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Chapter 4

IMPACTS OF FRESH AND HEATED SOYBEAN OIL ON CARDIOVASCULAR DISEASE

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ABSTRACT

Soybean oil is used as cooking oil worldwide. It is rich in polyunsaturated fatty acids and vitamin E. It also contains phytoestrogen, and genistein. It possesses antioxidant and anti-inflammatory activities. Most cooking oils are used repeatedly by consumers to save cost of food preparation. Many studies have been conducted to investigate the effects of its dietary consumption on health. Fresh soybean oil gives many beneficial effects on lipid profile and blood pressure, while heated soybean oil is detrimental to health such as hypertension, dyslipidemia and it also promotes atherosclerosis. The detrimental effects of the soybean oil are likely due to diminished antioxidant content upon heating. This review discusses the effects of fresh and heated soybean oil on cardiovascular disease which includes dyslipidemia, hypertension, and coronary heart disease.

Keywords: vegetable oil, hypertension, dyslipidemia, atherosclerosis, health, heart disease

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INTRODUCTION

Cardiovascular disease is a major cause of morbidity and mortality worldwide. High fat diet is known as one of important risk factors for cardiovascular disease, which includes hypertension, atherosclerosis and cardiac-related diseases. Oxidative stress is strongly believed to play a major role in the development of these diseases (Siti et al. 2015). Increased oxidative stress leads to many pathological changes such as damage to endothelial cells and mitochondria, and even it alters the activities of enzymes (Hao et al. 2011; Kamisah et al. 2014). Therefore, it is hypothesized that antioxidants either from diet or supplements may prevent or reduce the development of oxidative insult.

Soybean oil is rich in antioxidants. It is produced from the seeds of *Glycine max* and the second most commonly used vegetable oil globally (Statista 2016). The oil has a big variety of usage. It is used for salad dressing, frying, baking, shortenings and many others (SoyConnection 2016). It has been shown to possess antioxidant and antiinflammatory properties in ovariectomized rats (Hassan and Abdel-Wahhab 2012; El Wakf et al. 2014). However, long term (more than 9 months) consumption of soybean oil may increase oxidative stress in heart and liver, as shown in rats due to its high content of polyunsaturated fatty acids (PUFA) which is susceptible to oxidative insult (Ima-Nirwana et al. 1996).

Cooking oil is usually used repeatedly for frying to reduce cost in food preparation (Azman et al. 2012). However, this practice is unhealthy due to production of harmful products in the heated oil. Several complex chemical reactions take place in the oil during heating at high temperature which are dependent on many factors like temperature, duration of heating, type of frying materials and oils, as well as the amount of oxygen and antioxidant presence (Choe and Min 2007; Leskova et al. 2006). Fatty acid configuration of the repeatedly heated oils also changes from *cis* to *trans* isomer (Velasco et al. 2004). Peroxide value and malondialdehyde contents, two lipid peroxidation markers are increased with increasing frequency of heating of the oil (Kamisah et al. 2012; Jaarin and Kamisah 2012). The oxidative stability of the heated oil may be improved with addition of natural and synthetic antioxidants like curcumin, sesamol and γ-oryzanol (Ravi Kiran et al. 2015).

COMPOSITION OF SOYBEAN OIL

Fresh soybean oil contains about 15% saturated, 23% monounsaturated fatty acids (MUFA) and 62% PUFA (Ohara et al. 2008). The major saturated fatty acids in the oil are palmitic (16:0) and stearic (18:0) acids, whereas the major MUFA found in the oil is oleic acid (18:1). The main PUFA contained are linoleic (18:2) and α-linolenic (18:3) acids (Table 1). Linoleic acid is an omega-6 fatty acid, while α-linolenic acid is an omega-3 fatty acid. Compared to other vegetable oils, the soybean oil has lesser MUFA content than canola oil and virgin olive oil.

Soybean oil is considered having less desirable fatty acid composition, due to its lower MUFA composition than other edible oils (White 2007). Intake of edible oils rich in MUFA is considered healthier (Terés et al. 2008). One technique to produce soybean oil with higher content of MUFA and lower PUFA is by introducing mutations in two fatty acid desaturase 2 genes (FAD2-1A and FAD2-1B). These genes are responsible in converting oleic acid to linoleic acid. This technique increases the oleic acid content in wild type soybean from about 20% to 80% and to decrease linoleic acid from 50-60% to 4-8% (Haun et al. 2014) (Table 1). Another method is by partial hydrogenation. However, the negative impact of this method is production of *trans* fatty acids, the bad fatty acids which are harmful to health due to their bad effects on lipid profile (Lichtenstein et al. 2006). This oil in its fresh state only contains neligible amount of *trans* fatty acids (Lichtenstein et al. 2006).

