Special Article

Health-promoting effects of red palm oil: evidence from animal and human studies

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*The fruit of the oil palm tree (*Elaeis guineesis*) is the source of antioxidant-rich red palm oil. Red palm oil is a rich source of phytonutrients such as tocotrienols, tocopherols, carotenoids, phytosterols, squalene, and coenzyme Q10, all of which exhibit nutritional properties and oxidative stability. Mutagenic, nutritional, and toxicological studies have shown that red palm oil contains highly bioavailable β-carotene and vitamin A and is reasonably stable to heat without any adverse effects. This review provides a comprehensive overview of the nutritional properties of red palm oil. The possible antiatherogenic, antihemorrhagic, antihypertensive, anticancer, and anti-infective properties of red palm oil are examined. Moreover, evidence supporting the potential effectiveness of red palm oil to overcome vitamin A deficiency in children and pregnant women, to improve ocular complications of vitamin A deficiency, to protect against ischemic heart disease, to promote normal reproduction in males and females, to aid in the management of diabetes, to ameliorate the adverse effects of chemotherapy, and to aid in managing hypobaric conditions is presented.*

INTRODUCTION

The fruit of the oil palm tree (*Elaeis guineesis*) is the source of red palm oil. The oil palm is a perennial crop tree and has the highest oil yield compared with other leading oilseed crops in terms of oil yield per hectare.[1] Currently, Malaysia and Indonesia are the leading producers of palm oil.[2] The oil palm is a unique crop that can produce two types of oil, namely palm oil from the fibrous mesocarp (which has a brilliant, deep red-orange pulp) and palm kernel oil (which resembles coconut oil) from the kernel.[3]

Crude palm oil can be processed into various downstream products, although phytonutrients are partially removed during processing. Refined, bleached, and deodorized palm oil, the major processed product, is obtained from the bleaching and deodorization of crude palm oil. During the refining process, the carotenes that give crude palm oil its red-orange color become decomposed, resulting in refined, bleached, and deodorized palm oil, which has a light yellow color and retains part of the other phytonutrients.[4] Refined, bleached, and deodorized palm oil is a versatile oil widely used in more than 150 countries worldwide.[5] Red palm oil, on the other hand, is obtained through the novel processes of pretreatment, deacidification, and deodorization using molecular distillation, which allow about 80% of the carotenes and vitamins present in crude palm oil to be retained.[4] As a result, red palm oil has a distinctive flavor and aroma and is rich in

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doi: 10.1093/nutrit/nuw054

Table 1 **Health benefits of phytonutrients found in red palm oil**[a]

Phytonutrient (amount)	Composition[b] and health benefits
Vitamin E (717–863 ppm)	*Composition*: α-tocopherol (19%), α-tocotrienol (29%), γ-tocotrienol (41%), δ-tocotrienol (10%) *Health benefits*: anticancer, antiangiogenic, antioxidant, antiatherosclerotic, cardioprotective, and neuroprotective properties; inhibits cholesterol synthesis; aids in diabetes management
Carotenoids (600–750 ppm)	*Composition*: phytoene (0.2%), phytofluene (0.6%), β-carotene (41.0%), α-carotene (41.3%), *cis*-α-carotene (10.2%), ζ-carotene (0.6%), γ-carotene (0.8%), δ-carotene (0.8%), neurosporene (0.2%), β-zeacarotene (1.3%), α-zeacarotene (0.5%), lycopene (1.0%) *Health benefits*: provitamin A activity; cardioprotective and anticancer activity; prevents night blindness
Phytosterols (325–365 ppm)	*Composition*: cholesterol (6.6–11.5 ppm), campesterol (76–83 ppm), stigmasterol (59–64 ppm), β-sitosterol (187–218 ppm), unknown (<6 ppm) *Health benefits*: cholesterol-lowering properties, anticancer activity, enhances immune function
Squalene (14–15 ppm)	*Health benefits*: cardioprotective, radioprotective, and anticancer activity; inhibits cholesterol synthesis
Ubiquinone (18–25 ppm)	*Health benefits*: enhances production of cellular energy; antioxidative properties; cardioprotective and anticancer activity

Abbreviation: ppm, parts per million.
[a]Adapted from Loganathan et al.[13]
[b]Composition obtained from Tay et al.[6]

phytonutrients such as carotenes (which give the oil a bright red color), vitamin E, phytosterols, squalene, and coenzyme Q10.[6] Red palm oil has been known for its versatility as both a food and a health remedy for centuries. It was valued as a sacred food by the pharaohs of ancient Egypt.[7] Red palm oil is traditionally used in the tropical rain forest regions of West Africa[2] and northeastern Brazil.[8] Despite the high production and use of refined palm oil in countries like Malaysia and Indonesia, the nutritional potential of red palm oil has been underutilized in these countries.[9] Its nutritional properties are conferred mainly via its constituent phytonutrients, which are listed in Table 1. The purpose of this review, which is based on data from animal and human studies, is to provide a comprehensive overview of the nutritional benefits of red palm oil.

BIOAVAILABILITY AND BIODISTRIBUTION OF RED PALM OIL

Vitamin A occurs naturally in animal products. Good sources of vitamin A are cheese, butter, eggs, liver, and fish.[10] Vegetarians obtain their required vitamin A from carotenoids, which are found in plants, especially orange, green, and yellow vegetables and some fruits.[11] Red palm oil is considered one of the world's richest natural plant sources of carotenoids, which give the oil and fruit their brilliant orange-red color.[11] About 600 types of naturally occurring carotenoids are known,[12] 13 of which are found in palm oil: phytoene, phytofluene, *cis*-β-carotene, β-carotene, α-carotene, *cis*-α-carotene, ζ-carotene, γ-carotene, δ-carotene, neurosporene, β-zeacarotene, α-zeacarotene, and lycopene.[6] The major carotenes are β-carotene and α-carotene, accounting for 41.0% and 41.3%, respectively, of the total carotenoids present in commercial red palm oil.[6] Only 10% of the 600 known carotenoids are believed to have provitamin A activity. The α-, β-, and γ-carotenes are the only carotenes of red palm oil that show quantifiable provitamin A activity.[13] Red palm oil contains 15 times more retinol (provitamin A) equivalents than carrots, 300 times more than tomatoes,[4] and 44 times more than leafy vegetables.[9]

Carotenoids are fat-soluble pigments that require fat for conversion into vitamin A. Both vitamin A and β-carotene are absorbed, together with fat, in the small intestine in the presence of bile and pancreatic secretions.[12,14] Bioavailability of β-carotene and vitamin A is greater with the simultaneous intake of fats.[14] A minimum of 5 g of fat is required for optimal absorption of carotenoids.[12] Thus, red palm oil offers promise for the treatment of vitamin A deficiency. In humans, the half-life of vitamin A is 200 to 300 days[15]; hence, vitamin A status is not disturbed by slight fluctuations in vitamin A consumption. Ninety percent of vitamin A is stored in the liver, 1.5% is found in blood, and the remainder is stored in other tissues. β-Carotene levels, on the other hand, return to baseline levels within 20 to 30 days of the cessation of supplementation.[15] Provitamin A carotenoids in red palm oil are highly bioavailable, efficiently converted to retinols, and stored well in the liver.

A multicenter 20-week trial conducted in 5 European regions (Grenoble, France; Coleraine, Northern Ireland; Cork, Republic of Ireland; Zeist, the Netherlands; and Madrid, Spain) evaluated serum responses of carotenoids and tocopherols in 400 healthy volunteers given 100 mg of α-tocopherol in corn oil, 15 mg of carotenoids (red palm oil, lutein-rich Marigold extract, or lycopene-rich tomato extract) in corn oil, or corn oil placebo.[16] After 20 weeks, the α-tocopherol–supplemented group showed increased α-tocopherol levels and decreased γ-tocopherol levels. The red palm oil–supplemented group had marked increases in α-carotene (14-fold) and β-carotene (5-fold). Lutein supplementation, on the other hand, increased levels of lutein (5-fold), zeaxanthin (2-fold), and ketocarotenoids. Lastly, lycopene supplementation increased

serum lutein levels (2-fold). Different rates of benign carotenodermia (95% with red palm oil, 40% with lutein, and 25% with lycopene) were observed in an additional study in Spanish volunteers. Clearly, each carotenoid is metabolized differently in the human body, and several aspects of carotenoid absorption, transportation, clearance, tissue deposition, and utilization are still poorly understood.[16]

In a randomized, crossover trial, van het Hof et al.[17] compared the bioavailability of carotenes following consumption of a lunch fortified with red palm oil (25 mg/d) or synthetic all-*trans* β-carotenes (25 mg/d) in 72 healthy volunteers. Supplementation for 4 days was followed by a 10-day washout period. Both synthetic and natural palm oil carotenoids had comparable effects, with improved plasma β-carotene levels observed after 4 days of supplementation. The power of the study, however, is limited by the carryover effect of red palm oil supplementation used with a short washout period.

