

**Review Article**

Toxicity Associated with the Consumption of Thermally-oxidized Cooking Oils: A Literature Review of Experimental Studies

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Abstract: Use of cooking oils in culinary practices, especially in deep-frying is a very old method of food preparation largely utilized across the world. Apart being a quick method of frying, deep-frying (100°C to 180°C) confers to the cooked food the unique physico-chemical properties (modification of the texture, proteins denaturation, water vaporization, etc.) desired by the consumer. However, oil heated at relatively very high temperature (>180°C) could lead to the formation of toxic compounds which may pose detrimental effect on health of the consumers of fried foods. Several pathological conditions or diseases may be in part or fully associated with the consumption of food by-products of thermally-oxidized oils. In this study, we have overviewed most valuable published literatures on toxicity effects related to the ingestion of thermally-oxidized cooking oils on liver, kidney and cardiovascular system. Thus, this article aims to alert the general public for a better understanding of the health risks associated with frying oils, to serve as a stimulus for scientists to foster the research activities which could potentially contribute to reduce the burden of this issue and to help develop or reinforce regulation policies in most developing countries concerning the use of frying oils in food preparation.

Keywords: Cooking Oil, Health Hazard, Reactive Oxidative Stress, Toxicity

1. Introduction

Vegetable oils are any oils obtained through extractive methods from a broad category of crops, including seeds, nuts, cereal, grains, and fruits. These oils play an essential role in our feeding habit [1]. Some decades ago, till to date, there is considerable growth in the production and consumption of vegetable oils across the world. This situation continues to encourage reports from several food science specialists regarding the possible health risks to consumers of fried foods [2].

Frying is a food preparation processes and deep-frying among other methods remains very popular in several parts of the world including Niger republic in particular. Factors such as temperature, heating process, length of immersion and quality of the frying container are reported to cause most

physical and chemical changes in cooked food and oil [3-4].

Oil heated under appropriate heating system with thermal treatment ranging from 100°C to 180°C [5-7], oxidation may lead to complex chemical reactions, which associate the thermolytic and the oxidative mechanisms. However, oil heated in the presence of air and food at higher temperatures (>180°C) and for long time, may lead to several chemical transformations which could later produce toxic substances like lipid oxidation products (LOPs), volatile substances, unwanted monomers, polymers, isomers and free radicals [8-10]; fried food in return will absorb such noxious products, and subsequently absorbed into the gastrointestinal system and later to systemic circulation after consumption [11]. Aldehydes were reported to cause toxicity effects in the body [12-20]. Indeed, aldehydes such as 4-hydroxyalkenals, malondialdehyde, acrolein and crotonaldehyde, have received particular attention since discovered to significantly

contribute in the alterations of several cell functions, which mostly depend on the formation of covalent adducts with cellular proteins [21]. For instance, the presence of aldehyde-protein adducts has been demonstrated to be associated with the development of most oxidative stress-related inflammatory pathologies such as hypertension, atherosclerosis, diabetes, metabolic syndrome, and cancer [22-25]. Polar compounds isolated from fried oil were postulated to play a vital contributory role in the pathogenesis of inflammation [26]. Cyclic fatty acid monomers (CFAM) from heated vegetable oils were reported to increase the levels of makers of oxidative stress and inflammation in Wistar rats [27]. Polycyclic aromatic hydrocarbons from repeatedly heated coconut oil were reported to be responsible for

oxidative stress via enhancement of reactive oxygen species generation and lipid peroxidation, thus leading to the formation of preneoplastic lesions in rat liver [28].

To date, experimental animal models such as mice, rabbit, rats, etc. have been used to investigate the relationships between the consumption of fat and the development of various degenerative diseases [29-32]. The possible relationship between the consumption or the exposure of thermally-oxidized cooking oils and some pathological conditions is schematically demonstrated in Figure 1. The present review aims to give an overview on the toxicity potential of the degradation products of thermally-oxidized cooking oils.