Heating soybean oil using an electric oven for more than five times on the other hand, had increased the composition of saturated fatty acids comprising myristic, palmitic and stearic acids and reduced PUFA (linoleic and linolenic acids), from about 15% to 21% and 62% to 48%, respectively. The oleic acid was also increased from about 23% to 31% (Awney 2011). A similar trend was also seen when the oil was used repeatedly for frying more than five times in an open wok (Kamisah et al. 2012). Caprylic acid (C8:0), a short chain saturated fatty acid which was initially absent in fresh soybean oil, started to build up in the oil after two hours of heating at 180°C. After 16 hours of heating, more than 3000 ppm of this fatty acid was detected (Kim et al. 2013). It is one of major fatty acids from the decomposition of unsaturated fatty acids (Frankel 1985). These findings are suggestive that regardless of heating methods, fatty acid composition is altered in thermally oxidized soybean oil.

Table 1. Fatty acid composition (%)* in some vegetable oils

Fatty acid		Soybean oil	High-oleic soybean oil	Canola oil	Palm oil	Virgin olive oil	Sunflower oil	Safflower oil
12:0	Lauric acid	-	-	-	-	-	0.02	-
14:0	Myristic acid	0.1	-	-	-	-	0.09	0.1
16:0	Palmitic acid	10.5	7.0	3.8	43.5	14.6	36.2	6.7
16:1	Palmitoleic acid	-	-	0.2	-	1.7	0.12	0.08
17:0	Margaric acid	-	-	-	-	0.2	0.02	0.04
17:1	Margaroleic acid	-	-	-	-	0.3	-	-
18:0	Stearic acid	3.6	5.0	1.9	4.0	3.3	2.8	2.4
18:1	Oleic acid	23.2	80.0	59.0	38.7	80.8	28.0	11.5
18:2	Linoleic acid	54.5	4.0	21.2	10.6	10.2	62.2	79.0
18:3	Linolenic acid	7.2	4.0	11.2	0.2	0.8	0.16	0.15
20:0	Arachidic acid	0.3	-	0.5	-	0.5	0.21	-
20:1	Gadoleic acid	0.2	-	1.5	-	0.4	0.18	-
22:0	Behenic acid	0.4	-	0.3	-	0.1	-	-
22:1	Erucic acid	0	-	0.4	-	-	-	-
24:0	Lignoceric acid	-	-	-	-	<0.1	-	-
SFA		14.9	12.0	6.5	47.5	18.7	39.34	9.24
MUFA		23.4	80.0	61.1	38.7	83.2	28.3	11.58
PUFA		61.7	8.0	32.4	10.8	11.0	62.36	79.15

* The highest values possible.

Sources: Alvarruiz et al. (2015); Aniolowska & Kita (2016); Ohara et al. (2008); Orsavova et al. (2015); Haun et al. (2014).

Isoflavones or phytoestrogens are present in a little amount in crude soybean oil compared to other soybean-based products (Yue et al. 2007), and sometimes not detectable at all (Bhagwat et al. 2008). The isoflavones found are genistein, genistin, daidzin and daidzen with an average content of about 45 μg/kg refined oil (Zhao et al. 2015), while in the crude oil it is around 200 mg/kg oil (Yue et al. 2007). It also contains vitamin E which are α-, β-, γ- and δ-tocopherol and some α-tocotrienol with a total content of about 710 mg/kg oil. In heated soybean oil, the vitamin E content was greatly reduced (Adam et al. 2007). Rats consuming oxidized soybean oil had higher vitamin E catabolic and turn over rate (Liu and Huang 1996). The phytosterols found in the oil are campesterol, stigmasterol and β-sitosterol, which are about 850 mg/kg oil, considered lower than other vegetable oils such as oat and rice bran oils (Tong et al. 2014). There is no published report regarding the effects of heating on other micronutrients in the oil.

IMPACTS ON CARDIOVASCULAR DISEASES

Dyslipidemia

Composition of fatty acids in consumed oils affects plasma lipid profile in humans and experimental animals. Compared to animal fats in exception of fish oil, vegetable oils have better beneficial effects on health. It is believed that diet rich in saturated fat would increase cholesterol lipids, while MUFA and PUFA reduce cholesterol lipids (Krauss et al. 2000). With the current technology, vegetable oils have been modified to meet certain needs in food industry such as to improve oxidative stability and to increase shelf life (Clemente and Cahoon 2009). Therefore, the impacts of these modified oils on plasma lipid profile are also altered.

