Cancer Association of South Africa (CANSA)

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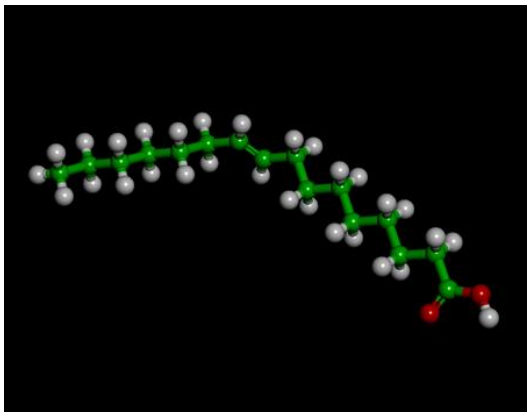
Fact Sheet on Palmitoleic Acid (Omega-7)

Introduction

Most people are aware of the following polyunsaturated fatty acids (PUFAS), namely Omega-3, Omega-6, Omega-9 and Omega-12. Most people are also aware of the wide-ranging benefits of Omega-3. There is, however, another category of fatty acid called Omega-7 in which the site of unsaturation is seven carbon atoms from the end of the carbon chain. The two most common omega-7 fatty acids in nature are palmitoleic acid and vaccenic acid. Whereas Omega-3, -6, -9, and -12 are polyunsaturated fatty acids (PUFAS), Omega-7 (Palmitoleic Acid) is a monounsaturated fatty acid (MUFA).



[Picture Credit: Palmitoleic Acid]

Palmitoleic acid (Omega-7) can be abbreviated as $16{:}1\Delta^{9}$. Dietary sources of palmitoleic acid include a variety of animal oils, vegetable oils, and marine oils. Macadamia oil (*Macadamia integrifolia*) and sea buckthorn oil (*Hippophaë rhamnoides*) are botanical sources with high concentrations, containing 17% and 19% (minimum) to 29% (maximum) of palmitoleic acid, respectively.

Palmitoleic acid has the formula $CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$.

Frigolet, M.E. & Gutiérrez-Aquilar, R. 2017. The Role of the Novel Lipokine Palmitoleic Acid in Health and Disease. *Adv Nutr*. 2017 Jan 17;8(1):173S-181S. doi: 10.3945/an.115.011130. Print 2017 Jan.
"The monounsaturated fatty acid palmitoleate (palmitoleic acid) is one of the most abundant fatty acids in serum and tissues, particularly adipose tissue and liver. Its endogenous production by stearoyl-CoA desaturase 1 gives rise to its cis isoform, cis-palmitoleate. Although trans-palmitoleate is also synthesized in humans, it is mainly found as an exogenous source in ruminant fat and dairy products. Recently, palmitoleate was considered to be a lipokine based on evidence demonstrating its release from adipose tissue and its metabolic effects on distant organs. After this finding, research has been performed to determine whether palmitoleate has beneficial effects on metabolism and to elucidate the underlying mechanisms. Thus, the aim of this work was to review the current status of knowledge about palmitoleate, its metabolism, and its influence on metabolic abnormalities. Results have shown mixed cardiovascular effects, direct or inverse correlations with

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

obesity, and hepatosteatosis, but a significant amelioration or prevention of insulin resistance and diabetes. Finally, the induction of palmitoleate release from adipose tissue, dietary intake, and its supplementation are all interventions with a potential impact on certain metabolic diseases."

