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Red Palm Oil and Its Antioxidant Potential in Reducing Oxidative Stress in HIV/AIDS and TB Patients

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1. Introduction

1.1 HIV and TB

Scientific evidence has shown that HIV infection is caused by a retrovirus, the Human Immunodeficiency Virus (HIV) which is a ribonucleic acid (RNA) virus so designated because of its genome that encodes an unusual enzyme, reverse transcriptase (RT) that enables the virus to make copies of its own genome as DNA in its host's cells (human T4 helper lymphocytes) (Oguntibeju *et al.*, 2008).

The drastic increase in the number of people infected with HIV is not peculiar to a particular racial group, country or community despite multidimensional efforts which have been made to combat this scourge (Weiss, 1996; Oguntibeju *et al.*, 2007a). It is reported that the virus selectively attacks and depletes T-lymphocyte bearing $CD4^+$ cells (T-helper cells) causing a predisposition to opportunistic infections and malignancies (Weiss, 1996) and ultimately resulting in Acquired Immunodeficiency Syndrome (AIDS).

The cellular receptors to HIV are cells that express the $CD4^+$ T cell receptor ($CD4^+$ T-cells or T4-cells) as well as other white blood cells including monocytes and macrophages. Glial cells in the central nervous system, chromaffin cells in the intestine and Langerhans cells in mucous membranes and skin that express $CD4^+$ T cell receptors can also be infected (Paxon *et al.*, 1996). The possibility that there are other cellular targets apart from $CD4^+$T-cells is proved by the likelihood of neurons that can be infected. This creates the possibility of the presence of co-receptors in addition to $CD4^+$ T cells to mediate fusion between HIV and its target cells (Grossman and Heberman, 1997).

Recognition of the $CD4^+$ T-cells by HIV-1 envelope glycoprotein (gp120) to which the virus binds and enters host cells to initiate rapid replication cycles (Oguntibeju *et al.*, 2007b) depicts significant cytopathic consequences of HIV infection of $CD4^+$ T-cells (Bartlett, 1998) and is an important factor in the initiation of HIV infection. The shed virions which are immunogenic, stimulate B cells to produce humoral antibodies and plasma cells through lymphoid hyperplasia that ultimately results in decreased number of infected cells as the $CD4^+$ T-cells migrate through the germinal cells. The depletion in the number of $CD4^+$ T-cells exceeds the formation of new cells and may maintain this phase for many years resulting in general disorganization of the lymphoid nodes, loss of lymphoid function and integrity.

2. Physiological and biochemical mechanisms of the role of oxidative stress in HIV/AIDS & TB disease complications

After initial infection of the human host, the pace of immunodeficiency development, susceptibility to infection and malignancies become manifest and are generally associated with the rate of $CD4^+$ decline (Enger *et al.*, 1996). The rate of $CD4^+$ decline varies considerably from person to person and is not constant throughout all the stages of HIV infection. Though the virological and immunological process that take place during the period of rapid fall in the number of $CD4^+$ T-cells are poorly understood, Koot *et al.* (1996) reported that acceleration of the decline of $CD4^+$ T-cells heralds the progression of the disease that is associated with the increasing rate of HIV-1 replication *in vivo* and declining cell-mediated immune response. Studies have shown that the host immunological alterations due to HIV infection result in progressive development of opportunistic infections and malignancy and is chiefly mediated /induced by deregulation of a cytokine profile production of ROS which also plays a role in the viral replication. *In vitro* studies have shown activation of viral replication by induction of TNFαβ (Allard *et al.*, 1998).

Das and co-workers (1990) stated that excessive production of reactive oxygen species (ROS) such as superoxide anions, OH^- radicals and H_2O_2, may be related to increased activation of PMN leucocytes during infection. This is influenced by the pro-oxidant effect of TNFα produced by the activated macrophages during the course of HIV infection and secretion of pro-inflammatory cytokines IL-1, IL-6, and IL-8 (Kiedzierska and Crowe, 2001). Gil *et al.* (2003) further established the presence of substantial oxidative stress in HIV infection which they attributed to the role of viral proteins that increases ROS intracellularly, therefore increasing the apoptotic index and depleting the $CD4^+$ T-lymphocyte population. The ROS thus produced can attack the double bonds in polyunsaturated fatty acids, inducing lipid peroxidation which may result in more oxidative cellular damage to the membrane lipids, proteins or DNA. Chronic oxidative stress experienced by patients infected by HIV leads to a condition in which there is increased consumption of antioxidants (such as Vitamin C, and E , selenium, and carotenoids) as well as micronutrients/ trace elements (Januga *et al.*, 2002). Stephen (2006), therefore, concluded that persistent chronic inflammation such as found in HIV infection places a long-term strain on antioxidant defenses, impair immune functions, increases the severity of the disease as well as increases the antioxidant requirement by the infected individual.

