Clinical Applications of Omega-7 & Omega-3 Fatty Acids in Cardiovascular Health

Fatty acids are the building blocks of fats. Of particular interest is the role that select fatty acids may play in cardiovascular disease and other disease states. Omega-3 fatty acids have been widely studied for decades, with well-established benefits to maintaining multiple aspects of cardiovascular health. Emerging science on omega-7 fatty acids is also promising, specifically in regards to lipid metabolism.

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A FOCUS ON OMEGA-7 & OMEGA-3

Supplemental omega-3s—specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)—are recommended for a number of applications to support specific functioning throughout the body, as well as for general health support. And a growing body of nutritional research suggests that omega-7s also hold promise for targeted approaches as well. The focus of this paper is on the potential clinical applications of specific omega-3s and omega-7s to support cardiovascular health—for reversing early risk factors, managing cardiometabolic conditions, and curbing cardiovascular disease progression.

OMEGA-7 BACKGROUND

All mentions of omega-7 (n-7) described in this paper refer exclusively to one of the most common omega-7s—palmitoleic acid, or its ester form palmitoleate. Palmitoleic acid is a 16-carbon fatty acid that can naturally occur as a *cis*-isomer (C16:1n-7, *cis*-9-hexadecenoic acid) and *trans*-isomer. In its *cis*-isomer form, it is a monounsaturated fatty acid (MUFA). Only recently has palmitoleic acid been recognized as anything more than a building block of phospholipids in membranes. 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. Palmitoleic acid is a MUFA like oleic acid (omega-9). But while approximately 90% of dietary intake of MUFAs is oleic acid (found in olive and other vegetable oils), very few foods naturally provide significant amounts of palmitoleic acid (see Table 1). Dietary intake may comprise less than 4% of total energy. Primary sources include plant oils (e.g., macadamia nut oil) and fish oils.[1] In fact, it was first identified after isolation from herring and cod liver oils in 1906.[2]

Unlike omega-3 fatty acids, palmitoleic acid can be produced within the body as a product of lipogenesis (fatty acid synthesis). It is primarily synthesized in the liver with the aid of stearoyl-coenzyme-A desaturase (SCD) enzymes. It is then used in the formation of triglycerides, packaged in very low-density lipoprotein (VLDL), and secreted into the blood.[2] Palmitoleic acid can also be synthesized in adipose tissue, where it is thought to be the most highly regulated fatty acid.[3]

Although considered a "minor" fatty acid, palmitoleic acid can be found throughout the body—ranking fifth among the most abundant fatty acids in most commonly measured tissue and blood lipid fractions.[4-7] Often palmitoleic acid is converted into several other members of the omega-7 family, such as palmitolinoleic acid (16:2n7) and rumenic acid (18:2n7), and therefore is considered the parent omega-7 fatty acid.[7]

Table 1. **Common Food Sources of n-7 Palmitoleic Acid**[1]

Dietary Source	Palmitoleic Acid (g/100 g of Fatty Acids)
Macadamia nut oil	17.3%
Cod liver oil	7.1%
Salmon	6.0%
Olive oil	1.4%
Eggs	0.3%
Soybean oil	0.08%

PALMITOLEIC ACID VS. PALMITIC ACID

It's important to note the difference between palmitoleic acid and its precursor palmitic acid (16:0), a *saturated* fatty acid that is the most common fatty acid found in living organisms. However, the desaturase enzymes that make palmitoleic acid have a weak affinity to its precursor palmitic acid—which is why only small amounts of palmitoleic acid are generally found in the body.[4,8] The ratio between palmitoleic acid and palmitic acid levels in plasma is known as the desaturation index.

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. Research suggests that it is one of the most atherogenic fatty acids. It has been shown to decrease fat oxidation and daily energy expenditure, which can lead to obesity. Palmitic acid has also been associated with inflammation and insulin resistance.[5,7,9]

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).[7] 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.

ENDOGENOUS PALMITOLEIC ACID EXAMINATIONS

Numerous studies and analyses have been conducted to establish associations between endogenous fatty acid concentrations and/or dietary intake to varying states of disease and health. Endogenous concentrations of essential omega-3s reflect dietary consumption, but fatty acids such as palmitoleic acid that can be synthesized in the body and consumed in the diet make scientific interpretation of serum and tissue fatty acid profiles more difficult. And fatty acid synthesis can be influenced by many factors.