Weimann, E., Silva, M.B.B., Murata, G.M., Bortolon, J.R., Dermargos, A., Curi, R. & Hatanaka, E. 2018.
"This study investigated the effects of palmitoleic acid on different phases of the healing process. Macroscopic analyses were performed on wounds in rats with or without palmitoleic acid treatment, and the results showed that palmitoleic acid directly hastened wound closure. The topical treatment of wounds with palmitoleic acid resulted in smaller wounds than those observed in the control group. The anti-inflammatory activity of palmitoleic acid may be responsible for healing, especially in the stages of granulation tissue formation and remodelling. Palmitoleic acid modified TNF-α, IL-1β, IL-6, CINC-2α/β, MIP-3α and VEGF-α profiles at the wound site 24, 48, 120, 216 and 288 hours post-wounding. Assays assessing neutrophil migration and exudate formation in sterile inflammatory air pouches revealed that palmitoleic acid had potent anti-inflammatory activity, inhibiting the LPS-induced release of TNF-α (73.14%, p≤0.05), IL-1β (66.19%, p≤0.001), IL-6 (75.19%, p≤0.001), MIP-3α (70.38%, p≤0.05), and l-selectin (16%, p≤0.05). Palmitoleic acid also inhibited LPS-stimulated neutrophil migration. We concluded that palmitoleic acid accelerates wound healing via an anti-inflammatory effect."

Good Sources of Palmitoleic Acid
A good source of Palmitoleic Acid is obtained from the oil of the Macadamia plant (*Macadamia integrifolia)*. Macadamias are large, spreading evergreen trees reaching 10 to 15 metres high and almost as wide. Macadamias are considered to be among the finest table nuts in the world. It contains high quantities of oil, and are, therefore, very fattening.

[Picture Credit: Macadamia]

Another excellent source of Palmitoleic Acid is obtained from oil from the seeds of the Sea Buckthorn plant.

[Picture Credit: Sea Buckthorn]

Sea Buckthorn (*Hipophaë rhamnoides*) is an arborescent armed, deciduous shrub or tree sometimes reaching up to18 metres. Its crown is irregular in shape with spiny, grey branches. The fruit is edible and has a tart, bittersweet taste. Its fruit is rich in Vitamins C, E, K, B_1 and B_2, as well as niacinamide, pantothenic acid, carotenoids and other substances such as oil, sugar, malic acid, amino acids and pectin.

The plant is considered a general panacea (a solution or remedy for all difficulties or diseases) and extensive use is made of its roots, stems, leaves, flowers, fruits and seed. Oil from the fruit acts as an antioxidant and is traditionally used to treat wounds, frost bite and pathological problems of the

alimentary mucous membranes. Serotonin (5-hydroxy-tryptamine) extracted from sea buckthorn possesses anti-tumour capabilities.

Omega-7 is quoted to be high in *palmitoleic acid* (not present in Omega-3, -6 or -9) which is effective against a range of life-threatening disorders – including cancer. Omega-7, in its natural source (i.e. macadamia nuts and sea buckthorn), is quoted to be a double-edged sword as it also contains high levels of *palmitic acid. Palmitic acid is a thick, gooey palm oil*, which in turn raises the risk of certain life-threatening disorders. It is essential when acquiring Omega-7 (palmitoleic acid) to ascertain that it has been 'purified' of palmitic acid.

Palmitoleic Acid (Omega-7) Fights the Factors of Metabolic Syndrome

Metabolic syndrome is a major contributor to the following:

- Elevated glucose and insulin resistance
- Lipid disturbances [causing high triglycerides and low High Density Lipoprotein (HDL)]
- High blood pressure
- Central obesity ('apple shape') – a well-known contributing factor to the increase in the risk of certain cancers like cancer of the prostate, kidney, breast, ovaries, colon, pancreas, cervix, thyroid and endometrium
- Chronic Inflammation which is also known to increase the risk for certain cancers

If one has metabolic syndrome, it means that one is possibly already along the road to heart disease, diabetes, certain cancers and other life-threatening disorders.