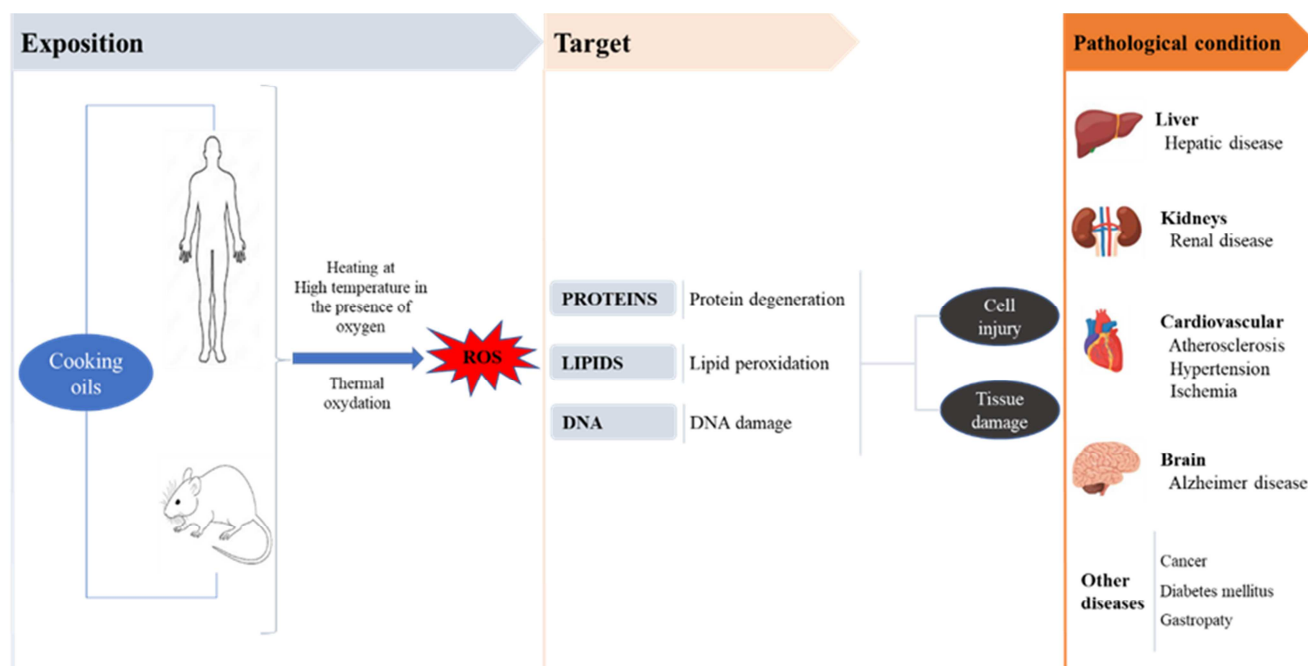


Figure 1. Illustration of possible pathway towards the development of certain pathological conditions as a result of cooking oil ingestion [adapted from 38].

2. Thermal Degradation Products of Cooking Oils and Their Possible Toxicological Effects After Ingestion

Toxicological effects in many tissues or organs through

cellular injury, enzyme damage and nucleic acid mutagenesis have been reported to be associated with the consumption of most of these highly oxidized cytotoxic agents as contaminants in food and cooking oil [33-39]. Table 1 presents a summative assessment of experimental studies investigating the toxicity effects of thermally-oxidized cooking oil.

Table 1. A summative assessment of information on cooking oils and their toxicities.

Type of oil	Method of cooking	Animal model	Key findings	Ref.
Soybean oil and sunflower oil	Repeatedly heated	Sprague Dawley rats	Adverse clinicopathological, toxicological and pathological effects with weight losses	[8]
Palm olein	Repeatedly Heated	Sprague Dawley rats	Impaired activity of blood pressure-regulating enzymes and increase of lipid peroxidation	[10]
Sunflower oil	Heated	Sprague Dawley rats	Altered lipid profile parameters	[15]
Coconut oil	Repeatedly heated	Wistar rats	Increased lipid peroxidation; formation of preneoplastic lesions in liver	[28]
Palm oil	Heated	Wistar strain albino rats	Deleterious effects on biochemical indices	[40]
Canola, sunflower and olive oils	Heated	Rabbit	Impaired the liver function and destroy its histological structure	[41]

