomes of the ACE assay, which revealed an IC_{50} value of 454 mg/mL of FSS which was higher than the regular soy sauce with an IC_{50} value of

Table 1. Antihypertensive effects of condiments prepared using fermented legumes.

Type of legume-based condiment	Type of cell culture / animal model	Effective dose	Route and duration of supplementation	Outcome	Reference
Chinese traditional fermented soy sauce	Male SD rat	10 mL/kg body weight with a high-fat diet	Oral gavage for 12 weeks	• Ameliorated hypertension-associated kidney injury; • Promoted blood pressure-lowering effects	Zhong *et al.* (2021)
Ganjang	Male SD rat	10 mL/kg body weight per day	Oral administration for nine weeks	• Suppressed mRNA expression of RAAS-related genes (renin, angiotensin II type 1 receptor, and mineral corticoid receptor); • Decreased reabsorption of sodium ion; • Lowered the risk of hypertension	Mun *et al.* (2017)
Doenjang	Male SD rats	10 mL/kg body weight per day	Oral administration for eight weeks	• Increased excretion of sodium and potassium; • Decreased level of serum renin and aldosterone; • Suppressed expression of angiotensin II type 1 receptor, mineral corticoid receptor, and ACE; • Attenuated development of high blood pressure despite the high sodium content	Mun *et al.* (2019)
Doenjang	3T3-L1 adipocytes	N/A	N/A	• Downregulated expression of genes encoding angiotensinogen, renin, and aldosterone-releasing factor; • Reduced activity of ACE and angiotensin II receptor	Woo *et al.* (2020)
Korean soybean paste	Male SHR	5 mg/kg body weight	Single or triple injection of synthetic HHL into the femoral vein	• Novel tripeptides, HHL with an IC_{50} value of 2.2 µg/mL isolated from the Korean soybean paste; • Both single and triple injections of synthetic HHL significantly reduced SBP in SH rats	Shin *et al.* (2001)
Miso	Dahl S and SD rats of both sexes	A diet containing 10% (w/w) of dry red *miso*	*Ad libitum* feeding for 11 weeks	• The blood pressure of Dahl S and SD rats of both sexes fed with a high-salt diet containing *miso* (2.3% salt) were significantly lower than rats fed with a high-salt diet (2.3% salt) only; • The development of hypertension was not associated with *miso* intake	Watanabe *et al.* (2006)

Type of legume-based condiment	Type of cell culture / animal model	Effective dose	Route and duration of supplementation	Outcome	Reference
Miso soup	Male Dahl S rats	A low-salt diet with 10% *miso* soup	*Ad libitum* feeding for eight weeks	• Attenuated glomerular sclerosis in the kidney; • Decreased urinary protein excretion; • Decreased collagen infiltration in the heart; • Regulated the excretion of sodium and potassium	Yoshinaga *et al.* (2012)
Miso	Female Dahl S rats	A low-salt diet with 5% (w/v) *miso* soup	*Ad libitum* feeding for 12 weeks	• Increased free water clearance and osmolar clearance in the *miso* group; • Increased excretion of urinary dopamine which led to reduced formation of lipid peroxides and decreased oxidative stress in the brain; • The attenuation of SBP in the *miso*-fed group was associated with the excretion of urinary dopamine	Du *et al.* (2014)
Miso	Male SHRSP	90% normal diet with 10% *miso*	*Ad libitum* feeding for two months	• Attenuated degeneration of glomeruli in the kidney; • Reduced formation of haemorrhagic macules in the brain; • Reduced incidence of stroke; • Attenuated development of high blood pressure	Watanabe *et al.* (2017)
Miso	Male Dahl S rats	50 mg *miso* extract daily	Bolus IP injection for four days ——— Continuous subcutaneous infusion for 14 days	• Antihypertensive effects of *miso* were primarily contributed by substances < 5 kDa; • Increased natriuresis and diuresis were not observed, suggesting a different mechanism involved in the regulation of blood pressure; • The supplementation of *miso via* IP or subcutaneous route was more effective in reducing blood pressure than oral route; • The underlying mechanisms remain unclear	Shimizu *et al.* (2015)
Fermented African locust bean condiment	Male Wistar rat (streptozotocin-induced diabetic model)	Basal diet supplemented with 10% fermented African locust bean condiment	Oral administration for 14 days	• Significant reduction in ACE activity was potentially contributed by isoflavones in African locust bean; • Phenolic extract from the fermented African locust bean showed a higher ACE inhibitory activity than the fermented soybean and Bambara groundnut	Ademiluyi and Oboh (2015)

Table 2. Antihypertensive effects of modified condiments prepared using fermented legumes.