In a single-dose pharmacokinetic model, both the metabolic activity and the bioavailability of vitamin A and carotenes were studied using a stable isotope reference method.[18] Twelve healthy volunteers were given 10 g of red palm oil in blended juice (2.4 mg of β-carotene and 1.8 mg of α-carotene) coadministered with a small amount of deuterium-labeled vitamin A ester (retinyl-acetate). Triglyceride-rich lipoprotein measured 8.5 hours after the intervention contained a lower ratio of β-carotene to α-carotene, implying that the vitamin A activity of β-carotene was substantially greater than that of α-carotene.[18]

An 8-week study of red palm oil supplementation (1.5 mg of β-carotene) in patients with cystic fibrosis was conducted at the Cystic Fibrosis Center in Heidelberg, Germany.[19] The majority of patients with cystic fibrosis have pancreatic insufficiency, which leads to a deficiency of nonenzymatic antioxidants caused by malabsorption of lipids and lipophilic vitamins. Interestingly, daily supplementation of the diet with red palm oil was found to improve plasma β-carotene, retinol, and α-carotene levels in patients with cystic fibrosis.[19]

In a recent randomized controlled model with a 2-week washout period, biofortified cassava gari was compared with an equal amount of red palm oil–fortified cassava gari for its effectiveness in improving vitamin A status in 8 healthy well-nourished American women.[20] Participants were provided with cassava gari–based breakfast meals that contained biofortified gari (1 mg of carotene), red palm oil–fortified gari (1 mg of β-carotene), or unfortified gari (0.3 mg of retinyl palmitate, reference supplement). Interestingly, both biofortified and red palm oil–fortified gari meals efficiently increased plasma concentrations of β-carotene, α-carotene, and retinyl palmitate.[20]

SAFETY, MUTAGENECITY, AND TOXICOLOGY OF PALM OIL

The safety of both crude palm oil and refined, bleached, and deodorized palm oil has been studied extensively in mutagenicity, nutritional, and toxicological studies, with no adverse effects reported. When fats are subjected to heat, thermal oxidation occurs and mutagens are formed. Heating can also lead to deterioration of the nutritional quality of the oil. Repeatedly heated crude palm oil and refined palm oil were tested for mutagenicity to determine the safety of edibility. Using *Salmonella typhimurium* strains TA100 and TA98 in the Ames test, no mutagens were detected when extracts of these oils were metabolically activated using the S9 fraction of rat liver microsomes.[21] This study demonstrates that these oils are suitable for use as a frying medium. Furthermore, despite repeated frying, the oils remained chemically stable and were safe for consumption.[21] Numerous studies conducted in India and included in the present review used the unrefined, unbleached, crude palm oil of edible-grade quality, yet the oil was termed *red palm oil* in the published reports because it was rich in carotenoids.

Nutritional and toxicological studies were conducted in weanling Wistar/NIN albino rats in 28-day and 90-day feeding studies.[22] Nutritional and toxicological effects of a protein-free diet vs a diet containing 10% casein protein with 10% fat (peanut oil, crude palm oil, or refined, bleached, and deodorized palm oil) were compared. No adverse effects on growth rate, feed efficiency, digestibility, fat absorption, nitrogen balance, phosphorus and calcium retention, serum enzymes, or blood hematology were found for any of the fats tested. Levels of lipids in tissue (after 28 days of feeding) and blood (after a longer 90-day feeding period) were comparable in all 3 groups fed oil (crude palm oil, refined, bleached, and deodorized palm oil, or peanut oil). Hence, when compared with peanut oil and refined, bleached, and deodorized palm oil, crude palm oil was found to possess similar nutritional quality and showed no toxicity.[22]

Hepatic drug-metabolizing enzymes, used to assess detoxification in a host, were studied in 3 generations of Wistar/NIN/inbred albino rats.[23] The effects of supplementation with red palm oil (10% of total fat) on various phase I and phase II metabolic pathways were compared with those of refined, bleached, and deodorized palm oil and refined, bleached, and deodorized palm olein. Carcinogens are metabolized instantaneously, producing a complex mixture of yields. Phase II glutathione *S*-transferase activity was measured in the livers of F3-generation mice. Feeding was extended for an additional generation (F4) for another 9 weeks. Red

Table 2 **Recommended dietary allowance (RDA) for vitamin A**[a]

Category	Age	RDA for vitamin A (μg RE)	Amount of red palm oil that supplies the RDA (g)
Infants	0–12 mo	400–500	5.7–7.1
Children	1–8 y	300–400	4.3–5.7
Adults			
Males	9–70 y	600–900	8.6–12.9
Females	9–70 y	600–700	8.6–10
Pregnancy	14–50 y	750–770	10.7–11
Lactation	14–50 y	1200–1300	17.1–18.6

Abbreviation: RE, retinol equivalents.
[a]RDA for vitamin A adapted from the Institute of Medicine.[25]

palm oil supplementation was found to increase levels of glutathione *S*-transferase, a detoxifying phase II enzyme; moreover, no induction of phase I enzymes or increase in total cytochrome P450, both of which indicate metabolization of phenobarbitone and polycyclic aromatic hydrocarbon, was found. Hence, the protection against chemical carcinogens provided by red palm oil was likely attributable to carotenoid content.[23] The tolerance and effective antioxidant potential of ordered doses (0, 1, 2, and 4 mL) of red palm oil was studied in a 7-week animal study. Red palm oil supplementation was found to enhance the concentration of antioxidants in red blood cells and liver. In addition, animals fed red palm oil also had normal liver architecture. On the basis of the data collected thus far, red palm oil appears safe for consumption and supplementation.[24]

RECOMMENDED DIETARY ALLOWANCE FOR VITAMIN A

The total amount of vitamin A in food is expressed as micrograms of retinol equivalents (RE). One hundred grams of red palm oil contains approximately 7000 RE. Table 2 shows the Recommended Dietary Allowance (RDA) for vitamin A as established by the Institute of Medicine for different populations.[25] An estimated 1 teaspoon (5 g) of red palm oil will supply the RDA for vitamin A for infants and children, whereas double this amount (10 g) will supply the RDA for adults and pregnant women. The contribution of the different phytonutrients in red palm oil, based on the estimated amounts of red palm oil needed to meet the RDA for vitamin A, is shown in Table 3. A comprehensive review of 62 controlled trials examined the correlation between health outcomes and plasma concentrations of carotenoids.[26] On the basis of the findings, a carotenoid health index with 5 categories of risk was proposed: <1μM (very high risk), 1–1.5μM (high risk), 1.5–2.5μM (moderate risk), 2.5–4μM (low risk), and >4μM (very low risk).[26]

VITAMIN A AND DISEASE PREVENTION

The therapeutic efficacy of red palm oil in various disorders has been researched extensively. In particular, supplemental red palm oil for vitamin A deficiency has been studied thoroughly in children, pregnant women, and lactating mothers. Other diseases, including cardiovascular complications, diabetes, cancer, and reproductive complications, have also been investigated, primarily in animal models. The section below describes evidence from animal and human trials that assessed the potential health benefits of red palm oil on various conditions.