Progression of HIV to AIDS in developed countries after initial infection is about 10-12 years for adults in the absence of antiviral therapy. However, some individuals manifest full blown AIDS within 5 years of infection whereas others survive long term (>10 years) asymptomatic HIV-1 infection without a significant decline in $CD4^+$ T-cell count. Such delay in the progression of HIV to AIDS may be attributed to either infection with genetically defective HIV-1 variants or effective host antiviral immune response where the individual has active cytotoxic T-cell responses against HIV-1 infected cells (Haase, 1999).

Ever since Robert Koch made the landmark discovery that tuberculosis is caused by the infectious agent *Mycobacterium tuberculosis* (Koch, 1882), it has remained a major global health threat. Although in developed countries the rates of infection has fallen in the past century, the number is now again increasing which results in over 2000 deaths in developed countries annually due to changes in social structures in cities, the HIV epidemic, and failure to improve treatment programs (Frieden *et al.*, 1995). The increased death rate recorded as a result of poverty, poor living conditions and inadequate medical care in

developing/Third World countries is further compounded by the emergence of multi-drug resistance where antibiotics are either of inferior quality, or are not used for a sufficient period of time to control the disease (O'Brien, 2001).

The recent increase in reported pulmonary tuberculosis (PTB) cases globally can be attributed to the increased susceptibility to opportunistic infections in HIV-infected persons. The highest prevalence of cases is reported to be in Asia (China, India, Indonesia, Bangladesh and Pakistan) and Africa with over 90% of global TB infections and deaths annually. TB cases occur predominantly in the economically productive 15-49 year age group (Dye *et al.*, 1999). Like HIV infection, TB also has a long latency period with symptomatic presentation occurring from 3 months to decades after establishment of the infection (Jagirdar and Zagzag, 1996).

TB is caused by an obligate pathogen that does not replicate outside its host environment (Mathema *et al.*, 2006) and is spread by aerosolization of droplets bearing *M. tuberculosis* particles released from the lung or larynx during coughing, sneezing, or talking in poorly ventilated areas. The particles of 1-5 μm in diameter, are inhaled and phagocytosed by resident alveolar macrophages. A vigorous immune response involving cytokines and a large number of chemokines ensues (Roach *et al.*, 2002). Protective immunity is characterized by granuloma formation that consists of primarily activated *M. tuberculosis* infected macrophages and T-cells. Medlar (1955), noted tissue necrosis and cavitations in over 10% of presumed immuno-competent patients and postulated that this was due to non-containment of continual bacterial replication (doubling time of 25-32 hours) that resulted in disease symptoms and its associated pathology. This response presumably initially limits infection to the primary site of invasion (the lung parenchyma and local draining lymph nodes known as the Ghon complex) in the majority of immuno-competent individuals (Bloom and Murray, 1992,).

Increased reactive oxygen species (ROS) has been reported in patients with TB. Excessive endogenously produced ROS in activated phagocytes of TB patients that escape to its surroundings can damage tissue or cellular DNA as well as impair immune function (Madebo *et al.*, 2003). It has been shown that the bactericidal potency of the myeloperoxidase-H_2O_2-halide system of neutrophilic granules demonstrates the bactericidal activities of the phagocytes that invariably produce increased ROS and reactive nitrogen intermediates (RNI) during phagocytic respiratory burst. Lower antioxidant potential as shown by a significant reduction of enzymatic antioxidants (superoxide dismutase, catalase) and non-enzymatic antioxidants (glutathione) as well as high malondialdehyde (MDA) concentrations suggest increases in the generation of ROS due to lipid peroxidation (Reddy *et al.*, 2004).

Di Massio and co-workers (1991), reported significantly reduced vitamin C and α-tocopherol levels in TB patients. These are integral components of antioxidants, which, when present in sufficient quantity, may act synergistically to protect cells from oxidative stress induced damage in TB patients. Several factors such as inadequate nutrients, malnutrition, nutrient malabsorption, low food intake, inadequate nutrient release from the liver, acute infections including other than HIV, may be the cause of low or impaired antioxidant capacity in TB patients (Das *et al.*, 1990).