Many studies had been conducted to investigate the effects of soybean oil on lipid profile. In rats fed diet containing 20% fat either in the form of fish oil or soybean oil, the soybean group had higher plasma total cholesterol (TC), triglyceride (TG) and low density lipoprotein cholesterol (LDL), the bad cholesterol than the fish oil-fed group. However, the soybean oil also increased high density lipoprotein cholesterol (HDL), the good cholesterol (Park and Park 2009). When compared to oat and rice bran oils, soybean oil increased plasma TC and LDL after 30 days feeding period in rats but had comparable plasma HDL and TG. The MUFA contents in the oils were comparable, but soybean oil had slightly higher PUFA. Both oat and rice bran oils promoted more fecal lipid and bile acid excretion (Tong et al. 2014), which may explain the hypocholesterolemic effect of the oils compared to the soybean oil.

As mentioned before, soybean is genetically modified or the oil is partially hydrogenated to improve its fatty acid composition. Many varieties have been developed like low-saturated fatty acid soybean oil, high-oleic acid soybean oil and low-α-linolenic acid soybean oil (Haun et al. 2014; Lichtenstein et al. 2006). The effects on plasma lipid profile of these varieties and partially hydrogenated soybean oil were compared with the wild type soybean oil. In moderately hyperlipidemic subjects (male and female) who consumed diets containing these oils for 35 days, the partially hydrogenated soybean oil significantly increased TC, LDL and apolipoprotein B (apo B) levels, as well as the ratio of TC:HDL in these subjects, indicating the negative impact of hydrogenation on cardiovascular risk factors. The high-oleic acid soybean oil increased the levels of HDL and apolipoprotein A (Apo A), the good lipid parameters compared to the other groups (Lichtenstein et al. 2006). Buriti oil (*Mauritia flexuosa*) which contains about 92% of MUFA also showed more superior effects on plasma lipid profile than wild type soybean oil (Aquino Jde et al. 2015). The findings of these studies proved that consumption of dietaries with higher content of MUFA is beneficial to plasma lipid profile.

Unfortunately, this assumption is not always true since canola oil which is rich in MUFA (about 59%) (Ohara et al. 2008) was reported to shorten survival time in stroke-prone spontaneously hypertensive rats as well as increased TC and LDL (Cai et al. in press). Soybean oil containing diet (10%) for 26 weeks was shown to significantly reduce plasma TC, free cholesterol and TG in spontaneously hypertensive rats compared to canola oil (Ohara et al. 2008), suggestive that the culprit is other than the fatty acid that yet to be discovered. It is believed that the high content of phytosterol in the canola oil is responsible for the detrimental effect of the oil (Ratnayake et al. 2000). It is further confirmed by an addition of phytosterol into soybean oil which later increased systolic blood pressure and promoted the onset of stroke, hence reduced survival time (Ogawa et al. 2003).

In daily cooking activities, there is a tendency for cooking oil to be used repeatedly. Soybean oil which was heated repeatedly more than 5 times and fed to rats for 12 weeks, increased plasma total cholesterol and LDL, as well as a reduction in HDL level when compared to the group that was fed fresh soybean oil (Awney 2011). In ovariectomized rat fed a high-cholesterol diet, an atherosclerotic model, feeding once-heated and five-time-heated soybean oil elevated plasma levels of TC, LDL and reduced HDL level (Adam et al. 2008).

Atherosclerosis

Atheroslerosis is a phenomenon characterized by hardening of blood vessel wall due to accumulation of white blood cells and and proliferation of intimal smooth muscle cells. One factor that enhances the formation of atherosclerotic plaque is high-fat diet. Therefore, atherosclerosis is strongly associated with altered lipid profile, which are elevated LDL and reduced HDL. In relation to this, atherogenic indices, defined by the ratios of the logarithm values of TG/HDL, LDL/HDL, TC/HDL (Nikniaz et al. 2016) and the ratio of (LDL+VLDL)/HDL (Hassan and Abdel-Wahhab 2012), are used as a sensitive predictor of plasma atherogenicity in promoting atherosclerosis and cardiovascular risk (Dobiásová and Frohlich 2001).

Ovariectomy increased TC, TG, LDL and VLDL, as well as decreased HDL levels due to estrogen deficiency in rats. Suplementation of soybean oil in diet reversed the negative impacts of ovariectomy on the blood lipid profile, hence reduced the atherogenic index in these rats (Hassan and Abdel-Wahhab 2012). In human subjects with moderate hypercholesterolemia, dietary soybean product as the main food component had significantly increased HDL level and then reduced the atherogenic index (LDL/HDL) when compared with the group that consumed cows' milk product. However, when the cows' milk products and soybean oil were combined in the diet, no significant reduction in the HDL level and ratio was seen (Kurowska et al. 1997). The findings were suggestive of the positive effects of soybean products including soybean oil on lipid profile and its antiatherogenic potential.