Vitamin A deficiency

Deficiency of vitamin A or retinol is a public health problem, listed as the most widespread nutritional deficiency worldwide.[11] Vitamin A deficiency results from liver disorders, malabsorption of fat, or inadequate dietary intake of vitamin A. Provitamin A can be cleaved to yield retinaldehyde and, thus, retinol and retinoic acid.[27]

Children. According to the World Health Organization (WHO), about 190 million preschool children in underdeveloped countries, especially countries in Africa and Southeast Asia, are vitamin A deficient.[28] Infants and children have higher vitamin A requirements to promote rapid growth and better immunity to infections. Vitamin A deficiency in children causes visual impairment, blindness, stunting, anemia, respiratory disease, increased risk of infection, and mortality due to common childhood infections such as diarrhea and measles. A Cochrane meta-analysis of 194 795 children showed that vitamin A supplementation could lower the incidence of several illnesses and reduce childhood mortality by 23%.[29]

In South Africa, van Stuijvenberg et al.[30] compared the effect of supplementation on the vitamin A status of primary school children using biscuits fortified with either red palm oil as a source of β-carotene or synthetic β-carotene (both provided 34% of the RDA for vitamin A in children, or 1.43 mg of β-carotene), with placebo provided as a control. Biscuits were distributed on school days for 6 months to 265 children aged 5 to 11 years who attended a rural primary school in the province of KwaZulu-Natal. The increase in serum retinol levels from baseline to 6 months was identical in all 3 groups. The authors reported 2 confounding factors. First, a new school lunch program was introduced during the last 4 weeks of the study (providing 233 RE of β-carotene per day, or 33% of the RDA for vitamin A). Second, the last batch of red palm oil–fortified biscuits

Table 3 **Contribution of phytonutrients based on estimated recommended amounts of red palm oil (RPO)[a]**

Phytonutrient	5 g of RPO (1 tsp)	10 g of RPO (2 tsp)	18 g of RPO (1 tbsp)
Total carotene	3.3 g	6.7 g	12.0 g
β-Carotene	1.3 g	2.7 g	4.8 g
α-Carotene	1.3 g	2.7 g	4.8 g
Other carotenes	0.7 g	1.3 g	2.4 g
Total vitamin E	4.1 g	8.1 g	14.6 g
α-Tocopherol	0.8 g	1.5 g	2.8 g
α-Tocotrienol	1.2 g	2.3 g	4.2 g
γ-Tocotrienol	1.7 g	3.3 g	6.0 g
δ-Tocotrienol	0.4 g	0.8 g	1.4 g
Coenzyme Q10	0.1 g	0.2 g	0.4 g
Phytosterols	1.6 g	3.2 g	5.8 g
Campesterol	0.2 g	0.5 g	0.9 g
Stigmasterol	0.3 g	0.6 g	1.1 g
β-Sitosterol	1.0 g	2.0 g	3.6 g
Cholesterol and other unknown phytosterols	0.0 g	0.1 g	0.2 g

Abbreviations: tbsp, tablespoon; tsp, teaspoon; RPO, red palm oil.
[a]Adapted from Tay et al.[6]

provided only half of the intended RDA for vitamin A because the red palm oil shortening had degraded under unsuitable storage conditions.[30] Nevertheless, this study reported good acceptance of red palm oil–fortified biscuits, indicating a feasible approach to address vitamin A deficiency among children.[30,31] The same authors conducted follow-up studies[31,32] in a different region where there was no school lunch program to confound the results. A similar design was employed, but the amount of the RDA supplied (30%) was slightly lower, the number of students (n = 432) aged 5 to 11 years from rural primary schools in KwaZulu-Natal was larger, and the study duration (3 months) was shorter. The provitamin A status of both groups who received β-carotene–fortified biscuits improved to a similar extent, whether biscuits were fortified with red palm oil or synthetic β-carotene.[31]

In Burkina Faso, the effect on vitamin A status of adding red palm oil to school meals was studied in primary schools in the cities of Kaya (north-central area) and Bogande (eastern area).[33] The sites were chosen carefully to ensure red palm oil was neither produced in the area nor used in a supplementation program. In Kaya, 239 pupils (aged 7–12 years) from 15 intervention schools participated in a study of the pre–post test effect of red palm oil supplementation on serum retinols. Red palm oil, provided at 15 mL (containing15 000 µg of retinol activity equivalents [RAEs]) per individual, 3 times per week for 1 year, was incorporated into the school lunch program. After the end of the intervention, serum retinol levels had increased and the rate of low serum retinol levels had declined. In a similar study in Bogande, pre–post tests were performed in 3 groups: group 1, negative control group who received regular school lunch; group 2, positive control group who received the regular school lunch and a single vitamin A capsule (60 mg) at the end of the school period; and group 3, who received red palm oil (a total of 76.5 mg RAEs over the test period). Comparable improvement in serum retinol levels and a decline in the rate of low serum retinol levels were reported in both the vitamin A–supplemented group and the red palm oil–supplemented group. These results indicate that a low dose of red palm oil, taken regularly, improves vitamin A in individuals with deficiency.[33]

In India, Manorama et al.[34] conducted 3 studies to evaluate the following: (1) the pre–post test effects of red palm oil on serum retinol levels; (2) the efficacy of red palm oil as a vitamin A supplement; and (3) the sustainability of serum retinol levels over a period of nonsupplementation after supplementation with red palm oil vs vitamin A. In the first trial, a 2-month intervention, vitamin A–deficient children (n = 24) aged 7 to 9 years of low socioeconomic status in a government-subsidized home in Hyderabad were given the Indian sweet, suji halwa, either fortified with red palm oil (2400 µg of β-carotene) or as prepared as placebo using peanut oil, as an evening snack. The group that received the placebo snack was given oral supplementation with 600 µg of vitamin A drops. Improvement in serum retinol levels and liver retinol stores was similar in both groups. In the second trial, mildly to severely vitamin A–deficient children (n = 26) aged 7 to 12 years from government schools in Hyderabad were given an evening snack of fortified suji halwa, similar to that given in the first trial, or a massive single dose of synthetic vitamin A (100 000 IU). After 1 month, a twofold improvement in serum retinol levels was reported in both groups. In addition, although the baseline level of β-carotene was low in both groups, the red palm oil–fortified group showed more than 3-fold improvement in β-carotene levels. In the third trial, vitamin A–deficient children (n = 36) aged 7 to 9 years from an interior village (Nakhaur, Orissa) were given dietary supplementation for 1 month and called for a follow-up after 6 months. Children were assigned to 1 of 3 groups: control, given 100 000 IU of vitamin A as a single massive dose; the Indian sweet besan laddhu, fortified with 4 g of red palm oil (50 000 IU of vitamin A); or besan laddhu fortified with 8 g of red palm oil (100 000 IU of vitamin A). After 6 months, upon cessation of supplementation, the group that received the red palm oil–fortified snack (8 g) had retinol levels comparable with those of the control group who received the single dose of vitamin A.[34] Red palm oil is an efficient source of bioavailable β-carotene; hence, supplementation with red palm oil twice or thrice yearly is recommended to maintain sufficient vitamin A status.[35]

In a similar, comparative, 15-day study, children (n = 36) aged 7 to 9 years old in Nakhour village, Orissa, were given a massive dose of vitamin A (50 000 IU) or the Indian sweet besan laddhu fortified with either 4 g of red palm oil (25 000 IU) or 8 g of red palm oil (50 000 IU).[36] Serum retinol levels were evaluated at baseline, after 15 days of supplementation, and after 3 months of supplementation. Compared with levels at baseline, serum retinol after both the massive vitamin A dose and the snack fortified with 4 g of red palm oil doubled, whereas levels after 8 g of red palm oil tripled. Moreover, 8 g of red palm oil conferred similar protection as the massive vitamin A dose after both the initial supplementation period and the postsupplementation period. Rather than continual supplementation, periodic supplementation at 3-month intervals was suggested for dietary supplementation programs to maintain normal childhood vitamin A status.[36]

Pregnancy and lactation. According to WHO, about 19 million pregnant women in underdeveloped countries are vitamin A deficient, especially in Africa and Southeast Asia.[28] During pregnancy and lactation, women are vulnerable to vitamin A deficiency because additional vitamin A is required to support maternal and fetal tissue growth as well as lactation.[37] Lactating mothers have been encouraged to supplement their diet with carotenoid-rich red palm oil to increase retinol levels in maternal serum and breast milk.[38]

The impact on vitamin A status of 8 mL of red palm oil (2400 µg of β-carotene) or 8 mL of peanut oil in sachets was studied in 170 pregnant women and their infants.[39] Pregnant women recruited from Niloufer Hospital, Hyderabad, received 8 weeks of supplementation, beginning at 26–28 weeks of gestation and ending at 35–36 weeks. Higher retinol levels in mothers and infants were reported, as was a decreased incidence of maternal anemia.

