Introduction to omega-7 fatty acids and palmitoleic acid

Omega-7 fatty acids are a category of unsaturated fatty acids. All fatty acids share a common basic hydro-carbon chain structure, with each carbon in the chain separated by a single or double bond. Omega-7 fatty acids all have the first carbon-carbon double bond at the 7th carbon counting backwards from the omega carbon. The most common omega-7 fatty acid is palmitoleic acid. Palmitoleic acid is a 16-carbon fatty acid that can naturally occur as a trans-isomer and a cis-isomer (C16:1n-7, cis-9-hexadecenoic acid). In its cis-isomer form, it is a monounsaturated fatty acid (MUFA).

Structure of palmitoleic acid (C16:1n-7)

Palmitoleic Acid

Only recently has palmitoleic acid been recognized as anything more than a building block of phospholipids in membranes, and emerging research suggests that it may play a protective role in a variety of cardiometabolic functions.

Dietary palmitoleic acid is thought to be readily absorbed from the diet. However, very few foods naturally provide significant amounts of palmitoleic acid (see Table 1). Primary sources include plant oils such as macadamia nut oil and sea buckthorn.

Table 1: Common food sources of palmitoleic

<table>
<thead>
<tr>
<th>Dietary Source</th>
<th>Palmitoleic Acid (g/100 g of Fatty Acids)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macadamia nut oil</td>
<td>17.3%</td>
</tr>
<tr>
<td>Cod liver oil</td>
<td>7.1%</td>
</tr>
<tr>
<td>Salmon</td>
<td>6.0%</td>
</tr>
<tr>
<td>Olive oil</td>
<td>1.4%</td>
</tr>
<tr>
<td>Eggs</td>
<td>0.3%</td>
</tr>
<tr>
<td>Soybean oil</td>
<td>0.08%</td>
</tr>
</tbody>
</table>

It is important to note the difference between palmitoleic acid and its precursor palmitic acid (16:0), a saturated fatty acid. Palmitic acid is found in most fats and oils, including palm products (e.g., palm oils), meats, and dairy products (e.g., cheese, butter). It is also commonly added to processed foods as a texturizing agent. Consumption of palmitic acid and other saturated fats is a rising concern due to negative health effects, particularly markers of cardiometabolic disorders. From both a consumer and healthcare professional standpoint, the distinction is important because dietary and other natural sources of beneficial n-7 palmitoleic acid may also contain higher concentrations of palmitic acid. For example, one analysis of pulp oil from 4 species of the sea buckthorn shrub showed a range of 32% to 42% palmitoleic acid—but also 34% to 41% palmitic acid (percentages of total fatty acids). Likewise,
commercially available omega-7 supplements may also contain higher levels of potentially harmful palmitic acid if the source materials are not processed to help remove it.

Palmitoleic acid can be produced endogenously within the body as a product of *de novo lipogenesis*, the process of lipid synthesis from excess carbohydrates\(^3\). It is primarily synthesized in the liver through the action of stearoyl-coenzyme-A desaturase (SCD), a key enzyme involved in *de novo lipogenesis*\(^3\). Data suggests that POA negatively feeds back on SCD enzymes to inhibit and potentially controls *de novo lipogenesis*\(^3\). *De novo lipogenesis* can be increased by dietary factors including high carbohydrate, high fat and saturated fat, energy imbalance, excess glucose, excess fructose, and chronic alcohol intake\(^3-5\), and epidemiological cohort studies that have adequately controlled for these factors show that palmitoleic acid is associated with a beneficial lipid profile\(^6\).

**Clinical evidence for palmitoleic acid**

A double-blind, randomized, placebo-controlled trial in humans demonstrated beneficial cardiometabolic effects of palmitoleic acid\(^7\). 60 subjects with dyslipidemia and baseline high sensitivity C-reactive protein (hsCRP) between 2 and 5 mg/L (raised) were randomized to receive a purified omega-7 preparation containing 220.5mg of palmitoleic acid or placebo control (medium chain triglyceride) daily for 30 days. All subjects were instructed to maintain their usual food intake patterns throughout the study. After the 30 day supplementation period, subjects in the POA group had experienced a 44% reduction in plasma hsCRP\(^7\). This is relevant therapeutically, as hsCRP is a sensitive and dynamic indicator of inflammation has been associated with an increased risk of coronary heart disease, fatal and non-fatal heart attack, and stroke, after adjustment for age and sex\(^8\), and individuals with LDL cholesterol less than 70mg/dL (.8mmol/L) and hsCRP concentrations below 2mg/L had reduced cardiovascular risk than those with LDL cholesterol below 70mg/dL and hsCRP above 2mg/L\(^9\).

