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Potential of Bioactive Components in Tempe for the Treatment of Obesity

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ABSTRACT

Obesity has become a global health issue and is one of the factors that trigger degenerative diseases. The correct food consumption management could be a solution for treating obesity. Soybean is a food that is rich in bioactive components and has antiobesity properties through various mechanisms. In Indonesia, nearly 60% of the soybeans are consumed in the form of tempe. The process of fermenting soybeans into tempe causes a bioconversion of nutrients and bioactive components, improving the active physiological abilities. The bioactive components that play a role in the treatment of obesity are isoflavones, proteins, and peptides. These bioactive components help in reducing body weight, lowering the body fat ratio and improve lipid profile. Thus, optimation and popularization of tempe as a functional food in the daily menu supported with correct tempe processing could be a solution in treating obesity.

Keywords: isoflavones, obesity, protein, soybean, tempe

INTRODUCTION

Obesity has become a worldwide health issue and is believed to be one of the factors that trigger degenerative diseases and metabolic problems such as diabetes mellitus (DM), coronary heart diseases (CHD), dyslipidemia, hypertension, and arthritis (Yuliana *et al.* 2011; Velasquez & Bhathena 2007). WHO (2014) highlighted that 65% of the world population is overweight and obese and has a higher mortality risk than malnourished people. Based on the WHO standard, a BMI greater than 25 kg/m^2 is categorized as overweight, and a BMI greater than 30 kg/m^2 is categorized as obese.

Aside from the lack of physical activities, poor food consumption pattern such as excessive consumption of foods rich in fat and carbohydrate is considered as a main cause of obesity (WHO 2011). Therefore, strategies in treating obesity include reduction of the amount of energy absorbed by the body, using appetite suppressants, inhibiting nutrient absorption, increasing metabolism, and lipid modulation (inhibiting the differentiation and proliferation of adipocytes, and reducing lipogenesis and increasing lipolysis) (Yun 2010).

Complications due to obesity and other degenerative diseases have encouraged the consumption of low-energy, low-fat, high-fiber, and antioxidant-rich foods (Bhathena & Velasquez 2002). Soybeans have been reported to contain such quality, it has various bioactive components which have active physiological properties in treating obesity (Bhathena & Velasquez 2002; Velasquez & Bhathena 2007). In Indonesia, nearly 60% of soybeans are consumed in the form of tempe with an average tempe consumption of 10.1 kg per person per year (Astawan *et al.* 2017). The process of fermenting soybeans into tempe can also improve its nutritional value and benefits for health (Nout & Kries 2005; Astawan 2008).

Many studies pertaining to the use of soybeans and soybean products in the treatment of obesity have been conducted, however not many discuss the possibilities of utilizing tempe which is a fermented soybean product as a component in treating obesity. Against this backdrop, the review will discuss the possibilities of using tempe as a soybean-derived functional food in the treatment of obesity.

1. The Bioactive components of soybeans and tempe

The main ingredient of tempe is soybeans (*Glycine max*), therefore bioactive components of soybeans (Table 1) would most likely be found in tempe, or might even be more "activated" due to the fermentation process. Tempe is made from soybean through a number of steps, namely soaking, boiling, removing the cotyledon husk, adding mold (the mold *Rhizopus* spp.), and fermenting at 30-37°C for 36-48 hours (Nout & Kries 2005). Fermentation changes various compo-

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nents in soybeans, producing tempe which has an enhanced nutritional content and improved bioactive components and is more beneficial for health than soybeans (Astawan *et al.* 2017). Table 1 shows the bioactive components in soybean and the benefit for health.

The technology of tempe-making is "adopted" in food technology as the term Solid State Bioconversion (SSB) or Solid State Fermentation (SSF) by exploiting various molds which are usually used in traditional fermentation processes such as *Rhizopus* sp, *Aspergillus* sp., *Bacillus* sp., *et cetera* (Maiti & Majumdar 2012; McCue *et al* . 2005; Sanchez-Magana *et al.* 2014). Fermentation of soybeans using the mold *Rhizopus* spp. is favored because the application is simple and able to produce products with a palatable flavor (Sanchez-Magana *et al.* 2014; Wijaya *et al.* 2007).

Fermentation will increase the content of small molecules such as free fatty acids and amino acids (Ali *et al.* 2016) and the isoflavone aglycone (Haron *et al.* 2009), as well as produce bioactive peptides (Gibbs *et al.* 2004). This is due to the enzymatic activity of microorganisms which works on the soybean substrate, for example, lactic acid bacteria (BAL), mold, and yeast (Gibbs *et al.* 2004; Barus *et al.* 2008). Singh *et al.* (2014) reported that fermentation with BAL is also commonly used for the production of bioactive peptides. These bioactive components will lend active physiological properties for health.