Type of legume-based condiment	Modification	Type of cell culture / animal model	Effective dose	Route and duration of supplementation	Outcome	Reference
Salt-free soy sauce	Direct removal of salt and fermentation in 20% ethanol medium	Caco-2 cell monolayer	375 mg of salt-free soy sauce powder in 7.5 mL of Hank's balanced salt solution (HBSS) buffer	N/A	• Three dipeptides, Ala-Phe, Phe-Ile, and Ile-Phe from salt-free soy sauce were able to move across caco-2 cell monolayers; • Only Ala-Phe and Ile-Phe exhibited ACE inhibitory activity, indicating the importance of amino acid sequence in determining the antihypertensive effects and transportability of peptides; • IC_{50} values of Ala-Phe and Ile-Phe were 165.3 and 65.8 μmol/L, respectively	Zhu *et al.* (2008)
Salt-free soy sauce	Direct removal of salt and fermentation in 20% ethanol medium	Male SHR	200 mg salt-free soy sauce powder/kg body weight per day	Oral administration for 13 weeks	• No significant difference was observed in ACE inhibitory activity in blood and organs, including lung, kidney, heart, and aorta, and between the salt-free soy sauce and control group; • A significantly high constrictive response against angiotensin II in the salt-free soy sauce group; • Suggested that the intake of salt-free soy sauce may be effective in preventing age-related sclerosis	Matsui *et al.* (2010)

Type of legume-based condiment	Modification	Type of cell culture / animal model	Effective dose	Route and duration of supplementation	Outcome	Reference
GABA-rich soy sauce	Conducted *moromi* fermentation using lactic acid bacteria, *Lactobacillus rennini*	Male SHR	0.033 or 3.3 mL/kg body weight of GABA-rich soy sauce	Single oral administration	• Significantly attenuated development of hypertension as compared to potassium-rich soy sauce and regular soy sauce; • Imposed inhibitory effect on RSNA, which decreased the reabsorption and retention of sodium; • Short-term hypotensive effect of GABA-rich soy sauce was more effective than its long-term hypotensive effect; • The concentration of GABA in the hypothalamus was the same between the GABA-rich soy sauce group and the control group, suggesting GABA-rich soy sauce exerted its hypotensive effect peripherally; • Exerted inhibitory effect on vascular hypertrophy	Yamakoshi *et al.* (2007)
		Male SHR and Wistar-Kyoto rats	A standard diet with 3.9% (w/w) GABA-rich soy sauce	Oral administration for six weeks		
Fermented soybean seasoning	Increased the ratio of soybean to wheat and altered fermentation conditions (shorter fermentation time and higher fermentation temperature)	Male SHR	A standard diet containing FSS (10%, v/w)	Oral administration for 11 weeks	• Total peptide content in FSS was 2.7 times higher than regular soy sauce; • Significant attenuation of SBP in SHR-consuming FSS; • High-dose group had a significantly lower SBP than low-dose group, indicating that FSS regulated blood pressure in a dose-dependent manner; • Antihypertensive effects of FSS were mainly contributed by nine dipeptides and a non-protein amino acid, nicotianamine	Nakahara *et al.* (2010)
		Male Dahl S rats	Low-dose group: a standard diet containing 5% (v/w) FSS; high-dose group: a standard diet containing 10% (v/w) FSS	Oral administration for six weeks		
		Male SHR	FSS peptide fraction (125, 250, or 500 mg/kg) or FSS nicotianamine fraction (250 or 500 mg/kg)	Single oral administration	• FSS peptide fraction had a significant effect in lowering SBP of SHR, meanwhile nicotianamine fraction did not; • Both serum aldosterone level and ACE activity in the lungs of the FSS group were significantly lower than the control group	Nakahara *et al.* (2011)
		Male SHR	2000 mg/kg body weight of FSS	Single oral administration	• Antihypertensive dipeptides, Gly-Tyr and Ser-Tyr, were detected in plasma for four hours, suggesting that both peptides resisted gastrointestinal digestion and were absorbed in their intact form	Nakahara *et al.* (2011)

