

## Review Article

# Heated cooking oils and its effect on blood pressure and possible mechanism: a review

Kamsiah Jaarin<sup>1</sup>, Norliana Masbah<sup>1</sup>, Siti Hawa Nordin<sup>1,2</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia; <sup>2</sup>Department of Basic Medical Sciences, Faculty of Medicine, Universiti Sultan Zainal Abidin, Terengganu, Malaysia

Received September 19, 2015; Accepted December 4, 2015; Epub February 15, 2016; Published February 29, 2016

**Abstract:** Studies have shown that oxidative stress and endothelial dysfunction involved in the development of hypertension. Repeated heating of cooking oils caused thermal oxidation which produces harmful products including free radicals. Hence, repeatedly heated cooking oils may be responsible for an increase in blood pressure or hypertension. The present review compared the effect of few heated vegetable oils on blood pressure and possible mechanisms of the blood pressure raising effect were discussed. Studies have reported that heated oils cause oxidative stress, vascular inflammation leading to endothelial dysfunction. The impaired endothelial function then may interfere with the homeostasis of endothelial derived relaxing and constricting factors. This subsequently leads to an increase in vascular reactivity and blood pressure.

**Keywords:** Heating, cooking oils, blood pressure, vascular reactivity, inflammation

## Materials and methods

Ovid Medline (published between 1946 and 2015) and Scopus (published between 1946 and 2015) database were used for articles collection. The search strategy involved a combination of the following sets of keywords (1) heated OR therm\* OR oxidised OR oxidized AND; (2) vegetable oil\* AND; (3) hypertens\* OR blood pressure OR vascular OR endotheli\*.

## Introduction

Hypertension has been associated with cardiovascular morbidity and mortality due to stroke, myocardial infarction and kidney failure [1]. The prevalence of hypertension amongst Malaysian aged more than 30 years old has increased from 32.9% in 1996 to 40.5% in 2004 [2]. By 2025, 29% of the world's adult populations are expected to have hypertension [3]. Many factors contribute to blood pressure (BP) variation including genetic factors, dietary habit and lifestyle. Various studies in humans and animals have been performed to determine the role of saturated and unsaturated fatty acids in hypertension [4-7]. Consumption of diet rich in un-

saturated fatty acids was found to decrease BP [8, 9]. Olive oil, a main ingredient of the Mediterranean diet, was found to decrease systolic and diastolic BP [10]. There is a high tendency for public to reuse the frying oils in cooking to save cost of food preparation [11]. This practice is detrimental to health as repeatedly heated oils undergo a series of chemical reaction known as thermal oxidation. Thermal oxidation products of heated oils include free radicals which are implicated in the pathogenesis of many diseases including hypertension [12]. Oxidative stress which is an imbalance between production of reactive oxygen species (ROS) and antioxidant dependence system is capable to induce lipid peroxidation and free radicals formation. Oxidative stress and lipid peroxidation have been implicated in the pathogenesis of hypertension and atherosclerosis [13-15]. Oxidative stress-induced endothelial injury impairs endothelial-dependent vasodilation which subsequently increases vascular reactivity and resistance. ROS may enhance sequestration of nitric oxide-forming peroxynitrite which itself is a free radical. Furthermore, ROS cause vascular inflammation and activation of growth sig-

## Heated cooking oils and blood pressure

**Table 1.** Effect of heated oil on blood pressure

Studies	Effect
Osim et al., 1996 (palm oil)	↑
Soriguer et al., 2003 (human study)	↑
Yen PL et al., 2010 (Soy oil)	No changes
Jaarin K et al., 2011 (Soy oil)	↑
Jaarin K et al., 2011 (Palm oil)	↑
Nurul-Iman BS et al., 2013	↑
Bautista R et al., 2013	No changes
Hamsi MA et al., 2014 (virgin coconut oil)	↑
Beshel FN et al., 2014 (palm oil)	↑
Jaarin K et al., 2015 (Corn oil)	↑

↑ indicates increase.

nalling pathway [16, 17]. Evidences suggest link between oxidative stress and hypertension. Hypertensive patients have been reported to have high levels of malondialdehyde (MDA) which is a breakdown product of lipid peroxidation and lower antioxidant activities. A recent study has demonstrated linear positive correlation between blood pressure and oxidative stress [18]. On the other hand, there was a negative correlation between blood pressure and antioxidant activities [19]. Previous studies have shown that heated oils cause lipid peroxidation and increase risk of atherosclerosis [20, 21].

Since heated oil cause lipid peroxidation and oxidative stress play important roles in CVD including hypertension [22]. This review article compare the effect of heated monosaturated and polyunsaturated cooking oils on blood pressure. The possible mechanism of blood pressure raising effect of heated oil was highlighted.

### The effect of heated vegetable oils on blood pressure (BP)

Earlier studies in humans and animals have been done to determine the relationship between heated cooking oil and hypertension. The earlier study that described the detrimental effect of heated vegetable oil on blood pressure was done by Osim et al., 1996 [23]. The study reported the mean arterial blood pressure of rats following chronic consumption of a diet that contained 15% oxidized palm oil was significantly increased compared to the control and fresh oil group. The detrimental effect of

thermal-oxidized oil on blood pressure was further demonstrated in human by Soriguer et al., 2003 [12]. The study reported that polar compounds which indicate the degradation degree of cooking oil were strongly and positively associated with high blood pressure. On the other hand, the concentration of monounsaturated fatty acids and serum phospholipids were negatively correlated to hypertension.

