

# **RED PALM OIL - HEALTH BENEFITS AND THEIR MOLECULAR EXECUTORS**

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Abstract: Red palm oil (RPO) has been a nutritional vantage amidst mankind since ancient times, but the dietary and healing benefits are now being rediscovered in various aspects of human health. Owing to its compositional richness, RPO is even being recommended as vitamin supplement besides being used as healthy cooking oil loaded with micronutrients and antioxidants. Recent research studies have dissected the molecular mechanisms underlying biological actions of RPO as well as its tocotrienols rich fraction (TRF) in cardiovascular health, vitamin deficiency, reproductive health and cerebral health. The present review elaborates on nutritional composition and health benefits of RPO, with a focus on the molecular executors of these actions. We include the documented as well as potential usages, of RPO for human wellbeing. This shall invoke the researchers working in the area of human nutrition to take up research programs for exploring the benefits of RPO in newer and unexplored pathological indications.

Keywords: Cardiovascular Health, Clinical Trials, Tocotrienol-Rich-Fraction, Oxidative Stress

#### **INTRODUCTION**

Red Palm Oil (RPO), derived from fleshy red mesocarp of the oil palm fruit (Elaeis guineensis), is a part of the ancient nutritional heritage. Its first documented dietary consumption was from an Egyptian excavation of a tomb dated 3000 BC, in1897 [1]. West African societies have a long history recognizing RPO as a nutritional haven – it has been used as a primary source of dietary fat as well as a remedy for illnesses. Dutch colonial expeditions to South-East Asia introduced the plant in Indonesia [2] and today it is the largest producer of palm oil across world, followed by Malaysia, producing nearly 27 million metric tonnes in 2011. [http://www.indexmundi.com/agriculture/?commodity= palm-oil&graph=production]. Palm oil is finding applications in a variety of products such as cooking and frying medium, functional foods, nutraceuticals, soaps, detergents, cosmeceuticals and even as a biofuel. Such diverse applications and utility is directly reflected in it constituting 30% of the world's 170 million oils and fats produced in tons of 2010 [http://www.americanpalmoil.com/publications/Annual %20Report/MPOC-2010-Annual-Report.pdf].The high content of carotenoids confers this palm oil a dark red color and bestows RPO with medicinal properties, along with several other components. Nutritional assortment in red palm oil is diverse and so are its medicinal applications, which would be discussed extensively in the current review.

# Nutritional composition:

The uniqueness of RPO and its observed health benefits in comparison from other vegetable oils lies in its fatty acid composition and their position in the triglyceride structure. RPO contains a balanced saturated (SFA) and unsaturated fatty acids in approximately 1:1 ratio, 51% SFA, 38% monounsaturated fatty acid (MUFA) and 11% polyunsaturated fatty acid (PUFA) [3-5]. It is a cocktail of hydrophobic, yet bio-available, minor nutrients such tocopherols and tocotrienols, squalene. as phytosterols, coenzyme Q10, carotenoids like βcarotene and lycopene (Figure 1). Tocotrienols, which are at least 50 times more potent anti-oxidants than tocopherols, form 66-79% of the total vitamin E content of this oil (tocotrienols - 1015 ppm, tocopherols -133ppm), such an appreciable tocotrienols content makes RPO comparable to rice bran oil [6-7]. RPO is one of the richest sources of  $\beta$ -carotene with 500-800 mg of carotenoids per kg of RPO which is 15 times higher than carrots and 300 times of that in tomatoes [8].

