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Review

Possible role of red palm oil supplementation in reducing oxidative stress in HIV/AIDS and TB patients: A Review

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Infection by HIV and/ or TB is known to cause a persistent chronic inflammation. There are evidences that patients infected with HIV and/ or TB are under chronic oxidative stress with a resultant decrease in endogenous and nutritional antioxidants as well as other micronutrients. Oxidative stress due to over production of free radicals and antioxidant deficiency causes damage to vital biological macromolecules and organs and further contributes to disease complications, progression and morbidity. It has been reported that nutritional (micronutrients and vitamin antioxidants) supplements have been reported to reduce the severity of HIV infection/AIDS, improve immune status of the patients as well as their quality of life. Based on previous animal studies in our laboratory on animal models, in this review, we discuss the possible role of red palm oil in reducing oxidative stress and thus proposed that red palm oil supplementation could sufficiently scavenge free radicals, increase total antioxidant capacity with the potential to reduce disease progression and complications, increase survival and improve the general well being of people living with TB and HIV/AIDS.

Key words: Supplementation, oxidative stress, HIV, AIDS, tuberculosis, red palm oil.

BACKGROUND AND LITERATURE REVIEW

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 hosts cells (that is, 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 $CD4^+$ receptors (T-helper cells) causing a predisposition to opportunistic infections and malignancies (Weiss, 1996) thus 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 cells receptor can also be infected (Paxon et al., 1996). The possibility that there are other cellular targets apart from $CD4^+$ is proved by 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) as the virus binds to and enters host

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cells to initiate rapid replication cycles (Oguntibeju et al., 2007b) which 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 then stimulate B cells to produce humoral antibodies and plasma cells through lymphoid hyperplasia that ultimately results in decreased number of infected cells as the $CD4^+$ migrate through the germinal cells. The depletion in number of $CD4^+$ T-cells exceeds the formation of new cells and may maintain this phase for many years with resulting general disorganization of the lymphoid nodes, loss of lymphoid function and integrity.

After initial infection of the human host, the pace of immunodeficiency development, susceptibility to infection and malignancies became manifest and are generally associated with the rate of $CD4^+$ declines (Enger et al., 1996). This rate of $CD4^+$ decline varies considerably from person to person and is not constant throughout 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), however 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 results 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 NF$\alpha\beta$ (Allard et al., 1998).\z

Das et al. (1990) stated that excessive production of reactive oxygen species (ROS) such as superoxide anions, OH^- radicals, H_2O_2, may be related to an 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 (Kedzierska and Crowe, 2001). Gil et al. (2003) further established the presence of substantial oxidative stress in HIV infection which was attributed to the role of viral proteins that increases ROS intracellularly, therefore increasing the apoptotic index and depleting the $CD4^+$ T-lymphocytes. The ROS thus produced can then 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 with 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 micro-nutrients/ trace elements antioxidants (Januga et al., 2002). Stephen (2006), therefore, concluded that persistent chronic inflammation such as HIV infection place a long-term strain on antioxidant defenses, impairs immune functions, increases the severity of the disease as well as increases 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 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 which 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 annually and an estimated 10 infections per 100,000 persons 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 the 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 diseases (O'Brien, 2001).

The recent increase in reported pulmonary tuberculosis (PTB) cases globally can be attributed to the heightened susceptibility to opportunistic infection by 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 infection and death annually. TB cases occur predominantly in the economically productive 15 - 49 years 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 an obligate pathogen that does not replicate outside of its host environment (Mathema et al., 2006) and is spread by aerosolization of droplets bearing *M. tuberculosis* particles released from the lung or laryngeal disease 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 h) 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 the 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. High 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 produced increased ROS and reactive nitrogen intermediates (RNI) during phagocytic respiratory burst and that lower antioxidant potential as shown by significant reduction of enzymatic antioxidants (superoxide dismutase, catalase) and non-enzymatic antioxidants (glutathione) as well as high MDA concentrations suggesting increased generation of ROS due to lipid peroxidation (Reddy et al., 2004).

Di Massio et al. (1991), reported significantly reduced vitamin C and α- tocopherol that 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 nutrient, malnutrition, nutrient mal-absorption, 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 patient (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 (Jargairdar and Zagzag, 1996). The progression and nature of disease may be affected by factors such as conditions that impacts on the host immune system that is 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 of the bacilli.