Subsequent studies were undertaken to determine the link between heated oil and blood pressure with emphasis on possible mechanisms of action [24-32]. Jaarin et al., 2011 reported that fresh palm and soy oil had no effect on blood pressure (BP) [27]. However, in contrast, heated twice, five times and ten times palm and soy oil increase blood pressure. The percentage increased in blood pressure with heated twice palm oil (2HPO), heated five times palm oil (5HPO) and heated ten times palm oil (10HPO) were 22.4%, 23.9% and 25.4% respectively. The same study demonstrated that heated once soy oil (1HSO), heated twice soy (2HSO), heated five times soy oil (5HSO) and ten times soy oil (10HSO) increase BP. The percentage increase in BP with soy oil were 16%, 23.0%, 25.9% and 34.4% respectively. It thus appears that heated soy oil had a more detrimental effect on blood pressure (BP) as the significant increase in BP was already noted with 1HSO and the percentage increase was higher with heated ten times soy (34.4%) compared to palm oil (25.4%). In this study, it was reported that once heated soy oil (1HSO) already caused 16% increase in BP compared to palm oil. This study stated that the percentage increase in BP was higher with increasing heating frequency [27]. Jaarin K et al., 2015 (unpublished data) reported a similar increase in BP occurred with heated corn oil. The study reported that five times heated corn oil (5HCO) and ten times heated corn oil (10HCO) produced 14.5% and 15.3% increase in blood pressure respectively. Thus, it appears that the percentage increase in BP was significantly lower for heated corn oil compared to heated palm and soy oil. The reason was unclear although both soy and corn oil are polyunsaturated oil. However, the effect of heated oil on BP was not supported by Bautista et al., 2014 as their study reported that heated canola oil had no significant effect on BP despite reduced acetylcholine-induced vasorelaxation and increased PE-induced vasocon-

## Heated cooking oils and blood pressure

**Table 2.** Effect of heated oil on acetylcholine-induced vasodilation and phenylephrine-induced vasoconstriction

Studies	Acetylcholine-induced vasodilation	Phenylephrine-induced vasoconstriction
Osim et al., 1996 (palm oil)	Not done	Not done
Owu DU et al., 1997 (palm oil)	↓	↑ (Noradrenaline)
Soriguer et al., 2003 (human)	Not done	Not done
Yen PL et al., 2010 (Soy oil)	Not done	Not done
Jaarin K et al., 2011 (Soy oil)	↓	↑
Jaarin K et al., 2011 (Palm oil)	↓	↑
Nurul-Iman BS et al., 2013	↓	↑
Bautista R et al., 2013	↓	No changes
Hamsi MA et al., 2014 (virgin coconut oil)	↓	↑
Jaarin K et al., 2015 (Corn oil)	↓	↑

Symbols indicate: ↑ increase; ↓ decrease.

striction [32]. This finding was in line with Yen et al., 2010 that demonstrated heated soy oil had no effect on BP in Spontaneously Hypertensive rats (SHR) and normotensive rats [33]. The type of animal used in the studies and the duration of the study contributed to the discrepancy in the finding. Yen et al., 2010 and Bautista et al., 2014 used SHR rats and Wistar rats respectively [32, 33], whereas the previously mentioned studies [24-31] used Sprague-Dawley rats. The duration of study may be attributed to the different finding as the previously mentioned studies [24-31] studied the effect for 24 weeks, whilst Yen et al., 2010 and Bautista et al., 2014 studied the effect for shorter period which was for 10 weeks [32, 33]. Finding by Nurul-Iman et al., 2013 was in line with Leong et al., 2009 which reported that heated 5 times palm oil increase blood pressure [24-26, 30]. However, the blood pressure raising effect of palm oil was attenuated by supplementation of virgin coconut oil (VCO) which is rich in antioxidants. The protective effect of antioxidants on heated vegetable oil was also demonstrated by Perez-Herrera et al., 2013. This study reported that olive oil polyphenols protected oxidative stress induced by thermal oxidation of oil [34]. This finding again supported the role of stress oxidative and antioxidants in heated oil-induced hypertension. Although fresh VCO protects heated-oil induced hypertension, in contrast five times (5VCO) and ten times heated virgin oil (10HVCO) increase BP [31]. Recent study by Beshel et al., 2014 demonstrated that rats fed with photooxidized and thermally oxidized palm oil had increased blood pressure

while reduced glomerular filtration rate (GFR) and renal plasma flow [35]. This study give a possibility that heated oil may adversely affect renovascular system thus increase BP [35]. The effect of heated oil on BP was summarized in **Table 1**.

### Vascular reactivity

The blood pressure was determined by total peripheral resistance and cardiac output. The effect of heated oils on vascular resistance was determined by measuring the ability of the blood

vessel to contract (vasoconstriction) and relax (vasorelaxation) in response to certain concentrations of acetylcholine (ACH) or phenylephrine (PE). This study is called vascular reactivity study. Standard organ bath procedures in determining the vascular reactivity are invasive and practically suitable for animal study only. In human studies, the vascular response to vasoactive substances such as ACH and sodium nitroprusside can be done non-invasively via laser Doppler fluximetry or imager combined with iontophoresis of the vasoactive substances across the skin for microvascular endothelial function assessment [36], however to the best of our knowledge, no study had been done to see the effect of heated oil consumption in vascular response using this technique. Alternatively, flow-mediated dilation (FMD) is another non-invasive method to look at vascular reactivity and endothelial function. This method use flow stimulus, or more precisely shear stress instead of endothelial-dependent vasodilator drugs in order to provoke the endothelium to release NO with subsequent endothelium-dependent dilation (EDD) [37]. Human study by Williams et al. 2001 shown there was no change in EDD after meals rich in heated olive and safflower oils [38]. Similarly, partially hydrogenated soy bean oil also demonstrated no difference on postprandial FMD [39]. However these studies investigated in a small-size sample and short-term duration.

Heated oils had been reported to attenuate acetylcholine-induced vasorelaxation and enhanced PE-induced vasoconstriction in the

**Table 3.** Effect of heated oil on inflammatory biomarkers

Studies	VCAM	ICAM	CRP
Sutherland WHF et al., 2007	↑	Not done	Not done
Ng CY et al., 2012a (soy oil)	↑	↑	Not done
Ng CY et al., 2012b (palm oil)	↑	↑	Not done
Bautista R et al., 2013	↑	Not done	Not done
Hamsi MA et al., 2014 (virgin coconut oil)	↑	↑	↑
Jaarin K et al., 2015 (Corn oil)	↑	↑	↑

Abbreviations: VCAM, vascular cell adhesion molecule; ICAM, intercellular adhesion molecule; CRP, C-reactive protein. Symbols ↑ indicate increase. a, b indicate studies by the same author in the same year.

blood vessel of rat fed heated oils [24-26, 30, 32]. These findings suggested that heated oil increase vascular reactivity and promoting vasoconstriction. Thus, it may be responsible for the blood pressure raising effect of heated oil. Study by Owu et al. 1997 shows rather similar altered response except that this study used noradrenaline as the contracting factor instead of phenylephrine [40]. These studies suggested that heated oils cause vasoconstriction and thus it increase BP. Effects of fresh and heated oil on vascular reactivity were summarized in **Table 2**.