Presentation of disease is variable as regards the pathology as well as infections in a variety of tissues such as the meninges, lymph nodes, and tissue of the spine, where response to antibiotic medication/treatment to clear the bacilli from tissues, partial reversal of the granulomatous process and subsequent clearance from the sputum may be found in clinical

cases (Jargirdar and Zagzag, 1996). The progression and nature of disease may be affected by factors such as conditions that negatively impact on the host immune system (for example, poorly controlled diabetes mellitus, renal failure, chemotherapy, malnutrition or intrinsic host susceptibility (Madebo *et al*., 2003). Host susceptibility has been known to affect endogenous re-activation and exogenous re-infection by the bacilli.

3. Reactive oxygen species and reactive nitrogen species and their effects on biological macromolecules and organs

Reactive oxygen species / reactive nitrogen species (ROS/ RNS) are constantly being formed in living organisms (Ceconi *et al*., 2003). In the course of oxygen metabolism, 1- 5% of all inhaled oxygen becomes ROS (Berk, 2007). Endogenously, ROS are produced from various sources such as mitochondria, activated macrophages and leucocytes, oxidase enzyme (NADPH), cyclo-oxygenase and lipoxygenase (Zalba *et al.,* 2006). Reactive oxygen species have oxidation ability and are classified either as free radicals (superoxide anion O_2^-, hydroxyl radical $OH^\bullet$, nitric oxide NO) or as non-free radicals (hydrogen peroxide H_2O_2, peroxynitrite $ONOO^-$) (Higashi *et al*., 2006). Previous studies have shown the involvement of ROS in physiological and pathophysiological conditions (Fortuño *et al*., 2005; Berk, 2007; Heistad *et al*., 2009). At low concentrations, ROS are involved in normal cell signaling pathways (smooth muscle and endothelial cell growth, apoptosis and survival) and in the remodeling of vessel walls (Fortuño *et al*., 2005; Heistad *et al.,* 2009). At high concentrations, ROS are identified as harmful compounds and constitute an important risk factor for the development of many diseases such as cardiovascular diseases (Maxwell & Lip, 1997; Heistad *et al*., 2009).

4. Oxidative stress

Oxidative stress occurs when there is a dysfunction in the overall balance between the production of reactive oxygen and nitrogen species and the antioxidant defense mechanisms (Ceconi *et al.,* 2003; Berk, 2007; Barbosa *et al.,* 2008).

Oxidative stress is believed to play a critical role in the complications and pathophysiology of HIV/AIDS, TB and cardiovascular diseases (Heistad *et al.,* 2009). In the context of oxidative stress in HIV/AIDS and TB, the major vascular ROS is the superoxide anion (O_2^-) which is predominantly generated by the NADPH oxidase enzyme (Fortuño *et al*., 2005). Superoxide is normally dismutased to hydrogen peroxide (H_2O_2) by a family of superoxide dismutase (intracellular Cu/Zn SOD, MnSOD or extracellular Cu/Zn SOD) (Hamilton *et al*., 2004). Hydrogen peroxide is converted into oxygen and water by catalase enzymes or by glutathione peroxidase (GPx) in the presence of reduced glutathione (Hamilton *et al*., 2004; Zalba *et al*., 2006). In the pathophysiological process of oxidative stress, excess superoxide has many effects, superoxide combines with NO to form peroxynitrite. Peroxynitrite is a highly toxic oxidant which causes damage to cells of the vascular wall through oxidation of lipids (lipid peroxidation), proteins (protein nitrosilation) and nucleic acids with superoxide. This causes vascular dysfunction by removing the protective effects of NO (Heistad *et al*., 2009), initiates the development of vascular inflammatory state (Hamilton *et al*., 2004), facilitates the oxidation of LDL, causing development of artherosclerotic lesions (Zalba *et al*., 2006) and triggers apoptotic cell death (Ceconi *et al*., 2003).

Accumulating evidence has suggested that oxidative stress, mainly through lipid peroxidation, represents an important risk factor in the development of cardiovascular

diseases and complications in HIV/AIDS and TB (Waterfall *et al.*, 1997; Ceconi *et al.*, 2003). In fact, lipid peroxidation leads to membrane disruption and release of highly reactive free radicals (such as MDA) which can severely alter the cellular function (Ceconi *et al.*, 2003) (Table 1).