Reactive oxygen species and reactive nitrogen species

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 $O_2^{\cdot-}$, 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 (Heistad et al., 2009). The pathophysiology of CVD and IHD is multi-factorial but it has been shown that the underlying pathogenesis is the deposition of fatty material, mainly LDL cholesterol, on the inner vascular wall of the blood vessels of the heart (Maxwell and Lip, 1997).

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 pathophysiology of cardiovascular diseases such as artherosclerosis, stroke and hypertension (Heistad et al., 2009). In the context of oxidative stress in CVD and IHD, the major vascular ROS which is superoxide anion ($O_2^{\cdot-}$) 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, Mn SOD or extracellular Cu/Zn SOD) (Hamilton et al., 2004). Hydrogen peroxide is scavenged 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 vascular cell damage through oxidation of lipids (lipid peroxidation), proteins (protein nitrosilation) and nucleic acids with superoxide. 1) This causes vascular dysfunction by removing the protective effects of NO (Heistad et al., 2009); 2) Initiates the development of vascular inflammatory state (Hamilton et al., 2003)

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

Oxidants	Reactions
Production of superoxide	O_2 + electron $\longrightarrow$ O_2
NADPH – oxidase	$2O_2$ + NADPH $\rightarrow$ $2O_2^-$ + NADP + H^+
Superoxide dismutase	O_2^- + O_2^- + $2H^+$ $\longrightarrow$ H_2O_2 + O_2
Calalase	H_2O_2 $\longrightarrow$ $2H_2O$ + O_2
Myeloperoxidase	H_2O_2 + x^- + H^+ $\longrightarrow$ HOX + H_2O
Glutathione peroxidase (Se-dependant)	2GSH + R-O-OH $\rightarrow$ GSSG + H2O + ROH
Fenton reaction	Fe^{2+} + H_2O_2 $\longrightarrow$ Fe^{3+} OH + OH^-
Iron-catalyzed Haber Weiss reaction	O_2^- + H_2O_2 $\longrightarrow$ O_2 + OH + OH^-
Glucose-6-phosphate dehydrogenase	G-6-P + NADP $\longrightarrow$ 6-Phosphogluconate + NADPH + H^+
Glutathionine reductase	G-S-S-G+NADPH + H^+ $\rightarrow$ 2GSH + NADH

Source: Murray, 2000.

3) Facilitates the oxidation of LDL, causing development of artherosclerotic lesions (Zalba et al., 2006); 4) 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 CVD and IHD (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) that can severely alter the cellular function (Ceconi et al., 2003) (Table 1).

Activation of oxygen

Oxygen is essential for energy metabolism and respiretion but it 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 a powerful oxidant units-protonated form (Gebicki 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-protein and NADH dehydrogenase have also been implicated as possible sites of super-oxide and hydrogen peroxide formation (Waterfall et al., 1997). Various oxidative processes including oxidation hydroxylations, dealkylations, deaminations, dehalogenation and desaturation occur on 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.

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 plasmallema-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 and Lip, 1997).