#### Heated oil and inflammatory biomarkers

Vascular inflammation, oxidative stress and vascular dysfunction have been reported to play an important role in pathogenesis of cardiovascular disease particularly hypertension and atherosclerosis [41-45]. The activated endothelium expresses adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1) and other chemotactic cytokines to accelerate and localise the inflammatory process [28, 29, 44]. At the same time, endothelial activation leads to reduction in the bioavailability of endothelium-derived vasoactive compounds such as NO, thus impairing endothelial function [45]. Altogether, these responses close a vicious, interlinking cycle between inflammation, oxidative stress and endothelial dysfunction leading to the development of hypertension.

Studies have shown that heated palm and soy caused an increase in aortic VCAM-1 and ICAM-1 expression (**Table 4**). The aortic VCAM-1 and ICAM-1 expression were found to be higher in rats fed with heated five times and ten times

palm and soy oil [28, 29]. A similar finding was noted for heated corn oil as heated once (1HCO), heated five times (5HCO) and ten times (10HCO) corn oil produced a significant increase in soluble VCAM-1 (sVCAM-1), ICAM-1 (sICAM-1) and C-reactive protein (unpublished data by Jaarin K et al., 2015). The effect of heated oil on inflammatory biomarkers was supported by Hamsi MA et al., 2015 which reported that ten times heated virgin coconut

oil caused significant increase in (sVCAM-1), ICAM-1 (sICAM-1) and C-reactive protein [31]. Bautista et al., 2014 supported that heated once and 10 ten times canola oil induced presence of nitrotyrosine in the aorta which indicate endothelial dysfunction [32]. Postprandial inflammatory response was increased after ingestion of heated sunflower oil as evidenced by increased NFkB and other inflammatory molecules like TNF- $\alpha$ , IL-1 $\beta$  and IL-6 in a randomized crossover study [46]. The effect of heated oil on inflammatory biomarkers was summarized in **Table 3**.

#### Correlation between blood pressure, VCAM-1 and ICAM-1 (Table 4)

Ng et al., 2012 demonstrated that there were strong positive correlation between VCAM-1, ICAM-1 and BP for heated palm oil and soy oil [28, 29]. The *r* values for VCAM-1 were 0.625, 0.751 respectively and the *r* value for ICAM-1 were 0.364, 0.627 respectively (**Table 4**). Hamsi et al. 2015 reported significant positive correlation between changes in BP with sVCAM-1, sICAM-1 and C reactive protein with *r* values of 0.592, 0.722 and 0.615 respectively [31]. However, only soluble ICAM-1 had a significant positive correlation with blood pressure for the corn oil (unpublished data by Jaarin K et al., 2015). Vascular dysfunction was also noted with long term feeding with food fried with canola oil [32]. The strong positive correlation between blood pressure and inflammatory biomarkers suggests that vascular inflammation plays important roles in pathogenesis of hypertension with heated oil. These studies, therefore suggest that heated oil induces vascular inflammation which may contribute to vascular dysfunction and hypertension.

## Heated cooking oils and blood pressure

**Table 4.** Correlation between blood pressure (BP) and VCAM-1 or ICAM-1 with heated oil

Studies	VCAM-1 & BP	ICAM-1 & BP	CRP & BP
Ng CY et al., 2012b (palm oil)	r = 0.625	r = 0.364	Not done
Ng CY et al., 2012a (soy oil)	r = 0.751	r = 0.627	Not done
Hamsi MA et al., 2014 (virgin coconut oil)	r = 0.592	r = 0.722	R = 0.615
Jaarin K et al., 2015 (corn oil)	r = 0.125	r = 0.345	Not done

a, b indicate studies by the same author in the same year.

### Oxidative stress

At high temperature heated oil undergoes a series of chemical reactions which include oxidation, hydrolysis, polymerization and isomerization. The reactions are deleterious to the stability of fatty acids and other biochemical parameters of the oil [47, 48]. Thermally heated cooking oil has been shown to cause 15-fold, 8-fold, 39-fold, 19-fold, 8.5-fold, 2.5-fold, increase in free fatty acid, peroxide value, *p*-anisidine value, total oxidation value, thiobarbituric acid-reactive substances (TBARS) value and trans fatty acid isomers respectively compared to the control [49]. The primary lipid oxidation products such as peroxides and hydro peroxides are unstable; they react rapidly with each other to form secondary lipid oxidation products. The products include volatile are alcohols, aldehydes, acids and ketones. Whilst the non-volatile compounds which includes carbonyls, polymeric and cyclic fatty acids. Several studies have examined the effect of heated vegetable oils on oxidative stress biomarkers in animal fed heated oil. The earlier study by Suomela et al., 2005 demonstrated that lipoprotein triacylglycerol and total lipids were more oxidized in pigs fed with diet rich in oxidized sunflower seed oil [50]. Adam et al., 2008 and 2009 demonstrated that heated palm and soy oil increased malondialdehyde (MDA) in rats fed heated oils [20, 21]. Yen et al., 2010 reported that heated soy oil increase thiobarbituric acid-reactive substances (TBARS) in rats [33]. The intake of heated sunflower oil-contained breakfast reduced plasma GSH levels and GSH/GSSG ratio, increased protein carbonyl levels and induced a higher gene expression of NADPH oxidase subunits, Nrf2-Keap 1 activation while addition of natural or artificial antioxidants could reduce postprandial oxidative parameters [34]. Total phenolics deteriorated with successive frying of virgin olive oil with only 20-30% of total phenolics left in the oil