Lietz et al.[40,41] conducted 2 studies on the effect of red palm oil on provitamin A activity in pregnant and lactating women in drought-prone rural villages in Tanzania. In the first study, pregnant women in the third trimester were allocated to receive red palm oil (12 g/d) or sunflower oil (12 g/d) or staple food and were encouraged to maintain their practice of eating dark green vegetables.[40] Tanzanian staple foods comprise sorghum, millet, maize, sweet potatoes, legumes, and green vegetables, whereas fish, meat, and eggs are rarely eaten. An amount of oil sufficient for 6 months, according to household size, was provided from the beginning of the third trimester to 3 months postpartum. Increased provitamin A activity, as shown by α-carotene and β-carotene levels, was found in both breast milk and plasma in red palm oil–supplemented groups. Retinol levels in breast milk remained stable in both the sunflower oil–supplemented and the red palm oil–supplemented groups.[40]

In a second follow-up study, which had a similar design, carotenoid levels in both plasma and breast milk were studied.[41] Levels of hydrocarbon carotenoids (α-carotene and β-carotene) were higher and levels of xanthophylls (lutein and zeaxanthin) lower in plasma than in breast milk in the red palm oil–supplemented group. Appreciable amounts of provitamin A and xanthophylls in breast milk of nursing mothers were found in the red palm oil–supplemented group. Xanthophylls are present in the macular pigment and protect photoreceptor cells against photooxidative damage.[41]

In another study with a similar design, also conducted in Tanzanian women in the third trimester of pregnancy, the effect of red palm oil, sunflower oil, or staple food on milk cytokines and prevalence of subclinical breast inflammation was investigated.[42] Mothers were encouraged to breastfeed because breast milk is rich in immunologically active components that promote infant health and immunity. A significant decrease in milk Na^+/K^+ was found in sunflower oil–compared with red palm oil–supplemented participants. The study was limited, however, because it was not randomized and double-blinded.[42]

In a short-term 10-day study, Honduran mother–infant pairs (n = 98) were assigned to receive either red palm oil supplementation (15 ml, equivalent to 15 mg of β-carotene and 6.8 mg α-carotene), β-carotene supplements (15 mg), or placebo (corn starch).[43] Short-term intake of red palm oil by the mothers was found to increase α-carotene and β-carotene in maternal plasma and breast milk. A significant increase in β-carotene compared with α-carotene was found in infant plasma. Improved vitamin A status in infants, possibly via metabolism of β-carotene in the maternal diet to retinols or more bioavailable α-carotene, was suggested.[43]

A survey was conducted in Nigerian women at different stages of pregnancy (n = 200) to determine the correlation between vitamin A status, habitual diet, present health, and morbidity status. Four-fifths of the women reported consuming red palm oil. It is speculated that frequent episodes of malaria, anemia, and subclinical infections, such as upper respiratory tract and urinary tract infections, were related to a high prevalence of vitamin A deficiency. Both the typical food preparation method – which involved heating oil to the point of smoking for at least 10 minutes and boiling green vegetables before adding them to the sauce – and the low intakes of liver (≈3 times per month) were thought to be related to low levels of bioavailable vitamin A. This study indicates that vitamin A deficiency is still prevalent in pregnant Nigerian

women.[44] Education about food preparation and the heat stability of red palm oil may be beneficial to this group.

A longitudinal pre–post-intervention study was performed to evaluate the effectiveness of red palm oil as a source of vitamin A among mother–child (aged 1–3 years) pairs (n = 210) in an area of Burkina Faso where red palm oil is not consumed.[45] Intake of breast milk, red palm oil, and fruit contributed to a significant increase in dietary vitamin A among children, whereas intake of red palm oil and vegetables significantly increased dietary vitamin A among mothers. Red palm oil was shown to significantly increase serum retinol levels in both mothers and children.[45]

Mosha et al.[46] conducted a study as part of an ongoing effort to enrich locally produced staples with vitamin A. The local staple, cassava flour, was fortified with red palm oil. Red palm oil–fortified cassava flour (providing 1920 RE/d) was used to prepare weaning and normal family meals for preschool children (n = 162) and pregnant and lactating women (n = 68). The 20-month pilot study was conducted in 5 villages in the rural district of Kigoma, Tanzania, which had high levels of disorders related to vitamin A deficiency and undernourishment. Although the Kigoma district is among the largest producers of red palm oil, it is an area of low red palm oil consumption, owing to lack of nutritional awareness by mothers and an unacceptable flavor, especially to children. In 3 pilot villages, community-level nutrition education programs were conducted to train mothers to prepare red palm oil–fortified cassava flour. The remaining 2 villages served as controls and prepared cassava flour in the traditional manner; they did not participate in the cassava flour fortification program or the feeding trials. Red palm oil–fortified cassava flour was reported to be highly acceptable. Serum retinol levels and growth rate improved among preschool children who consumed red palm oil–fortified cassava flour. Serum retinol concentrations also increased in pregnant and lactating women. Hence, fortification of staple foods with red palm oil can be an inexpensive, feasible, and workable way to address vitamin A deficiency.[46]

A cluster-randomized cross-sectional dietary intake survey was conducted among 587 households of mother–child dyads to assess the prevalence of vitamin A deficiency in Akwa Ibom, Nigeria.[47] This assessment was part of the HarvestPlus program to introduce provitamin A–biofortified cassava as a sustainable food in Nigeria. Participants were reported to have iron deficiency on the basis of low ferritin and high transferrin levels. This population was found to have adequate vitamin A status, which was attributed to relatively high red palm oil consumption that accounted for 50% to 60% of the daily vitamin A intake. The prevalence of vitamin A deficiency among the children, however, is a still a concern. According to the authors, this could be related to several factors, such as infection status, efficiency of provitamin A bioconversion from the diet, and degradation of vitamin A. Participants had higher levels of retinol carriers (ie, retinol-binding proteins) compared with serum retinol levels, indicating adequate retinol liver stores.[47]

Visual impairment due to vitamin A deficiency in children. According to WHO, an estimated 2.8 million preschool-aged children are at risk of nutritional blindness or active xerophthalmia due to vitamin A deficiency in low-income countries.[48] Approximately 250 000 to 500 000 children with vitamin A deficiency become blind yearly, half of whom die within a year of losing their vision.[48] The ocular signs of progressive vitamin A deficiency in children, as graded by WHO, are night blindness, conjunctival xerosis, Bitot's spots, corneal xerosis, corneal ulcer/keratomalacia, and corneal scarring.[11] Severe vitamin A deficiency distresses ocular tissue by reducing regeneration of visual pigment upon exposure to bright light or causes lasting damage to the epithelium of the cornea and conjunctiva. Classical ocular manifestations of vitamin A deficiency range from less serious Bitot's spots and night blindness to severe xerophthalmia and keratomalacia resulting in blindness.[9]

In a 1937 hospital-based study, Aykroyd and Wright[49] investigated the effects of red palm oil emulsion compared with cod liver oil emulsion (both supplying vitamin A at 500 IU/d) in infants and children with keratomalacia or corneal ulceration. Marked clinical improvement with red palm oil treatment was observed within 14 days. The two treatments showed comparable efficacy. Red palm oil was better tolerated than cod liver, which tended to aggravate diarrhea, and was more palatable.[49]

Two studies conducted in India reported a reduction in Bitot's spots after red palm oil supplementation.[50,51] Bitot's spots are areas with abnormal squamous cell proliferation and keratinization of the conjunctiva, which lead to the formation of patches. In the first study, Sivan et al.[50] provided participants with a red palm oil–fortified noon meal to assess the acceptability of red palm oil, the effects of red palm oil on vitamin A status, and morbidity. Preschool children (n = 923) from 35 daycare centers in the Vivekananda Kendra Rural Development Programme in Tamil Nadu, a region with a high prevalence of xerophthalmia, were chosen. A standard noon meal fortified with 5 mL of either red palm oil or peanut oil was provided for 10 months. The red palm oil group had better vitamin A status, lower incidence and greater disappearance of