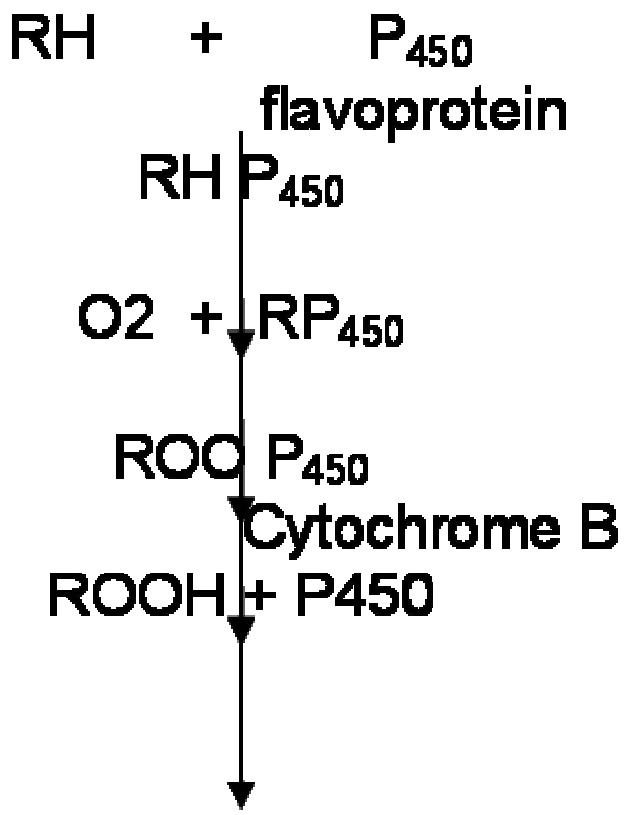

Figure 1. Schematic presentation of the cytochrome P450 electron transport (Valko et al., 2007).

Antioxidants

Maxwell and Lip (1997) reported that a set of scavenging systems called antioxidants has evolved to protect and limit the potential threat of oxidative stress. These include: preventive antioxidant enzymes such as superoxide dismutases (SOD), catalase and glutathione peroxidase; preventive antioxidant proteins such as the iron-binding protein transferrin, copper-binding proteins, caeruloplasmin and albumin; preventive low molecular weight molecules divided into two groups: water-soluble molecules such as vitamin C, urate, polyphenol (flavonoids) and thiol groups (glutathione); and lipid-soluble antioxidants such as vitamin E (alpha-tocopherol, tocotrienols), ubiquinol-10 (reduced coenzyme Q10) and beta-carotene. Most of these antioxidants are derived from dietary sources (fruits and vegetables including red palm oil).

Red palm oil

Several studies have illustrated that RPO is a rich cocktail of lipid-soluble antioxidants such as carotenoids (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 an ischemia/reperfusion model of oxidative stress (Esterhuyse et al., 2005; Bester et al., 2006; Engelbrecht et al., 2006; Kruger et al., 2007) and modulation of the serum lipid profile in rats.

Red palm oil (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/ micronutrient compounds such as tocopherol, tocotrienol, lycopene, squalene, Co-enzyme $Q_{10,}$ phytsterol, 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 that is α and β carotenes (Sundram et al., 2003) with its wide range of protective properties against disease, 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 et al. (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, 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 acid has also been identified as part of its constituents (Sundram et al., 2003).

A number of human feeding studies reported that palm oil diets showed a reduction of blood cholesterol values ranging from 7 to 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 palm olein rich oil diet is identical to oleic-acid rich diet.

A study on fifty-one Pakistani adults showed that those given palm oil rich diets performed better than sunflower

oil. Palm oil increased HDL-cholesterol and Apo A-1 levels (Farooq et al., 1996). A group of research scientists in Beijing, China compared the effects of palm oil, soybean oil, peanut oil and lard (Zhang et al., 1997a; Zhang et al., 1997b).

Sundram et al. (1992) performed a dietary intervention study on a free-living Dutch population which 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 with 70% of palm oil. The palm oil diet did not raise serum total cholesterol and LDL-cholesterol and caused a significant increase in the HDL-cholesterol and a significant reduction in LDL-triglycerides.

The effect of palm olein and of canola oil on plasma lipids was 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). 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 diet containing palm oil (olein), corn oil and coconut oil on serum cholesterol. Coconut oil raised serum total cholesterol by more than 10% where as both corn and palm oil diet reduced the total cholesterol; 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 soy oil for five weeks, with a six-week wash-out period, had comparable blood cholesterol levels. However, the blood triglycerides were increased by 28% on the soybean oil diet.