Type of legume-based condiment	Modification	Type of cell culture / animal model	Effective dose	Route and duration of supplementation	Outcome	Reference
Casein *miso* paste	The substitution of steamed soybeans for sodium caseinate	Male SHR	1.8 g/kg body weight	Single oral administration	• *Miso* paste with 16% casein exhibited the highest ACE inhibitory activity; • After 60 days of fermentation, the ACE inhibitory activity of casein *miso* paste was about six times higher than the regular *miso* paste; • Tripeptides, VPP, and IPP contributed to the major antihypertensive effects of casein *miso* paste; • SBP in SHR administered with casein *miso* paste was significantly lower than the general *miso* paste	Inoue *et al.* (2009)
Marukome MK-34-1 *miso* (shinki *miso*)	Reduced percentage of malted rice, shorter fermentation period, and used different strains of koji starter	Male SHRSP	5% (w/v) shinki *miso* solution	*Ad libitum* feeding for four weeks	• Antihypertensive substances of *shinki miso* were found to have molecular weight < 3 kDa; • The weight of the aortic wall of the *shinki miso* group was significantly lower than the regular *miso* and control groups; • Significant lower oxidative stress in the *shinki miso* group; • No significant difference in urinary sodium excretion between the *shinki miso* group and the control group; • A significant reduction of SBP in both SHRSP and Dahl S rats fed with *shinki miso*	Tomari *et al.* (2019)
		Male Dahl S rats	*Awase miso* (mixture of 5% regular *miso* and 5% *shinki miso* solution at a ratio of 2:1 (v/v))	*Ad libitum* feeding for four weeks	• A significant reduction of SBP in the *awase miso* group with no significant difference in urinary sodium excretion between the *awase miso* group and the regular *miso* group	

1620 mg/mL. FSS also exhibited a stronger antihypertensive effect in Dahl S rats compared to regular soy sauce. Purification of substances in FSS has led to the identification of nine dipeptides and a non-protein amino acid, nicotinamide, which might have contributed to the antihypertensive effects of FSS. Interestingly, nicotinamide with an IC_{50} value of 0.26 mg/mL was proved to exhibit the strongest ACE inhibitory activity. A further study was conducted by Nakahara *et al*. (2011) to elucidate the mechanism of FSS in lowering blood pressure. Compared with the previous study, a peptide fraction of FSS exhibited a significant effect in lowering the SBP of SHR while the nicotianamine fraction did not. Additionally, the ingestion of FSS in SHR led to the suppression of ACE activity and aldosterone levels in serum, demonstrating the blood pressure-lowering effect of FSS through the regulation of the RAAS system. Two dipeptides, Gly-Tyr and Ser-Tyr, isolated from FSS remained intact after being subjected to an *in-vitro* gastrointestinal digestion. This finding was further supported by the detection of both dipeptides in the plasma of SHR after the ingestion of FSS. Besides, it was discovered that the ACE activity in the lung and the serum aldosterone level of SHR were reduced significantly following the administration of FSS. This finding indicated the antihypertensive effect of FSS *via* the inhibition of ACE activity. A low-sodium soy sauce was developed and tested among the Japanese population (Nakamura *et al*., 2003). This trial demonstrated that the consumption of low-sodium soy sauce had a significant effect in lowering DBP among people aged 40 or above.

The antihypertensive activity of soy sauce was elevated through the reformulation of raw ingredients used in fermentation, which aimed to increase the release of antihypertensive peptides. This formulation included the reduction or total removal of salt for higher enzymatic activity, changing of the ratio of the substrate, and selection of starter culture (Yamakoshi *et al*., 2007; Zhu *et al*., 2008; Matsui *et al*., 2010; Nakahara *et al*., 2010; 2011). Although emerging technologies have been applied to modify soy sauce, concerns regarding the high operating cost and compromised quality due to the removal of flavour-contributing compounds have arisen (Luo *et al*., 2009; Fidaleo *et al*., 2012). Consequently, the application of technologies for modifying commercial soy sauce has been limited. Thus, it is imperative to improve the technology feasibility and cost-effectiveness for the modification of soy sauce.

