

# Plant Nutraceuticals for Cardiovascular Diseases with Special Emphasis to the Medicinal Herb Fenugreek (*Trigonella Foenum-Graecum* L.)

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**Abstract:** Cardio Vascular diseases have assumed alarming proportions globally primarily due to life style changes, changing food habits and sedentary habits. Food plays an important role in regulating body functions and more so the cardio vascular functions. Obesity is a major cause of CVD and is related to nutrition and exercise. Excess fat in body gets deposited in adipose tissue, blood vessels, nerves and joints and often promotes diabetes, hypertension and renal disorders. All these can be regulated to a large extent by taking proper health supplements and regulating nutrition. Functional food rich in protein and fibers and less in calorific value can help in reducing reactive oxygen species and risks of myocardial infraction and improve quality of life. Nutraceuticals offer this possibility. Nutrition therapy focuses on maintaining optimal nutrition, modifying nutritional contents and controlling blood pressure. This paper reviews the role of nutraceuticals and dietary supplements from plant sources with special emphasis to medicinal herb fenugreek (*Trigonella foenum-graecum* L.) for enhancing good health and reducing risks of cardio vascular diseases.

**Keywords:** nutraceuticals, cardiovascular diseases, hypertension, diabetes, chronic heart disease, fenugreek

**Abbreviations:** **ACE:** Angiotensin-converting enzyme; **CHD:** Coronary Heart Disease; **CVD:** Cardio Vascular Diseases; **HAART:** Highly Active Antiretroviral Combination Therapy; **HDL-C:** High Density Lipid-Cholesterol; **HTN:** Hypertension; **GI:** Glycemic Index; **LDL-C:** Low Density Lipid-Cholesterol; **LPP:** lipid Peroxidation Process ; **MUFA:** Mono Unsaturated Fatty Acids; **NFκB:** Nuclear Factor Kappa B; **Om3:** Omega 3; **PUFA:** Poly Unsaturated Fatty Acids; **SFA:** Saturated Fatty Acid; **Terp:** Terpenenes; **TG:** Tri- Glycerides; **TC:** total cholesterol; **VLDL:** Very Low Density Lipid

## INTRODUCTION

Cardio Vascular Diseases (CVD) result in the death of over 6.5 million people worldwide every year and atherosclerosis of the coronary arteries is the cause of most incidences. There is a wide range of risk factors associated with the development of CVD, including family

history, hypertension, raised serum cholesterol, diabetes, smoking, poor diet and lack of exercise. Changing levels of prosperity and availability of fast food to kids are leading to imbalance to body intake and energy used. Myocardial infarctions (MIs) occur in patients who have established Coronary heart disease (CHD) where there

is severe and/or prolonged impaired supply of oxygenated blood to the cardiac tissue. Primarily obesity is responsible for hypertension, (HTN), dyslipidemia, with a co morbid disease risk including type 2 diabetes, heart disease [1]. India shows a steadily increasing trend of HT [2] with the potential of becoming the ‘hypertension capital of the world [3]. About 25 % of Indians who live in urban areas are reported to be hypertensive [4; 5] and 57% of all stroke deaths and 24 % of all cardiovascular deaths in Eastern Asia are associated with hypertension (HT) [6]. Coronary heart disease (CHD) is responsible for 52 % of the 870,000 deaths that occur annually from cardiovascular disease in the United States.

The term 'nutraceutical' was coined from 'nutrition' and 'pharmaceutical' in 1989 by DeFelice and was originally defined as ‘a food (or part of the food) that provides “medical or health benefits, including the prevention and/or treatment of a disease”’. Nutraceuticals may range from isolated nutrients, dietary supplements, herbal products as well as processed products from cereals and soups to genetically engineered ‘designer’ foods. Ethnobotanical and pharmacognostical studies have been carried out on Traditional medicines for health benefits [7-9]. USA has 190 billion dollar market for health foods and supplements meant to improve health. Plant sources provide major dietary supplements as they contain vitamins, minerals, nutrients, carbohydrates, fats and proteins. Such food can be from algal source like *Spirulina* sp, garlic, soy or a specific component of a food like omega-3 oil from Salmon. Fenugreek (*Trigonella foenum-graecum* L.)

seed is used extensively as a spice, but it also contains saponins, isoleucine and galactomannans which are known to have beneficial health effects, especially in diabetic [10-11, 59-65]. In this review we

concentrate mainly on plant sources with some specific examples from the medicinal herb fenugreek.

