

Cancer Association of South Africa (CANSA)

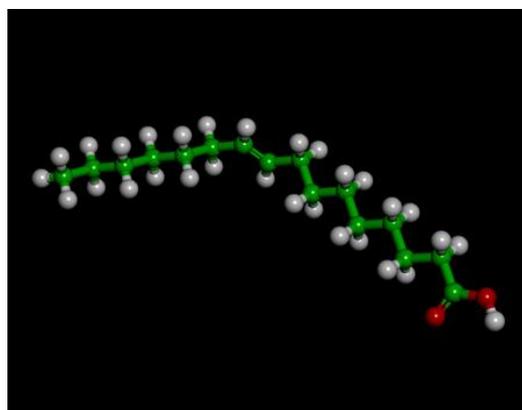


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Fact Sheet on Palmitoleic Acid (Omega-7)

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 Δ^7 . 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 $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$.

Yang, Z.H., Pryor, M., Noguchi, A., Sampson, M., Johnson, B., Pryor, M., Donkor, K., Amar, M. & Remaley, A.T. 2019.

Scope: Palmitoleic acid (palmitoleate; C16:1 n-7), an omega-7 monounsaturated fatty acid (MUFA) found in plants and marine sources, has been shown to favorably modulate lipid and glucose metabolism. However, its impact on atherosclerosis has not been examined in detail.

Methods and results: LDL receptor knock out (LDLR-KO) mice are fed a Western diet supplemented with 5% (w/w) palmitoleate concentrate, oleic-rich olive oil, or none (control) for 12 weeks. Dietary palmitoleate increases hepatic C16:1 levels, improves plasma and hepatic lipid/lipoprotein profiles ($\approx 40\%$ decrease in triglycerides), and reduces the atherosclerotic plaque area by $\approx 45\%$ compared with control or olive oil group ($p < 0.05$). These favorable changes are accompanied by the downregulation of key genes, such as Srebp1c, Scd1, Il-1 β , and Tnf α . ApoB-depleted plasma from mice fed palmitoleate has increased cholesterol efflux capacity by 20% from ABCA1-expressing cells

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($p < 0.05$). A beneficial effect of palmitoleate on glucose metabolism (54% decreased in HOMA-IR, $p < 0.05$) is also observed.

Conclusions: Dietary-supplemented palmitoleate reduces atherosclerosis development in LDLR-KO mice, and is associated with improvement of lipid and glucose metabolism and favorable changes in regulatory genes involved in lipogenesis and inflammation. These findings imply the potential role of dietary palmitoleate in the prevention of cardiovascular disease and diet-induced metabolic disorders.

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-1 β , IL-6, CINC-2 α/β , MIP-3 α 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%, $p \leq 0.05$), IL-1 β (66.19%, $p \leq 0.001$), IL-6 (75.19%, $p \leq 0.001$), MIP-3 α (70.38%, $p \leq 0.05$), and I-selectin (16%, $p \leq 0.05$). 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 (*Hipphaë rhamnoides*) is an arborescent armed, deciduous shrub or tree sometimes reaching up to 18 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, B₁ and B₂, 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.

González-Becerra, K., Ramos-Lopez, O., Barrón-Cabrera, E., Riezu-Boj, J.I., Milagro, F.I., Martínez-López, E. & Martínez, J.A. 2019.

Background: Chronic illnesses like obesity, type 2 diabetes (T2D) and cardiovascular diseases, are worldwide major causes of morbidity and mortality. These pathological conditions involve interactions between environmental, genetic, and epigenetic factors. Recent advances in nutriepigenomics are contributing to clarify the role of some nutritional factors, including dietary fatty acids in gene expression regulation. This systematic review assesses currently available information concerning the role of the different fatty acids on epigenetic mechanisms that affect the development of chronic diseases or induce protective effects on metabolic alterations.

Methods: A targeted search was conducted in the PubMed/Medline databases using the keywords "fatty acids and epigenetic". The data were analyzed according to the PRISMA-P guidelines.

Results: Consumption fatty acids like n-3 PUFA: EPA and DHA, and MUFA: oleic and palmitoleic acid was associated with an improvement of metabolic alterations. On the other hand, fatty acids that have been associated with the presence or development of obesity, T2D, pro-inflammatory profile, atherosclerosis and IR were n-6 PUFA, saturated fatty acids (stearic and palmitic), and trans fatty acids (elaidic), have been also linked with epigenetic changes.

Conclusions: Fatty acids can regulate gene expression by modifying epigenetic mechanisms and consequently result in positive or negative impacts on metabolic outcomes.

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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).

Acosta-Montaño, P., Rodríguez-Velázquez, E., Ibarra-López, E., Frayde-Gómez, H., Mas-Oliva, J., Delgado-Coello, B., Rivero, I.A., Alatorre-Meda, M., Aguilera, J., Guevara-Olaya L, & García-González, V. 2019.

“Metabolic overload by saturated fatty acids (SFA), which comprises β -cell function, and impaired glucose-stimulated insulin secretion are frequently observed in patients suffering from obesity and type 2 diabetes mellitus. The increase of intracellular Ca^{2+} triggers insulin granule release, therefore several mechanisms regulate Ca^{2+} efflux within the β -cells, among others, the plasma membrane Ca^{2+} -ATPase (PMCA). In this work, we describe that lipotoxicity mediated mainly by the saturated palmitic acid (PA) (16C) is associated with loss of protein homeostasis (proteostasis) and potentially cell viability, a phenomenon that was induced to a lesser extent by stearic (18C), myristic (14C) and lauric (12C) acids. PA was localized on endoplasmic reticulum, activating arms of the unfolded protein response (UPR), as also promoted by lipopolysaccharides (LPS)-endotoxins. In particular, our findings demonstrate an alteration in PMCA1/4 expression caused by PA and LPS which trigger the UPR, affecting not only insulin release and contributing to β -cell mass reduction, but also increasing reactive nitrogen species. Nonetheless, stearic acid (SA) did not show these effects. Remarkably, the proteolytic degradation of PMCA1/4 prompted by PA and LPS was avoided by the action of

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monounsaturated fatty acids such as oleic and palmitoleic acid. Oleic acid recovered cell viability after treatment with PA/LPS and, more interestingly, relieved endoplasmic reticulum (ER) stress. While palmitoleic acid improved the insulin release, this fatty acid seems to have more relevant effects upon the expression of regulatory pumps of intracellular Ca^{2+} . Therefore, chain length and unsaturation of fatty acids are determinant cues in proteostasis of β -cells and, consequently, on the regulation of calcium and insulin secretion.”

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 (PPAR α), in adipose tissue. However, in liver, the effects of palmitoleic acid on glucose metabolism and the role of PPAR α remain unknown.

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

METHODS: C57BL6 and PPAR α 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 PPAR α . Palmitoleic acid treatment did not increase AMPK phosphorylation, modulate glucokinase or increase FGF-21 in liver of PPAR α 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 PPAR α .

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

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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).

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

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Omega-7

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Palmitoleic Acid

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