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**Fig.1:** Minor constituents responsible for diverse biological actions of RPO

The medicinal benefit of this oil despite being high on SFA is being resolved by scientific studies on fatty acid metabolism. In the small intestine, dietary triacylglycerols (TAGs) are attacked by the pancreatic lipase at the sn-1 and sn-3 position, yielding free fatty acids and 2-monoacylglycerol (2-MAG). The "sn-2 hypothesis" states that it is the 2-MAG which is more readily absorbed in the small intestine, the sn-1 and sn-3 fatty acids cleaved off being precipitated as insoluble calcium and magnesium salts requiring higher amounts of bile salts for absorption. Thus, the fatty acid at sn-2 position is the actual form of "fat" being utilized by the body. In case of RPO only 3% palmitic acid (SFA) is at the sn-2 position, majority at this is occupied by oleic acid. The enormity of sn-2 positioned fatty acid is such that it renders the source as "more" atherogenic. RPO thus despite being SFA rich oil, actually behaves as MUFA rich oil [9]. Furthermore, owing to its high antioxidant content RPO defies the rancidity-prone nature of other edible oils and has longer shelf life and stability, and thus can be used as such without hydrogenation [10]. The compositional richness of RPO as spelt out above, though known, is only now being investigated and exploited scientifically. Although one of the earliest research enquiries on the dietary importance of RPO date to 1929 [11], but trials on animal models and human studies to define its mode of action are only recent advancements. The chasm of molecular information is extremely wide and warrants detailed research. Recent pre-clinical and clinical studies on RPO supplementation as well as its purified fractions are being reviewed in this article.

# Pathological conditions and RPO supplementation:

RPO supplementation has shown merits in various disease models, the broadest category being cardiovascular complications (Figure 2). Combating vitamin A deficiency, alleviating oxidative damage, inflammation and maintenance of male reproductive health have been topics of adjunct studies.



**Fig.2:** Molecular signaling capabilities of RPO in preservation of cardiovascular health

# Cardiovascular health (CDVH)

Cardiovascular borne risk factors: Serum complications and dietary fat have a long associative history. Before any edible fat is introduced to the markets for public consumption, it is assessed for its influence on various cardiovascular disease risk factors viz., cholesterol, blood pressure, pre-diabetes/diabetes, body weight, magnitude of physical activity etc. Of these factors, RPO has been adjudged repeatedly on the blood lipid and cholesterol profile. In a recent study, male Sprague-Dawley rats were fed red palm olein, palm olein, corn oil and coconut oil as 15% additional supplement in the normal rat feed. The most beneficial observation was a significant dip in the LDLC and TC levels and elevated HDLC upon supplementation of red palm olein and palm olein, which could not be matched by corn oil or coconut oil [12]. This effect was recapitulated in an earlier study with weaning male Wistar rats chronically fed red palm olein, palm olein and palm oil stripped of vitamin E content (SPO). The HDLC content of blood in the red palm olein fed group was higher than that in palm olein and SPO fed group, while LDLC content was drastically depreciated in comparison to other groups. TC levels in the red palm olein group though were above those in other groups, depreciated within the group. The TG levels also dipped significantly [13].

As oils are heated to high temperatures, the compositional changes may not correlate with the studies carried out by direct oral consumption of the dietary oil. Evidence shows that RPO does not alter the serum lipid profile despite heating up to 5 times. In one of such studies animals fed with fresh RPO, one time heated RPO and five times heated RPO showed similar effects on serum cholesterol and lipid peroxidation. Even long term feeding with heated RPO had no deranging effect on serum TG, HDLC and TC/HDLC ratio [14]. The human trials assessing the dietary inclusion of RPO indicate similar benefits. A 30 day study where 31 volunteers were given RPO supplement (Palmvitee – prepared by Palm Oil Research Institute of Malaysia) on

daily basis along with their routine diet led to a reduction in the TC and LDLC in all participants. Moreover, the LDLC/HDLC ratio dipped to a significant 78%. [15]. Another human study conducted on comparative assessment of coconut oil, corn oil and palm olein consumption over a 5 week period indicated decreased serum cholesterol, LDLC and LDLC/HDLC by 8%, in 123 Malaysian volunteers validating the non-hyper cholesterolemic effects of palm oil [16].