Thus, the impact of palm oil on serum lipids is more like that of mono-unsaturated rather than saturated oil. There appears to be several explanations: (1) Palm oil is made up of 50% unsaturated fats. It is not totally saturated and the saturated fatty acids present are palmitic (90%) and stearic (10%). Stearic acid does not elevate blood cholesterol and palmitic acid does not raise blood cholesterol level in people whose blood cholesterol level is in normal range (Hayes, 1993; Hayes et al., 1995, 1991; Khosla and Hayes, 1994, 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; Mcintosh et al., 1991). (3) The position of the saturated and unsaturated fatty acid chains in a triglyceride backbone of palm oil molecule determines whether the fat will elevate cholesterol level in the blood (Kritchevsky, 1988, 1996). In palm oil, 75% of the unsaturated fatty acid chains are found in position 2 of the carbon atom of the triglyceride backbone molecule (Padley et al., 1986). This could explain why palm oil is not cholesterol-elevating. (4) It has an anti-clotting effect and prevents the formation of thrombus in the blood vessels. Blood clotting can be induced by injury to the blood vessel wall and the alteration in the aggregating properties of blood platelets. Hornstra (1988) in the Netherlands first demonstrated that palm oil has anti-clotting effect and is as anti-thrombotic as the highly unsaturated sunflower seed oil. A human study (Kooyenga et al., 1997 and Tomeo et al., 1995) 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 that prevents blood-clotting (prostacyclin) or decreases the formation of a blood-clotting hormone thromboxane (Sugano and Imaizumi, 1991; Sundram et al., 1990; Ng et al., 1992). Thus scientific evidence indicates that the palm oil diet is anti-thrombotic.

Studies in animals confirmed that palm oil do not promote the formation of plaques in the arteries. Fatty deposits are made up of mainly fats and cholesterol (Hornstra, 1988). A Netherlands study was conducted on rabbits to test the effect of palm oil on atherosclerosis (Hornstra, 1988). After feeding the rabbits for one and a half years, palm oil and sunflower oil diets caused the lowest degree of atherosclerosis in comparison with fish oil linseed oil and olive oil. Similarly, Kurfeld et al. (1990) in the United states, also using the 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 the 14-month feeding period, coconut oil fed rabbits had the most atherosclerosis lesions, while in palm oil-fed rabbits, the number of lesions was no different from that with the other oils.

More than 70% of the vitamin A intake in the 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 process by acting as oxygen and peroxyl radical scavengers. Their synergistic action with other anti-oxidants make them an even more potent compound.

It has been suggested that different individual compounds with variables anti-oxidant activity 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 resulted in an inhibition of lipid peroxidation

significantly greater than the sum of the individual effects (Zhang et al., 1992). This may suggest that a cocktail of anti-oxidants may have a far more profound anti-oxidative effect due to the synergistic action of the individuals (Zhang et al., 1992).

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 might provide the ultimate dietary supplement to fight disease associated with oxidative stress (Van Rooyen et al., 2008).

In our research group, we are aiming at investigating the oxidative stress biomarkers, antioxidant levels and quality of life of patients with HIV/TB before and after red palm oil supplementation. We will also investigate the effect of RPO administered as a nutritional supplement to reduce oxidative stress, increase antioxidant levels and general sense of well-being as well as establish the pro-vitamin A efficacy of RPO. In addition, we plan: 1) To establish the prevalence and extent of oxidative stress in TB and HIV infected individuals. 2) To obtain information on the dietary intake of antioxidants in the South Western part of Nigeria. 3) To investigate the effects of RPO on oxidative stress biomarkers in TB and/ HIV positive subjects. 4) To investigate the potential of RPO to improve the antioxidant status of TB/ HIV positive subjects. 5) To assess the progression and severity of the diseases as measured by $CD4^+$, $CD8^+$ and viral load following administration of RPO. 6) To assess possible improvement in the immune system following administration of RPO to the TB and HIV infected subjects and to establish pro-vitamin A efficacy of RPO in the different groups of participants. 7) To determine whether RPO will improve the quality of life as measured by a sense of well being, increased weight, strength, comfort level, self image after the administration of RPO.

Conclusively, it could be said that oxidative stress plays a role in inflammatory and chronic disease such HIV/AIDS and TB and contribute significantly to depletion of immune factors, micronutrients and progression of disease and that red palm oil could potentially retard the process because of rich antioxidants.

REFERENCES

Allard JP, Aghdassi E, Chau J, Tam C, Koracs CM, Salit E, Walmsley SL (1998). Effect if vitamin E and C supplementation on oxidative stress and viral load in HIV- Infected subjects. AIDS 12: 1653-1659

Barbosa KB, Bressan J, Zulet MA, Martínez Hernández JA (2008). Influence of dietary intake on plasma biomarkers of oxidative stress in humans. Anales del Sistema Sanitario de Navarra 31(3): 259-80.

Bartlett JD (1998). Natural history and classification of HIV infection Chapter 2 In: Medical Management of Infection 1-15. Bartlett, JG (Ed.). Barltimore: Port City Press.