Type of oil	Method of cooking	Animal model	Key findings	Ref.
Palm oil	Repeatedly heated	Sprague Dawley rats	Increased lipid peroxidation and total cholesterol; oxidative damage	[42]
Sunflower oil and palm oil	Reused edible	Wistar rats	Induced toxicity; damage the vital internal organs	[43]
Virgin coconut oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure and inflammatory biomarkers	[44]
Palm oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure; adverse remodelling, and increased vascular cell adhesion	[45]
Palm oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure, lipid peroxidation and decreased antioxidant enzymes	[46]
Palm kernel oil and soya oil	Fresh and heated	Albino Wister rats	Increased level of lipids in blood (hyperlipidaemia)	[47]
Sunflower	Heated	Wistar rats	Reduced feeding and body weight; lipid-lowering action and damage to liver and kidneys; decreased serum concentration of anti-ovalbumin immunoglobulin	[48]
Soybean oil	Repeatedly heated	Breast cancer murine model	Aggravated breast cancer metastasis	[49]
Canola oil	Heated	Mice	Exaggerated development of inflammatory bowel disease and IBD-associated colon tumorigenesis	[50]
Soybean oil	Heated	Broiler chickens	Induced oxidative stress in intestines; increase in cytokine levels	[51]
Fatty acids; soybean lipoxidase	Heated	Caco-2; smooth muscle cells	Induced oxidative stress and exacerbate atherogenesis	[52]
Cooking fat	Heated	Human	Impaired endothelial function	[53]
Vegetable cooking oil	Repeatedly heated	Wistar rats	Induced toxicity to blood cells and damage several internal organs (jejunum, colon and liver)	[54]
Palm oil	Repeatedly heated	Rabbit	Damage to liver, heart, kidney, lung, brain, spleen and muscles cells	[55]
Palm oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure	[56]
Palm oil	Repeatedly heated	Sprague Dawley rats	Increased lipid peroxidation	[57]
Palm, rapeseed, soybean, sunflower and virgin olive oils	Heated		Altered biochemical indices	[58]
Coconut oil, bulk oil, used cooking oil and pig oil	Used cooking	Wistar Rats	Induced oxidative stress and inflammation	[59]
Soybean oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure; increased inflammation; altered proteinoid production and adverse vascular remodel	[60]
Commercial oil	Heated	Wistar rats	Decreased retroperitoneal tissue weights and lipid contents	[61]
Soy oil	Repeatedly heated	Sprague Dawley rats	Increased atherogenic properties (risk of atherosclerosis)	[62]
Mustard oil	Heated	Wistar rats	Induced the formation of local tissue cell hyperplasia (tumorigenic)	[63]
Vegetable cooking oil	Reused	Albino rats	Increased levels of enzymes in the blood which is indicative of liver damage	[64]
Palm oil	Repeatedly heated	Wistar rats	Damage to liver cells	[65]
Corn oil	Heated		Increased atherogenic properties (risk of atherosclerosis)	[66]
Dietary lipids	Heated	New Zealand White rabbits	Increased levels of fatty streak lesions, a “fingerprint” of atherosclerosis	[67]
Palm oil and soybean oil	Repeatedly heated	Sprague Dawley rats	Impaired endothelium-dependent vasorelaxations and augmentation of contractile responses	[68]
Olive, soybean and palm oils	Repeatedly heated	Human	Impaired vascular endothelial function	[69]
Sunflower and olive oils	Heated	Human	Increased blood pressure	[70]
Soy oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure	[71]
Palm oil	Repeatedly heated	Sprague Dawley rats	Increased blood pressure; necrosis of cardiac tissue	[72]
Soybean oil	Heated	Wistar rats	Altered metabolism of the class of compounds derived from arachidonic acid; increased oxidative stress	[73]
Mustard oil	Repeatedly heated	Wistar rats	Damage to heart, liver, kidney and small intestine cells	[74]
Virgin coconut	Used-cooking	Mice	Altered haematological parameters	[75]
Canola oil	Heated	Wistar rats	Increased adipose tissue and early endothelial dysfunction	[76]
Palm oil	Heated	Swiss Albino mice	Damage liver and kidney cells	[77]
Palm oil	Heated	Rabbits	Altered kidney function	[78]