## CARBOHYDRATES

Blood glucose level is associated with fat metabolism. Carbohydrates taken by body are converted to glucose. Starchy food takes long time to get digested to increase blood glucose level. The measure of a food ability to elevate blood glucose levels is referred to its Glycemic Index (GI). Simple sugars have high GI as they cause rapid increase in blood glucose levels. An increased uptake of sugar can increase triglyceride level in the blood. High GI food causes storage of body fat. But instead of storing the extra glucose as glycogen like the muscles and liver do, the fat cell stores the excess glucose as fat. The higher the glucose rises, the more of it will be used in fat cells. Fructose which is a component of the most common disaccharide, sucrose, is considered the most hypertriglyceridemic monosaccharide. The hypertriglyceridemic effect of sucrose is only seen when substantial quantities are consumed (>140 g/day) and when a relatively high proportion of dietary fat is derived from saturated fatty acids.

Fructose promotes triglyceride synthesis and VLDL production in the liver. The effect of sucrose on VLDL metabolism is more pronounced in individuals with elevated blood triglyceride and insulin concentrations as well as in obese subjects, especially with abdominal obesity. Oligosaccharides inulin and oligofructose (fructans) which are composed of linear chains of fructose units linked to a terminal sucrose molecule are good for CVD. Oligosaccharides are water soluble, and the water-binding capacity and gelling tendency increase with the number of hexose units. In plants, inulin is used as an energy reserve and osmo-regulator. Inulin occurs, for

instance, in onions, garlic, banana, leeks, and asparagus. One study in hyperlipidemic subjects showed significantly lower total and LDL cholesterol concentrations after a diet rich in inulin (18 g/day) compared with the control diet [12]. Brighenti *et al.* [13] observed lower cholesterol and triglyceride levels in men consuming 9 g of inulin added to a rice breakfast cereal for 4 weeks. As regards polysaccharides, fenugreek galactomanan containing high ratio of galactose substitution is considered vital in the food industry [14], since it reduces glucose absorption in the human digestive system by having high hydrophilic properties and constituting viscosity solutions (*i.e.* energy intake reduction). Moreover, it can also reduce blood- and plasma glucose as well as cholesterol content in both human and animals (*i.e.* hyperglycemia and type 2 diabetic prevention).

#### **ANTI HIV**

Protein inhibitors of proteinases are ubiquitous. Plant protease inhibitors have been described as endogenous regulators of proteolytic activity. These inhibitors form stable complexes with target proteases to block, alter or prevent access to the enzyme active site. These proteins are known to be involved in many biological functions, such as blood coagulation, platelet aggregation, anti-carcinogenesis, antiparasitic agent and granulocyte cytopoietic activity as storage proteins [15]. Recent studies have employed protease inhibitors as new drugs in highly active antiretroviral combination therapy (HAART) to increase the life expectancy in HIV-positive patients [16]. They may be synthesized constitutively during normal development or may be induced in response to insect and pathogen attacks [17]. These findings have thus attracted interest in developing insect-resistant transgenic crops expressing a trypsin inhibitor gene [18].

Oddepally *et al.* [19] purified and characterized stable Kunitz trypsin inhibitor from *Trigonella foenum-graecum* L. (fenugreek) seeds. It showed high trypsin and chymotrypsin inhibitory activity.