after eighth frying [51]. Andrikopoulos et al., 2002 and Adam et al., 2007 demonstrated that heating reduces vitamin E concentration of heated oil [51, 52]. Adam et al., 2007 reported that more than 50% of  $\alpha$ -tocopherol and  $\alpha$ -tocotrienol were destroyed after once heating [52]. After five times heating

ing, more than 95% of  $\alpha$ -tocopherol and  $\alpha$ -tocotrienol in the palm oil were destroyed. After five times heating 82% of  $\alpha$ -tocopherol in the soy oil was destroyed.  $\gamma$ -tocopherol and  $\delta$ -tocotrienol appear to be more heat stable compared to  $\alpha$  isomers. Ingestion of thermally oxidized sunflower oil increased postprandial plasma peroxides (5-11%) significantly in a trial for both men with stable coronary artery disease and healthy men [53]. These findings therefore suggested that heating cause oxidative stress which may contribute to vascular dysfunction and hypertension.

### Nitric oxide and blood pressure regulating enzymes

Vascular endothelium produces a vast range of chemical mediators to regulate cellular adhesion, smooth muscle cell proliferation and vascular wall inflammation. Endothelial cells produce endothelial derived relaxing factors (EDRF) such as nitric oxide (NO) and prostacyclin ( $\text{PGI}_2$ ). NO is widely recognized as an important endothelium-derived vasodilator in regulating blood pressure. NO activates guanylate cyclase which increases the formation of cyclic guanosine monophosphate (cGMP), which ultimately causes vascular smooth muscle relaxation [54]. Prostanoids such thromboxane  $\text{A}_2$  ( $\text{TXA}_2$ ) also produced by the vascular endothelial cells to cause vasoconstriction. Imbalance or increase in  $\text{TXA}_2$  over ( $\text{PGI}_2$ ) ( $\text{TXA}_2/\text{PGI}_2$ ) ratio may contribute to an increase in total peripheral resistance and hence hypertension. Excessive free radicals can induce endothelial dysfunction [45, 55]. Endothelial dysfunction may lead to reduction in NO availability. The reduction in availability of NO may result from both reduced production and increased breakdown of NO [56]. Free radicals react with NO to generate peroxynitrite, a highly pro-oxidative

## Heated cooking oils and blood pressure

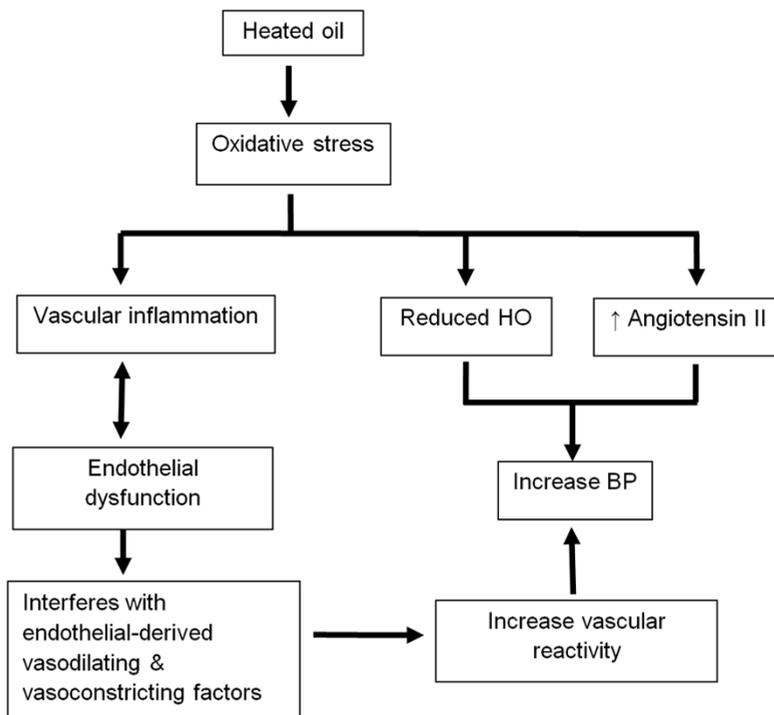
species that propagate the chain of lipid peroxidation [45], leading to oxidative stress. Prolonged consumption of heated oil was found to profoundly decrease nitric oxide (NO) in rats [25, 26, 30]. Leong et al., 2009 suggested that reduction in NO may be responsible for attenuation of endothelium-dependent relaxation response by acetylcholine and increased vasoconstriction response to phenylephrine [26]. Yen et al., 2010 however reported an elevation in plasma NO in spontaneously hypertensive rats (SHR) fed heated oil for ten weeks [33]. The elevation is thought to be due to the release of NO from endothelial cells to combat pro-hypertensive state [57]. Based on these findings, the release of NO during acute ingestion of heated oil might be initially an adaptive action to fight against hypertension, but it eventually becomes maladaptive after a chronic period. Nurul-Iman et al., 2013 reported that heated oil produced reduction in NO. The reduction in NO with heated palm oil improved with virgin coconut oil [30]. Again, this finding supports that heated oil caused oxidative stress which subsequently contribute to reduction in NO.

Prostacyclin (PGI<sub>2</sub>) is another substance that plays an assisting role with NO in regulating blood pressure. Ng et al., 2012 has shown that repeatedly heated soybean oil increases plasma TXA<sub>2</sub>/PGI<sub>2</sub> ratio in experimental rats [28]. This finding was consistent with Hamsi et al., 2015 which demonstrated that heated virgin coconut oil increase thromboxane B<sub>2</sub> while reducing PGI<sub>2</sub> [31]. These results may suggest heated oil not only reduces NO but might cause an imbalance between vasodilation or and vasoconstriction factors produce by vascular endothelium. While PGI<sub>2</sub> protects against elevated blood pressure and leukocytes adhesion, thromboxane A<sub>2</sub> (TXA<sub>2</sub>) triggers platelet aggregation and vasoconstriction, counteracting the function of PGI<sub>2</sub>. An increase in TXA<sub>2</sub>/PGI<sub>2</sub> ratio potentiate vasoconstriction effect of TXA<sub>2</sub> and attenuates vasodilation action of PGI<sub>2</sub>, leading to the elevation of blood pressure [28]. Reduction in PGI<sub>2</sub> observed in heated oil groups may be due to the increased oxidative stress as it has been reported to impair the aortic generation of PGI<sub>2</sub> in rats [58]. Therefore, it is suggested that excessive oxidation compounds from lipid oxidation may induce oxida-

tive stress and impairs endothelial function which regulates blood pressure [59-61].