Hypertension: Hypertension which is determined by the pressure exerted by the blood pumping action of heart on the arteries, and flexibility and size of the arteries, is an important risk factor to be monitored for CVDH maintenance [17]. Expedited loss of cardiomyocytes accompanies hypertension and contributes to development of ventricular dysfunction and heart failure. The spontaneously hypertensive rat (SHR) model was evaluated for effect of long term (13 weeks) consumption of several edible oils - fish, canola, olive, palm and soyabean, on number of left ventricular cardiomyocytes. It was observed that the RPO fed animals had 60% more cardiomyocytes than the control animals, superseding the 30% preserved cardiomyocytes in olive oil fed group. Correlating with this, the systolic blood pressure of the palm oil fed animals was 15% lower than in the control animals [18]. In another 4 week study performed on Sprague-Dawley rats, fed on RPO, followed by a weeklong administration of buthionine sulfoximine for inhibition of GSH (reduced glutathione) synthesis and hence attenuating the glutathione antioxidant system, it was found that the palm oil fed group showed lower agedependent increase in mean arterial pressure and pressor response to inhibitor, without changing the heart rate or body weight compared to the buthionine sulfoximine and control groups. RPO also elevated the levels of various vasodilators – prostaglandin I2 (PGI2), nitric oxide (NO), and aortic cGMP, and decreased the levels of vasoconstrictors - thromboxane A2 (TxA2) and aortic cAMP. The inhibitor-induced increase in various isoprotanes and thromboxane A2, and the reduction in kidney GSH were positively attenuated by palm oil [19]. The study establishes RPO"s potential to alleviate oxidative stress induced hypertension by regulating the secretions of the endothelial lining.

High salt diet has been identified as one of the major life style related risk factor for hypertension by WHO and several agencies such as NIH/National Heart, Lung, and Blood Institute, USA [20]. RPO supplementation when evaluated on the Dahl-Salt Sensitive Rat Model has proved its merit in protecting against hypertension, oxidative stress and associated endothelial dysfunction. Dahl-Salt sensitive rats were fed either a high salt (HS) or low salt (LS) diet with or without PO (Carotino, 5 g/kg daily) for four weeks. High salt induced group displayed an elevated mean arterial

pressure as an outcome of the molecular imbalance comprising decreased nitric oxide, prostacyclins and reduced glutathione (GSH): oxidized glutathione (GSSG) ratio. Moreover, plasma isoprotanes and thromboxane A2, aortic and renal vascular resistance as well as aortic superoxide ion concentration were increased. In the PO supplemented animals - HS and LS, the salt induced hypertension as indicated by the mean arterial pressure, falls at the end of 4 weeks. PO reduced plasma TxA2 and vascular resistance of the renal and aortic arteries and increased the GSH: GSSG ratio as well as NO in the LS group. The HS-induced elevation in isoprotanes and superoxide production and reduction in kidney GSH: GSSG ratio, were alleviated by PO supplementation. PO fed animals also displayed a reduced vessel wall-thickness: lumen diameter ratio and a greater relaxant effect of mesenteric arteries to acetylcholine. The effect of PO supplementation was most marked on the mortality via salt induced hypertension – the HS group showed only 58% survival at the end of the study, but on PO supplementation 100% survival was observed [21].

With these observations, it is alluring to speculate that PGI2, TxA2 and NO are key elicitors of RPO"s normalizing effects on hemodynamic and antihypertensive outcomes and its supplementation might prove beneficial to control blood pressure *via* reigning PGI2:TxA2 and NO secretion in pre-hypertensive patients, though this warrants detailed investigations.

Ischemia Reperfusion Injury: RPO has supplementation been most extensively investigated in ex-vivo model of isolated perfused rat heart model of Ischaemia-Reperfusion Injury (IR injury Benefits of PO (olein fraction) supplementation have been evaluated in excised hearts of Wistar rats subjected to global ischaemia followed by reperfusion. The antioxidant enzyme system of the PO supplemented groups subjected to IR stress was potentiated while markers of oxidative stress such as depreciated. lipid peroxidation products were Histopathological evaluation also showed a decrease in extent of myocardial tissue edema and the focal loss of myocardial fibers following PO supplementation [22].