#### **ANTI OBESITY AGENT**

Obesity is associated with many diseases, particularly diabetes, hypertension, osteoarthritis, and heart disease. Natural products can target different obesity genes and/or different stages of the adipocyte life cycle which may help in reduction of obesity. Several polyunsaturated fatty acids also show combinations of anti-obesity actions, including upregulation of mitochondrial biogenesis, induction of  $\beta$ -oxidation, and suppression of adipocyte lipogenesis [20]. Possible anti-obesity therapeutics from *Trigonella foenum-graecum* L. have been described recently [21]. Dietary fat is not directly absorbed by the intestine unless the fat has been subjected to the action of pancreatic lipase. Therefore, pancreatic lipase is one of the most widely studied mechanisms for determining natural products' potential efficacy as anti-obesity agents [22]. Among treatments for obesity, one of the most promising strategies in the effort to reduce energy intake through gastrointestinal mechanisms, without altering the central mechanisms, is the development of nutrient digestion and absorption inhibitors [22].

#### **LIPID PROFILES**

Fat provides body with store of energy and insulation from the cold and it protects body organs from physical damage. In fact all of the cells in animal body are surrounded by a membrane of fat. Fatty acids are central point for dietary recommendations for heart health. Brain, spinal cord and entire nervous system are largely made from fat. Dietary fats are necessary for the proper absorption of fat-soluble vitamins, and scientists

recently discovered that some fats in the diet are used for sending signals to the brain to control how much you eat. Some of the hormones such as testosterone and estrogen are also made from fats. In fact next to water fat is the most abundant substance in the human body, ideally averaging about 10% to 20 % of total body weight. Lipids are essential constituents of cell membrane but non-essential triglyceride levels regulate body functions.

Triacylglycerols also known as Triglycerides (TGs) are the primary constituents of vegetable oil and animal fats. Esterification of polyalcohol Glycerol, with one two or three fatty acids results in monoglycerides, diglycerides or TG, respectively. Triglycerides (TGs) (also known as triacylglycerols) are the primary constituents of vegetable oil and animal fats. Fatty acids can be of three types: saturated fatty acids (SFAs) which have no double bonds and are termed as “saturated” with hydrogen atom. Mono Unsaturated Fatty Acids (MUFA) have one double bond *e.g.* Oleic acid; Poly Unsaturated Fatty Acids (PUFAs) Which have one more than one double bond. *Cis*-versus *trans* fatty acids are also important. Beef, lamb and dairy products contain naturally occurring *trans* fatty acids in limited amounts. Most *trans* fatty acids are produced during chemical hydrogenation of unsaturated fats when some of the *cis*-isomers are converted to the *trans*-configuration instead of undergoing complete hydrogenation.

Areas like brain and liver, rich in polyunsaturated fatty acids, when experience a lipid peroxidation process (LPP) resulted by free radicals attack on their cell lipid membrane undergo an oxidative deterioration of their polyunsaturated lipids which produces several toxic by-products [23]. This process

also inactivates main components in living cells such as DNA and rest of biomolecules in biological systems [24]. So far, the inhibitory impact of fenugreek crude extract on the LPP has been found to be extremely useful [23].

## HEALTHY FATS

For decades, fatty acids have been a focus of dietary recommendations for heart health. Lipids are transported as lipoproteins in the blood. These include very low-density lipoprotein-cholesterol (VLDL-C), LDL-C and high density lipoprotein-cholesterol (HDL-C). LDL-C is removed from the circulation by binding with both plasma membranes and HDL-C, and is a less concentrated form of cholesterol. An increased level of LDL-C can result from a deficiency in the binding mechanism and is known as type II hypercholesterolaemia. Hypercholesterolaemia is known to be an important risk factor in the development of atherosclerosis and CHD, and studies have shown that a 1 % decrease in serum cholesterol can lead to a 2 % reduction in mortality. The aims of treatment are to increase HDL-C and decrease total cholesterol and LDL-C. A number of mechanisms implicated in the cholesterol-lowering activity of the isoflavones include altered thyroid status, enhanced bile acid excretion, leading to reduced rates of cholesterol absorption, and up-regulation of LDL receptors.