Bitot's spots, and higher serum β-carotene levels than the control group, and red palm oil was as acceptable as the control oil.[50] In a follow-up study with a shorter intervention of 7 months, additional control groups received vitamin A retinol palmitate (400 RE or 800 RE) or peanut oil (5 mL or 10 mL), and an experimental group received red palm oil (5 mL [400 RE] or 10 mL [800 RE]). Six groups comprising a smaller number (n = 334) of preschool children from the Vivekananda Kendra preschool in Ramanathapuram, Tamil Nadu, were recruited to assess the effectiveness and determine the optimal dose of supplementation. Sivan et al.[51] reported that a lower dose of red palm oil, 5 mL/d, improved vitamin A status as well as the 8 mL dose used by Mahapatra and Manorama.[36] Red palm oil at 5 mL/d was sufficient to improve retinol, β-carotene, and α-tocopherol status. Furthermore, red palm oil conferred better protection than synthetic vitamin A, and no new cases of Bitot's spots were reported in either group that received supplementation.[51]

The Nutrition Foundation of India conducted a multicentric study in Trivandrum, Coimbatore, and New Delhi.[52] Although participants – children, pregnant, and lactating women – initially did not like red palm oil because of its odor and color, they eventually accepted it. Red palm oil supplementation was found to increase the rate of disappearance of Bitot's spots in Coimbatore and Trivandrum. In New Delhi, it was found to significantly improve conjunctival impression cytology. In addition, 54% of children with conjunctival impression cytology had normal findings after 6 months of red palm oil supplementation. After 5 months of supplementation, 80% of participants with vitamin A deficiency had normal vitamin A levels. Hence, a small amount of red palm oil (4–10 g/d) was adequate to improve vitamin A status in children and adults.[52]

Ocular manifestations of vitamin A deficiency still exist in underprivileged communities in Malaysia.[53] Vitamin A deficiency is prevalent in preschool and primary school–aged children from rubber plantations and aboriginal Orang Asli children. The acceptability and order of preference of 3 different red palm oil–fortified local snacks, namely spring roll, curry puff, and doughnut, was tested with 26 preschool children from 2 preschools in an Orang Asli settlement in Sungai Tekir, Negeri Sembilan. The snack was fortified with 5 mL of red palm oil (providing 300 RE/d), which contributed two-thirds of the recommended nutrient intake for vitamin A in Malaysian children. The percentage of carotenoid retention in the snacks varied (100% in doughnut, 84% in spring roll, and 35% in curry puff) depending on the different heating conditions used to prepare the snacks. The acceptability of all snacks tested was high (82%–100%). The children preferred spring roll the most and doughnut the least.[54] Red palm oil–fortified snacks can be used to combat vitamin A deficiency among Orang Asli[54] and underprivileged children in Malaysia.

In 1963, a study was conducted in 3- to 13-year-old Indonesian boys (n = 52) living in orphanages in Jakarta, Java, with obvious ocular symptoms of vitamin A deficiency and minor symptoms of xerophthalmia.[55] The children were assigned to 1 of 5 groups to receive sugar (2 g/kg body weight), skim milk powder (2 g/kg body weight), coconut oil (1 g/kg body weight), red palm oil (providing β-carotene at 410 μg/kg body weight), or 2000 IU of vitamin A acetate for 22 days during mealtimes. Remarkably, red palm oil was found to cure night blindness in these children. Compared with the other groups, the red palm oil group showed increased serum vitamin A levels after 1 week of supplementation, and levels were sustained thereafter.[55]

In 1967, Lian et al.[56] conducted a 2-week intervention in 5 Javanese villages to improve vitamin A intake in preschool children (n = 226) aged 1 to 5 years with xerophthalmia. Villages 1 and 2 were assigned to receive red palm oil as vitamin supplement (4 mL/d = 3000 IU of provitamin A), village 3 was assigned to receive refined, bleached, and deodorized palm oil, village 4 received no supplement, and village 5 was supplemented with skim milk fortified with vitamins A and D (2400 IU of vitamin A). Interestingly, villages supplemented with red palm oil showed reduced incidence of xerophthalmia and increased levels of vitamin A. Moreover, children supplemented with vitamin A–fortified skim milk showed increased serum levels of vitamin A, indicating vitamin A can be absorbed even in conjunction with a diet low in fat.[56]

Use of red palm oil for cardiovascular-related complications

The health effects of red palm oil other than overcoming vitamin A deficiency have been widely studied. Animal models are commonly used to gain mechanistic insight into the pathogenesis of disease. This section addresses the potential therapeutic efficacy of red palm oil as an adjuvant in disease prevention and treatment, assessed mainly from the results of animal studies but also from human dietary interventions.

Ischemic reperfusion. According to the WHO, ischemic heart disease is the leading cause of death worldwide in middle- and high-income countries.[57] Ischemic heart disease or coronary artery disease is caused by insufficient blood supply to the heart muscle (myocardium). Extensive studies in animals have documented the

cardioprotective role of red palm oil against ischemic reperfusion injury in the heart via several mechanisms,[58] namely by activation of cardioprotective pathways, including mitogen-activated protein kinases (MAPKs),[59] nitric oxide–cyclic guanosine 3′,5′-monophosphate (NO-cGMP),[60–62] matrix metalloproteinase-2 (MMP-2),[63] and connexin-43 (Cx43)[64]; enhancement of the prosurvival signals protein kinase B (PKB)[65,66] and phosphoinositide-3-kinase–protein kinase B (P13K-PKB)[66]; attenuation of the proapototic markers c-Jun N terminal kinase (JNK),[59,65] poly(ADP-ribose) polymerase (PARP) cleavage,[59,65,66] and caspase-3[59]; and reduction of myocardial tissue injury by reducing lactate dehydrogenase levels.[67]

Red palm oil–based baking fat (providing 0.58 mg of red palm oil per kilogram of body weight per day) was incorporated into normal rat chow for 6 weeks in a rat model of hyperlipidemia.[62] Red palm oil supplementation improved aortic output recovery and increased levels of cGMP, which protects against myocardial ischemia. Dietary red palm oil was speculated to improve myocardial ischemic tolerance by raising nitric oxide (NO) concentrations and restoring NO-cGMP signaling in the heart.[60–62]

Nitric oxide plays an important role in regulating cardiac and vascular function and protecting against tissue reperfusion. During ischemic reperfusion, elevated production of myocardial NO confers protection against ischemia/reperfusion damage. In a 6-week reperfusion cardiac functionality test, male Long-Evans rats received a control diet, a high-cholesterol (2% cholesterol) diet, a control diet with red palm oil (7 g per kilogram of diet), or a high-cholesterol (2% cholesterol) diet with red palm oil (7 g per kilogram of diet).[60] Improvement in aortic output recovery in animals supplemented with red palm oil was hypothesized to be linked to NO-cGMP activation and inhibition of the cyclic adenosine monophosphate (cAMP) pathway. It was postulated that, during ischemia, NO formation protects the myocardium by increasing tissue cGMP (an endogenous intracellular cardioprotectant) and reducing cytosolic cAMP-regulated calcium influx.[60]

In a continuation study, Esterhuyse et al.[61] investigated the role of the NO-cGMP pathway on myocardial ischemic tolerance in a rat model of hyperlipidemia.[61] Mediated by cGMP, NO confers a cardioprotective effect against the consequences of ischemia/reperfusion. To study these effects, a diet similar to that in the earlier study[62] was used, and 2 groups were added to mimic animals with hyperlipidemia by adding 2% cholesterol to the diet in the control and experimental groups. In addition to the previous observations,[62] under hypoxic conditions, NO levels in cardiomyocytes were elevated in the group fed red palm oil, while NO synthase activity was elevated in the group fed red palm oil and cholesterol. Hence, dietary red palm oil could improve myocardial ischemic tolerance by enhanced NO and NO-cGMP signaling.[61]

Extracellular signal-regulated protein kinase (ERK), p38, and JNK are major MAPKs.[65] Mitogen-activated protein kinases and PI3K/PKB play pivotal roles in cell growth, differentiation, apoptosis,[65] and metabolism.[65,66] Engelbrecht et al.[65] investigated the role of the PKB and MAPKs pathways in myocardial ischemic tolerance.[65] A dietary design similar to that used by Esterhuyse et al.[62] was adopted. Serine-threonine kinase PKB and p38 MAPKs were reported to have cardioprotective effects against ischemia/reperfusion injury. Protein kinase B and PI3K/PKB also promote survival of cardiomyocytes.[58] Compared with the control, red palm oil was found to increase aortic output recovery. During reperfusion, this protection is accompanied by an increase in cardioprotective PKB and p38 phosphorylation, a decrease in proapototic JNK54 and JNK46 phosphorylation, and attenuation of proapototic PARP cleavage. The author recommends daily supplementation with red palm oil at 0.58 mg/kg body weight for cardioprotection.[62] Hence, red palm oil can directly influence MAPK signaling to protect cardiomyoctes from ischemia/reperfusion-induced apoptosis or injury.[65]