Understandably, analyses of endogenous palmitoleic acid concentrations in humans report mixed findings—similar to research on other fatty acids that can be synthesized in the body and consumed in the diet (e.g., oleic acid). Interpreting and comparing these various studies and analyses is also challenging for a number of other reasons, including:

- A variety of tissue and blood measurements for palmitoleic acid have been used—and many evaluate single samples.
- Dietary and metabolic factors can also impact results:
  - Desaturation of palmitic acid in cow's meat/milk may increase circulating palmitoleate.[10]
  - Excess energy consumption and low-fat, high-carbohydrate diets can stimulate lipogenesis in the liver that increases plasma palmitoleic acid concentration, as well as adipose concentration.[5,6]
- Increased body weight/fat may also induce enzymatic changes in desaturation that may influence measures.[6]
  - New research suggests that adipose tissue has reduced lipid synthesis capacity in obese mice and humans.[11]

- Gender: women appear to have more adipose tissue palmitoleate than men.[1]
- Pharmaceutical agents may also influence palmitoleate concentrations.
    - Anti-diabetic thiazolidinediones (TZDs) have been shown in human and animal studies to increase plasma palmitoleate, suggesting a role in insulin sensitivity.[12]

Following are a few studies that have attempted to establish relationships with endogenous palmitoleic acid concentration to various metabolic functions and health states. It is important to note that these epidemiologic analyses DO NOT reflect specific dietary interventions or supplementation with palmitoleic acid.

- In a regression analysis of 134 men with no known metabolic disorders, plasma palmitoleic acid concentration was independently associated with plasma triglycerides and waist circumference. *Note: The 33 subjects in the highest quartile of triglycerides (≥ 1.05 mmol/l) had a mean value of 1.75 mmol/l—just above the 1.70 mmol/l normal range cutoff.*[13]
- A study of a Mediterranean population of overweight and obese subjects demonstrated that overweight subjects had significantly higher adipose tissue concentrations of palmitoleic acid than obese and morbidly obese subjects. *Note: In this case, plasma palmitoleic acid was suggested to be an important predictor of a more favorable BMI.*[5]
- In a subset analysis of control subjects from a previous study, a positive association was shown for adipose tissue concentration of palmitoleic acid and obesity. *Note: This association was attenuated in subjects with low carbohydrate intake.*[12]
- In a 3-arm analysis of metabolic syndrome (n=27), obese (n=43), and control (n=24) subjects, plasma palmitoleic acid concentrations were higher in metabolic syndrome subjects than in control—but not in obese subjects. *Note: "Metabolic syndrome" subjects had abdominal obesity plus 2 other diagnostic markers, and the "obese" classification allowed for an additional diagnostic marker of metabolic syndrome (e.g., hyperlipidemia).*[14]
- In a nested control study of children genetically predisposed to type 1 diabetes, non-fasting serum samples demonstrated that palmitoleic acid (and other fatty acids) were positively associated with risk of advanced β-cell autoimmunity. *Note: The associated fatty acids are all present in milk/meat. And early milk consumption has been associated with development of preclinical and type 1 diabetes.*[10]
- An analysis of 39 non-diabetic, obese subjects—10 insulin resistant (IR) and 10 insulin sensitive (IS)—showed no significant difference between groups in either plasma or VLDL palmitoleic acid concentrations. *Note: "However, our study does not preclude the possibility that plasma palmitoleate availability may be related to insulin sensitivity in lean subjects or that palmitoleate availability within muscle and liver tissue might be different in IS and IR subjects."*[15]
- A cross-sectional study of 162 diabetic subjects—a majority with non-alcoholic fatty liver disease (NAFLD)—suggested an association with higher liver fat content and palmitoleate in red blood cell membranes. *Note: The authors suggested this was due to increased endogenous lipogenesis caused by obesity and insulin resistance.*[16]

Recent larger, long-term examinations suggest more positive trends between endogenous palmitoleate concentrations and insulin sensitivity, lipid metabolism, and/or body weight. For example, many of the factors that may have influenced outcomes in other studies were taken into consideration a prospective cohort of 3,630 men and women from the Cardiovascular Health Study (1992-2006).