The benefits of PO supplementation were further corroborated by findings of cardiac functionality tests in Long-Evans rats fed on a control diet or control diet plus 7g RPO per kg diet for six weeks. RPO fed animals showed elevated cGMP levels during ischaemia against the control animals/pre-ischaemic stage, indicating effect of RPO supplementation in boosting NO-cGMP axis [23]. The authors hypothesize that the RPO mediated elevated cGMP tends to control the cAMP regulated Ca2+ influx and on the other hand allows opening of sarcolemmal-K+ ATP channels to extrude the excess Ca2+, thereby rendering protection against IR injury by keeping the intracellular [Ca2+] under check.

Besides the free radical insult, IR injury also stimulates signaling cascades mediated by several signaling molecules, receptors and kinases. Mitogen activated protein kinases (MAPK) are a family of serinethreonine kinases which are best characterized and responsible for determining the effects of IR injury. MAPK family consists of extracellular signal-regulated protein kinases (ERK1/2), c-Jun NH2-terminal kinases (JNK) and p38 and these members are involved in cell proliferation, differentiation and apoptosis. Phosphoinositide 3-kinase (PI-3K) is another key initiator of protective responses in IR injury which acts via the Akt/protein kinase B [24-25]. Red palm oil supplementation in IR injury model showed higher aortic output recovery accompanied by a boost in p38-MAPK phosphorylation during reperfusion [26]. Similarly, JNK54 and JNK46 phosphorylation status was enhanced from 20 minute perfusion stage to 10 minute reperfusion stage in the control group, but significantly decreased in the RPO group. ERK phosphorylation, though increased due to IR injury, was unaffected by RPO consumption. Akt/PKB phosphorylation at Ser473 and activation, a pro-survival signal, was shown to be enhanced in the 10 minute reperfusion stage. The prosurvival effect was also confirmed by the attenuated poly-(ADP-ribose) polymerase (PARP) cleavage though no significant effect was seen on attenuation ofcaspase-3 activation [26].

A similar study examining RPO supplementation in combination with hyper-cholesteremic diet showed diminished aortic output recovery in the cholesterol supplemented diet while significant group improvement was observed with RPO supplementation. As previous study. this was p38 accompanied with decreased and JNK phosphorylation and enhanced phosphorylation of the ERK MAPK at the 10 minute reperfusion stage against the 20 minute perfusion stage. However, contrary to the previous study, the apoptotic markers, caspase-3 and PARP, complied with the pro-survival effect of RPO - a depreciated caspase-3 against higher total caspase-3 and a lower level of cleaved PARP [27]. These studies are important pointers to the underlying molecular players responsible for the benefits of RPO. It is hypothesized that Akt/PKB activation is a key prosurvival signal responsible for cardio-protective action of RPO. Akt activated downstream of PI-3K is an initiator of several downstream pathways which aid cell survival such as phosphorylation and activation of mTOR to further activate p90 ribosomal S6 kinase in the nucleus where it phosphorylates and inactivates pro-apoptotic protein BAD at serine 112 [28], phosphorylation and inactivation of initiator caspase-9,

phosphorylation and activation of NOS and secretion of NO [25].



**Figure.3:** Physiological disturbances under hypobaric hypoxia and functional attributes of RPO to potentially counter the pathologies (Broken arrows indicate known benefits of RPO supplementations in these pathological indications)