S/N	Oxidants	Reactions
1.	Production of superoxide	O_2 + electron ⟶ O_2
2.	NADPH – oxidase	$2O_2$ + NADPH ⟶ $2O_2^-$ + NADP + H^+
3.	Superoxide dismutase	O_2^- + O_2^- + $2H^+$ ⟶ H_2O_2 + O_2
4.	Calalase	H_2O_2 ⟶ $2H_2O$ + O_2
5.	Myeloperoxidase	H_2O_2 + x^- + H^+ ⟶ HOX + H_2O
6.	Glutathione peroxidase (Se-dependant)	2GSH + R-O-OH ⟶ GSSG + H2O + ROH
7.	Fenton reaction	Fe^{2+} + H_2O_2 ⟶ Fe^{3+} OH + OH^-
8.	Iron-catalyzed Haber Weiss reaction	O_2^- + H_2O_2 ⟶ O_2 + OH + OH^-
9.	Glucose-6-phosphate dehydrogenase	G-6-P + NADP ⟶ 6-Phosphogluconate + NADPH + H^+
10.	Glutathione reductase	G-S-S-G+NADPH + H^+ ⟶ 2GSH + NADH

Source: Murray, 2000

Table 1. Reactions in relation to oxidative stress in blood cells and various tissues.

5. Activation of oxygen

Oxygen is essential for energy metabolism and respiration but is has been implicated in many disease and degenerative conditions (Ceconi *et al.*, 2003). Activation of oxygen may occur by two different mechanisms: absorption of sufficient energy to reverse the spin on one of the unpaired electrons and monovalent reduction. Non-activated oxygen is a bi-radical. It can be activated by either reversing the spin on one of the unpaired electrons to form the singlet state or by reduction. In the monovalent reduction of oxygen, superoxide (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (OH) and finally, water (H_2O) is formed. Superoxide forms the hydroxyl radical (OOH) which is the protonated form of the superoxide anion radical (Gebick and Bielski, 1981; Ceconi *et al.*, 2003).

Numerous enzymes (peroxidases) use hydrogen peroxide as a substrate in oxidation reactions involving the synthesis of complex organic molecules. Haber and Weiss (1994) identified the hydroxyl radical as the oxidizing species in the reaction between H_2O_2 and ferrous salts.

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH + OH^-$$

Most oxygen is consumed by the cytochrome oxidase enzyme in the mitochondrial electron transport system. Isolated mitochondria produce H_2O_2 and O^{2-} in the presence of NADH (Loschen *et al.*, 1974). The various Fe-S-proteins and NADH dehydrogenase have also been implicated as possible sites of superoxide and hydrogen peroxide formation (Waterfall *et al.*, 1997). Various oxidative processes including oxidation hydroxylations, dealkylations, deaminations, dehalogenation and desaturation occur in the smooth endoplasmic reticulum. Mixed function oxygenases that contain a heme moiety add an oxygen atom into an organic substrate using NADPH as the electron donor. The generalized reaction catalyzed by cytochrome P_{450} is:

$$RH + NADPH + H^+ + O_2 \longrightarrow ROH + NADP^+ + H_3O$$

Superoxide is produced by microsomal NADPH dependent electron transport involving cytochrome P_{450} (Valko *et al.*, 2007). One possible site at which this may occur is shown in Figure 1:

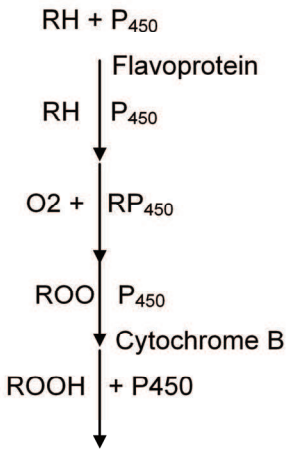

Fig. 1. Schematic presentation of the cytochrome P450 electron transport (Valko *et al.*, 2007).