Berk BC (2007). Novel approaches to treat oxidative stress and cardiovascular diseases. Transactions of the American Clinical and Climatological Association 118: 209-14.

Bester DJ, van Rooyen J, Du Toit EF, Esterhuyse AJ (2006). Red palm oil protects against the consequences of oxidative stress when supplemented with dislipidaemic diets. Med Tech SA 20: 3-8.

Bonanome A, Grundy SM (1988). Effect of dietary stearic acid and plasma cholesterol and lipoprotein levels. New Eng. J. Med. *318:1124-12487*.

Bloom BR, Murray B (1992). Tuberculosis: Commentary on a re-emergent killer. Sci. 257: 1055-1064.

Ceconi C, Boraso A, Cargnoni A, Ferrari R (2003). Oxidative stress in cardiovascular disease: myth or fact? Archives of Biochemistry and Biophysics 420 (2): 217-21.

Choudhury N, Tan L, Truswell AS (1995). Comparison of palm olein and olive oil : Effects on plasma lipids and Vitamins E in young adults. Am. J. Clin. Nutr. 61: 1043-1051

Das UN, Podma M, Sogar PS, Ramesh G, Koratkar R (1990). Stimulation of free radical generation in human leucocytes by various agents including NF is a calmodulin – dependent process. Biochem Biophys Res. Commun. 67: 1030-6.

Di Massio P, Murphy M, Seis H (1991) Antioxidant defense systems: the role of carotenoids, tocopherols and thios. Am. J. Nutr. 53: (suppl) 1945 – 2005.

Dye CS, Scheele P, Dulin V, Pathanira, Raviglione MC (1999) Global burden of Tuberculosis, estimated incidence, prevalence and mortality. W.H.O. Global Surveillance and Monitoring Project, JAMA 282: 677-686.

Ebong PE, Owu DU, Isong EU (1999). Influence of palm oil (*Elaesis guineensis*) on health. Plant food for Human Nutr. 53:209-222.

Edem DO (2002). Palm oil: biochemical, physiological, nutritional, haematological and toxicological aspects of: a review. Plant Foods Hum. Nutr. 57: 319-41.

Engelbrecht AM, Esterhuyse AJ, du Toit EF. Lochner A, van Rooyen J (2006). P38-MAPK and PKB/Akt, possible role players in red palm oil-induced protection of the isolated perfused rat heart? J. Nutr. Biochem. 17: 265-271.

Enger CN, Graham and Peng Y (1996) Survival from early, intermediate and late stages of HIV infection. J. Am. Med. Assoc. 275:1329-1334.

Esterbauer H, Schaur J.S, Zollner H, (1991): Chemistry and biochemistry of 4-hydroxynonenal, malondialdehyde and related aldehydes. Free Radic. Biol. Med 11:81-128.

Esterhuyse AJ, Du Toit EF, Van Rooyen J. (2005): Dietary red palm oil supplementation protects against the consequences of global ischemia in the isolated perfused rat heart. Asian Pac. J. Clin. Nutr. 2005: 14(4): 340-347 (a).

Farooq A, Amir ID, Syed AA (1996). Dietary fats and coronary risk factors modification-a human study. Proceedings of PIPOC

Fortuño A, San José, G, Moreno MU, Díez J, Zalba G (2005). Oxidative stress and vascular remodeling. Exp. Physiol. 90 (4): 457-66.

Fridorich I (1970). Quantitative aspects of the production of superoxide anion radical by milk zanthine oxidae. J. Biol. Chem. 245:4053-4057.

Frieden TR, Fujiwara PI, Washko RM, and Hamburg MA.(1995). Tuberculosis in New York City – turning the tide. N. Engl. J. Med. 333:229-233.

Gebick JM, Bielski BHJ (1981). Comparison of the capacities of the dihydroxyl and superoxide radicals to initiate chain oxide of linoleic acid. J. Am. Chem. Soc. 103:7020-7022.

Gil L, Martinez G, Gonzalez I, Tarinas A, Alvarez A, Giuliani A, Molina R, Tapanes R, Perez J, Leon OS (2003). Contribution of characterization of oxidative stress in HIV/AIDS patients. Pharmacol. Res. 47 (3): 217 – 24.