Before adjustments, higher plasma palmitoleic acid concentrations were independently correlated to greater body mass index and intake of carbohydrate, protein, and alcohol. After multivariable-adjusted linear regression in consideration of those correlations, higher palmitoleic acid concentrations were associated with beneficial effects, including:

- Lower ratio of total cholesterol to HDL
- Lower LDL cholesterol
- Higher HDL cholesterol
- Decreased levels of fibrinogen

However, palmitoleic acid concentrations were also associated with greater adiposity, higher triglycerides, and (in men) greater insulin resistance—without overall associations with diabetes incidence. The investigators stated that the findings suggest that circulating palmitoleate may have direct regulatory benefits on some metabolic pathways (as shown in animal studies), but might reflect underlying lifestyle traits (e.g., carbohydrate intake, energy imbalance) that confound findings.[6]

A positive association between palmitoleic acid and insulin sensitivity was demonstrated in a recent analysis of subjects at risk of developing type 2 diabetes who followed a 9-month lifestyle intervention that included regular exercise, fiber intake, and restriction of <30% of total fat (≤10% saturated fat). Circulating palmitoleate at baseline demonstrated:

- Positive correlation to insulin sensitivity—independent of age, gender, or adiposity.
- No association with age, serum high sensitivity C-reactive protein (hs-CRP, a marker of inflammation), or measures of adiposity adjusted for age and gender—including body weight, BMI, waist circumference, total fat, and visceral fat.

In subjects with high baseline palmitoleate, investigators also noted a higher chance to observe an increase in insulin sensitivity (independent of adiposity change) when compared to subjects with low baseline levels.[17]

DIETARY OMEGA-7 INVESTIGATIONS

A number of studies have examined the benefits of diets lower in saturated fats and higher in MUFAs (e.g., Mediterranean-style diets). As stated earlier, a majority of dietary MUFAs are omega-9s, and there are a limited number of common foods that provide a significant source of palmitoleic acid. Therefore, understandably few dietary intervention studies with a palmitoleic acid focus have been conducted to date. These clinical and in vivo studies suggest, however, that a palmitoleic acid-rich diet may favorably influence lipid metabolism.

A 12-week, 4-arm study in hamsters compared a lowfat, low-cholesterol diet (10% fat, 0.1% cholesterol) enriched with macadamia, palm, canola, or safflower oils to evaluate lipoprotein profiles and aortic cholesterol accumulation. Macadamia oil demonstrated:[18]

- Lower non-HDL cholesterol and triglycerides compared to palm and coconut oils

- Higher HDL cholesterol compared to coconut, canola, and safflower oils

As with endogenous fatty acid profile evaluations, human dietary interventions with palmitoleic acid-rich foods have also shown mixed results. Assuring consistent dietary intake in human clinical research is difficult, and the design of some studies include varying dietary protocols that may have influenced outcomes and make comparison difficult. In 4 recent small clinical studies, however, short-term consumption of macadamia nuts generally demonstrated:[19-22]

- Reduction in total cholesterol
- Reduction in triglycerides
- Positive effects on LDL and HDL cholesterol were also sometimes observed

PALMITOLEIC ACID STUDIES

Research to date suggests that palmitoleic acid may offer protective health benefits in many areas where palmitic acid negatively affects functioning. In vitro and in vivo studies have consistently demonstrated positive effects in the regulation and pathophysiology of lipid and glucose metabolism. (See summary in Table 2.)

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. 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."[11]

- In a laboratory study of L6 muscle cells from rats, palmitoleic acid caused a significant reduction in insulin signaling and insulin-stimulated glucose transport.[23]
- In a study with human pancreas islets, saturated palmitic acid increased β-cell DNA fragmentation and decreased β-cell proliferation. But monounsaturated palmitoleic acid did not affect DNA fragmentation and induced β-cell proliferation—as well as prevented the deleterious effects of both palmitic acid and high glucose concentration.[24]
- In a laboratory study, palmitoleic acid demonstrated cell protective properties by inhibiting lipoaptosis (cell death) activity induced by the endoplasmic reticulum (ER) stress response after exposure to palmitate[25]
- Lipodemic analyses in mice and liver cells demonstrated lipokine-like activity to beneficially influence several functions involved in insulin regulation and lipid metabolism.[11]
- 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, and lowered plasma and hepatic triglycerides. It also downregulated mRNA expressions of pro-inflammatory adipocytokine genes (TNF-α, resistin) in white adipose tissue and lipogenic genes (SREBP-1, FAS, SCD-1) in the liver.[26]
- In a series of food studies with rats, the satiety effects of various free form fatty acids were compared to control—including palmitoleic acid, palmitic acid, and oleic acid. Palmitoleic acid elevated levels of the satiety hormone cholecystokinin (CCK), and food intake was reduced.[27]

Table 2. **Summary of Palmitoleic Acid Research**[11,23-33]