Omega-7 works in five distinct ways to reduce most of metabolic syndrome's harmful effects on one's health:

- It reduces insulin resistance and lowers blood glucose
- It suppresses fat production and accumulation
- It normalises abnormal lipid profiles (including raising beneficial HDL-cholesterol)
- It fights obesity
- It powerfully suppresses the inflammation that drives metabolic syndrome

The following table shows how different drugs compare to Omega-7 in fighting metabolic syndrome:

Metabolic Syndrome Parameter	Statins (Lipitor and others)	Fibrates (Lopid and others)	Glitzones (Actos and others)	Sulfonylureas (Glipizide and others)	Palmitoleic Acid (Omega-7)
LDL ('bad' cholesterol)	Reduce	Reduce	Increase	No effect	Reduce
HDL ('good' cholesterol)	Little effect May decrease	Increase	Increase	Decrease	Increase
Blood sugar	May increase	No effect	Reduce	Reduce Increases insulin	Reduce

Insulin Resistance	May worsen	No effect	Reduce	May improve	Reduce
Body weight/ Composition	Increase weight Decrease fat-free mass	Mazy increase weight and fat mass	Decrease fat	Increase	Reduce appetite
Inflammation	May reduce	May reduce	Reduce	No effect	Reduce
Side effects	Muscle pain (myalgia), may increase risk of diabetes	Gallstones, muscle pain	May increase risk of cardiovascular death	Increased risk of cardiovascular death	None known

(Yang, Miyahara & Hatnaka, 2011; Stefan, et al., 2010; Experimental Animal Laboratory, 2008; Green, 2012; Martinez, 2013).

De Souza, C.O., Teixeira, A.A.S., Biondo, L.A., Lima Junior, E.A., Batatinha, H.A.P. & Rosa Neto, J.C. 2017.

BACKGROUND: Palmitoleic acid, since described as lipokine, increases glucose uptake by modulation of 5'AMP-activated protein kinase (AMPK), as well as increasing lipolysis by activation of peroxisome proliferator-activated receptor-α (PPARα), in adipose tissue. However, in liver, the effects of palmitoleic acid on glucose metabolism and the role of PPARα remain unknown.

OBJECTIVE: To investigate whether palmitoleic acid improved the hepatic insulin sensitivity of obese mice.

METHODS: C57BL6 and PPARα knockout (KO) mice were fed for 12 weeks with a standard diet (SD) or high-fat diet (HF), and in the last 2 weeks were treated with oleic or palmitoleic acid.

RESULTS: Palmitoleic acid promoted a faster uptake of glucose in the body, associated with higher insulin concentration; however, even when stimulated with insulin, palmitoleic acid did not modulate the insulin pathway (AKT, IRS). Palmitoleic acid increased the phosphorylation of AMPK, upregulated glucokinase and downregulated SREBP-1. Regarding AMPK downstream, palmitoleic acid increased the production of FGF-21 and stimulated the expression of PPARα. Palmitoleic acid treatment did not increase AMPK phosphorylation, modulate glucokinase or increase FGF-21 in liver of PPARα KO mice.

CONCLUSIONS: In mice fed with a high-fat diet, palmitoleic acid supplementation stimulated the uptake of glucose in liver through activation of AMPK and FGF-21, dependent on PPARα.

Palmitoleic Acid (Omega-7) Fights Inflammation

There is a close connection between fat tissue and the chronic, low-grade inflammation that is associated with metabolic syndrome. The connection may be related to an enzyme known as SCD1 (stearoyl-CoA desaturase 1).

When scientists remove SCD1 activity in laboratory animals, their levels of fat tissue inflammation fall sharply, and their ability to respond to insulin (insulin sensitivity) rises. In the laboratory, adding omega-7 to cultures of fat cells triggers these same benefits by suppressing SCD1 activity.

Animal studies show significantly reduced levels of fat-related inflammatory cytokines (signalling molecules) following administration of omega-7. The livers of supplemented animals show significant reductions in the number of activated inflammatory cells, an effect that may help prevent

fatty liver disease. Many of these beneficial anti-inflammatory effects may arise from the ability of omega-7 to deactivate the master inflammatory regulation complex called *NF-kappaB*.