In the peroxisomes and glyoxysomes, compartmentalized enzymes involved in the B-oxidation of fatty acids and glyoxylic acid cycle includes glycolate oxidase, catalase and various peroxidases. Glycolate oxidase produces H_2O_2 in a two-electron transfer from glycolate to oxygen (Lindqvist *et al.*, 1991). Xanthine oxidase, urate oxidase and NADH oxidase generate superoxide as a consequence of the oxidation of their substrates (Fridovich, 1970). The xanthine oxidase reaction is often used *in vitro* as a source of superoxide producing one mole of superoxide during the conversion of xanthine to uric acid (Fridovich, 1970). A superoxide-generating NADPH oxidase activity has been clearly identified in plasmalemma-enriched fractions (Valko *et al.*, 2007). These flavopoteins may produce superoxide by the redox cycling of certain quinones or nitrogenous compounds and NADPH oxidase reduces Fe^{3+} to Fe^{2+} converting it to a form that can be transported. Dysfunction of NADPH oxidase results in the formation of superoxide (Maxwell & Lip, 1997).

6. Mechanism of action of antioxidants in improving the immune status of AIDS and TB patients

Antioxidants are compounds that dispose, scavenge and suppress the formation of free radicals or oppose their actions. Free radicals, primarily the ROS, superoxide and hydroxyl radicals, which are highly reactive, with an unpaired electron in an atomic or molecular orbit, are generated under physiological conditions during aerobic metabolism (Semba & Tang, 1999; Champe *et al*., 2005). Because free radicals are potentially toxic, they normally are inactivated or scavenged by antioxidants before they can damage lipids, proteins or nucleic acids.

Superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px) are the primary antioxidant enzymes involved in the direct elimination of ROS whereas glutathione transferase, glucose-6-phosphate dehydrogenase (G6PD) and copper-binding ceruloplasmin are secondary antioxidant enzymes which assist in maintaining a steady concentration of glutathione and NADPH required for optimal functioning of the primary antioxidant enzymes (Kiremidjian-Schumacher *et al*., 1994; Champe *et al*., 2005). Antioxidant enzymes require micronutrients such as selenium, iron, copper, zinc and manganese as cofactors for optimal catalytic activity and to act as effective antioxidant defence mechanisms. If homeostasis between the rate of formation of free radicals and the rate of neutralization of free radicals is not maintained, oxidative damage, known as oxidative stress occurs which further damages the already compromised immune system and consequently enhances HIV and TB progression (Cunningham-Rundles, 2001; Cunningham-Rundles *et al*., 2005) and it has been reported that most of these antioxidants are derived from dietary sources (fruits and vegetables including red palm oil (Maxwell & Lip, 1997; Ebong *et al*., 1999; Edem, 2002; Van Rooyen *et al*., 2008).

7. Mechanism of action of red palm oil in improving the immune status of patients with AIDS and TB

Several studies have illustrated that red palm oil (RPO) is a rich cocktail of lipid-soluble antioxidants such as carotenoids (mostly α- and β-carotene, lycopenes), vitamin E (in the form of α- , β-, δ- tocotrienols and tocopherol) and ubiquinone (mostly coenzyme Q_{10}) (Ebong *et al*., 1999; Edem, 2002; Van Rooyen *et al*., 2008).

Feeding experiments using various animal models have highlighted that red palm oil is beneficial to health by reducing oxidative stress (Ebong *et al*., 1999). Many studies have demonstrated the protective effects of red palm oil in a cardiac ischaemia/perfusion model of oxidative stress (Esterhuyse *et al*., 2005; Bester *et al*., 2006; Engelbrecht *et al*., 2006) and modulation of the serum lipid profile in rats.

RPO is widely used as cooking oil in West and Central Africa and plays an essential role in meeting energy and essential fatty acid needs in many regions of the world. It contains many beneficial antioxidants and micronutrient compounds such as tocopherol, tocotrienol, lycopene, squalene, co-enzyme Q_{10}, physterol, glycolipids, phosphatides, calcium, phosphorus, iron, riboflavin, chlorophil, xanthophil, flavonoids, phospholipids, and carotenoid in addition to the equal proportion of saturated and unsaturated fatty acids such as oleic acid, linolenic acid, palmitic acid, linoleic acid, stearic acid and arachidic acid. It is known to be the richest source of carotenoids in terms of provitamin A equivalents i.e α and β carotenes (Sundram *et al*., 2003) with its wide range of protective properties against disease

and aging as well as being modulators for cellular processes / functions where photo-oxidative processes predominate by acting as scavengers of oxygen and peroxyl radicals (Van Rooyen *et al.*, 2008). Sebinova and co-workers (1991) documented the increased protection derived from a combination of tocopherol and tocotrienol and further revealed that tocotrienol offers a more efficient protection than tocopherol as it is preferentially consumed by ROS. It has been shown that fresh RPO has no adverse effect on body weight and morphology of body tissues. It also lowers the level of serum lipids and inhibits tumour growth (Kritchevsky, 2000), enhances intestinal uptake of protein and the metabolism of sulphur-amino acids and promotes reproductive capacity (Ebong *et al.*, 1999). Calcium, phosphorous, iron, riboflavin, chlorophyll, xanthophylls, flavonoids and phospholipids and equal proportion of saturated and unsaturated fatty acids have also been identified as part of its constituents (Sundram *et al.*, 2003).