The cardio-protective potential of RPO is also extended to its influence on reduction in myocardial infarct size. In one of the recent studies, male Wistar rats were fed either a standard rat chow or a 2% cholesterol supplemented diet (hyper-cholesteremic diet) for nine weeks, beyond week 4, diet was supplemented with RPO for the last five weeks. At the end of feeding period hearts were isolated, perfused and subjected to global ischaemia followed by reperfusion. Notable parameters assessed included size of the infarct and MMP<sub>2</sub> zymography. A larger infarct was noted in rats consuming hypercholesteremic diet as compared to the normal control diet, but on supplementation of RPO along with the hyper-cholesteremic diet the infarct size was depreciated to the extent comparable of normal diet controls [29]. PO supplementation has also been shown to have anti-arrhythmogenic benefits in a model of sudden cardiac death to simulate the severe heart attack in humans. Male hooded Wistar rats were supplemented with test diet – normal diet with 12% fat from various sources for one year before inducing IR injury. In case of PO supplemented diet ventricular fibrillation decreased in comparison to the control diet which was supplemented with sheep fat [30]. Recently, the up-regulation of myocardial connexion-43 has been shown to be associated with suppression of early postischemic-reperfusion-related ventricular tachycardia and electrically inducible ventricular fibrillation after 5 weeks of RPO feeding to Spontaneously Hypertensive Rat Model and Wistar-Kyoto rats. This protection could be due to the enhanced cell-cell communication due to connexin-43 accumulation [31].

Haemostasis:Consumption of RPO is also seen topositivelyinfluencehaemostasisin

hyperfibrinogenaemic phenotype. In a randomized, controlled, single blind parallel study comprising fifty nine hyper-fibrinogenaemic individuals who consumed red palm olein, palm olein or sunflower oil (25g/day) for 4 weeks, significant decrease in pro-thrombotic tissue plasminogen activator antigen in the RPO group was reported [32]. This promising action can be attributed to the rich tocotrienols content of RPO and is being further investigated in a clinical trial sponsored by MPOB [http://clinicaltrials.gov/ct2/show/NCT01631838]. To summarize, as the emerging molecular data suggests, RPO incorporation in the diet is beneficial for the heart and the vascular system. Regular consumption can warrant maintenance of a healthy heart, as well as alleviation from various pathological conditions plaguing the cardiovascular system in the times when lifestyle related disorders are rampant.

# Vitamin A Deficiency:

Vitamin A deficiency, though scantily known in the developed nations, is a stark and alarming reality in the developing and third world countries. WHO estimates 33% of pre-school children and 15% of the pregnant women in these countries to be biochemically deficient for vitamin A and are at grave risk for associated disorders. These disorders include impairment of vision, increased risk of xeropthalmia, morbidity and mortality due to weak immune system etc [http://whqlibdoc.who.int/publications/2009/97892415 98019 eng.pdf]. RPO being the richest natural source of readily bio-available beta-carotene, offers a compliant solution to vitamin A deficiency. It can be incorporated as a dietary supplement, in-home fortificant, fortified foods distributed in targeted supplementary program, and fortified staple food products [7].

In a study conducted on pre-school children fed with RPO for a 10 month period showed improvement in the physiological vitamin A status indicated by higher blood beta-carotene levels and faster disappearance and depreciated recurrence of Bitot"s spots (conjunctival lesions located near the corneal limbus indicating vitamin A deficiency) [33]. In another such study on school children, supplementation of RPO was compared with oral Vitamin A palmitate and it was observed that serum vitamin A levels and the fall in Dehydroretinol/Retinol ratio were comparable in both the cases indicating a similar liver saturation with vitamin A, demonstrating RPO"s potential to deliver bio-available beta-carotene [34]. In a similar study, consumption of biscuits fortified with RPO as a source of  $\beta$ -carotene (400 ppm total carotenoids), by school children for twelve months, was proven equally effective as biscuits fortified with synthetic  $\beta$ -carotene in raising the serum retinol concentrations. Also, fortification with RPO was economical and had a shelflife of up to 6 months. It also boosted the immune

(alleviated morbidity from respiratory and diarrhea related complications) and cognitive functions [35].