The amount and types of bioactive components produced during the fermentation of tempe are influenced by the enzymatic activities of the microorganisms. Efriwati and Nuraida (2013) demonstrated that differences during the tempe production process will yield different macronutrient components (carbohydrate, fat, and protein) in the tempe and also differences in the isoflavone content. Differences in the tempe production method create a possibility for different microbes to exist and to take part in the tempe fermentation process (Barus *et al.* 2008). The differences in microorganisms will determine the differences in proteolytic, lipolytic, and glycolytic activities, and these will determine differences in the bioconversion of fat, protein, carbohydrate and other components (Tope 2014).

A number of *in vitro* tests revealed a few bioactive components in soybeans and products derived from soybeans that play a role in the treatment of obesity such as phenolic (isoflavone) component and peptides. Some of the mechanisms of these components can be seen in Table 2.

Table 1. The bioactive components in soybeans and the benefits for health (Sugano 2006)

Component	Health benefits
Protein	Hypocholesterolemic, antiatherogenic, reduces weight
Peptide	Easily absorbed, reduces weight
Lectin	Immunity, anticarcinogenic
Trypsin inhibitor	Anticarcinogenic
Dietary fiber	Improves the function of the digestive tract, prevents colon cancer, regulates the metabolism of fat
Oligosaccharide	Prebiotic, improves the function of the digestive tract
Phytin	Regulates carbohydrate metabolism, anticarcinogenic, aids in mineral absorption
Saponin	Regulates fat metabolism, antioxidant
Isoflavone	Esterogen functions, prevents osteoporosis, anticarcinogenic
Linoleic acid	Essential fatty acid, hypocholesterolemic
Linolenic acid	Essential fatty acid, hypocholesterolemic, improves the function of the cardiovascular system, antiallergy
Lecithin	Increases the metabolism of fat, maintains nervous functions
Tocopherol	Antioxidant, prevents cardiovascular diseases
Sterol	Hypocholesterolemic, prevents prostate cancer
Vitamin K	Aids in blood clotting, prevents osteoporosis
Mg	Essential mineral, prevents cardiovascular problems

Table 2. Bioactive components in tempe for the treatment of obesity

Product	Bioactive component	Research method	Active physiological properties	References
Soybean tempe with *R.oligosporus* NRRL 2710	E peptide and I peptide	Antioxidant through the ferric thiocyanate method	Positive antioxidant activity, and E peptide also has an ACE inhibition property with an IC_{50} of 0.6±0.1µM	Gibbs *et al.* (2004)
Solid state bioprocessed soybeans with *R.oligosporus*	Phenolic component	Inhibition of amylase, α-glucosidase, and antioxidant through the DPPH method	Maximum inhibition of amylase on day 4 of fermentation with an inhibition index (AI) of 2.08. Highest glucosidase inhibition on day 6 of fermentation, AI=1.1. A correlation of R=0.85 between antioxidant activity and amylase inhibition	McCue *et al.* (2005)
Solid state bioconversion (SSB) of soybeans with *R.oligosporus*	Phenolic component	Inhibition of amylase, α-glucosidase, and antioxidant through the DPPH method	Highest antioxidant on fermentation day 4, 57.4% higher than soybeans without fermentation, highest amylase inhibition on day 6 of fermentation, AI=3.6, highest glucosidase inhibition on day 6 of fermentation, AI = 2.0	Maiti and Majumdar (2012)

1.1. *Phenolic component and isoflavone*

In Indonesia, soybeans are processed into tempe, tofu, soy sauce, *tauco*, and soymilk. Among those soybean products, tempe is the food with the highest isoflavone aglycone thus provide higher bioavailability compared to other soybean products (Haron *et al.* 2009). Raw tempe has an isoflavone content of 54 mg/100 g (bb), while tofu and soymilk have a lower isoflavone content of 43 and 28 mg/100 g (bb), respectively.

Mold fermentation helps activate the soybean's isoflavone component (Figure 1) from the glycone form (daidzin and genistin) to aglycone (daidzein and genistein) that are more readily absorbed by the body (Astawan 2008) and also increases the antioxidant activity (Astawan *et al.* 2013). Efriwati and Nuraida (2013) found that the genistein and daidzein contents of tempe were 9.4-10.0 and 93.4-101.2 mg/100 g tempe (b.k), respectively. Haron *et al.* (2009) found that the total isoflavone aglycone was 54 mg/100 g tempe (b.k) with almost identical amounts of daidzein and genistein, 26±6 mg and 28±11 mg.