Consumption of once- and five-time-heated soybean oil for 4 months in ovariectomized rats fed a high-fat diet had negatively altered serum lipid profile by increasing TC, LDL and TG as well as decreasing HDL (Adam et al. 2008). From histomorphometric study, the thermally oxidized oil had increased thickness of the aortic intima and media in the rats, which were similar in both groups of once- and five-time-heated oil. When observed under electron microscope, the aortic endothelial cells showed early signs of apoptosis in both heated oil groups, with increased thickness of subendothelial layers. Rats fed with fresh soybean oil showed no obvious aortic ultrastructural changes (Adam et al. 2009). Apoptosis occurs due to an accumulation of oxidized LDL in macrophages during the progression of atherosclerosis (Shi et al. 2007). Ng et al. (2012) also reported similar findings. They observed increases in aortic wall thickness and area as well as circumferential wall tension in normotensive rats fed five- and ten-time-heated soybean oils for 6 months. Elastic lamella in the aortic tunica intima of the groups was disarrayed and fragmented, together with increased expressions of adhesion molecules. The changes seen in these studies can be collectively concluded that prolonged intake of heated soybean oil may contribute to the progression of atherosclerosis.

Hypertension

Positive effects of soybean oil on hypertension have been demonstrated in many studies. Feeding dietary soybean oil for 12 weeks had reduced blood pressure in spontaneously hypertensive rats (Aguila et al. 2005). However, substitution of corn oil with soybean oil in hypertensive rats increased mean arterial blood pressure (Mattson et al. 2005). Meanwhile in humans, soybean oil incorporated into diet decreased diastolic blood pressure after 3 months in hypertensive subjects but no effect was seen on systolic blood pressure. The effects were comparable to olive oil-treated group. Both oils also reduced plasma tissue-type plasminogen activator antigen (t-PA), plasminogen activator inhibitor antigen (PAI-1) and prothrombin fragments. These findings suggest that soybean oil may cause hyperfibrinolysis and thrombin generation, both are important factors in progressing hypertension (Trifiletti et al. 2005). The beneficial effects of soybean oil in reducing hypertension are believed via many mechanisms. It is possible that the protective effect of the oil could also be due to angiotensin-converting enzyme inhibitory properties, just like the soybean protein, which also possesses hypotensive effects via inhibition on the enzyme (Yang et al. 2008), or reduction in renal cyclooxygenase-2 expression (Ohara et al. 2008) and/or restoration of plasma nitric oxide levels (Simão et al. 2010). Angiotensin-converting enzyme is responsible to convert angiotensin I to angiotensin II, which the latter is a potent vasoconstrictor, resulting in a raised blood pressure (Taylor and Pool 2011). While cyclooxygenase-2 enzyme stimulates renin-angiotensin-aldosterone system, also leading to increased arterial pressure (Quadri et al. 2016).

When compared with olive oil, soybean oil supplementation for 2 weeks was not effective to reduce blood pressure in normotensive female rats. High-oleic acid content in the olive oil was believed to be responsible for the hypotensive effect of oil (Terés et al. 2008). An epidemiology study also showed an inverse relationship between diastolic blood pressure and oleic acid intake (Miura et al. 2013). Therefore, modification of the soybean oil producing high-oleic soybean oil is expected to improve the hypotensive property of the oil. A recently published systematic review on the substitution of high-oleic vegetable oils for vegetable oils rich in saturated fatty acids suggested that the use of novel high-oleic soybean oil would give favorable effects on plasma lipid profile and cardiovascular health (Huth et al. 2015). So far, there is no scientific report on the effects of high-oleic soybean oil on cardiovascular disease.