Consumption of soya foods (*Glycine max* (L). Merr.) (min of 25 gm/day) reduces chronic heart diseases. They are source of isoflavones, Curcumin from *Curcuma longa* L. for making curry and *Glycine max* (soya) isoflavones possess cancer chemopreventive properties [25; 26]. Vegetables and fruits also contain Flavonoids *e.g.* onion, grapes, red wine, apples, and cherries strengthen the

tiny capillaries that carry oxygen and essential nutrients to all cells [27].

## **FIBERS**

A combination of soluble and insoluble fibers play important role in reduced risk of MI in hypercholesterolemic subjects. The soluble fibers were guar gum and pectin, and the insoluble fibers were soy fiber, pea fiber, and corn bran. Cereal fibers are better as compared to fibers from vegetables and fruits. The dietary fiber was associated with a significant reduction of the risk for CHD of approximately 27 %. Also, fruit and vegetable consumption was associated with a significant reduction of CHD risk (23 and 14 %, respectively), while for cereals, no significant association was found. This may be related to the fact that most of the cereals consumed were refined and low in dietary fiber. The fibers from psyllium (*Plantago ovate* Forssk.) have been used for glucose control in diabetic patient and to reduce lipid level in hyperlipidemia [28]. Psyllium husk is rich in soluble fiber, and meta-analyses of studies indicate that it can reduce the LDL cholesterol level 7-9 %. Buckwheat seed proteins also act similar to natural fibers present in the food [29]. Guar gum is the natural gum that produces the highest viscosity, and human studies have shown that it reduces the total and LDL cholesterol levels significantly. Pectin has also been investigated thoroughly and shown to have significant effects on blood cholesterol levels. The main mechanism behind the lipid-lowering effect of soluble fiber is probably that the lipids decrease the uptake of bile acids in the intestine. It is estimated that an intake of 5 to 10 g of viscous fiber per day can reduce the LDL cholesterol level by 5%, a reduction similar to that of a daily intake of 1 to 3 g of plant sterols and 25 g of soy protein.

Fenugreek seed's endosperm is rich of soluble fiber and almost 50% (30% – soluble dietary fiber, 20% –insoluble dietary fibers) of its dry weight consists of dietary edible fiber [30]. From this view, fenugreek can possibly adjust glucose-containing levels in plasma with imposing direct disruption on its absorption in the digestion process and also by delay in stomach emptying [31]. According to *in vivo* studies, soluble fiber from fenugreek seems to decrease in reabsorption of bile constituents in small intestine, through binding cholesterol and bile acids, and disruption in the enterohepatic cycle. Then, the need for cholesterol in bile acid biosynthesis is boosted and blood cholesterol content remarkably reduces [10].

## **ENERGY BALANCE LEADS TO ACCUMULATIONS OF FATS**

If energy intake is more and energy consumption is less the extra energy is stored in body in fats. An increase in central adiposity- the accumulation of body fat in the abdominal area – is associated with greater risk of cardiovascular disease. Consumption of herbal stimulants, like green tea, caffeine, ephedrine, chitosen also help in body weight loss [32]. Green tea extract may promote weight loss by decreasing appetite [33]. Some of the other ingredients recommended to reduce body weight include a complex blend of fenugreek, *Gymnema sylvestre* R.Br. , chitosan and glucomannan and vitamin C in the dietary supplement significantly reduced body weight [34]. *Momordica charantia* L. , *Capsicum sp* containing capsaicin, conjugated linoleic acid (CLA) possesses potential anti obese properties [35].

## **NIACIN AND CVD**

Nicotinic acid or niacin or niacinamide is used for hyperlipidemia and used for curing diabetes. In other words, niacin raises HDL

cholesterol more than other lipid-lowering involved factors. *Polypodium leucotomos* (L.) J. Sm. is used orally to prevent psoriasis, vitiligo, skin cancer and other cancers. Walnuts and flax are source of PUFA and may contribute to mental and visual functions.