The bioconversion of glycone isoflavone and the improved bioavailability of isoflavone would increase the active physiological properties of tempe in comparison to soybean, for example in condition such as hypotriacylglycerol (Watanabe *et al.* 2006) and hypocholesterolemic (Astuti 1997) that usually occur in obesity cases. Figure 1 shows the chemical structure of soybean isoflavones according to Shao *et al.* (2009).

Isoflavones also play many roles in the inhibition of carbohydrate-digesting enzymes. Lee and Lee (2001) demonstrated that genistein is an effective α-glucosidase enzyme inhibitor, is reversible, slow-binding and non-competitive. The product of soybean fermentation using *R. oligosporus* demonstrated an amylase inhibition of 1.5-2.0 AI (Amylase Inhibition Index) which correlated with the total phenol value (R=0.59) (McCue *et al.* 2005; Maiti & Majumdar 2012).

In addition, Genistein also has a potential as an antiobesity through the activation of the AMP-activated kinase (AMPK) in the inhibition of lipid differentiation (Hwang *et al.* 2005). Genistein (20-200 uM) could significantly inhibit 90% of adipose tissue differentiation from 3T3-L1 cells and also induce apoptosis (43%) in mature adipose tissue (Hwang *et al.* 2005). *In vivo* testing of 0.2% genistein + 0.5% L-carnitine in C57BL/6J rats with high-fat feed demonstrated a decrease in body weight of 254% after 12 weeks of the experiment. This was believed to be due to a PPAR activation inhibition mechanism (Yang *et al.* 2006). Numerous benefits of soybean isoflavones and their increased amount in tempe create an opportunity to utilize tempe in the treatment of obesity.

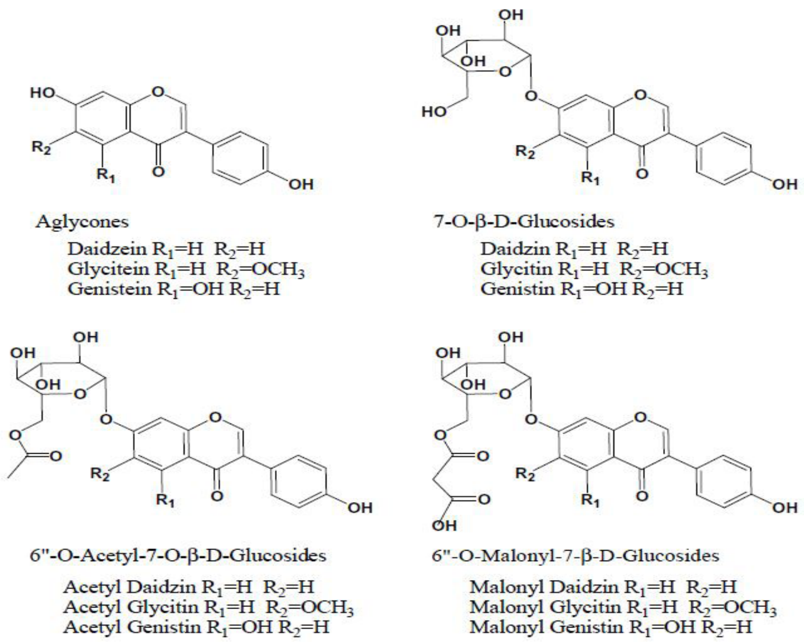

Figure 1. The chemical structure of soybean isoflavones (Shao *et al.* 2009)

1.2. ***Protein and or peptides***

Other components of soybeans that play a part in obesity treatment are protein and peptides. Wang and Huang (1984) discovered a protein found in soybean, sunflower seeds, peanuts, and cucumber seeds which have an antiobesity potential through a lipase inhibition mechanism. The inhibition effect was strongly influenced by heat and the role of protease and was not dependent on the amount of the enzyme lipase but depended on the amount of substrate. A large amount of substrate eliminated the lipase inhibition effect, thus in the application, limitation of fat consumption was also required for an optimum lipase inhibition benefit.

The lipase inhibition mechanism is believed to be through the binding of protein on the surface of the substrate micelle, preventing the normal lipase function which works on the interfacial area between the medium (water) and the surface of the micelle (Wang & Huang 1984). This soybean protein component is believed to still be present in tempe, or the lipase inhibition activity in tempe could still be maintained by other, smaller proteins or peptides produced through tempe fermentation. Gibbs *et al.* (2004) demonstrated an increase in dissolved protein in tempe compared to soybean, plus antioxidant properties and other active physiological actvities.