	Results	Areas of Potential Benefits: Weight/BMI	Insulin/Glucose	Fat/Lipids	Inflammation
IN VITRO & IN VIVO	Dimopoulos et al.[23] ▪ Promoted muscle glucose transport in skeletal muscle cells		√		
	Maedler et al.[24] ▪ Stimulated pancreatic β-cell proliferation ▪ Improved survival of β-cells after exposure to palmitic acid		√		
	Akazawa et al.[25] ▪ Inhibited saturated palmitic acid-induced apoptosis in hepatocytes ▪ Inhibited palmitic acid-induced ER stress ▪ Inhibited palmitic acid-induced dysregulation of proapoptotic Bcl-2 proteins			√	
	Cao et al.[11] ▪ Stimulated muscle insulin action ▪ Inhibited hepatic triglycerides ▪ Suppressed cytokine expression in adipocyte fractions ▪ Decreased expression of hepatic lipogenic enzymes (related to insulin sensitivity)		√	√	√
	Yang et al.[26] ▪ Reduced body weight increase ▪ Significantly increased insulin sensitivity ▪ Lowered plasma glucose and insulin levels ▪ Lowered plasma and hepatic triglycerides ▪ Downregulated mRNA expression of adipocytokines (TNF-α, resistin) ▪ Downregulated mRNA expression of lipogenic genes (SREBP-1, FAS, SCD-1)	√	√	√	√
	Yang et al.[27] ▪ Elevated levels of CCK (satiety) ▪ Reduced food intake	√			
	Burns et al.[28] ▪ Improved insulin sensitivity		√		
	Duckett et al.[29] ▪ Reduced weight gain ▪ Reduced intramuscular adipocyte size	√		√	
	Cleveland Clinic Foundation[30†] ▪ Reduced aortic cholesterol deposition ▪ Increased HDL cholesterol			√	
CLINICAL†	Green[31] ▪ Reduced hs-CRP†† ▪ Reduced TG ▪ Reduced LDL-C, non-HDL-C & TChol			√	√
	Martinez[32] ▪ Reduced hs-CRP ▪ Reduced TG ▪ Reduced LDL-C, non-HDL-C & TChol ▪ Increased HDL-C ▪ Reduced weight			√	√
	Martinez[33] ▪ Reduced hs-CRP levels ▪ Reduced TG ▪ Reduced LDL-C, non-HDL-C & TChol ▪ Increased HDL-C	√		√	√

†† In a subgroup analysis of subjects with elevated hs-CRP at baseline.
† Conducted with a purified palmitoleic acid preparation containing only the *cis*-isomer form.

- Infusion of palmitoleic acid in obese lambs appeared to favorably affect insulin signaling to alter plasma glucose.[28]
- Administration of an omega-7-enriched oil to obese sheep increased circulating palmitoleic acid and reduced average daily weight gains and intramuscular adipocyte size.[29]
- A purified preparation of palmitoleic acid (to help remove palmitic acid and retain the *cis*-isomer form of palmitoleic acid) was evaluated in the Apo-E mouse model of artherosclerois. Palmitoleic acid demonstrated a consistent antiatherogenic effect compared to control, as well as an 85% increase in HDL levels.[30]

CLINICAL STUDIES WITH PURIFIED PALMITOLEIC ACID

Three preliminary human studies have been conducted with an omega-7 preparation containing the same purified palmitoleic acid (PPOA) mentioned in the animal study above. Data on the potential metabolic benefits of palmitoleic acid in humans are limited due to the multiple variables that constitute fatty acid synthesis. However, it has been proposed that the hormone-like activity demonstrated in animal research may help explain why even small doses have repeatedly yielded improvement in serum lipids in these studies.[31-33]

Dosing Feasibility Study. Subjects of varying health states were randomly assigned to receive either 210 mg of PPOA (n=13) or 840 mg PPOA (n=14). High response rates were seen following PPOA that included:[31]

- Decreases in LDL cholesterol
  - Range of 12% to 19% decrease with 210 mg PPOA
  - Range of 3.9% to 30% decrease with 840 mg PPOA
- Decreases in total cholesterol
  - Range of 3% to15% decrease with 210 mg PPOA
  - Range of 3.9% to 30% decrease with 840 mg PPOA
- Declining trend in non-HDL cholesterol (See Table 3)

There were no changes in baseline or post-treatment glucose values in either group, and both dosages were well tolerated. Three subjects in the study presented with elevated hs-CRP levels at baseline (ranging from 2.2. to 3.7 mg/L). In a separate subgroup analysis, these subjects showed a mean reduction of 73% in hs-CRP with only 210 mg of PPOA daily.[31]