Fenugreek seeds contain several abundant (L-tryptophan and lysine rich proteins, mucilaginous fiber) and rare (saponins, coumarin, fenugreekine, nicotinic acid, saponin, phytic acid, scopoletin and trigonelline) chemical ingredients, which are beneficial for many of therapeutic cases, since they lower blood glucose level (anti diabetic function) and inhibit cholesterol absorption (hypercholesterolemia function) as a result of saponin-cholesterol complex formation in the body [36]. The saponin content in the fenugreek seed as a haemolytic agent has a key role in the curing hyperlipidaemic patients [23; 36]. Moreover, its hypoglycaemic effect is greatly refers to two major substances; trigonelline and 4-hydroxyisoleucine [23] as an insulin stimulant amino acid.

## ANTIOXIDANTS

Many antioxidants decrease risk of coronary heart disease and have free radical scavenging effect. Arguments for the health benefits of antioxidants are largely correlated to diet composition vs disease and morbidity in populations. The consumption of antioxidant-rich foods results in the maintenance of higher antioxidant levels in blood serum [37-40]. Reduction of atherosclerotic heart disease in association with antioxidant rich diets is hypothesized to be related to a reduction in the oxidative polymerization of low-density lipoproteins and consequent lesion formation and plaque build-up in key coronary arteries [41]. Antioxidants have free radical scavenging effect which decreases risk of coronary heart

disease which include in reduction of atherosclerotic heart disease [42; 43; 44]. Studies of lipid metabolism have shown that it is not the high cholesterol levels that cause atherosclerosis and CHD but rather the oxidised low-density lipoprotein-cholesterol (LDL-C). The use of antioxidants would therefore be expected to reduce the incidence of CHD and this has been shown in epidemiological studies. Antioxidant rich diets lessen oxidative polymerization of low-density lipoproteins which cause plaque buildup in key coronary arteries [41].

Reduction in reactive oxygen species also results in protection of DNA from destruction [45]. Consumption of fruits and vegetables rich in antioxidants results in higher antioxidant levels in blood serum. One of the richest sources of antioxidants in the human diet is potato tubers (*Solanum tuberosum* L.) [46]. Their antioxidant content decreases a great deal atherosclerotic processes, inhibits cholesterol accumulation in blood serum and enhances the resistance of the vascular walls [37] found that anthocyanins from a blueberry extract were absorbed in their intact glycosylated and acylated forms and were associated with an increase in serum antioxidant status. Use of effective lipid lowering agents such as Statins-HMGCoA reductase inhibitors improves the lipid level profile: reduces elevated LDL, help in decreasing TG and increasing HDL. Lowering of Low Density Lipoprotein LDL-C ( $\leq 70$  mg/dL) for those with chronic CHD promotes better health. Positive results have been achieved by combining therapeutic modalities to target both the endogenous and exogenous pathways of cholesterol synthesis. Green tea and black teas contain antioxidants which control atherosclerosis by fibrinolytic mechanisms and reduce mortality by myocardial infarction (MI) [38; 39; 47-51].

Fenugreek seed has desired *in vitro* and *ex vivo* antioxidant activity, indicating its therapeutic value for human health as they can protect living cells from any unpredictable damage, ethanol toxicity, premature aging, and tumor formation. This property may arise from its ability to modulate enzymes corresponding to concentrations of oxidized cell products [10; 52].