Grossman Z, Heberman RB,(1997). T-cell homeostasis in HIV infection is neither failing nor blind: Modified cell count reflects an adaptive response of the host. Nat. Med. 3: 486-490.

Haber, F, Weiss J (1994). The catalyticed decomposition of hydropen peroxide by iron salts. Proc. Roya Soc. A. 147-332.

Haase AT (1999). Population biology of HIV-infection: viral load and CD4+T-cell demographics and dynamics in lymphatic tissues. Ann. Rev Immunol., 17: 625-656.

Hamilton CA, Miller WH, Al-Benna S, Brosnan MJ, Drummond RD, McBride MW, Dominiczak A F (2004). Strategies to reduce oxidative stress in cardiovascular disease. Clin.Sci. 106 (3): 219-34.

Hayes KC, Pronczuk A., and khosla , P. (1995). A rationale for plasma cholesterol modulation by dietary fatty acids: Modelling the human response in animals. J. Nutr. Biochem. 6:188-194.

Hayes KC (1993). Specific dietary fat without reducing saturated fatty acids does not significantly lower plasma cholesterol concentrations

in normal males. Am. J. Clin. Nutr. 55:675-681.
Hayes KC, Pronczuk A, Lindsey S, Diersen-Scchade D (1991). Dietary saturated fatty acids (12:0,14:0,16:0) differ in their impact on plasma cholesterol and lipoproteins in human primates. Am. J. Clin. Nutr. 53:491-498.
Heistad DD, Wakisaka Y, Miller J, Chu, Y, Pena-Silva R (2009). Novel aspects of oxidative stress in cardiovascular diseases. Circ. J. 73 (2): 201-07.
Higashi Y, Jitsuiki D, Chayama K, Yoshizumi M (2006). Edaravone (3-methyl-1-phenyl-2-pyrazolin-5-one), a novel free radical scavenger, for treatment of cardiovascular diseases. Recent Patents on Cardiovascular Drug Discovery 1 (1):85-93.
Holub BJ, Silicilia F, Mahadevappa VG (1989). Effect tocotrienol derivatives on collagen and ADP-induced human platelet aggregation. Presented at PORIM International Palm Oil Development Conference, Sept 5-6, Kuala Lumpur.
Hornstra G (1988). Dietary lipids and cardiovascular disease: Effects of palm oil. Oleagineux 43:75-81
Jagirdar J, Zagzag D (1996). Pathology and insights into pathogenesis TB. pp. 467 – 482 in Tuberculosis 1st Ed. Little Brown and Company. New York N. Y.
Januga P, Jaruga B, Gackowski D, Olczak A, Halota W, Pawlowska, Olinski R (2002). Supplementation with antioxidant vitamins prevents oxidative modification of DNA in lymphocytes of HIV infected patients. Free Rad. Biol. Med. 32: 414-420.
Khosla P, Hayes KC (1992). Comparison between effects of dietary saturated (16:0), monounsaturated (18:1) and polyunsaturated (18:2) fatty acids on plasma lipoprotein metabolism in Cebus and Rhesus monkeys fed cholesterol-free diets. Am. J. Clin. Nutr. 55:51-62.
Khosla P, Hayes KC (1994): Cholesterolaemic effects of the saturated fatty acids of palm oil. Food Nutr. Bull. 15:119-125.
Kiedzierska K, Crowe SM (2001). Cytokines and HIV: Interaction and clinical implications. Antivir Chem. Chemother 12: 133 – 150.
Koch R (1882). Die aetiology der Tuberculese. Klinische Wochenschr. 19:221-230.
Koji Uchida (2000): Role of Reactive Aldehyde in Cardiovascular Diseases. Free Radic. Biol.28(12): 168-1696.
Koot M, Van't B, Wout A, Koot NA (1996). Relation between changes in cellular load evaluation of viral phenotype and the clonal composition of virus type infection. J. Infect Dis. 173:349-354.
Kooyenga DK, Gerler M, Watkins TR, Gapor A, Diakoumakis E, Bierenbaum ML (1997): Palm oil antioxidant effects in patients with hyper-lipidaemia and carotid stenosis-2 year experience. Asia Pacific J. Clin. Nutr.6:1:72-75
Krichevsky D (1988): Effects of triglyceride structure, and lipid metabolism. J Nutr. Rev. 46:177.
Kritchevsky D (2000). Impact of red palm oil on human nutrition and health. Food Nutr Bull. 21: 182-88.
Kritchevsky D (1996). Influence of triglyceride structure on experimental atherosclerosis in rabbits. FASEB J.10:A187.
Kurfeld D, Davidson LM, Lopex-Guisa JM (1990): Palm and other edible oils: atherosclerosis study in rabbits. FASEB 4: February.
Lindquist Y, Branden CL, Mathews FS, Lederer F (1991). Spinnach ghycolate oxidase and yeast flagrant cytochrome are structurally homologous and evolutionary related enzymes with distinctly different function and flavin mononucleotive binding. J. Bio. Chem. 266:3198-3207.
Loschen, G., Azzi, Richter, C., and Flohebp, L. 91974). Superoxide radicals as precursors of mitochondrial hydrogen peroxide. FASEB 42:68-72.
Madebo T, Lindtjdrn B, Aukrust P, Berge R (2003). Circulating anti-oxidants and lipid peroxidation products in untreated tuberculosis patients in Ethopia. Am. J. Clin. Nutr. 78: 117-22.