In a follow-up study by Engelbrecht et al.,[66] the association between the PI3K/PKB signaling pathway and ischemic reperfusion was studied in the same model[65] as described previously. Red palm oil supplementation was found to improve the percentage of rate-pressure product recovery after 10 to 30 minutes of reperfusion. It also protected against ischemia/reperfusion-induced injury via activation of the prosurvival pathways PKB/Akt and P13-K/PKB and attenuation of proapototic PARP cleavage.[66]

Using a hypercholesterolemic model and design similar to that used by Esterhuyse et al.,[62] Kruger et al.[59] conducted further studies on the influence of red palm oil on MAPK phosphorylation and apoptosis in ischemia/reperfusion injury. Cell survival or death by apoptosis depends on the dynamic balance between ERK and stress-activated JNK and p38-MAPK. As observed in earlier studies, significant improvement in aortic output was observed in the red palm oil–supplemented group. Interestingly, red palm oil supplementation was found to reduce the stress-activated proapoptotic JNK and p38-MAPK phosphorylation associated with cardioprotection after ischemia/reperfusion-induced injury, to improve the ERK phosphorylation that promotes survival of the cardiomyocytes, and to attenuate proapoptotic caspase-3 and PARP cleavage. Hence, red palm oil was found to have a cardioprotective effect against diet-induced hypercholesterolemia.[59]

In another mechanism study by the same group, the effect of red palm oil supplementation on myocardial MMP-2 activation and PKB phosphorylation was investigated.[67] Matrix metalloproteinases are a family of endopeptides that assist cell migration and tissue remodeling. During ischemic injury, activation of MMP-2 prevents recovery and leads to greater cardiac infarct size. The release of lactate dehydrogenase from the heart muscle is a surrogate of myocardial tissue injury and disease. In a 5-week animal study, the effects of red palm oil, sunflower oil, and control were compared. Myocardial infarct size after ischemic/reperfusion injury was significantly reduced in the red palm oil group compared with the sunflower oil and control groups. Red palm oil supplementation also reduced lactate dehydrogenase concentrations in the reperfusion coronary effluent.[67] As reported previously, red palm oil protects against ischemia/reperfusion-induced injury by activating prosurvival PKB/Akt phosphorylation[65,66] and is not affected by activation of the MMP-2 pathway.[67]

In an extended study, the association between red palm oil supplementation and MMP-2 activity was further investigated in a hyperlipidemic animal model. Male Wistar rats were fed either a hypercholesterolemic diet with 2% cholesterol or standard chow diet for 9 weeks.[63] An additional 2 groups received the same diet for 4 weeks, and beyond that they were supplemented with red palm oil until week 9. Red palm oil supplementation was found to protect the hearts of the hyperlipidemic rats from ischemia/reperfusion injury. Infarct size was also reduced in both normal and hyperlipidemic animals supplemented with red palm oil. Contrary to a previous finding by Bester et al.,[68] the protective effect of red palm oil against ischemia/reperfusion injury in hyperlipidemic rats was proposed to be mediated by MMP-2.[63]

The effect of red palm oil supplementation (200 μL/d) on arrhythmia was studied in male, spontaneously hypertensive rats and nonhypertensive Wistar–Kyoto rats.[64] Myocardial intercellular Cx43 synchronizes the myocardium, permitting electrical and molecular signal propagation in cardiomyocytes. Upon prolonged ischemia, Cx43 dephosphorylation occurs, causing modification of the gap junction and prompting electrical uncoupling. After 5 weeks of red palm oil feeding, spontaneously hypertensive rats showed improved cell-to-cell communication via upregulation of Cx43 mRNA, Cx43 protein, and phosphorylated Cx43, all associated with suppression of early postreperfusion-induced arrhythmia and electrically inducible ventricular fibrillation.[64]

Atherogenic dyslipidemia. Atherogenic dyslipidemia refers to increased concentrations of small, dense, low-density lipoprotein (LDL) particles, decreased concentrations of high-density lipoprotein (HDL) particles, and increased levels of triglycerides in blood. Evidence of the antiatherogenic properties of red palm oil is available from both human and animal studies.

In a parallel human study in a Chinese population, Zhang et al.[68] assigned volunteers to receive either red palm oil or soybean oil for 42 days. Dietary fat contributed 28% of total calories, and the test oil contributed two-thirds of the total dietary fat. Red palm oil and soybean oil had a similar effect on serum lipid levels. Levels of antioxidants, however, namely serum β-carotene, α-carotene, lycopene, and α-tocopherol, were higher in the red palm oil group than in the soybean oil group. Red palm oil was also well accepted by the volunteers as a new edible oil.[68]

Kritchevsky et al.[69] conducted 2 studies in an atherogenic rabbit model using 0.1% and 0.2% cholesterol intake for 90 and 60 days, respectively.[69] The atherogenic potential of different palm oils with different percentages of palmitic acid at the *sn*-2 position was tested. The test fats (14% of total energy) compared were refined, bleached, and deodorized palm oil, red palm oil, and interesterified randomized palm oil. Levels of serum and liver lipids and liver weight relative to body weight were comparable in all 3 groups. High-density lipoprotein cholesterol was highest in rabbits fed refined, bleached, and deodorized palm oil. Atherosclerosis was most severe in the group fed randomized palm oil, followed by the group fed refined, bleached, and deodorized palm oil (26% lesser), and lastly, the group fed red palm oil (45% lesser). Higher amounts of antioxidants (carotenoids and vitamin E) in red palm oil than in refined, bleached, and deodorized palm oil conferred better antiatherogenic potency.[69,70]

The effects of different vegetable oils (red palm olein, palm olein, corn oil, and coconut oil) fed for 4 and 8 weeks were studied by examining lipid profiles in a Sprague Dawley rat model. Groups supplemented with red palm oil, palm olein, and coconut oil showed decreased LDL cholesterol compared with the control group fed standard rat chow.[71] With all oils studied, total cholesterol was unchanged at week 4 but was lower after week 8. Interestingly, red palm oil was found to increase HDL cholesterol and decrease LDL cholesterol.[71]

The effects of various antioxidants on the lipid profile were studied in a weaning male Wistar rat model fed 18% red palm oil, 18% palm olein, or 18% vitamin E–stripped palm olein for 12 weeks. Kamisah et al.[72] showed that the atherogenicity index, ie, the ratio of total cholesterol to HDL cholesterol, could be reduced by palm olein and red palm oil, a finding attributed to the antioxidant content of both oils. No adverse effect on the lipid profile was observed. Instead, owing to their

high antioxidant content and balanced fatty acid composition, red palm oil and palm olein exhibited hypocholesterolemic activity and were deemed to be more effective in reducing LDL cholesterol and the ratio of total cholesterol to HDL cholesterol.[72]

In a study by Wilson et al.,[73] Golden Syrian hamsters were fed red palm oil, palm olein, palm olein with red palm oil extract (palm olein–red palm oil), or coconut oil. Levels of plasma cholesterol and aortic accumulation of cholesterol were compared between groups. Animals fed palm–based oils had lower plasma total cholesterol, VLDL cholesterol, and LDL cholesterol as well as higher HDL cholesterol compared with animals fed coconut oil. The aortas of hamsters fed red palm oil showed the least amount of atherogenesis as well as a marked ratio of free cholesterol to esterified cholesterol.[73]

Most of the fats consumed in the modern diet are subjected to heat during the cooking process.[74] Palm oil is more resistant to thermal oxidation than other vegetable oils and fats, and hence it is widely used as heavy-duty frying oil.[75] Owing to both its high oleic acid content and its vitamin E content, palm olein has a favorable health profile and shows good heat stability.[76] Heating of oil causes oxidation, which is the major form of deterioration. This causes a significant loss of oil quality, promoting changes in functional, sensory, and nutritional values and decreasing the safety of both heated oils and food products cooked in oil. Oxidation promotes formation of harmful new compounds like diacylglycerols, monoglycerols, monomers, polymers, free fatty acids, and other oxidative substances.[77] In a long-term (20 wk) study, animals were fed a basal diet fortified with 15% wt/wt fresh red palm oil, red palm oil heated once, or red palm oil heated up to 5 times. Interestingly, no adverse effect on serum triglycerides, HDL cholesterol, or the ratio of total cholesterol to HDL cholesterol was found following long-term feeding of fresh and heated red palm oil. Both fresh and heated red palm oil had similar effects on serum cholesterol and lipid peroxidation.[74]