Antihypertensive effects of soybean paste

Soybean paste is one of the oldest condiments consumed worldwide, particularly in countries such as China, Japan, and Korea. Similar to soy sauce, the initial fermentation of soybean paste involves the degradation of proteins and starches, leading to the formation of macromolecules such as peptides and reducing sugars. Meanwhile, the flavour and colour of soybean paste are the products of the Maillard reaction that occurs during the second stage of soybean paste fermentation (Shin and Jeong, 2015; Kusumoto *et al*., 2021; Yue *et al*., 2021). Additionally, volatile components that contribute to the aroma profile of soybean paste are released. Thus, the organoleptic properties of a soybean paste are greatly dependent on the biochemical conversion of the substrate. Besides, intrinsic and extrinsic factors including pH, temperature, humidity, and salinity play an important role in constructing the sensory profile of soybean paste. Therefore, soybean pastes originating from different countries vary in taste, aroma, and appearance as they are fermented under different conditions and handling processes. For instance, *miso* from Japan and *doenjang* from Korea are prepared from *koji* and *meju*, respectively (Allwood *et al*., 2021; Kusumoto *et al*., 2021; Han *et al*., 2021; Adebo *et al*., 2022).

Several studies have been conducted to assess the antihypertensive activity of *miso*. Interestingly, results have shown that the consumption of *miso* is not directly related to the development of hypertension. Furthermore, the consumption of *miso* was found to improve the condition of hypertension through the regulation of potassium and sodium excretion, downregulation of RAAS, and attenuation of kidney damage related to the progression of hypertension. An *in-vivo* study using Dahl S and SD rats revealed that the daily intake of the traditional *miso* significantly attenuated the increment of blood pressure (Watanabe *et al*., 2006). In addition, the inclusion of *miso* in the diet of Dahl S rats and stroke-prone spontaneously hypertensive rats (SHRSPs) revealed that the *miso* significantly decreased blood pressure, and delayed kidney and brain damage (Yoshinaga *et al*., 2012; Watanabe *et al*., 2017). Similarly, Du *et al*. (2014) demonstrated that the intake of *miso* significantly reduced the development of hypertension in Dahl S rats. It was suggested the suppression of SBP was associated with elevated natriuresis and diuresis. Interestingly, lower oxidative stress in the brain of the *miso* group was related to higher activity of dopamine, indicating that increased natriuresis and diuresis were mediated by elevated excretion of dopamine. These results demonstrated that the suppression of SBP was associated with dopaminergic activity. An *in-vivo* study was conducted by Shimizu *et al*. (2015) to assess the blood pressure-lowering effect of *miso* extract. The *miso* extract was injected into the Dahl S rat through either bolus intraperitoneal (IP) injection or subcutaneous infusion. The results demonstrated that both administration methods significantly attenuated SBP in Dahl S rats. Compared to oral administration, the supplementation of *miso* through IP or subcutaneous injection was more effective in lowering blood pressure, suggesting that a different mechanism was involved in the regulation of blood pressure. Meanwhile, a cross-sectional study was conducted among Japanese aged 50 years or above to discover the association between the consumption of *miso* and blood pressure (Ito *et al*., 2017). Although the consumption of *miso* soup did not significantly lower the blood pressure in elderly individuals, the results indicated that the occurrence of hypertension is not associated with the consumption frequency of *miso* soup. Similarly, a cross-sectional study was conducted based on the data retrieved from the Japan National Health and Nutrition Survey (NHNS) 2012. The study aimed to investigate the relationship between the portion size of *miso* and the prevalence of hypertension. The results revealed that a larger portion size of *miso* did not lead to a higher prevalence of hypertension (Okada *et al*., 2018). In a recent study, the antihypertensive effects of Korean traditional soybean paste, *doenjang*, were tested in SD rats. Despite consuming high salt content, the SBP of rats fed with a high-salt diet with *doenjang* (8% salt) showed no significant difference compared to the rats fed with a normal diet (0.3% salt). The findings suggested that the decreased renin level and the increased excretion of sodium and potassium attenuated the development of hypertension in rats consuming *doenjang* (Mun *et al*., 2019). Antihypertensive effects of *doenjang* were further assessed by Woo *et al*. (2020) using 3T3-L1 adipocytes. The results showed that the ACE of adipocytes treated with *doenjang* was inhibited by the downregulation of RAAS-related genes. In addition, an *in-vitro* study conducted by Shin *et al*. (2001) led to the discovery of a novel ACE inhibitory tripeptide, His-His-Leu (HHL), isolated from Korean soybean paste. Further study was conducted to assess the antihypertensive effects of HHL, which found that the tripeptide significantly reduced the SBP in SH rats.