### **PLANT STEROLS**

Aggressive risk reduction therapies are indicated for patients with CHD to improve survival reduce recurrent events and improve quality life. HMGCoA reductase inhibitors (statins) are used in CHD to target the reduction of elevated LDL and to improve the lipid level profile. Foods enriched with plant stanols or sterols lower serum cholesterol levels by reducing intestinal absorption of cholesterol. Use of effective lipid lowering agents is critical to achieve target lipid levels in the growing numbers number of persons at risk for CHD. Lowering of Low Density Lipoprotein LDL-C ( $\leq 70$  mg/dL) for those with chronic CHD may require combining therapeutic modalities to target both the endogenous and exogenous pathways of cholesterol synthesis to obtain positive results. Plant sterols are natural compounds present as minor components of vegetable oils, nuts, seeds, legume, fruits, vegetables and grains. The most abundant plant sterols include sitosterol, campesterol and stigmasterol with typical daily intakes ranging from 150 to 400 mg/day. Plants stanols are the saturated counterparts of plant sterols and occur more scarcely in nature. Combined or liberate state of sterol compounds ( *e.g.*  $\beta$ -sitosterol, stigmasterol, cholesterol) and steroidal sapogenins (*e.g.* diosgenin, tigogenin and their C-25 epimers) can easily be found or detected in all parts of fenugreek plant [53],

mainly in flowers and young pods in early reproductive growth stages, and then subsequently accumulate, specially the latter one, in matured seeds [54]. Average diets provide only 20 to 50 mg of plant stanols/day. These minor levels of intake are of little significance but an enhanced daily consumption of 800 to 3000 mg of plant sterols or stanols/day has been found to lower LDL-C by 6-20 % without changing HDL-C or TG levels [45].

### **OMEGA-3 FATTY ACIDS AND TERPENENES FUNCTION**

Long chain omega (n)-3 PUFA have been associated with cardiovascular health benefits. Prescription omega-3 fatty acids significantly lower triglycerides (TGs) by approximately 25 % but may slightly raise low density lipoprotein (LDL) and only modestly increase high density lipoprotein (HDL). Low carbohydrate diets have been shown to significantly lower TGs and raise HDL slightly compared to a standard low calorie diet. Dietary fats that are high in monounsaturates have a better metabolic profile and help improve lipid profiles. Some studies have suggested that these fats particularly the omega-3-fatty acids, have a beneficial effect on body weight as well [55]. Omega-3-fatty acids from fish oils contain Docosahexaenoic acid (DHA) which is one of the major components of grey matter in the brain, and is important in the retina, testes, and present at high levels in fish oil. The major source is marine algae; consequently the largest commercial source is fish feeding off the algae. Many of the important body functions are thought to require adequate tissue levels of DHA, particularly brain and eye functions, and there is a growing trend to enrich a large number of foods with DHA, the virtues of which are widely extolled in the media. DHA is produced in the body from EPA by desaturation and elongation reactions.

Several investigations have emphasized that omega-3 consumption decreases the risk of infecting by chronic diseases such as diabetes and heart disease [56]. Omega 3 has numerous benefits; among which anti-inflammatory and anti-oxidant effects are the most remarkable [56]. The essential oil from the seeds of fenugreek is nearly full of terpenes such that a mixture of antioxidants with these nutrients, accompany the fenugreek essential oil with the capability of fighting cancer tumors, viruses, and free radicals [57]. Recently, it has been unveiled that terpenes that are simply absorbed by the gut, have a determining role in the scavenging of cholesterol metabolism [58]. The  $\beta$ -pinene, as a terpene, existence in fenugreek essential oil can inhibit the activity of enzymes related to type 2 diabetes (*i.e.*  $\alpha$ -amylase, maltase) in plasma and pancreas [57].

The supplementation of omega-3 with fenugreek terpenes (Om3/terp) can outstandingly (1) hamper  $\alpha$ -amylase by 46% and maltase by 37% , which are mainly responsible of diabetes in plasma and pancreas,(2) regulate the hypertension related enzymes in both plasma and kidney, (3) decrease the concentrations of glucose, TG, total cholesterol (TC), and LDL-C in plasma and liver of diabetic rats, and (4) increase the amounts of HDL-cholesterol level to maintain the homeostasis status in blood lipid [57]. The Om3/terp formulation can also be taken in to account for future food prospect in view of anti-diabetic, anti-hypertensive and hypolipidaemic activities. Overall, the inhibitory effect of fenugreek essential oil, containing omega-3 fatty acids, on the activity of plasma angiotensin-converting enzyme (ACE) which is directly associated with diabetic diseases, has been confirmed by Hamden *et al.* [57].