In the clinical intervention study with palmitoleic acid\(^7\), subjects supplemented with palmitoleic acid also experienced an 8% reduction in LDL cholesterol and 15% reduction in plasma triglycerides, as well as a 5% increase in plasma HDL\(^7\). These improvements in lipids are important due to the causative role of LDL in
atherosclerosis development (reference), and the contribution of high triglycerides to atherogenic dyslipidemia and small dense HDL and LDL particles\textsuperscript{10,11}. Overall, the results of this clinical study with palmitoleic acid suggest that it is a reasonable therapeutic approach in helping maintain healthy lipid levels in patients with diagnosed lipid disorders. Omega-7 and palmitoleic acid supplementation has already been adopted in North America, spearheaded by practices such as The Cleveland Clinic.

Pre-clinical studies suggest that palmitoleic acid is a regulator of metabolic health

Several pre-clinical studies have begun to shed light on palmitoleic acid’s mechanisms of action, and \textit{in vitro} and \textit{in vivo} studies have consistently demonstrated positive effects in the regulation and pathophysiology of lipid and glucose metabolism. In landmark research from Harvard University, over 400 fatty acids were screened and it was suggested that palmitoleic acid functions as a ‘lipokine’ - a lipid with hormone-like biological activity\textsuperscript{12}. They also suggested that the ester form circulating in the blood serves as a communicator to distant organs and assists in the regulation of metabolic homeostasis. The investigators proposed that it might be "the only fatty acid that could substantially change serum fatty acid composition in relation to alterations in lipid metabolism in adipose tissue"\textsuperscript{12}.

Several studies have demonstrated a beneficial effect of palmitoleic acid on Insulin sensitivity and glucose uptake. In a 4-week, placebo-controlled study of diabetic mice, palmitoleic acid administration significantly increased insulin sensitivity (as assessed by an insulin tolerance test), lowered plasma glucose and insulin levels\textsuperscript{13}. Mechanistically, palmitoleic acid has been shown \textit{in vitro} to promote muscle glucose transport in skeletal muscle cells\textsuperscript{14}, stimulated muscle insulin action\textsuperscript{12}, and stimulated insulin-secreting pancreatic beta-cell proliferation\textsuperscript{15}. Palmitoleic acid also downregulated mRNA expression of pro-inflammatory genes (TNF-\textalpha, resistin) in white adipose tissue\textsuperscript{13}, and reduced intramuscular adipocyte size\textsuperscript{16}, two actions that may have a positive knock-on effect on insulin sensitivity through improved insulin signaling.

Several reports of a positive effect of palmitoleic acid exist for body weight regulation in different animal models\textsuperscript{13,16}. Increases in ‘anorectic’ gut peptides such as cholecystokinin (CCK) may mediate this weight
reducing effect through an increase in satiety and a reduction in food intake, as palmitoleic acid supplementation has been shown to increase circulating CCK concentrations in pre-clinical models\textsuperscript{17}.

In terms of lipid metabolism, in a 4-week, placebo-controlled study of diabetic mice, palmitoleic acid administration significantly lowered plasma and hepatic triglycerides, and downregulated the expression of lipogenic genes (SREBP-1, FAS, SCD-1) in the liver\textsuperscript{13}. In addition to these effects on lipid metabolism, palmitoleic acid has been shown to reduce endoplasmic reticulum (ER-) stress in macrophages (a marker of atherosclerosis)\textsuperscript{18}.

**Conclusions**

Palmitoleic acid is an omega-7 fatty acid with mounting pre-clinical and clinical evidence supporting its role in metabolic control and cardiovascular health. In clinical studies, supplementation with palmitoleic acid has been shown to reduce plasma hsCRP and improve lipid profile, suggesting therapeutic benefit for patients with cardiovascular disease risk. There are few rich dietary sources of palmitoleic acid and these tend to be uncommon in the standard diet (e.g. macademia nut oil, sea buckthorn). Additionally, these often contain high amounts of the saturated fat palmitic acid, and so purified sources of palmitoleic acid are important for clinical intervention.

**REFERENCES**