2.1. Toxic Effects on Liver

Liver is an organ which plays a crucial role in lipid metabolism, in protein synthesis and has numerous functions in the body and participates in the regulation of biochemical parameters. Biochemical makers of hepatic function which include total protein, albumin, serum glutamic-pyruvic transaminase, serum glutaminoxaloacetic transaminase, alkaline phosphatase, etc. are the most frequently demanded tests. Many studies have reported the impact of oxidized cooking oils on biochemical makers of hepatic function. For

example, Ambreen et al. (2020) investigated the effect of daily used oxidized cooking oils (Canola, sunflower and olive oils) on hepatic function in laboratory animal model and found that repeatedly heated oil-fed groups significantly increased serum liver enzyme levels, which is clearly indicative of hepatic injury [41]. Heated palm oil was also reported to impair liver biomarkers in laboratory exposed animal models. Hailemariam et al. (2020), in their study found that heated palm oil which was administered to Swiss albino mice could negatively affect the serum liver enzyme levels [42]. Similar findings were reported in several studies [79, 80]. Heated mustard oil was also reported to contribute to the increase of

serum LDL cholesterol and triglycerides and the decrease of HDL in exposed Wistar rats [63]. Histopathological examination constituted another path of laboratory investigation which helps to explore the presence of possible alterations in cells or tissue abnormalities. The toxicity effect could be acute (hepatocytes with necrosis, degeneration, steatosis) or chronic (hepatitis with various forms of necrosis, fibrosis and cirrhosis). Numerous studies have investigated the effect of cooked and repeatedly cooked oils on liver. The ingestion of canola oil, sunflower oil and olive oil that were cooked for longer period were reported to be highly toxic as it alter the normal function of liver and damage its histological structure [41]. Shukla et al. (2003) in their study have evaluated the effect of fresh and heated mustard oil at 300°C for a period of 180 min and administered in Wistar rats (0.5 mL/day for 8 weeks). From the findings, authors have suggested that some constituents of mustard oil may be carcinogenic in nature since found to enhance the preneoplastic hepatic foci development in Wistar rats [63]. Islam et al. (2019) in their previous study found that raw and repeatedly fried mustard oil intake have caused metabolic and organ histological changes in exposed Wistar rat [74]. Syafruddin (2018) in his study have used a completely randomized design with 15 treatments and five replications to examine the effects of repeatedly heated palm oil on lipid profile, as well as liver tissue of experimental rats. The results of data analysis indicate a relationship between abusive heating of palm oils with liver injury [65]. Morshed et al. (2018) in their study have evaluated the effects of chronic consumption of long-time heated palm oil diet on histological changes in rabbit internal organs. Specific lesions that were reported concerning progressive changes in the liver include among others the formation of hepatic lobules [55].

2.2. Toxic Effects on Kidney

Kidneys are two bean-shaped organs which help filtrate extra water and wastes out of the living body and make urine. Biochemical indexes of kidney function which include urea, creatinine, serum electrolytes and uric acid are the most frequently ordered tests [81]. Many studies have reported the impact of oxidized cooking oils on biochemical indexes of kidney function. For example, Hailemariam et al. (2020) found that the administration of fried palm oil in Swiss Albino mice engender an increase of the kidney biomarkers (urea and creatinine) [77]. Another important indicator of renal injury is an increase in uric acid accumulation, suspected to accentuate acute injury to the kidney [82, 83]. Yingfang et al. (2020) investigated the effect of soybean oil alone and a mix of lard and soybean oil in cooking on renal metabolic activity in mice. Authors found that the increasing intake of soybean oil alone dramatically contributed to the increase of uric acid level in serum [84]. Several other studies have investigated the histological changes in kidneys of exposed animal models with thermally oxidized cooking oils. Morshed et al. (2018) examined the effects of long-time consumption of heated palm oil diet on the kidney of exposed rabbit and found that kidney of the heated palm oil diet groups developed abnormalities in

the structure of glomeruli and the renal tubules [55]. Shastry et al. (2011) reported that reused sunflower and palm oils changes in size of kidney and the presence of tubular cell in medullary region, cytoplasmic as well as nuclear vacuoles in exposed Wistar rats [43].