Marzuki A, Arshad F, Tariq AR, Kamsiah J (1991): Influence of dietary fat on plasma lipid profiles of Malaysian adolescents. Am. J. Clin Nutr.53:1010S-1014S
Mathena B, Kurepina NE, Bifani PJ, Kreiswirth BN, (2006). Molecular epidemiology of tuberculosis: Current insight. Clin. Microbiol. Rev. 19: 658-685.
Mattson FH, Grundy SM (1985): Comparison of effects of dietary saturated, monounsaturated and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. J. Lipid Res. 26:194-202.
Maxwell SR, Lip GY (1997). Free radicals and antioxidants in cardiovascular disease. Br. J. Clin. Pharmacol. 44 (4): 307-17.
Mclntosch GH, Whyte J, McAthur R, Nestle PJ (1991): Barley and wheat foods; Influence on plasma cholesterol cocntrations in hypercholesterolemic men. Am J. Clin Nutr. *1205-1209*
Medlar EM (1955). Necropsy studies of human pulmonary T. B. Ann. Rev. Tuberc 71 (2): 29 –55.
Ng, TKW, Hayes KC, de Witt GF, Jegathesan M, Satgunasingham N, Ong ASH, Tan DTS. (1992). Palmitic and oleic and exert similar effects on serum lipid profile in the normo-cholestrolemic humans. J. Am. Coll. Nutr. 11:383-390.
Ng TKW, Hassan K, Lim JB, Lye MS, Ishak R (1991). Non-hypercholestrolemic effects of a palm oil diet in Malasysian volunteers. Am J. Clin. Nutr. 53:1015S-1020S.
O'Brien RJ (2001). Tuberculosis: scientific blueprint for TB drug development Global Alliance for TB. Drug Development, New York, N.Y.
Oguntibeju OO, van der Heever WMJ, Van Schalkwyk FM (2008). Potential effects of nutrient supplement on the anthropometric profiles of HIV-positive patients: complementary medicine could have a role in the management of HIV/AIDS. Afr. J. Biomed. Res. 11: 13-22.
Oguntibeju OO, van der Heever WMJ, Van Schalkwyk FM (2007a). Interplay between Socio-demographic variables, nutritional and immune status of HIV-positive/AIDS patients. Pak. J. Biol Sci. 10 (20): 3592 – 3598.
Oguntibeju OO, van der Heever WMJ, Van Schalkwyk FM (2007b). A review of the epidemiology, biology and pathogenesis of HIV. J. Biol. Sci 7(8): 1296-1304.
Osim EE, Owu DU, Isong EU, Umoh IB (1994). Influence of chronic consumption of thermoxidixed and fresh palm oil on basal metabolic rate, body weight and morphology of tissue in rats. Discov. Innov. 6: 389-396.
Padley FB, Gunstone FO, Krishna DR (1986). Hardbook. Gunstone, F.D., Hardwood, J.L. and F.B. Padley eds., Chapman and Halls, New York p49.
Paxon WA, Martin SR, Tse D (1996). Relative resistance to HIV-1 infection of CD4 lymphocytes from persons who remain uninfected despite multiple sexual exposures. Nat. Med. 2: 412-417.
Qureshi A, Qureshi N, Hasler-Rapaczl.(1991a): Dietary tocotrienol reduce concentrations of plasma cholesterol, apoprotein B, thromboxane B2 and platelet factor 4 in pigs with inherited hyper-lipidemias. Am. J. Clin. Nutr. 53:1042S-1046S
Qureshi A, Burger WC, Prentice N, Bird HR, Sunde ML (1980). Regulation of Lipid metabolism in chicken liver by dietary cereals. J. *Nutr. 10:388-393*.
Qureshi A, Qureshi N, Wright JJK (1991b): Lowering of serum cholesterol in hypercholesterolemic humans by tocotrienols (palmvitee). Am J. Clin Nurt 53:1021S-1026S
Reddy YN, Murthy SV, Krishna DR, Prabhakar (2004). Role of Radicals and antioxidants in tuberculosis patients. Ind. J Tuberc 151: 213-18.
Roach DR, Bean AG, Demangel C, Frances MP, Briscoe H, Brilton WJ (2002). TNF regulates chemokine induction essential for cell recruitment, granuloma formatives and clearance of mycobacterium infection. J. Immunol. 168: 4620 – 27.
Sebinova E, Kagan V, Han D, Parker L (1991). Free radical recycling and inter-membrance mobility in the antioxidant properties of α – tocophenol and α – tocotrienol. Free Radical Biol. Med. 10: 263 – 275.
Sundram K, Ismail A, Hayes KC, Jeyamalar R, Pathmanathan R (1997). Trans celeidial fatty acids adversely affect the lipoprotein profile relative to specific saturated fatty acids in humans. J. Nutr. 127:3:5143-5203
Sundram K, Sambanthamurthi R, Tan YA (2003). Palm Fruit Chemistry. Asia Pac. J. Clin. Nutr. 12 (3):` 355 – 362.
Sundram K, Hornstra G, Houwelingen AC (1992). Replacement of dietry fat with palm oil: Effect on human serum lipid, lipropotein and apoprotein. Br. J. Nutr. 68:677-692.
Sundram K, Khor HT, Ong ASH (1990).Effect of dietary palm oil and its fractions on rat plasma and high density lipoprotein. Lipids 25(4):187-193
Stephen MS (2006). The pathogenesis of HIV infection: the stupuid may not be so dumb afterall. Retrov 3: 60.