Table 3. **Lipid Profile Changes with Varying Dosages of PPOA**[31]

Biomarker & Target Change		Low Dose Arm 210 mg PPOA (n=13)			High Dose Arm 840 mg PPOA(n=14)		
		Baseline/ 4 Weeks		Mean Change	Baseline/ 4 Weeks		Mean Change
TG	↓	128	118	-7.7%	146	130	-11.0%
LDL-C	↓	118	112	-5.1%	118	109	-7.6%
non-HDL-C	↓	143	136	-4.9%	147	135	-8.2%
TChol	↓	199	189	-5.0%	195	182	-6.7%

Shaded boxes represent p values<0.05 when compare to baseline

Table 4. **Subgroup Analysis of Subjects with Baseline TChol>200**[31]

Biomarker & Target Change		Low Dose Arm 210 mg PPOA (n=6)			High Dose Arm 840 mg PPOA (n=7)		
		Baseline/ 4 Weeks		Mean Change	Baseline/ 4 Weeks		Mean Change
TG	↓	100	93	-7.0%	180	153	-15.0%
LDL-C	↓	141	125	-11.3%	134	117	-12.7%
non-HDL-C	↓	161	143	-4.9%	170	147	-8.2%
TChol	↓	232	208	-10.3%	219	190	-13.2%

Shaded boxes represent p values<0.05 when compared to baseline

Almost half of the subjects had baseline total cholesterol>200 mg/dL. This subgroup analysis demonstrated (See Table 4):[31]

- Significant declines in total, non-HDL, and LDL cholesterol in both arms
- Decrease in triglycerides in both arms

Of note was that virtually all subjects with high LDL cholesterol values were concomitantly on statin and/or fibrate therapy at the time, yet both dosage groups still demonstrated >10% decreases in total and LDL cholesterol. The investigator suggested a possible complementary mechanism of action between statins and PPOA.[31]

Open Label Study. This study included 16 obese patients presenting with lipid disorders (hyperlipidemia, dyslipidemia), metabolic syndrome, and/or type 2 diabetes given a 420 mg dose of a purified omega-7 preparation (containing 210 mg PPOA like the low-dose arm in previous study) for 30 days, in addition to weight loss counseling and lifestyle guidance. A majority of subjects also presented with: elevated hs-CRP; medications for blood pressure and/or type 2 diabetes; and elevated triglycerides (mean 227 mg/dL). Subjects demonstrated the following mean changes (See Table 5):[32]

- Decrease in hs-CRP
- Decrease in triglycerides
- Decreases in LDL, non-HDL, and total cholesterol
- Increase in HDL cholesterol

Double-Blinded, Randomized, Placebo-Controlled Study. This study included 60 subjects with elevated hs-CRP at baseline (3 to10 mg/L) but with no diagnosed cardiometabolic conditions. Subjects instructed not to change normal food intake and received either a 420 mg dose of a purified omega-7 preparation (containing 210 mg PPOA) or placebo for 30 days. No noticeable changes were seen in the placebo arm, but the PPOA arm demonstrated the following mean changes (See Table 5):[33]

- Decrease in hs-CRP
- Decrease in triglycerides
- Decreases in LDL, non-HDL, and total cholesterol
- Higher than expected increase in HDL cholesterol when compared to placebo

Table 5. **Lipid Profile Changes with 210 mg PPOA**[32,33]

Biomarker	Target Change	Open Label Study (n=16)[32]	Placebo-Controlled Study (n=60)[33]
		Mean Change at 30 Days	Mean Change at 30 Days
hs-CRP	↓	-64%	-50%
TG	↓	-36%	-17%
LDL	↓	-10%	-7%
HDL	↑	+4%	+3%
non-HDL	↓	-17%	-9%
TChol	↓	-13%	-7%

Shaded boxes represent p values<0.01 when compared against placebo

These clinical studies suggest that PPOA may be a reasonable therapeutic approach in helping maintain healthy lipid levels in healthy patients and those with diagnosed lipid disorders. Omega-7 supplementation with PPOA has already been adapted in North America, spearheaded by practices such as The Cleveland Clinic.

OMEGA-3 BACKGROUND

Omega-3s are polyunsaturated fatty acids (PUFAs) with well-documented health benefits in over 20,000 published scientific papers. It's been nearly 4 decades since scientists first linked a diet rich in omega-3s and lower rates of heart disease in Greenland Eskimos.[34] Since then, certain omega-3s have been shown to be a powerful tool in the management of inflammatory-related chronic diseases, as well as supporting overall health.