Another possible mechanism by which heated oil increase BP is via affecting angiotensin converting enzymes (ACE) and heme oxygenase-1 (HO-1). Leong et al., 2012 reported that heated palm olein reduced heme-oxygenase [62]. Heme-oxygenase plays an importance role in modulating BP and vascular tone as the by-products of HO which are carbon monoxide (CO) and biliverdin which have antioxidant properties [63]. Sabaawy et al., 2001 reported over-expression of HO gene and increase in HO activity reduce BP [64]. Heme oxygenase (HO) and CO may contribute to the prevention of endothelial dysfunction. Increased in HO activity may be responsible for up regulation of antioxidant defence systems [65]. Reason for the reduction in HO with heated oil is not clear and postulated that it could be due to oxidative stress that overwhelming body antioxidants defence mechanism including HO system [62]. Interpretation of HO activity is not straight-forward since the oxidative stress-induced upregulation of HO gene expression, although cause increased HO protein, may reciprocally be associated with reduction of HO activity [66-68]. This phenomenon is due to the nuclear localization of HO-1 protein during stimulation by oxidative stress that mediates the protective genes as well as determines the active or non-active state of enzymatic activity [68]. Another theory is that peroxynitrite causes the inactivation of HO [67]. Leong et al., 2012 demonstrated that heated palm olein increased angiotensin converting enzymes (ACE) [62]. ACE is required for the formation of angiotensin I to angiotensin II which is a potent vasoconstrictor agent. Angiotensin II promoting oxidative stress via activation of NADPH oxidase that produces reactive oxygen species (ROS). The blood pressure raising effect of angiotensin II is mediated via the vasoconstriction property as well as reduction in NO secondary to interaction of ROS with NO to produce peroxynitrite. Since heated oil activated ACE activity therefore, the blood pressure raising effect of heated oil may be mediated via an increase in angiotensin II. The reason for activation of ACE with heated oil was unknown. There is possibility that reduction in NO activate ACE and vice versa as

## Heated cooking oils and blood pressure



**Figure 1.** Possible mechanism of blood pressure raising effect of heated oil.

Michael et al., 1997 reported that NO has antagonizing effect on angiotensin II [69].

Indeed, another study will be required to clarify this issue since ACE is membrane-bound protein which localized on plasma membranes of various cell types including vascular endothelial cells, renal and neuroepithelial cells while soluble plasma ACE may only reflect the turnover and clearance of the membrane-bound ACE. Therefore, tissue ACE is thought to be more important and convincing interpretation regarding ACE activity [70]. The link between ACE and heated oil consumption is extremely limited. Study by Beshel et al., 2014 which shows chronic consumption of heated palm oil caused decreased in GFR and renal blood flow while increased BP may reflect a possibility of renovascular hypertension and renin-angiotensin-aldosterone system (RAAS) dysregulation had been occurred [35].

### Conclusion

The current review showed that heated cooking oils increased BP. The magnitude of the increase in BP was more with repeated heating. Although once-, five- and ten-time-heated oils

increased BP, the percentage increase was higher with the oil which was reheated ten times compared to heated once. It was shown that at the smallest and highest heating frequency, the percentage increase was highest for heated soy compared to heated corn and palm oil. It was reported that the percentage increased in BP was lowest for corn oil compared to soy despite both is polyunsaturated oils. The blood pressure raising effect of heated oil was associated with an increase in inflammatory biomarkers VCAM-1, ICAM-1 and CRP which suggest that heated oil induce vascular inflammation leading to vascular dysfunction which interferes with the release of endothelium-

derived vasoactive compounds like nitric oxide, prostacyclin and thromboxane. The reduction in endothelial derived relaxant factors is responsible for an increase in vascular reactivity as reflected by attenuation of vascular relaxation response to acetylcholine and enhanced vasoconstriction response to phenylephrine. The increased in vascular reactivity is responsible for the rise in blood pressure. Activation of ACE and reduction in HO may contribute to blood pressure raising effect of heated oil which warrants further elucidation. The detrimental effect of heated oil on BP was most likely due to oxidative stress as reflected by an increase in peroxide value which was coupled with reduction in vitamin E content of heated oil. The oxidative stress causes vascular inflammation and dysfunction. The possible mechanism is explained in **Figure 1**.

### Acknowledgements

The authors would like to acknowledge Universiti Kebangsaan Malaysia for the financial support by grant GUP-2013-059.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Kamsiah Jaarin, Department of Pharmacology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: 60391459578; Fax: 60326938205; E-mail: kamsiah@ukm.edu.my