A number of human feeding studies reported that palm oil diets show a reduction of blood cholesterol values ranging from 7%-38% (Mattson and Grundy, 1985; Bonanome and Grundy, 1988). A comparative study in young Australian adults showed that the total blood cholesterol, triglycerides and HDL-cholesterol levels of those fed on palm oil (palm olein) and olive oil were lower than those fed on the usual Australian diet (Choudhury *et al.*, 1995). A double-blind cross-over study (Sundram, 1997) showed that a palm olein rich oil diet is identical to an oleic-acid rich diet.

A study on fifty-one Pakistani adults showed that those given palm oil rich diets performed better than those on sunflower oil. Palm oil was found to increase HDL-cholesterol and Apo A-1 levels (Farooq *et al*, 1996). A group in Beijing, China compared the effects of palm oil, soybean oil, peanut oil and lard (Zhang *et al,* 1997a; Zhang *et al*, 1997b) and reported that palm oil caused a significant increase in the HDL-cholesterol as well as a significant reduction in LDL-triglycerides.

Sundram and co-workers (1992) performed a dietary intervention study on a free-living Dutch population who normally consumes diets high in fats. Using a double blind cross-over study design consisting of two periods of six weeks of feeding, the normal fat intake of a group of 40 male volunteers was replaced by 70% palm oil. The palm oil diet did not raise serum total cholesterol and LDL-cholesterol, and caused a significant increase in the HDL-cholesterol as well as a significant reduction in LDL-triglycerides.

The effects of palm olein and of canola oil on plasma lipids were examined in double blind experiments in healthy Australian adults (Truswell *et al*, 1992). Palm oil performed better than canola oil in raising the HDL-cholesterol (Truswell *et al*, 1992). Other studies have demonstrated that RPO supplementation has beneficial or neutral effects on serum total cholesterol (Zhang *et al.*, 1997a).

A cross-over feeding study showed that the blood cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol levels of palm olein and olive oil diets were comparable (Ng *et al.*, 1992). A Malaysian study (Ng *et al.*, 1991) was conducted to compare the effects of a diet containing palm oil (olein), corn oil and coconut oil on serum cholesterol. Coconut oil was found to raise serum total cholesterol by more than 10% whereas both the corn and palm oil diets reduced the total cholesterol; the corn oil diet reduced the total cholesterol by 36% and palm oil by 19%. A similar cholesterol-lowering effect of palm oil was observed in 110 students in a study conducted in Malaysia (Marzuki *et al.*, 1991). The study compared the effect of palm oil with that of soybean oil. Volunteers fed on palm oil (olein) and soybean oil for five weeks, with a six-week wash-out period, showed comparable blood cholesterol levels. However, the blood triglycerides were increased by 28% in those on the soybean oil diet.

Thus, the impact of palm oil on serum lipids is more like that of a mono-unsaturated rather than saturated oil. There appears to be several explanations: (1) Palm oil is made up of 50% unsaturated fats and the saturated fatty acids present are palmitic (90%) and stearic (10%). Stearic acid as well as palmitic acid do not raise blood cholesterol levels in people whose blood cholesterol levels are in the normal range (Hayes, 1993; Hayes *et al*., 1995; Hayes *et al*., 1991, Khosla and Hayes, 1994; Khosla and Hayes, 1992). (2) The vitamin E, particularly the tocotrienol present in palm oil can suppress the synthesis of cholesterol in the liver (Qureshi *et al*., 1991a; Qureshi *et al*, 1991b; Qureshi *et al*, 1980; Mcltosh *et al*, 1991). (3) The position of the saturated and unsaturated fatty acid chains in a triglyceride backbone of the palm oil molecule determines whether the fat will elevate the cholesterol level in the blood (Kritchevsky, 1988; Kritchevsky, 1996). In palm oil, 87% of the unsaturated fatty acid chains are found in position 2 of the carbon atom of the triglyceride backbone molecule (Ong & Goh, 2002). This could explain why palm oil is not cholesterol-elevating. (4) It has an anti-clotting effect and prevents the formation of thrombi in the blood vessels. Hornstra (1988) in the Netherlands first demonstrated that palm oil has an anti-clotting effect, and is as anti-thrombotic as the highly unsaturated sunflower seed oil. A human study (Kooyenga *et al*., 1997) showed that tocotrienol (from palm oil) supplementation can reduce stenosis of patients with carotid atherosclerosis.