Omega-3s are "good fats" found in every cell in the human body. They are considered essential because they aren't produced by the body, so they must be obtained from foods or supplementation. The most widely researched omega-3s are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA supplements are commonly referred to as "fish oils" because coldwater fish such as mackerel, menhaden, salmon, and tuna are major sources. Other common sources include calamari, krill, and other marine animals.

Alpha-linolenic acid (ALA) is a plant-based omega-3 found in flaxseed, hemp, dark green vegetables, and nuts. ALA does not convey health benefits to the same degree when compared to similar doses of EPA or DHA. While ALA is converted by the human body to DHA or EPA, studies suggest that the overall conversion rate may be less than 1%.[35,36] ALA conversion is also limited in men.[37]

OMEGA-3s IN THE DIET

Although supplements are popular and dietary sources are plentiful, the increase in inflammatory-related chronic diseases—most notably heart disease—suggests that most people aren't getting enough. Another challenge is that the dietary consumption of omega-6s may be too high.

Human nutritional science has established that an adequate ratio of omega-6 and omega-3 fatty acids is an important component to promote a healthy and balanced diet. It is estimated that the ratio of omega-3s to omega-6 fatty acids in the average Western diet of a century ago was balanced at 1:1. But today that ratio is believed to be as high as 17:1, as consumers now eat fewer foods that are concentrated with anti-inflammatory omega-3s (fish, flax, dark green vegetables, nuts) and more foods that are high in pro-inflammatory omega-6s (processed cereals, red/processed meats).[38] While both types of fats are essential for health, this imbalance—coupled with a lack of regular physical activity—has directly contributed to a rise in lifestyle-related chronic diseases.[39,40]

In 2004 the U.S. Food and Drug Administration took an important step by issuing the following qualified health claim: "Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of CHD." However, there is still no official government RDI for omega-3s, and recommendations from leading health organization differ.

The lack of an official RDI may explain why so few consumers know what their optimal intake should be, and why so few doctors are making sure their patients are getting enough. In fact, a 2006 survey of 500 family physicians published in the *Journal of the American Board of Family Medicine* revealed that despite having knowledge of the benefits, fewer than 1 in 5 physicians prescribe omega-3s to their heart disease patients.[41]

As far as dietary consumption, preparation time/methods, taste/smell issues, and availability of fresh fare influence consumptions habits. Contamination is also a very real concern. In 2004 the FDA and Environmental Protection Agency, concerned over mercury and other contaminants in fish and shellfish, advised women of childbearing age and young children to avoid certain large species of fish and limit their consumption of other fish to 2 average meals a week. Fish oil supplements may also carry higher levels of heavy metals or contaminants.

OMEGA-3s & CARDIOVASUCLAR HEALTH

A number of studies of endogenous fatty acid profiles suggest that higher concentrations of omega-3s decrease the risk of a number of concerns that have been associated with cardiovascular disease development—including abdominal obesity, higher liver fat content, and elevated blood lipids.[5,14,15,42]

Omega-3 fatty acids (including EPA and DHA) have been examined in previous clinical and epidemiological research that has shown they may:[42-53]

- Keep cell membranes fluid, flexible, and permeable to function properly
- Reduce certain pro-inflammatory signals and activities (e.g., oxidative stress)
- Regulate genetic expression in favor of health
- Promote healthy blood flow and decrease the growth rate of atherosclerotic plaque
- Reduce LDL cholesterol levels
- Increase HDL cholesterol levels
- Reduce triglyceride levels
- Lower blood pressure (slightly)
- Decrease the risk of fatal arrhythmias
- Decrease the chance of stroke

Though EPA and DHA have individually shown to beneficially influence certain functions to a greater extent than the other, the bulk of research focuses on their combined use to support overall cardiovascular health. Their complementary effects also suggest their combined use to support cardiovascular health.[43]

Summary

Emerging research suggests that omega-7s offer a targeted approach to support healthy cholesterol and triglyceride metabolism, as well as improve markers of inflammation associated with cardiovascular disease development. Doses of 210 mg/day or purified palmitoleic acid have been suggested in preliminary clinical studies to be an effective, well-tolerated dose in a variety of patients.

The omega-3s EPA and DHA in combination are a well-established nutritional approach to support multiple cardiovascular functions, as well as support for overall health. Both omega-7s and omega-3s may offer viable clinical approaches to positively affect cardiovascular response and help manage and reverse cardiovascular risk factors.

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