Singh *et al.* (2014) stated that bioactive peptides from soybeans and its products also have antiobesity properties through a number of mechanisms such as anorexia or appetite suppression, inhibition of lipogenesis in the liver (decreasing the triglyceride and cholesterol levels in the blood), and inhibition of the activation of the hormone cholecystokinin (CCK), causing satiety. Jang *et al.* (2008) stated that in overweight rats induced by high-fat feed, supplementation of peptides from black soybeans for 13 weeks has shown weight loss, decreased leptin level and decreased appetite compared to the controls.

2. The Effect of soybeans and tempe in obesity treatment

A few *in vivo* studies related to the effect of soybean and or tempe consumption on obese test animals can be seen in Table 3. Obesity is usually associated with insulin resistance and abnormalities in lipid metabolism in the form of increased overall lipid production such as increased free fatty acids, triglycerides, and LDL (Yuliana *et al.* 2011). Metabolomic issues such as dyslipidemia and or diabetes as an effect of obesity can be managed by consuming soybeans, soybean products such as tempe, or soybean hydrolysate as a source of protein. Watanabe *et al.* (2006) and Astawan *et al.* (2015) demonstrated an improvement in lipid profile, especially an increase in HDL due to consumption of tempe feed (isocaloric) compared to consumption of casein or soybean.

Table 3. *In vivo* studies related to the effect of soybean and or tempe consumption on obesity treatment

Model	Feed and Amount	Time	Results	References
Wistar male rats	Three groups: casein, soybean, and tempe-GABA with *R. microspores* inoculum fermented aerobically and anaerobically. Isoprotein (30%), previously fed high-fat feed (20%)	6 weeks	No difference in weight. A significant difference in cholesterol and triacylglyceride levels in plasma, namely casein>soybean>tempe-GABA. The highest HDL in the tempe-GABA group. The highest LDL in the casein group.	Watanabe *et al.* (2006)
Adult male Sprague-Dawley rats and yellow KK mice, made obese	Three groups: casein, protein soybean isolate (SPI), and soybean protein hydrolysate (SPI-H) Low-calorie feed (60%), high protein (35%) and low fat (5%), previously fed high-fat feed (30%)	4 weeks	Adult rats: lower fat absorption in SPI and SPI-H compared to that in casein, total cholesterol, and blood glucose lower in SPI-H. Mice: significantly lower body fat in SPI and SPI-H than in casein.	Aoyama *et al.* 2000a
Male yellow KK mice, made obese	Four groups: casein (WPI), casein hydrolysate (WPI-H), soybean protein isolate (SPI), and soybean protein hydrolysate isolate (SPI-H) Feed as in Aoyama *et al.* 2000a	2 weeks	A significant descrease in the body weight of SPI-H rats compared to WPI and WPI-H. Total plasma cholesterol, blood glucose, and body fat level lower in SPI-H than in WPI and WPI-H.	Aoyama *et al.* 2000b
Obese (weight: 125 g) and normal (96 g) SHR/N-cp rats	Fours groups: 20% casein (normal), casein +0.1% isoflavone, casein +0.1% probiotic, casein +0.1% isoflavone +0.1% probiotic; Isocaloric.	20 weeks	The isoflavone group had a significant loss of body weight, epididymal, perirenal, subdiaphragmatic, ileal fat pad fat weight, and total cholesterol compared to the other treatments in obese rats.	Ali *et al.* 2004

An experiment using low calorie (60 %), high protein (35%) and low fat (5%) feed in obese rats demonstrated a decrease in body weight and an improvement in the condition of the body fat in rats fed with soybean protein isolate and soybean hydrolysate compared to those fed with casein and milk protein hydrolysate (Aoyama *et al.* 2000a, Aoyama *et al.* 2000b). The mechanism involved were decrease in perirenal fat and blood glucose concentration. Furthermore, Kagawa *et al.* (1996) suspected that the fat reduction effect was due to the activity of the tetrapeptide found in soybeans.

In addition to protein and or peptides activities, the decrease in body weight and the improvement in the lipid condition was also due to the activity of isoflavone (genistein, daidzein, and glycitein) (Ali *et al.* 2004) found in soybeans and tempe. Further, Watanabe *et al.* (2006) demonstrated that the protein, isoflavone and free amino acid components in tempe had a better hypotriacylglyceride effect than soybeans or casein.