2.3. Toxic Effects on Heart

Cardiovascular diseases constitute common diseases affecting heart and arteries. Adverse cardiovascular outcomes include among others coronary heart disease, atherosclerosis and stroke. Thermally oxidized oil products, have been reported in many studies as mediators of most vascular injury due to lipid and protein oxidation [85-87]. Among possible vascular changes, atherosclerosis is now considered as a major cause of coronary heart disease. Several studies have reported the possible implication of frequent dietary consumption of cooking oil in the pathogenesis of atherosclerosis [88-91]. Early evidence concerning the atherogenicity of thermally-stressed poly-unsaturated fatty acids rich oils was provided by two famous researchers, Kritchevsky and Tepper in 1967 [66]. They found that heating corn oil (20 min at 215°C) substantially increased its atherogenic properties. Rudel et al. (1995) in their study involving African green monkeys showed that diets enriched in palm oil and safflower oil respectively caused atherosclerosis. However, dietary with safflower oil which is a polyunsaturated fatty acid (18:2), appears with poor atherogenicity in these primates [92]. Staprans et al. (1996) investigated the contribution of oxidized dietary lipids in the development of atherosclerosis in rabbits [67]. Adam et al. (2008) explored the effects of repeatedly heated soy oil on the development of atherosclerosis using ovariectomized rats. Results have shown that repeated heating of soy oil causes an increase in lipid peroxidation, LDL and homocysteine level in rats [62]. These conditions may contribute to the pathogenesis of atherosclerosis especially in post-menopausal women [72]. In another study, Adam et al. (2008) have examined the effects of heated palm oil mixed with 2% cholesterol diet on certain biochemical indices in estrogen-deficient rats. Results have shown that repeatedly heated palm oil appears to increase lipid peroxidation and cholesterol level [42]. Tan et al. (2012) in their study found that repeatedly heated palm oils significantly contribute to the increase of the tunica intima thickness in aorta of the exposed animal models. Findings suggest that repeated heated palm oils have the potential to cause oxidative stress and inflammation which aggravates the development of atherosclerosis [57]. In the same year, another study from Aziz et al. (2012) reported that heated palm oil caused damage to vascular system [93]. Ni and Wayan (2016) in their research assignment found that the ingestion of used cooking oil could lead to atherosclerosis formation [59]. Endothelial dysfunction is another important event that contributes to the initiation and progression of vascular injury [94, 95] and also a predictor of hypertension [79, 80]. Appreciation of endothelial function has become an important means to detect arterial abnormalities and represents an early marker of cardiovascular diseases. Various studies have reported the

impairment of endothelial function following the consumption of cooking vegetable oils. Owu et al. (1997) examined the effect of palm oil in the diet on aortic responses to contracting and relaxing agents under standard organ bath procedures and found that chronic intake of thermally oxidized palm oil alters the function of aorta isolated from the rat. Free radicals that are generated during thermal oxidation of palm oil could generate modification after consumption which could in progress raise the plasma levels of cholesterol and low-density lipoprotein and thus alter the vascular smooth muscle function [96]. Michael et al. (1999) investigated the effect of the intake of used cooking fat that had been used for deep frying in a commercial fast-food restaurant and observed endothelial dysfunction in healthy men [53]. Similarly, Rueda-Clausen et al. (2007) found that the ingestion of fresh or cooked olive, soybean and palm oils causes detrimental acute effect in the endothelial function in healthy young men [69]. Jaarin et al. (2011) in their study reported that chronic consumption of repeatedly heated palm oil and soybean oil impaired the vascular system of adult male Sprague-Dawley rats [68]. Ng et al. (2012) investigated the effect of repeatedly heated palm oil on blood pressure, aortic morphometry, and vascular cell adhesion molecule-1 (VCAM-1) expression in rats and found that prolonged consumption of repeatedly heated palm oil appears to cause endothelial dysfunction, as reflected by the adverse vascular remodeling and the induction of VCAM-1 expression on endothelial cells [45]. Endothelial dysfunction is associated with vascular tone changes leading to the pathogenesis of hypertension. Several studies have demonstrated that oxidized oils provoked alterations in endothelial function leading to elevation of blood pressure in animal models. In a cross-sectional study which was conducted in southern Spain, Frederico et al. (2003) reported that the degradation products of the reuse sunflower oil, constitute an independent risk factor for hypertension [70]. Leong et al. (2008) reported that fresh palm oil has no deleterious effects on blood pressure and cardiac tissue but prolonged consumption of repeatedly heated palm oil (20 min at 180°C) may result in blood pressure elevation with injured cardiac tissue [72]. In 2009, the same research team came to explore the possible biochemical and vascular mechanisms involved in the increased blood pressure following chronic administration of repeatedly heated palm cooking oil (10 min at 180°C) and found that its intake causes an increase in blood pressure with impaired vasorelaxation in Sprague-Dawley rats [56]. Furthermore, in 2010, the same authors investigated the effect of consumed repeatedly heated soy oil (10 min at 180°C) on blood pressure, plasma nitric oxide, heme oxygenase and angiotensin-converting enzyme. The study recorded higher blood pressure and angiotensin-converting enzyme activity as the plasma nitric oxide and heme oxygenase-1 decreased [71]. In another study, Leong et al. (2012) verified whether heated palm oil affects blood pressure by increasing vascular reactivity or by affecting the blood pressure-regulating enzymes and lipid peroxidation in Sprague-Dawley rats. They observed that the consumption of thermally oxidized palm olein (10 min at 180°C) may affect the functions of enzymes