Generally, soybean paste has been subjected to modifications including the substitution of fermentation substrate and adjustment of fermentation conditions. For instance, a randomised controlled trial was carried out in Japan to assess the effect of low-sodium *miso* on blood pressure. However, there was no significant change in blood pressure between the intervention and control group after six weeks. Interestingly, DBP was significantly reduced in subjects aged above 40, suggesting that the blood pressure-lowering effect might be more profound in subjects with a higher risk of hypertension (Nakamura *et al*., 2003). In a clinical trial conducted by Mizuno *et al*. (2005), the hydrolysis of casein by *A. oryzae* led to the generation of tripeptides, VPP, and IPP with significant antihypertensive effects. Thus, a *miso* paste was developed by substituting soybeans with casein to enhance its antihypertensive effect. Compared to the regular *miso* paste, SBP was greatly reduced in SHR after being fed with casein *miso* paste. ACE inhibitory activity of casein *miso* paste was also higher than other *miso* pastes, which correlates with the higher concentration of antihypertensive peptides found in casein *miso* paste (Inoue *et al*., 2009). Tomari *et al*. (2019) developed a new type of *miso* with improved ACE inhibitory activity called Marukome MK-34-1 *miso* (*shinki miso*). An *in-vivo* study reported that *shinki miso* exhibited higher antihypertensive effects in SHRSP compared to regular *miso*. This finding conformed to the results obtained in the ACE assay which demonstrated that *shinki miso* (IC_{50} = 0.23 mg/mL) exhibited a stronger ACE inhibitory activity than the general *miso* (IC_{50} = 2.5 mg/mL). Considering that the general and *shinki miso* regulated blood pressure through different mechanisms, *awase miso* was created by combining both *shinki* and general *miso*. The *awase miso* was fed to Dahl S rats, and analysed in a comparison with the group fed with regular *miso*. The results demonstrated that the blood pressure was remarkably reduced in the *awase miso* group compared to the group fed with the general *miso* group. However, there was no significant difference in the urinary sodium between the group fed with *awase* and general *miso*. This finding indicated the possible attenuation of hypertension by *shinki miso* through the downregulation of RAAS instead of natriuresis. The formation of angiotensin II results in the generation of oxygen radicals which leads to increased oxidative stress. It was observed that the kidney of SHRSP fed with *shinki miso* had lower oxidative stress than SHRSP fed with general *miso*. However, there was no significant difference in aldosterone level in urine between *shinki miso* and the control group, which was contrary to the statement suggesting that *shinki miso* regulates blood pressure through the inhibition of RAAS. Additionally, a placebo-controlled intervention was carried out to evaluate the effects of *awase miso* on humans (Kondo *et al*., 2019). Despite consuming higher amounts of salt, the subjects in the *awase miso* group exhibited a significant reduction in night-time blood pressure. The underlying mechanism regulating the blood pressure remains unclear.

Despite its high sodium content, studies have shown that the consumption of soybean paste reduces the prevalence of hypertension. Studies have also shown that the modified soybean pastes exhibit enhanced antihypertensive activity, often linked to the presence of antihypertensive peptides. However, the underlying mechanisms and the exact causes contributing to the antihypertensive effects of soybean paste are not yet fully elucidated.

Antihypertensive effects of Douchi

Douchi is a traditional soy product that originated from China, and prepared through solid-state fermentation. Rather than soybean, black soybean is used in the making of *Douchi*. Pre-fermentation of steamed black soybeans involves inoculation of fungi or bacteria such as *Aspergillus*, *Mucor*, *Rhizopus*, or *Bacillus subtilis* to obtain *koji* (Endo *et al*., 2014; Mani and Ming, 2017). Despite the similar fermentation process, *Douchi* and soybean paste differ as soybeans in *Douchi* are not mashed (Nout, 2015). Moreover, distinct microbial communities have been found in *Douchi* and soybean paste, which contribute to their unique taste and flavour (Yang *et al*., 2019a; Yue *et al*., 2021). Nevertheless, a similar trend in metabolic activities has been observed in *Douchi* and soybean paste. The hydrolytic enzymes secreted by the fermenting microorganisms break down the large molecules during the early stage of fermentation. Small molecules formed at a later stage of fermentation contribute to the flavour of *Douchi*. The production of bioactive peptides with antihypertensive effects remains the main research focus considering their potential blood pressure-lowering effects (Li *et al*., 2019; Yang *et al*., 2019b).