### References

- [1] Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB and Stamler J. Blood pressure and end-stage renal disease in men. *N Engl J Med* 1996; 334: 13-18.
- [2] Rampal L, Rampal S, Azhar MZ and Rahman AR. Prevalence, awareness, treatment and control of hypertension in Malaysia: A national study of 16,440 subjects. *Public Health* 2008; 122: 11-18.
- [3] Ueshima H, Zhang H and Choudhury SR. Epidemiology of hypertension in China and Japan. *J Hum Hypertension* 2000; 14: 765-769.
- [4] Charnock JS, McLennan PL and Abeywardena MY. Dietary modulation of lipid metabolism and mechanical performance of the heart. *Mol Cell Biochem* 1992; 116: 19-25.
- [5] Grimsgaard S, Bona KH, Jacobsen BK and Bjerve KS. Plasma saturated and linoleic fatty acids are independently associated with blood pressure. *Hypertension* 1999; 34: 478-483.
- [6] Bayorh MA, Abukhalaf IK and Ganafa AA. Effect of palm oil on blood pressure, endothelial function and oxidative stress. *Asia Pac J Clin Nutr* 2005; 14: 325-339.
- [7] Ganafa AA, Socci RR, Eatman D, Silvestrov N, Abukhalaf IK and Bayorh MA. Effect of palm oil on oxidative stress-induced hypertension in Sprague-Dawley rats. *Am J Hypertens* 2002; 15: 725-731.
- [8] Bairati I, Roy L and Meyer F. Effects of a fish oil supplement on blood pressure and serum lipids in patients treated for coronary artery disease. *Can J Cardiol* 1992; 8: 41-46.
- [9] Mensink RP, Janssen MC and Katan MB. Effect on blood pressure of two diets differing in total fat but not in saturated and polyunsaturated fatty acids in healthy volunteers. *Am J Clin Nutr* 1988; 47: 976-980.
- [10] Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T and Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Am J Clin Nutr* 2004; 80: 1012-1018.
- [11] Azman A, Mohd Shahrul S, Chan SX, Noor-hazliza AP, Khairunnisak M, Nur Azlina MF, Qodriyah HM, Kamisah Y and Jaarin K. Level of knowledge, attitude and practice of night market outlet operator in Kuala Lumpur regarding the usage of repeatedly heated cooking oil. *Med J Malaysia* 2012; 67: 97-107.
- [12] Soriguer F, Rojo-Martínez G, Dobarganes MC, García Almeida JM, Esteva I, Beltrán M, Ruiz De Adana MS, Tinahones F, Gómez-Zumaquero JM, García-Fuentes E and González-Romero S. Hypertension is related to the degradation of dietary frying oils. *Am J Clin Nutr* 2003; 78: 1092-1097.
- [13] Rodrigo R, Prat H, Passalacqua W, Araya J, Guichard C and Bachler JP. Relationship between oxidative stress and essential hypertension. *Hypertens Res* 2007; 30: 1159-1167.
- [14] Ono Y, Mizuno K, Takahashi M, Miura Y and Watanabe T. Suppression of advanced glycation and lipoxidation end products by Angiotensin II type-1 receptor blocker candesartan in type 2 diabetic patients with essential hypertension. *Fukushima J Med Sci* 2013; 59: 69-75.
- [15] Baradaran A, Nasri H and Rafeian-Kopaei M. Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants. *J Res Med Sci* 2014; 19: 358-367.
- [16] Hausding M, Jurk K, Daub S, Kröller-Schön S, Stein J, Schwenk M, Oelze M, Mikhed Y, Kerahrudi JG, Kossmann S, Jansen T, Schulz E, Wenzel P, Reske-Kunz AB, Becker C, Münzel T, Grabbe S and Daiber A. CD40L contributes to angiotensin II-induced pro-thrombotic state, vascular inflammation, oxidative stress and endothelial dysfunction. *Basic Res Cardiol* 2013; 108: 386.
- [17] Chatterjee S and Fisher AB. Mechanotransduction in the endothelium: role of membrane proteins and reactive oxygen species in sensing, transduction, and transmission of the signal with altered blood flow. *Antioxid Redox Signal* 2014; 20: 899-913.
- [18] Korkmaz GG, Altınoglu E, Civelek S, Sozer V, Erdenen F, Tabak O and Uzun H. The association of oxidative stress markers with conventional risk factors in the metabolic syndrome. *Metabolism* 2013; 62: 828-835.
- [19] Muhammad SA, Bilbis LS, Saidu Y and Adamu Y. Effect of antioxidant mineral elements supplementation in the treatment of hypertension in albino rats. *Oxid Med Cell Longev* 2012; 2012: 134723.
- [20] Adam SK, Das S, Soelaiman IN, Umar NA and Jaarin K. Consumption of repeatedly heated soy oil increases serum parameters related to atherosclerosis in ovariectomized rats. *Tohoku J Exp Med* 2008; 215: 219-226.
- [21] Adam SK, Das S and Jaarin K. A detailed microscopic study of the changes in the aorta of experimental model of postmenopausal rats