Not only children, various clinical studies have shown that women in gestation and post-partum stages are highly benefited by RPO consumption. In one such study, 170 women at 16-24 weeks of gestation were recruited and supplemented with RPO dose equivalent to recommended dietary amount of beta-carotene (2,400µg) or groundnut oil to the control subjects for the rest of their pregnancy. The serum retinol level of the test group improved substantially over the control group and subsequently only 1.5% women in the test group had vitamin A deficiency (serum retinol levels < 0.7 µmol/L) against the control group with 9.7% such incidences. RPO also led to reduction in incidences of anaemia, low birth weight and preterm delivery associated with lower serum retinol levels in the 3rd trimester of the pregnancy [36]. It has been demonstrated that post parturition supplementation of RPO increased pro-vitamin A carotenoids in the maternal and infant serum by two-folds and in breast milk by 2.5 folds [37]. These findings validate the benefits offered by RPO in preserving maternal health and ensuring neonatal well-being.

# Male Reproductive Health:

Reproductive health preservation by RPO supplementation is probably an outcome of its" high pro-vitamin A carotenoid content which is converted to retinol, and is essential to spermatogenesis [38]. Further, administration of RPO to male Wistar rats along with standard rat chow for 60 days was shown to reduce caspase 3/7 activity, inhibiting apoptosis caused in rat sperm by the *in vivo* induction of hydroperoxide [39]. This benefit of RPO could be an outcome of presence of rich cocktail of phytonutrients with anti-oxidant activity.

# **Biological actions of tocotrienol rich fraction:**

Researchers have made efforts to fractionate and study the mechanisms of action of active ingredients of RPO. Tocotrienol-Rich-Fraction (TRF) is one such RPO fraction which is a rich source of tocotrienols (TCT), a vitamin E precursor known to be more potent than tocopherols in its biological actions. TRF has shown anti-ageing effects on human diploid fibroblasts as it reversed the morphology of senescent human diploid fibroblasts to resemble that of juvenile cells with decreased activity of SA-β-gal, lesser damaged DNA, and larger number of S-phase cells. Also TRF treatment could restore elongated telomere length in senescent human diploid fibroblasts [40]. Like RPO, TRF also promises to have cardioprotective properties, with the  $\gamma$ -TCT being more potent than  $\alpha$  and  $\delta$ -TCT. The action has been proposed to be mediated via the pro-survival Akt signaling in mice IR injury model [41]. TRF supplementation has been observed to decrease the myocardial infarct size, decreased expression and phosphorylation of c-Src and higher stabilization of 20S and 26S proteasomes in isolated perfused hearts subjected to IR injury [42]. TRF is also shown to improve vascular health via inhibiton of key ratecontrolling enzyme - HMG CoA reductase, in cholesterol synthesis which regulates serum cholesterol levels [43], this if studied in details may offer a safer alternate to statins, group of drugs targeting HMG CoA reductase. Further TRF supplementation also delimits aortic vascular cell adhesion molecule-1 (VCAM-1) expression besides controlling oxidative stress and inflammation in the vasculature, preventing the development of proatherosclerotic milieu [44].

TRF supplementation has also shown merits in neurodegenerative disorders, potentially owing to its chain breaking antioxidant activity which might protect lipid membranes from peroxidation. However, it is argued that neuroprotective effect of tocotrienols is majorly independent of its anti-oxidant properties and is likely to be mediated by controlling arachidonic acid metabolism in the neural tissue by blocking the activity of calcium dependent phospholipases (cPLA2) thereby prostaglandins, leukotrienes, regulating thromboxanes, isoprotanes production [45-47]. There are evidences that TRF, specifically α-TCT, directly interacts with the active site of lipoxygenase 12-LOX to prevent access of arachidonic acid to the enzyme and generation of downstream leukotrienes - Leukotriene A4, C4, D4, E4, B4 – having pro-inflammatory and vasoconstrictive properties promoting vascular leakage and vasogenic edema. Functionality of 12-LOX is regulated by c-Src mediated tyrosine phosphorylation. Palm oil derived  $\alpha$ -TCT blocks c-Src activity in nanomolar concentrations [48-50].