Hemostasis. Hemostasis is a process to stop bleeding from an injured blood vessel. It requires collective action of vascular, platelet, and plasma factors. Hemostatic abnormalities can cause excessive bleeding or thrombosis. In a randomized, controlled, single-blinded parallel study, free-living hyperfibrinogenemic volunteers (n = 59) were given baked products containing red palm oil, palm olein, or sunflower oil at 25 g/d (contributing 12% of total energy intake) for 4 weeks. The effects of these oils on lipid profile, hemostatic markers, and fibrin characteristics were compared. No hypercholesterolemic effect was found with red palm oil. Fibrinolytic risk markers for cardiovascular disease, namely plasma tissue plasminogen activator antigen, was significantly reduced in the red palm oil group.[78]

Hypertension. According to WHO, hypertensive heart disease is among the top 10 leading causes of death globally in middle- and high-income countries.[57] Hypertension is related to endothelial dysfunction and oxidative stress.

The cardioproctective effects of red palm oil on vascular endothelium were investigated in Dahl salt-sensitive hypertensive rats. Rats were grouped to receive a high-salt (8% sodium chloride) or a low-salt (0.3% sodium chloride) diet with or without red palm oil (5 g/kg daily). Following 4 weeks of feeding, red palm oil was found to decrease mean arterial pressure, plasma thromboxane, and vascular resistance of the renal and aortic arteries. In addition, an enhanced ratio of the oxidant reduced glutathione (GSH) to oxidized glutathione (GSSG) and increased NO levels were reported in the low-salt group. The high-salt diet supplemented with red palm oil induced an increase in isoprostane and aortic superoxide formation as well as a decrease in the kidney GSH:GSSG ratio. In the low-salt group, the beneficial effect of red palm oil was related to a decrease in the ratio of vessel wall thickness to lumen diameter as well as to a better relaxant response of mesenteric arteries to acetylcholine. At the end of the study, a markedly improved survival rate was observed in the high-salt–induced hypertension group supplemented with red palm oil: the control high-salt group had 58% survival, whereas high-salt group supplemented with red palm oil had 100% survival.[79]

The effects of high-oleic super olein, red palm oil, and palm olein on systolic blood pressure and heart rate were studied in 4-week-old spontaneously hypertensive rats and normotensive Wistar Kyoto rats.[80] Rats were fed either standard rat chow (controls) or a diet supplemented with 15% super olein, red palm oil, or palm olein for 15 weeks. Several hypertension-related cardiovascular parameters, particularly aortic media thickness, were reduced with all experimental oils, and heart size was reduced in rats fed super olein and palm olein. In addition, no lipid deposition on the thoracic-abdominal aorta was found in any of the supplemented groups. Better lipid profiles, as demonstrated by reduced LDL levels and a lower antiatherogenic index (ratio of total cholesterol to HDL cholesterol), were also observed in the groups fed super olein and red palm oil. The author claims the oils possess antihypertensive properties associated with improved serum lipoprotein profiles and reduced hypertension-related cardiac and vascular smooth muscle hypertrophy.[80]

The protective effect of rooibos herbal tea, red palm oil, and the combination of the two was studied on *tert*-butyl hydroperoxide (t-BHP)–induced oxidative stress and hepatotoxicity in Wistar rats. Rats (n = 80) were randomized to 8 groups: negative control (water), positive control (t-BHP), rooibos or red palm oil alone, rooibos and red palm oil in combination, rooibos with t-BHP, or red palm oil with t-BHP alone, and rooibos with both t-BHP and red palm oil. After 8 weeks of treatment, rooibos herbal tea, red palm oil, and the combination of the two were found to effectively protect against oxidative hepatotoxicity. The mechanism involves reduction in liver function enzymes, protection against lipid peroxidation, control of antioxidant activity, and restoration of redox status.[81]

Use of red palm oil in other diseases and health conditions

Cancer. According to WHO, cancer is the leading cause of morbidity and mortality worldwide. The common sites of cancers are breast, colon/rectum, lung, cervix, and stomach. Seventy percent of the world's cancer mortality occurs in Africa, Asia, and Central and South America.[82]

Red palm oil was found to aid in cancer management and to reduce the adverse effects of chemotherapy. Following a 1-week acclimatization period, 32 rats with azoxymethane-induced colon cancer were randomized into 4 groups to receive red palm oil or soybean oil (at 7% fat, normal level; or 14% fat, high-fat Western diet) for 13 weeks.[83] Aberrant crypt foci were used as a colonic tumor biomarker. Red palm oil supplementation was found to reduce the number of aberrant crypt foci and the amount of aberrant crypt activity compared with soybean oil. Red palm oil was also found to increase glutathione *S*-transferase activity in the liver. Glutathione *S*-transferase, an important carcinogenic biomarker, plays an important role as a detoxifying and carcinogen-metabolizing enzyme. Hence, red palm oil supplementation may be beneficial in the management of colon cancer.[83]

Anthracyclines (daunorubicin and doxorubicin) have gained prominence in chemotherapeutic practice in the treatment of systematic neoplasms and solid malignancies. Their clinical use, however, is hampered by adverse effects such as acute or chronic cardiac toxicity, chronic cardiomyopathy, and congestive heart failure. The cardioprotective effect of red palm oil was evaluated in a 4-week study of animals treated with daunorubicin (2 mg/kg body weight). Coadministration of red palm oil during daunorubicin treatment was found to improve aortic output and cardiac function, stabilize antioxidant enzymes (NO synthase and superoxide dismutase), and inhibit the stress-induced MAPK pathway.[84] Thus, red palm oil supplementation during chemotherapy may confer protective effects. These findings warrant confirmation in a human clinical trial.

Reproduction. Red palm oil was found to be beneficial for normal reproduction support in both male and female systems. Since red palm oil has no teratogenic effect, women of reproductive age in endemic areas of vitamin A deficiency can be safely supplemented with red palm oil.[85]

In a multigeneration animal breeding study, Manorama et al.[86] assessed the safety of hydrogenated vegetable oil with 30% mahua oil compared with peanut oil (control), red palm oil, and refined, bleached, and deodorized palm oil on reproductive performance and growth development in the third (F3) generation. Red palm oil, refined, bleached, and deodorized palm oil, and peanut oil were found to be safe for consumption, showing no adverse effects on reproductive performance (percentage conception, birth weight, litter size, weaning weight, sex ratio at birth and weaning, preweaning mortality, mating days), no effects on behavior of pups or adults (maturational landmarks and neurological reflexes), and no toxicological effects.[86]

Aboua et al.[87] fed supplemental red palm oil to male Wistar rats for over 60 days, targeting one complete cycle of spermatogenesis. They demonstrated that red palm oil could improve sperm count and motility, halt lipid peroxidation, scavenge formation of reactive oxygen species, elevate antioxidant activity (superoxide dismutase synthesis, catalase, and GSH), and protect epididymal sperm against damage from oxidative stress induced by hydroperoxide,. Hence, incorporation of red palm oil in the diet was proposed to be beneficial for men to combat adverse effects of oxidative stress, maintain sperm quality, and preserve fertility.[87] A long-term in vivo red palm oil feeding intervention to study complete spermatogenesis and epididymal maturation has been suggested.[88]

The impact of supplementation with red palm oil, iron, and vitamin C on vitamin A and hemoglobin status was studied in 15 adolescent girls.[89] Red palm oil retains about 85% of its carotene content after processing. Participants were supplemented with placebo for 30 days, followed by placebo plus iron (ferrous sulfate, 200 mg) for the next 45 days, followed by a red palm oil snack (supplying half the RDA of vitamin A) plus iron for a further 45 days, and lastly, a red palm oil snack plus iron plus vitamin C (25 mg) for another 45 days. Blood samples were collected at baseline and after every period of supplementation. Maximum hemoglobin levels were reached after supplementation with both red palm oil and iron instead of iron alone. The addition of

vitamin C resulted in further improvement in hemoglobin levels. Moreover, red palm oil significantly improved vitamin A and β-carotene levels.[89]

Diabetes. According to WHO, diabetes mellitus is among the top 10 leading causes of death in middle- and high-income countries worldwide.[57] Supplementation with red palm oil, rooibos tea extract, and a combination of the two for 7 weeks was found to upregulate antioxidant activity in streptozotocin-induced diabetic rats.[90] The animals exhibited effects of glycosuria, with weight loss due to decreased tissue protein and muscle mass, which mimics diabetic conditions in humans. Interestingly, the rats fed red palm oil and rooibos tea extract gained more weight. The liver plays a vital role in oxidation, detoxification, and free radical reactions; hence, biomarkers of oxidative stress in the liver are high at the primary stage of disease. Supplementation with red palm oil alone, rooibos extract alone, and the combination was found to improve liver superoxide dismutase and glutathione peroxidase as well as plasma oxygen radical antioxidant capacity (ORAC).[90] Evidence from human dietary intervention studies is needed to confirm these findings.