Zhang *et al*. (2006) reported that a tripeptide consisting of Phe, Ile, and Gly with ACE inhibitory activity was isolated from the fermented *Douchi*. This study also showed that fermentation and gastrointestinal digestion may enhance the ACE inhibitory activity of *Douchi*. The findings were further supported by research conducted by Wang *et al*. (2015) which showed that gastrointestinal digestion elevated the ACE inhibitory activity of fermented *Douchi*. On the other hand, Wang *et al.* (2013) showed that the antihypertensive properties of *Douchi* were mainly contributed by ACE inhibitory peptide rather than the synergistic effect of ACE inhibitory peptide and Maillard reaction product.

Antihypertensive effects of broad bean paste

Broad bean paste, also known as horse bean chili paste, *doubanjiang*, or Pixian *doubanjiang*, can be found in southwestern China. It is a semi-solid condiment traditionally added to Sichuan dishes due to its savoury and spicy taste (Lu *et al*., 2020; 2021; Yang *et al*., 2021). Studies have reported an elevated antihypertensive activity in the broad bean subjected to biochemical processes including enzymatic hydrolysis and fermentation, often associated with the release of bioactive peptides and GABA (Martineau-Côté *et al*., 2022).

Li *et al*. (2021) reported the isolation of four novel peptides exhibiting ACE inhibitory activity from water-soluble extract of fermented broad bean paste. The peptide RGLSK with an IC_{50} value of 87 mmol/L showed the highest ACE inhibitory activity among the peptides discovered. The findings suggested that the hydrogen bonds and coordinate bonds formed between RGLSK and S1 active sites, and Zn^{2+} of ACE stabilised the interaction in the RGLSK-ACE complex.

Antihypertensive effects of sufu

Sufu, commonly known as *fu-ru*, is a cheese-like condiment with a creamy texture made of fermented tofu (Cheng *et al*., 2009). The production of *sufu* starts with the making of tofu from soybeans. Pehtze is formed through solid-state fermentation of tofu following fungal inoculation using *Actinomucor* spp., *Mucor* spp., and *Rhizopus* spp. Pehtze overgrown with mycelium will be subjected to salting and ripening. Various types of *sufu* can be produced by adding different dressing mixtures such as red *koji*, spices, salt, sugar, and alcohol during ripening. Generally, *sufu* can be classified into red, white, and grey *sufu* (Han *et al*., 2001; Yasuda, 2011). Proteolytic and lipolytic activities during the fermentation of *sufu* lead to the generation of free amino acids and volatile organic acids that contribute to its flavour and aroma. The functional properties of a fermented *sufu* are mainly attributable to the bioactive peptides generated during the fermentation (Ma *et al*., 2013b; Cai *et al*., 2016).

An *in-vitro* study was conducted to investigate the antihypertensive properties of *sufu*. ACE inhibitory activity of *sufu* was determined throughout production, which was associated with peptide and sodium chloride concentrations. The results revealed a positive correlation between peptide content and ACE inhibitory activity. Meanwhile, salting decreased ACE inhibitory activity in *sufu*. Additionally, a prolonged fermentation of *sufu* will reduce ACE inhibitory activity due to extensive proteolysis. Similarly, GABA content increased during fermentation, and decreased during salting (Ma *et al*., 2013a). GABA content also showed a positive correlation with ACE inhibitory activity. Nevertheless, the antihypertensive mechanism of GABA in *sufu* remains uncertain.