# Hypobaric-hypoxia stressor and RPO supplementation:

Hypobaric-hypoxia is a physiological stress faced by people visiting high altitudes for occupational purposes, tourists participating in recreational activities organized at such locations or during long duration air travel. Rapid ascent and lowered oxygen bio-availability due to hypobaric situation ensues systemic oxidative stress, pulmonary and cardiovascular complications and cerebral/cognitive damages. Pathological condition addressed by RPO in the disease models studied so far, are also found in the complex and multi-faceted response of the human body to hypobaric hypoxia (Figure 3) [58-60]. In light of the observed benefits of RPO in diverse in vitro and in vivo studies, authors stress upon in-depth research on potential benefits of RPO supplementation under conditions of hypobaric hypoxia. Incorporation of RPO as a dietary supplement either as a cooking medium or direct oral consumption as a soft gel capsule (similar to cod liver oil capsules) to populations who are likely to be exposed to hypobaric hypoxia might prove favorable. The compositional

richness of RPO offers a safe, nutritional and unexplored vista that can be easily included in military rations, traveller kits, or flight meals. The success in recent human trials (as listed in table 1 and above text) affirms compliance by wide age-bracket, sex or ethnicities.

Table.1: Some of the recent human	trials exploiting the
nutritional richness of RPO	

DISORDER/		
DEFICIENCY and	FINDINGS	REFERENCE
TRIAL DESCRIPTION		
CARDIOVASCULAR HEALTH Hyperfibrinogenaemic South African volunteers given 25g/day - RPO, Palm olein, sunflower oil, for 4 weeks	Favourable lipid profile, controlled fibrinogenic tendencies	[32]
Chinese male adults given regular Chinese meal cooked in soyabean oil for 3 weeks followed by switching of cooking media to RPO for 6 weeks.	Neutral effects on serum lipid profile, elevated antioxidant status of the serum	[51]
Short-term and Long term consumption of RPO by middle aged Indian subjects, in comparison to groundnut oil. Cross-over studies were also included. VITAMIN A DEFICIENCY	Better performance on cardiovascular disease risk factors – lipid profiles, and platelet function.	[52]
Tanzanian women consuming RPO and further advised to consume dark green leafy vegetables for 6 months including a 3 month post-partum period.	Improved physiological carotenoid level – serum and breastmilk of young mothers	[53]
RPO made available in local markets and promoted through social media in Burkina Faso to women for incorporation in the family meal for a 30 day period	Improved physiological retinol levels in Young women pre-school children.	[54-55]
Incorporation of RPO in school lunch program and children fed for 1 year.	Improved physiological retinol levels and alleviation of vitamin A deficiency.	[56]
CEREBROVASCULAR HEALTH		
Tocopherol rich fraction of Palm oil fed to 50 subjects with 15-79% carotid stenosis.	Improved blood oxidative stress parameters and serum lipid profile. Regression in atherosclerotic plaque.	[57]

# CONCLUSION

In today's times of rampant lifestyle disorders in the developed nations and nutritional deficiency disorders in the developing world, RPO offers a nutritionally rich and economic option for fortification of our diets. The success in recent human trials affirms compliance by wide age-bracket, sex or ethnicities. Scientific evidences exist to claim that RPO and its fractions modulate the network purified of pathological signaling at various nodes to bring about its health benefits. RPO supplementation reinstates regulating cardiovascular health by vasodilation/vasoconstriction, controlling the oxidative damage, inflammation and tissue apoptosis due to IR injury, improves hemostasis, and arrhythmias. The antioxidant and vascular protection properties are also preservative in cerebrovascular disorders and neurodegeneration. Most importantly, it has emerged as an economic and effective nutritional supplement in the developing nations against vitamin A deficiency amongst children and pre-natal/post-partum health. The plethora of signaling moieties influenced by mere RPO dietary incorporation demand that we accept and propagate its use to a wider population and curb emerging health vulnerabilities.

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