involved in the regulation of blood pressure by increasing the angiotensin-converting enzyme level and decreasing heme oxygenase activity [10]. Jaarin et al. (2011) investigated the effects of heated palm and soy oils on blood pressure in adult male Sprague-Dawley rats and observed that the chronic ingestion of heated vegetable oils caused a significant increase in blood pressure with respect to increasing number of heating repetitions. The greater the number of heating repetition, the greater increase in blood pressure. Findings suggest that free radicals that are generated through thermal oxidation of the vegetable oils contributed to impaired nitric oxide bioavailability, and then the hypertension [68]. Ng et al. (2012) ascertained the role of inflammation in the blood pressure raising effect of heated soybean oil in male Sprague-Dawley rats and found that prolonged consumption of repeatedly heated soybean oil causes blood pressure elevation in 5 times heated palm oil and 10 times heated palm oil groups, which may be attributed to inflammation. The aortae of 5 times heated palm oil and 10 times heated palm oil groups were reported to engender vascular remodeling. Elastic lamellae were disorganized and fragmented in 5 times heated palm oil and 10 times heated palm oil-treated rats. VCAM-1 expression showed a significant positive correlation with blood pressure [60]. In a comparable study that was conducted in Malaysia, Hamsi et al. (2014) explored the effect of repeatedly heated virgin coconut oil (15 min at 180°C) on the blood pressure and inflammatory biomarkers and found that blood pressure increased significantly in the 5 times and 10 times heated virgin coconut oil groups compared to the control groups. The finding of the study suggests that thermally-oxidized vegetable cooking oils may induce inflammation which has been implicated in the impairment of endothelial function [44]. Kumeshini et al. (2016) studied the effect of repeatedly heated palm oil on the blood pressure in ovariectomized female Sprague-Dawley rats. By the end of the study, they constated an increase in systolic, diastolic and mean blood pressure in 5 times heated palm oil and 10 times heated palm oil compared to respective control [46].

3. Conclusion and Research Perspectives

This concise review on past and recent in vitro and in vivo toxicological studies provides an outline related to health issues associated with the degradation products of thermally-oxidized cooking oils. Policy makers, food service entities and consumers need to be aware that consumption of thermally oxidized cooking oils may lead to pathological conditions. Thus, progress through gathering evidence-based information needs regarding the dangers of consuming oxidized cooking oils should be encouraged. Such compiled information on awareness would be a valuable indicator which would help to implement oil management plans and to monitor oil quality. Today, what new research areas could help build upon what is known to date concerning the toxicity of thermally-oxidized cooking oil? These include assessments of the level of awareness regarding the usage of heated cooking oil, studies of the safety of cooking oil for public

consumption, studies of improved maintenance of oil quality by food vendors, studies towards the development of alternative cooking methods and studies on the major role of lipid oxidation products in the development of most pathological disorders in line with other complementary studies on potential therapeutic approaches as options that could help control these conditions.

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Conflicts Interest

The authors declare no conflict of interest.

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