## Heated cooking oils and blood pressure

- fed with repeatedly heated palm oil. *Int J Exp Pathol* 2009; 90: 321-327.
- [22] Ng CY, Leong XF, Masbah N, Adam SK, Yusof K and Jaarin K. Heated vegetable oils and cardiovascular risk factors. *Vascul Pharmacol* 2014; 61: 1-9.
- [23] Osim EE, Owu DU and Etta KM. Arterial pressure and lipid profile in rats following chronic ingestion of palm oil diets. *Afri J Med Med Sci* 1996; 25: 335-340.
- [24] Leong XF, Aishah A, Nor Aini U, Das S and Jaarin K. Heated palm oil causes rise in blood pressure and cardiac changes in heart muscle in experimental rats. *Arch Med Res* 2008; 39: 567-572.
- [25] Leong XF, Mustafa MR, Das S and Jaarin K. Association of elevated blood pressure and impaired vasorelaxation in experimental Sprague-Dawley rats fed with heated vegetable oil. *Lipids Health Dis* 2010; 9: 66.
- [26] Leong XF, Najib MN, Das S, Mustafa MR and Jaarin K. Intake of repeatedly heated palm oil causes elevation in blood pressure with impaired vasorelaxation in rats. *Tohoku J Exp Med* 2009; 219: 71-78.
- [27] Jaarin K, Mustafa MR and Leong XF. The effect of heated vegetable oils on blood pressure in rats. *Clinics* 2011; 66: 2125-2132.
- [28] Ng CY, Kamisah Y, Faizah O and Jaarin K. The role of repeatedly heated soybean oil in the development of hypertension in rats: association with vascular inflammation. *Int J Exp Pathol* 2012; 93: 377-387.
- [29] Ng CY, Kamisah Y, Faizah O, Jubri Z, Qodriyah HM and Jaarin K. Involvement of inflammation and adverse vascular remodelling in the blood pressure raising effect of repeatedly heated palm oil in rats. *Int J Vasc Med* 2012; 2012: 404025.
- [30] Nurul-Iman BS, Kamisah Y, Jaarin K and Qodriyah HM. Virgin coconut oil prevents blood pressure elevation and improves endothelial functions in rats fed with repeatedly heated palm oil. *Evid Based Complement Alternat Med* 2013; 2013: 629329.
- [31] Hamsi MA, Faizah O, Srijit D, Yusof K, Zar Chi T, Qodriyah HM, Zaiton Z, Adel E, Kogilavani S and Kamsiah J. Effect of consumption of fresh and heated virgin coconut oil on blood pressure and inflammatory biomarkers. *Alex J Med* 2015; 51: 53-63.
- [32] Bautista R, Carreon-Tores E, Luna-Luna M, Komera-Arenas Y, Franco M, Fragoso JM, López-Olmos V, Cruz-Robles D, Vargas-Barrón J, Vargas-Alarcón G and Pérez-Méndez O. Early endothelial nitrosylation and increased abdominal adiposity in Wistar rats after long-term consumption of food fried in canola oil. *Nutrition* 2014; 30: 1055-1060.
- [33] Yen PL, Chen BH, Yang FL and Lu YF. Effects of deep-frying oil on blood pressure and oxidative stress in spontaneously hypertensive and normotensive rats. *Nutrition* 2010; 26: 331-336.
- [34] Perez-Herrera A, Rangel-Zuniga OA, Delgado-Lista J, Marin C, Perez-Martinez P, Tasset I, Tunez I, Quintana-Navarro GM, Lopez-Segura F, Luque de Castro MD, Lopez-Miranda J, Camargo A and Perez-Jimenez F. The antioxidants in oils heated at frying temperature, whether natural or added, could protect against postprandial oxidative stress in obese people. *Food Chem* 2013; 138: 2250-2259.
- [35] Beshel FN, Antai AB and Osim EE. Chronic consumption of three forms of palm oil diets alters glomerular filtration rate and renal plasma flow. *Gen Physiol Biophys* 2014; 33: 251-256.
- [36] Al-Tahami BA, Yvonne-Tee GB, Halim AS, Ismail AA and Rasool AHG. Method optimization on the process of iontophoresis with laser Doppler fluximetry in the assessment of microvascular endothelial function. *Malaysian J Med Health Sci* 2007; 7: 35-40.
- [37] Corretti MC, Anderson TJ, Benjamin EJ, Celermajer D, Charbonneau F, Creager MA, Deanfield J, Drexler H, Gerhard-Herman M, Herrington D, Vallance P, Vita J and Vogel R. Guidelines for the ultrasound assessment of endothelial dependent flow-mediated vasodilation of the brachial artery: A report of the International Brachial Artery Reactivity Task Force. *J Am Coll Cardiol* 2002; 39: 257-265.
- [38] Williams MJ, Sutherland WH, McCormick MP, Yeoman D, de Jong SA and Walker RJ. Normal endothelial function after meals rich in olive or safflower oil previously used for deep frying. *Nutr Metab Cardiovasc Dis* 2001; 11: 147-152.
- [39] De Roos NM, Siebelink E, Bots ML, van Tol A, Schouten EG and Katan MB. Trans monosaturated fatty acids and saturated fatty acids have similar effects on postprandial flow-mediated vasodilation. *Eur J Clin Nutr* 2002; 56: 674-679.
- [40] Owu DU, Orié NN and Osim EE. Altered responses of isolated aortic smooth muscle following chronic ingestion of palm oil diets in rats. *Afr J Med Med Sci* 1997; 26: 83-86.
- [41] Griendling KK and FitzGerald GA. Oxidative Stress and cardiovascular Injury Part 1: Basic Mechanisms and In Vivo Monitoring of ROS. *Circulation* 2003; 108: 1912-1916.
- [42] Touyz RM. Molecular and cellular mechanism in vascular injury in hypertension: role of angiotensin II. *Curr Opin Nephrol Hypertens* 2005; 14: 125-131.
- [43] Mazor R, Itzhaki O, Sela S, Yagil Y, Cohen-Mazor M, Yagil C and Kristal B. Tumor Necrosis Factor- $\alpha$ : A possible priming agent for the poly-