Holub *et al*, (1989) reported that the vitamin E in palm oil inhibits platelets from "sticking" to each other. Other supporting evidence showed that a palm oil diet increases the production of a hormone, prostacyclin that prevents blood-clotting or decreases the formation of a blood-clotting hormone, thromboxane (Sundram *et al*., 1990; Ng *et al*., 1992).

Kurfeld *et al*. (1990) in the United states, using a rabbit model, compared the effects of palm oil with hydrogenated coconut oil, cottonseed oil, hydrogenated cottonseed oil, and an American fat blend containing a mixture of butterfat, tallow, lard, shortening, salad oil, peanut oil and corn oil. At the end of a 14-month feeding period, coconut oil fed rabbits showed the most atherosclerotic lesions, while palm oil-fed rabbits showed less lesions compared to the coconut oil fed rabbits.

More than 70% of the vitamin A intake in Third World countries comes from fruits and vegetables in the form of carotenoids (Van Rooyen *et al*., 2008). In humans and animals, carotenoids, an important constituent of palm oil, play an important role in protection against photo-oxidative processes by acting as oxygen and peroxyl radical scavengers. Their synergistic action with other antioxidants makes them an even more potent compound.

It has been suggested that different individual compounds exhibiting a variety of anti-oxidant activities may provide additional protection against oxidative stress when ingested simultaneously (Esterbauer *et al*., 1991). A combination of lipophilic anti-oxidants present in red palm oil results in an inhibition of lipid peroxidation which is significantly greater than the sum of the individual effects (Zhang *et al*., 1995). This suggests that a cocktail of anti-oxidants may have a far more profound anti-oxidative effect due to the synergistic action of the individual compounds (Zhang *et al*., 1995).

The antioxidant properties of RPO has been attributed to the synergistic actions of carotenoids and vitamin E in the presence of lycopene in a natural food environment and this might provide the ultimate dietary supplement to fight disease associated with oxidative stress (Van Rooyen *et al*., 2008).

Conclusively, it could be said that oxidative stress plays a role in inflammatory and chronic diseases such as HIV/AIDS and TB and contribute significantly to depletion of immune factors, micronutrients and also promotes the progression of disease. Red palm oil could

potentially retard the process due to its unique characteristics and also as it is known to be rich in several important antioxidants.

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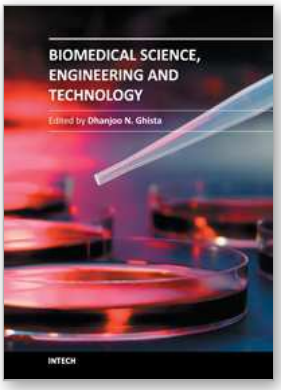

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This innovative book integrates the disciplines of biomedical science, biomedical engineering, biotechnology, physiological engineering, and hospital management technology. Herein, Biomedical science covers topics on disease pathways, models and treatment mechanisms, and the roles of red palm oil and phytomedicinal plants in reducing HIV and diabetes complications by enhancing antioxidant activity. Biomedical engineering coves topics of biomaterials (biodegradable polymers and magnetic nanomaterials), coronary stents, contact lenses, modelling of flows through tubes of varying cross-section, heart rate variability analysis of diabetic neuropathy, and EEG analysis in brain function assessment. Biotechnology covers the topics of hydrophobic interaction chromatography, protein scaffolds engineering, liposomes for construction of vaccines, induced pluripotent stem cells to fix genetic diseases by regenerative approaches, polymeric drug conjugates for improving the efficacy of anticancer drugs, and genetic modification of animals for agricultural use. Physiological engineering deals with mathematical modelling of physiological (cardiac, lung ventilation, glucose regulation) systems and formulation of indices for medical assessment (such as cardiac contractility, lung disease status, and diabetes risk). Finally, Hospital management science and technology involves the application of both biomedical engineering and industrial engineering for cost-effective operation of a hospital.

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