Hypobaric hypoxia. Hypobaric hypoxia is a condition in which the body is deprived of a sufficient oxygen supply due to reduced atmospheric pressure. This condition may lead to systematic oxidative stress, pulmonary and cardiovascular complications, and cerebral and cognitive damage. It usually occurs in sportsmen, travelers, soldiers, and people visiting high altitudes. Saxena et al.[91] studied the effects of red palm oil on acute hypobaric hypoxia in 2 experiments. In the first one, male Sprague Dawley rats were fed red palm oil (1 mL/d) and exposed to normoxic or hypoxic conditions. In the second one, two new groups (controls) were exposed to normoxic or hypoxic conditions. Red palm oil supplementation was found to expand the mean hypoxic threshold, reduce pulmonary transvascular damage and reinstate the integrity of the vascular barrier, reduce edema index in lung tissue, restore cellular redox status by increasing the GSH:GSSG ratio, decrease the lactate dehydrogenase concentration, and facilitate detoxification of reactive oxygen species. Hence, the antioxidant and vascular protective properties of red palm oil could be beneficial to individuals exposed to acute hypobaric hypoxia.[91]

Infection. Red palm oil was also found to have a positive effect on immune function. Cooper et al.[92] investigated the effect of red palm oil consumption on malaria in 207 children (aged 0 to 60 months) with fever in a malaria-endemic area in the state of Osun in western Nigeria. Levels of C-reactive protein, a biomarker of acute infection, are directly associated with infection, socioeconomic status, and nutritional intake. Beneficial effects of red palm oil were only observed in infected subjects more than 36 months old with low plasma retinol and α-carotene levels. Although C-reactive protein were elevated, red palm oil reduced the severity of infection in this age group.[92] The study limitation was most of the children had adequate vitamin A levels hence reducing the apparent protection of red palm oil against Malaria. The author suggested repeating red palm oil trial in a population where vitamin A deficiency is prevalent and red palm oil consumption is less but acceptable.

The inflammatory response forms part of the innate immune system, which is the first line of host defense against injury or infection by other organisms. Cytokines are directly implicated as pathophysiological mediators of myocardial depression in systemic sepsis and other forms of cardiovascular disease. Rooibos is a phenolic-rich South African herbal tea. The Langendorff system and the lipoposaccharide-induced inflammatory model were used to evaluate the anti-inflammatory effects of rooibos and red palm oil supplementation on baseline cardiac function.[93] Male Wistar rats were fed red palm oil (7 g per kilogram of diet) or rooibos, alone or in combination for 28 days and were divided into 2 groups. One group was injected with lipopolysaccharide to induce inflammation. Red palm oil and rooibos tea, when supplemented individually, resulted in increased plasma interleukin-10, a cardioproctective anti-inflammatory cytokine. The combination of rooibos and red palm oil increased endogenous myocardial interleukin-10, suggesting a cardioprotective anti-inflammatory effect.[93]

FUTURE DIRECTION AND CHALLENGES

Supplementation with red palm oil as a natural source of provitamin A could be a practical and economical approach to address vitamin A deficiency and other health-related ailments. Red palm oil can be promoted for use as a salad dressing, a cooking oil, or as part of a blended oil.[9] Carotenoid loss during storage and cooking of red palm oil is acceptable.[2] The major challenges to the use of red palm oil in food intervention programs to combat vitamin A deficiency were outlined by Burri.[2] Among these are the refining and processing of red palm oil and the acceptance of red palm oil's strong taste and aroma by consumers. Another consideration is the variation in carotenoid levels in red palm oil. Carotenoid concentrations vary with the fruit variety, the degree of palm fruit ripeness, the geographical location of plantations, the cooking method, and the storage conditions. Red palm oil should be processed to a concentrated

form of provitamin A supplement or carefully refined to remove color, odor, and taste to make it more palatable.[2]

Red palm oil intake varies by geographical region and local preference. Regular consumption of an appropriate amount of red palm oil can help to ensure adequate intake of vitamin A.[94] Following implementation of well-designed nutritional studies and programs to raise awareness of nutritional values and food preparation methods, red palm oil has become well accepted in Africa, Indonesia, India, China, and Malaysia. In a study in India, sensory evaluation of savory (murukku, tamarind rice, and upma) and sweet (suji halwa and cake) snacks prepared with crude palm oil was conducted by 15 panels of judges.[95] Acceptability of the food products prepared with a 1:1 blend of crude palm oil and peanut oil, with crude palm oil alone, with peanut oil alone, or with refined, bleached, and deodorized palm olein was evaluated. The most suitable food products for incorporation of crude palm oil were murukku as a savory snack and suji halwa as a sweet snack. A 1:1 blend of crude palm oil and peanut oil was well accepted by study participants. By blending the oils, the color and strong aroma of crude palm oil alone can be reduced and adequate β-carotene can be supplied. A 1:1 blending of crude palm oil with other edible oils was suggested for home cooking and school feeding programs.[95]

At present, red palm oil is not widely available in international markets, although its price is comparable to that of olive oil or other specialty fats. The cost of refining red palm oil compares unfavorably with the cost of producing vitamin A capsules, which are inexpensive and need to be supplied only twice yearly.[2] A 30-month social marketing strategy assessed the impact of red palm oil introduction in random samples of a target group of 10 000 mother–child pairs in areas of Burkina Faso where red palm oil is not consumed.[96] The promotional activities conducted through social marketing successfully increased awareness of red palm oil among the mothers. Moreover, red palm oil was well accepted by 45% of mothers and children after 24 months. Two-thirds of the participants had better knowledge and adequate vitamin A intake. This study also highlighted concern about positioning red palm oil as a food supplement instead of a cooking oil. Moreover, as demand increases, there will be challenges to increase production and sustain the cost.[96]

CONCLUSION

Red palm oil is rich in phytonutrients such as tocotrienols, tocopherols, carotenoids, phytosterols, squalene, and coenzyme Q10. Nutritional and toxicological studies have shown it contains highly bioavailable β-carotene and vitamin A and is reasonably stable to heat, forming no mutagens when heated. Promising data on bioavailability indicate the potential efficacy of red palm oil in combating vitamin A deficiency in children and pregnant women. Other health benefits include improvement of ocular complications; cardioprotective effects in ischemic heart disease; antiatherogenic, antihemorrhagic, antihypertensive, and anticancer properties; support of normal reproduction for both males and females; improved management of diabetes and chemotherapy; improved management of hypobaric conditions; and protection against infection. On the basis of the data collected thus far, further examination of red palm oil in large-scale human clinical studies is warranted.

Acknowledgments

Author contributions. R.L. performed the literature search. R.L., K.M.S., A.R., C.Y.M., and T.K.T. were involved in project conceptualization and design. R.L. and T.K.T. prepared the manuscript. K.M.S., A.R., and C.Y.M. edited the manuscript. All authors read and approved the manuscript.

Funding/support. This work was supported by research grants from the Malaysian Palm Oil Board (Project ID: PD16412), where the research allocation comes from the Malaysian government. The funder did not interfere with the design, conduct, or preparation of the review. Prior approval for publication is a requirement of the funding body.

Declaration of interest. R.L., C.Y.M., and T.K.T. are employees of the Malaysian Palm Oil Board. The other authors have no relevant interests to declare.

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