## Heated cooking oils and blood pressure

- morphonuclear Leukocyte-Reduced Nicotinamide-Adenine Dinucleotide Phosphate Oxidase in Hypertension. *Hypertension* 2010; 55: 353-362.
- [44] Kwon JS, Joung H, Kim YS, Shim YS, Ahn Y, Jeong MH and Kee HJ. Sulforaphane inhibits restenosis by suppressing inflammation and the proliferation of vascular smooth muscle cells. *Atherosclerosis* 2012; 225: 41-49.
- [45] Hsieh HJ, Liu CA, Huang B, Tseng AH and Wang DL. Shear-induced endothelial mechanotransduction: the interplay between reactive oxygen species (ROS) and nitric oxide (NO) and the pathophysiological implications. *J Biomed Sci* 2014; 21: 3.
- [46] Perez-Herrera A, Delgado-Lista J, Torres-Sanchez LA, Rangel-Zuniga OA, Camargo A, Moreno-Navarette JM, Garcia-Olvid B, Quintana-Navarro GM, Alcalá-Diaz JF, Muñoz-Lopez C, Lopez-Segura F, Fernandez-Real JM, Luque de Castro MD, Lopez-Miranda J and Perez-Jimenez F. The postprandial inflammatory response after ingestion of heated oils in obese persons is reduced by the presence of phenol compounds. *Mol Nutr Food Res* 2012; 56: 510-514.
- [47] Giua L, Blasi F, Simonetti MS and Cossignani L. Oxidative modifications of conjugated and unconjugated linoleic acid during heating. *Food Chem* 2013; 140: 680-685.
- [48] Rodrigues N, Malheiro R, Casal S, Asensio-S-Manzanera MC, Bento A and Pereira JA. Influence of spike lavender (*Lavandula latifolia* Med.) essential oil in the quality, stability and composition of soybean oil during microwave heating. *Food Chem Toxicol* 2012; 50: 2894-2901.
- [49] Awney HA. The effects of Bifidobacteria on the lipid profile and oxidative stress biomarkers of male rats fed thermally oxidized soybean oil. *Biomarkers* 2011; 16: 445-452.
- [50] Suomela JP, Ahotupa M and Kallio H. Triacylglycerol oxidation in pig lipoproteins after a diet rich in oxidized sunflower seed oil. *Lipids* 2005; 40: 437-444.
- [51] Andrikopoulos NK, Dedoussis GVZ, Falirea A, Kalogeropoulos N and Hatzinikola H. Deterioration of natural antioxidants species of vegetable oils during the domestic deep-frying and Pan-frying of potatoes. *Intern J Food Sci Nutr* 2002; 53: 351-363.
- [52] Adam SK, Sulaiman NA, Mat Top AG and Jaarin K. Heating reduces vitamin E content in palm and soy oils. *Malays J Biochem Mol Biol* 2007; 15: 76-79.
- [53] Sutherland WHF, Williams MJA, de Jong SA and McCormick MP. Ingestion of moderately thermally oxidized polyunsaturated fat decreases serum resistance to oxidation in men with coronary artery disease. *Nutr Res* 2007; 27: 265-272.
- [54] Gruetter CA, Barry BK, McNamara DB, Gruetter DY, Kadowitz PJ and Ignarro L. Relaxation of bovine coronary artery and activation of coronary arterial guanylate cyclase by nitric oxide, nitroprusside and a carcinogenic nitrosamine. *J Cyclic Nucleotide Res* 1979; 5: 211-224.
- [55] Guterbaum TJ, Braunstein TH, Fossum A, Holstein-Rathlou NH, Torp-Pedersen CT and Dominguez H. Endothelial nitric oxide synthase phosphorylation at threonine 495 and mitochondrial reactive oxygen species formation in response to a high H<sub>2</sub>O<sub>2</sub> concentration. *J Vasc Res* 2013; 50: 410-420.
- [56] Viridis A, Fritsch Neves M, Duranti E, Bernini G and Taddei S. Microvascular endothelial dysfunction in obesity and hypertension. *Curr Pharm Des* 2013; 19: 2382-2389.
- [57] Wu CC and Yen MH. Higher level of plasma nitric oxide in spontaneously hypertensive rats. *Am J Hypertens* 1999; 12: 476-482.
- [58] Toniolo A, Buccellati C, Pinna C, Gaion RM, Sala A and Bolego C. Cyclooxygenase-1 and prostacyclin production by endothelial cells in the presence of mild oxidative stress. *PLoS One* 2013; 8: e56683.
- [59] Yamamoto M, Suzuki A, Jokura H, Yamamoto N and Hase T. Glucosyl hesperidin prevents endothelial dysfunction and oxidative stress in spontaneously hypertensive rats. *Nutrition* 2008; 24: 470-476.
- [60] Gebhard C, Stähli BE, Shi Y, Camici GG, Akhmedov A, Hoegger L, Lohmann C, Matter CM, Hassa PO, Hottiger MO, Malinski T, Lüscher TF and Tanner FC. Poly (ADP-ribose) polymerase-1 protects from oxidative stress induced endothelial dysfunction. *Biochem Biophys Res Commun* 2011; 414: 641-646.
- [61] Gortan Cappellari G, Losurdo P, Mazzucco S, Panizon E, Jevnicar M, Macaluso L, Fabris B, Barazzoni R, Biolo G, Carretta R and Zanetti M. Treatment with n-3 polyunsaturated fatty acids reverses endothelial dysfunction and oxidative stress in experimental menopause. *J Nutr Biochem* 2013; 24: 371-379.
- [62] Leong XF, Salimon J, Mustafa MR and Jaarin K. Effect of repeatedly heated palm olein on blood pressure-regulating enzymes activity and lipid peroxidation in rats. *Malays J Med Sci* 2012; 19: 20-29.
- [63] Kawamura K, Ishikawa K, Wada Y, Kimura S, Matsumoto H, Kohro T, Itabe H, Kodama T and Maruyama Y. Bilirubin from heme oxygenase-1 attenuates vascular endothelial activation and dysfunction. *Arterioscler Thromb Vasc Biol* 2005; 25: 155-160.

## Heated cooking oils and blood pressure

- [64] Sabaawy HE, Zhang F, Nguyen X, Elhosseiny A, Nasjletti A, Schwartzman M, Dennery P, Kappas A and Abraham NG. Human heme-oxygenase-1 gene transfer lowers blood pressure and promotes growth in spontaneously hypertensive rats. *Hypertension* 2001; 38: 210-215.
- [65] Turkseven S, Kruger A, Mingone CJ, Kaminski P, Inaba M, Rodella LF, Ikehara S, Wolin MS and Abraham NG. Antioxidant mechanism of hemeoxygenase-1 involves an increase in superoxide dismutase and catalase in experimental diabetes. *AM J Physiol Heart Circ Physiol* 2005; 289: H701-H707.
- [66] Kawakami T, Puri N, Sodhi K, Bellner L, Takahashi T, Morita K, Rezzani R, Oury TD and Abraham NG. Reciprocal effects of oxidative stress on heme oxygenase expression and activity contributes to reno-vascular abnormalities in EC-SOD knockout mice. *Int J Hypertension* 2012; 2012: 740203.
- [67] Kinobe R, Ji Y and Nakatsu K. Peroxynitrite-mediated inactivation of heme oxygenases. *BMC Pharmacol* 2004; 4: 26.
- [68] Lin Q, Weis S, Yang G, Weng YH, Helston R, Rish K, Smith A, Bordner J, Polte T, Gaunitz F and Dennery PA. Heme Oxygenase-1 Protein Localizes to the Nucleus and Activates Transcription factors Important in Oxidative Stress. *J Biol Chem* 2007; 282: 20621-20633.
- [69] Michel JB, Feron O, Sase K, Prabhakar P and Michel T. Caveolin versus calmodulin. Counterbalancing allosteric modulators of endothelial nitric oxide synthase. *J Biol Chem* 1997; 272: 25907-25912.
- [70] Atlas SA. The Renin-Angiotensin Aldosterone System: Pathophysiological Role and Pharmacological Inhibition. *J Manag Care Pharm* 2007; 13: 9-20.