## PREVENTION OF CVD

Traditional foods worldwide which were rich in complex carbohydrates and low in fat are being replaced by a diet that is high in saturated fat and animal protein and low in fiber. Both adipose cells and tissues are affected by numerous hormones and compounds produced by other cells and body tissues which can affect health status. Anti-oxidants, dietary fibres, Omega-3 polyunsaturated fatty acids, vitamins, minerals also help in prevention and treatment of Cardio Vascular Diseases (CVD). Vegetables and crops are significant sources of antioxidants in human nutrition which are rich in polyphenols and ascorbic acid [40]. There are a wide range of risk factors associated with the development of CHD, hypertension, raised serum cholesterol and lack of exercise. Lipid lowering drugs are among the most prescribed medications in the world with more than 20 million people prescribed this class of drugs. Low carbohydrate diets have been shown to significantly lower TGs and raise HDL slightly compared to a standard low calorie diet [59-65].

Cholesterol lowering therapy with statins has been established as an effective method of reducing death and myocardial infarction among patients with CHD. Other widely used lipid altering drugs include fibrates, niacin. Statins also help in decreasing TG and increasing HDL that could contribute to the risk reduction. Other therapies with significant lipid lowering effects such as fibrates and niacin which lower triglycerides and raise HDL, also have shown to reduce CHD levels despite less potent effects on reducing LDL. It has been suggested that in combinational therapies with fibrate or nicotinic acid in addition to an LDL lowering drug should be given in high risk patients with low HDL cholesterol level.

LDL-C lowering can be enhanced by combining a statin which reduces hepatic cholesterol synthesis and increases hepatic LDL receptor activity with ezetimibe, a selective cholesterol absorption inhibitor that blocks cholesterol absorption at the intestinal brush border to reduce LDL-C. Trans-fatty acids have also come under dietary restriction. In contrast unsaturated fatty acids are considered to be heart healthy. Unsaturated fatty acids [both Monounsaturated (MUFAs) and polyunsaturated fatty acids (PUFAs)] are advocated as good source and decrease in saturated and trans fatty acids in dietary recommendations have been recommended [1-6; 59-65].

According to the lipid hypothesis for atherogenesis, apolipoprotein (apo) B containing lipoprotein enter the artery wall accumulate, are oxidized and become ligands for scavenger receptors on macrophages. They are taken up by and accumulate within macrophages, converting them into foam cells. In this way the process of atherogenesis begins. HDLs are the cholesterol efflux promoters. When an imbalance between influx occurs more foam cells form and atherosclerosis progresses. Not only is the concentration of apo-containing lipoprotein dramatically affected by the types of fat consumed, but their composition also is affected and these changes can affect the atherogenicity of the particles. An old assumption regarding fatty acids and their effects on atherosclerosis was that MUFAs (in olive oil) were neutral, SFAs were bad and PUFAs were good. Apolipoprotein A-V (apo-V) is secreted primarily from the liver as a 366 amino acid protein with high density lipoprotein (HDL) and is also associated with very low density lipoprotein (VLDL). ApoA-V is a strong modulator of circulating triglyceride and is

negatively correlated with serum triglyceride levels in animal model studies [2-6;59-65].

Increasing knowledge of the mechanisms relating excess adiposity to disease, and enhancement of our ability to mitigate these effects, depend on the continued development of our understanding of the functions of this tissue. Drugs used for obesity treatment can in theory , target and decrease food intake or energy absorption, or increase physical activity or basal metabolism/energy expenditure, but drugs currently approved for weight loss treatment target only a few of these.

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