There is now human data on how omega-7 can lower inflammation and reduce the resulting cardiovascular risk. In a pilot trial of adults with high levels of *C-reactive protein* (blood marker for inflammation), supplementation with 210mg a day of *omega-7* resulted in a robust 73% decrease of *C-reactive protein (CRP)*.

Those results were extended in a larger, randomised clinical trial, in which all patients had abnormally high CRP levels (greater than 3 mg/dL). In this study, 30 days of supplementation with 210 mg/day of palmitoleic acid resulted in a significant drop in CRP of 1.9 mg/dL – that is a 43% reduction in a dangerous cardiovascular risk marker. Moreover, by the end of the supplementation period, the average CRP level was reduced from greater than 4 mg/dL to 2.1 mg/dL. The health ramifications of this marked reduction in C-reactive protein are profound, especially in abdominally-obese individuals who often exhibit dangerously elevated levels of this inflammatory indicator (CRP). (NHLBI/AHA Conference Proceedings; Festa, *et al*., 2000; Shah, *et al*., 2008; Liu, *et al*., 2010; Yand, Miyahara & Hatanaka, 2011; Guo, *et al*., 2012; Green, 2012; Martinez, 2013).

De Souza, C.O., Vannice, G.K., Rosa Neto, J.C. & Calder, P.C. 2018.
"Although dietary fatty acids can modulate metabolic and immune responses, the effects of palmitoleic acid (16:1n-7) remain unclear. Since this monounsaturated fatty acid is described as a lipokine, studies with cell culture and rodent models have suggested it enhances whole body insulin sensitivity, stimulates insulin secretion by β cells, increases hepatic fatty acid oxidation, improves the blood lipid profile, and alters macrophage differentiation. However, human studies report elevated blood levels of palmitoleic acid in people with obesity and metabolic syndrome. These findings might be reflection of the level or activity of stearoyl-CoA desaturase-1, which synthesizes palmitoleate and is enhanced in liver and adipose tissue of obese patients. The aim of this review is to describe the immune-metabolic effects of palmitoleic acid observed in cell culture, animal models, and humans to answer the question of whether palmitoleic acid is a plausible nonpharmacological strategy to prevent, control, or ameliorate chronic metabolic and inflammatory disorders. Despite the beneficial effects observed in cell culture and in animal studies, there are insufficient human intervention studies to fully understand the physiological effects of palmitoleic acid. Therefore, more human-based research is needed to identify whether palmitoleic acid meets the promising therapeutic potential suggested by the preclinical research."

Palmitoleic Acid (Omega-7) Helps Manage Body Weight
The reason central or abdominal obesity ('apple shape') is a factor in metabolic syndrome is because it has such strong associations with certain cancers and cardiovascular disease risk. This is due, in large part, to the increased inflammation produced by fat tissue.

Omega-7 helps manage this factor of metabolic syndrome because it signals one's body to stop storing fat.

Animals fed diets rich in omega-7 show significant increases in stomach and intestinal hormones that promote the feeling of fullness (satiety). At the same time, such diets produce decreases in hunger-promoting hormones. The combined effect is a significant reduction in food intake.

Several statin drugs, while lowering cholesterol and triglycerides, also produce increases in body and liver fat deposition. Omega-7 does just the opposite. Omega-7 **reduces** the production of fat in the liver. Increases in liver fat can result in non-alcoholic fatty liver disease (NAFLD), which is considered a major manifestation of the metabolic syndrome - which can eventually lead to liver failure and even cancer.
(Elbassuoni, 2013; Festa, *et al*. 2000; Shah, Mehta & Reilly, 2012; Lu*, et al*., 2012; Yang, Takeo, & Katayama, 2013; Aguirre, *et al*., 2013; Pappachan, 2013; NHLBI/AHA Conference Proceedings; Burns, *et al*., 2012).

Adverse Effects of Palmitoleic Acid (Omega-7)
No significant adverse effects have been reported for Omega-7 fatty acids.
(Yang & Kallio, 2002; Yang, Kalimo, Marrila, *et al*., 1999; Farma Nord).

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