Truswell A. S, Choudhury N, Roberts DCK (1992). Double-bind comparison of plasma lipids in healthy subjects eating potato crisps fried in palm olein or canola oil. Nutr. Res. 12: S34-S52.
Van Rooyen J, Esterhuyse A. J, Engel brecht A, Toit E. F. (2008). Health benefits of natural carotenoid rich oil: a proposed mechanism of protection against ischaemia reperfusion injury. Asia Pac J. Clin Nutr 17: 316 – 19.
Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J (2007). Free radicals and antioxidants in normal physiological functions and human disease. Int. J. Biochem. Cell Biol. 39 (1): 44-84.
Waterfall AH, Singh G, Fry JR, Marsden CA (1997). The measurement of lipid peroxidation *in vivo*. Brain Res. Protocols 2: 217–22.
Weiss R (1996). HIV receptors and the pathogenesis of AIDS. Sci., 272: 1885-1886.
Zalba G, Fortuño A, Díez, J (2006). Oxidative stress and atherosclerosis in early chronic kidney disease. Nephrology, Dialysis, Transplantation 21 (10): 2686-90.
Zhang J, Wang CR, Dai J, Chen XS, Ge KY. (1997a): Palm oil diet may benefit mildly hyper-cholestrerolaemic Chinese adults. Asia Paci. J. Clin. Nutr. 6:1:22-25
Zhang J, Wang P, Wang CR, Chen XS, Ge KY (1997b): Non-hypercholesterolemic effects of a palm oil diet in Chinese adults. J. Nutr. 127(3): 5095-5135
Zhang J, Wang P, Wang P, Wang CR, Chen XS, Ge KY (1995): The effects of palm oil on serum lipids and thrombosis in Chinese adults. Paper presented at the 7th Asian Congress of Nutrition, /Beijing, China Oct. 7-11.