Tempe, which contain protein composition that has been fermented into peptides (similar to the condition in soybean protein hydrolysate) and supported by higher isoflavone component than soybeans (Haron *et al.* 2009) or soybean hydrolysate, is of course expected to have more benefits for health including for obesity treatment. Unfortunately, no studies in place aimed at pertaining to this subject. The author has not found any clinical studies regarding the use of tempe in humans for the purpose of obesity control. However, one human study conducted by Astuti (1997) has demonstrated the benefits of tempe in improving the lipid or dyslipidemia status which is also commonly found in obesity cases (Table 4).

Many clinical studies pertaining to the use of soybeans in obesity treatment have been

Table 4. Studies in humans pertaining to the effect of consuming soybeans and or tempe in obesity treatment (Astuti 1997)

Product	Research method	Results
Tempe formula-based food	24 volunteers (8 men, 16 women), daily consumption of a tempe-based drink for three months	A decline in total cholesterol (8.6% in men, 10.25% in women), a decline in LDL (12% in men, 9.67% in women), a decline in MDA (23% in men, 15% in women).

conducted. Cope *et al.* (2008) reported in a review that a number of soybean-based food products will reduce body weight and eliminate fat when consumed isocalorically. This was proven through *in vivo* testing using model animals, though there are very few supporting clinical studies in humans.

Zhang *et al.* (2013) have conducted a meta-analysis of the efficacy of the consumption of a soybean isoflavone supplement on body weight, fasting blood glucose, and insulin in post-menopausal non-Asian women. Nine studies with 528 panelists for the parameter of body weight, 11 studies with 1,182 panelists for the parameter of blood glucose, and 11 studies with 1,142 panelists for the parameter insulin have been analyzed. These studies have demonstrated significant weight loss and a decrease in blood glucose and insulin in post-menopausal female panelists who had been given isoflavone as a supplement compared to the control group which was given a placebo. Furthermore, supplementation of isoflavone for a short time (<6 months) could significantly decrease weight, while long-term supplementation (>6 months) could significantly decrease blood glucose. A more significant weight loss was achieved through the consumption of a low dosage of supplement (<100 mg) and for those who were overweight (BMI <30) compared to those who were obese (BMI >30).

3. Tempe as a functional food in obesity treatment

Considering the various potentials of the bioactive components in tempe as an antiobesity, tempe could be made into an appropriate diet menu. Yenrina *et al.* (2006) stated a survey of 2,080 households on Java Island revealed that they consumed processed soybean products such as tofu, tempe, *oncom*, soybean sprouts, tofu skin, and soy sauce in daily basis. Unfortunately, many of the processes involved frying, especially for tempe.

The frying process would increase fat intake (from the cooking oil absorbed by the product), indirectly increasing the caloric intake and could trigger obesity. Haron *et al.* (2009) stated that in 100 g raw tempe there is 205 ± 56 mg (dry weight) of isoflavone and the frying process would decrease the isoflavone by 45% to merely 113 ± 41 mg per 100 g (dry weight) of fried tempe. The correct tempe processing such as boiling or braising without frying or other processes that involve little fat could be considered as an alternative (Muaris 2016) in the optimation of tempe in obesity treatment diets.

Daily consumption of tempe in adequate amounts could support the daily plant-based protein and isoflavone intake. In 1995, the US FDA declared that a minimum of 25 grams of plant-based protein needs to be consumed daily as a part of a low fat and low cholesterol diet. Utari *et al.* (2011) suggested consumption of at least medium-sized slices of tempe (approximately 150 grams of tempe/day) cooked by steaming or boiling to improve the lipid profile. Consumption of that amount of tempe is equivalent to the consumption of 35 mg/day of isoflavone and is in line with the recommended daily isoflavone consumption which is 30-100 mg/day (Messina & Messina 2003). The effectiveness of tempe as a functional food in obesity cannot be achieved in a short time or with a certain dossage. Consuming tempe regularly with appropriate processing in the long term should be incorporated in the healthy living habit.

CONCLUSION

Based on the literature study, it is known that soybeans are beneficial in the treatment of obesity and its complications. Soybeans help reduce body weight and improve the body lipid condition. The bioactive components which are presumed to play a role are soybean protein, peptides, and isoflavone. The fermentation of soybeans into tempe can increase the amount and ability of these bioactive components. Optimation and popularization of tempe consumption as a functional food in the daily diet, supported with correct tempe processing (without frying), could be a solution in obesity treatment.

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