On repeated heating, soybean oil loses its beneficial effects due to destruction of the minor components like vitamin E (Adam et al. 2007) and alteration of fatty acid composition ((Awney 2011; Adam et al. 2008). Soybean oil has significantly increased peroxide value after being heated twice (Leong et al. 2010). Normotensive rats that were fed once-, twice-, five-time- and ten-time-heated soybean oil for 6 months had significantly higher systolic blood pressure than fresh soybean oil group. The elevation in blood pressure was associated with reductions in plasma nitric oxide level and vascular relaxatory response, as well as an increase in vascular contraction (Jaarin et al. 2011). Raised activity of plasma angiotensin-converting enzyme and lower plasma heme oxygenase activity were also noted in rats that were fed heated soybean oil (Leong et al. 2010). Heme oxygenase is involved in blood pressure regulation by reducing the activity of angiotensin II (Stec et al. 2012). Similarly, Ng et al. (2012) also demonstrated that five- and ten-time-heated soybean oil also increased blood pressure in normotensive rats as early as one month of feeding period. In these rats, the heated oils also increased plasma thromboxane and prostacycline ratio after 6 months. Thromboxane promotes vasoconstriction, while prostacycline has the opposite effect (Muzaffar et al. 2011).

Contrary to above studies, Yen et al. (2010) reported that heated soybean oil diet for 10 weeks failed to increase systolic blood pressure in normotensive rats and feeding the diet to spontaneously hypertensive rats did not further increase the blood pressure. The discrepancy in these findings could be due to the difference in baseline systolic blood pressure. In Yen et al. (2010) study, the baseline (week 0 of feeding) systolic blood pressure in the both normotensive and hypertensive rats were about 140 mmHg. While in Ng et al. (2012) study, it was about 110 mmHg in normotensive rats, which was later elevated to about 145 mmHg after 24 weeks. This might explain the difference in both studies.

Coronary Heart Disease

A study by Aguila et al. (2004) showed that long term intake of soybean oil for 13 weeks had mild effect on myocardial structures in spontaneously hypertensive rats. It somehow decreased the damage to cardiomyocytes and intramyocardial vessels induced by hypertension in these rats. Its effect was similar to that of olive oil, suggestive that both oils had some cardioprotective effects. The cardioprotective effects of soybean oil were also reported by Ribeiro et al. (2010). In their study, soybean supplementation (100 μl) intramuscularly for 15 days had increased left ventrivular contractility without affecting systolic and diastolic blood pressure in rats. The inotropic response might be associated with increased myosin ATPase and Na^+-K^+ATPase activities as well as increased expressions of sodium-calcium exchanger and sarcoplasmic reticulum calcium pump (SERCA2a) observed in these rats compared to the control. These parameters are involved in myocardial mechanics.

A study conducted on Finnish subjects (676 men and 591 women) without known coronary heart disease, showed that replacement of dairy fat with vegetable oil, primarily soybean oil in the diet for 6 years, significantly reduced the incidence of major cardiovascular event or coronary heart disease death by 67% in men and 60% in women. The intervention diet contained less saturated fat and rich in PUFA, in particular α-linolenic acid (Turpeinen et al. 1979; Miettinen et al. 1983). Many other studies had reported the beneficial effects of high intake of α-linolenic acid on coronary heart disease (Zatonski et al. 2008; Albert et al. 2008). However, a recent study conducted in Dutch population showed that α-linolenic acid intake had no association with coronary heart disease incidence, but a low intake of the fatty acid might be a risk factor for incident stroke (de Goede et al. 2011).

A randomized, single-blind trial was conducted in two groups of patients with coronary artery diseases (such as myocardial infarction, angina pectoris and stroke). A group consumed a local diet similar to the step I National Cholesterol Education Program (NCEP) prudent diet and served as the control, while another group (intervention group) consumed an Indo-Mediterranean diet, which was rich in α-linolenic acid, had increased intake of whole grains and mustard or soybean oil. After 2 years, the intervention group had significantly lower serum cholesterol levels, fewer non-fatal myocardial infarction, sudden cardiac death and cardiovascular events than the control group (Singh et al. 2002). The protective effects of soybean oil are most probably due to its rich content of omega-3 (α-linolenic acid) (Covington

2004). The fatty acid is an essential fatty acid, can be only obtained through diet or supplementation. Omega-3 fatty acids have been shown to possess antiarrhythmic (Christou et al. 2015) and antithrombotic (Li et al. 2015) properties.

Intake of partially hydrogenated soybean oil in the diet had increased the level of lipoprotein[a] in healthy male subjects. Hydrogenation had significantly increased the percentages of *trans* fatty acids in the soybean oil (Almendingen et al. 1995). The liporoptein[a] is highlighted as an independent cardiovascular risk factor, which is assoaciated with coronary artery disease (Nordestgaard et al. 2010). However, no published study was reported on the effects of heated soybean oil consumption on coronary artery disease.

CONCLUSION

Fresh soybean oil gives many beneficial effects on lipid profile, blood pressure and other cardiovascular diseases due to its fatty acid composition and antioxidant properties. However, consumption of heated soybean oil may impose hazardous effects on cardiovascular disease.

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