A low-salt *sufu* was developed by Ma *et al*. (2014) to assess the effects of *in-vitro* digestion, heat treatment, and pH on its ACE inhibitory activity. The ACE inhibitory activity of low-salt *sufu* showed a significant increment after being subjected to *in-vitro* digestion. Moreover, the low-salt *sufu* digested by pepsin and α-chymotrypsin exhibited the highest ACE inhibitory activity (IC_{50} = 0.015 mg/mL). Meanwhile, an increasing trend in ACE inhibitory activity of low salt *sufu* was observed when the pH decreased. These findings indicated that gastrointestinal digestion may enhance the antihypertensive effects of low salt *sufu*. The low salt *sufu* also exhibited remarkable thermostability as no significant difference was observed in its ACE inhibitory activity when heated at various temperatures.

Antihypertensive effects of fermented African locust bean

African locust bean (*Parkia biglobosa*) seeds are commonly used as an ingredient in local condiments through solid-state fermentation. Fermented African locust bean has a pungent smell and a spheroid shape of dark greyish colour. It is widely consumed across West Africa by different socio-ethnic groups. Depending on the surroundings and equipment used, the fermentation of African locust beans is typically spontaneous. Generally, *Bacillus* spp. are the principal microorganisms that drive the fermentation of African locust beans (Olasupo and Okorie, 2019; Ugwuanyi and Okpara, 2020). Studies have revealed that the hypotensive effects of African locust bean are mainly contributed by phenolic and flavonoid compounds. Studies have also suggested that the blood pressure-lowering effect of the African locust bean works mainly through the inhibition of ACE and regulation of nitric oxide, acting as a vasodilator (Saleh *et al*., 2021).

In 2015, Ademiluyi and Oboh (2015) evaluated the blood pressure-lowering effect of fermented African locust beans through *in-vitro* and *in-vivo* studies. The results showed that daily consumption of a diet supplemented with 10% fermented African locust bean produced a significant effect in reducing ACE activity in the lungs of a diabetic rat. Additionally, an *in-vitro* study was conducted to investigate the ACE inhibitory activity of phenolic extract derived from the fermented locust bean. The reported IC_{50} of the fermented African locust bean was 136 mg/mL, which was higher than that of the fermented Bambara groundnut and soybean. In addition, a cross-sectional study was carried out to investigate the association between the consumption of fermented African locust beans and the hypertension incidence among residents of Bogou and Goumou-kope (Ognatan *et al*., 2011). The clinical results revealed a significantly low blood pressure among the subjects from Bogou (n = 100) who had habitually consumed fermented African locust beans for at least five years compared with those from Goumou-Kope (n = 100) who had never consumed fermented African locust beans. The results indicated the antihypertensive effects of fermented African locust beans was associated with its long-term consumption. Rather than the bioactive peptides, the antihypertensive effects of fermented African locust bean have been associated with its phenolic and flavonoid compounds. However, its mechanism of action remains inconclusive, which necessitates further research to identify the bioactive compounds with antihypertensive effects present in the fermented African locust bean.

Conclusion

Studies have revealed that an intake of legume-based condiments had no association with the development of hypertension despite their high sodium content. On the contrary, the consumption of legume-based condiments was found to exert a positive effect on blood pressure, and protect against hypertension-associated organ damage. Generally, legume-based condiments regulate blood pressure through the suppression of RAAS and/or impart vasodilation effect through natriuresis. The inhibition of RAAS was often linked to the presence of ACE-inhibitory peptides generated during the fermentation of condiments. However, the presence of other bioactive components that may work synergistically with the ACE inhibitory peptides should not be neglected. It was demonstrated that with slight modifications, such as fermentation condition and salt concentration, the antihypertensive effects of legume-based condiments can be enhanced. Nevertheless, current studies have mainly focused on the modification and evaluation of nutraceutical properties of soy sauce and *miso*. Studies have revealed that condiments such as fermented African locust beans, *sufu*, *Douchi*, *etc.* exhibit remarkable antihypertensive effects. Preceding research is therefore essential to obtain fundamental knowledge before attempting to modify legume-based condiments to enhance their antihypertensive effects. Concerning the implementation of a national salt reduction strategy, researchers and manufacturers should consider consumer preference when performing modification and reformulation of legume-based condiments to improve their marketability. In conclusion, legume-based condiments have shown promising results in the management of hypertension, demonstrating its potential functional food that can be incorporated into the daily diet. However, future studies are necessary to determine the active constituents and the underlying mechanisms contributing to their hypotensive effects.

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