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MANAGEMENT OF HYPERCHOLESTEROLEMIA THROUGH MAXIMUM NATURAL SOURCES AVAILABLE IN PAKISTAN

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ABSTRACT: Familial Hypercholesterolemia (FH) is the congenital disease related to premature artery disease caused by mutations are mostly found within the low-density lipoprotein receptor sequence and alter the genes encoding proteins involved in the metabolism of low-density lipoproteins (LDL). Genetic testing can ensure the disorder and is extremely helpful for cascade screening. FH is one of the foremost common genetic disorders, this disorder remains principally unseen and its management is commonly suboptimal. Despite the availability of numerous pharmacologic medications to significantly lower LDL-C levels, FH patients are frequently not effectively treated. Therapeutic lifestyle changes usually inadequate to attain fascinating cholesterol levels. This is often notably true for top risk patients; but, additionally, low-risk patients, whose cholesterin levels aren't essentially faraway from counseled targets, have either sub-optimal or maybe considerably magnified lipid levels. Nutraceuticals are products that stand on the boundary between food and medicine, supplying additional amounts of certain nutrients with positive health effects. Many nutraceuticals are prompt to boost plasma lipid profile. Typically, a diagnosis will be made using a combination of clinical factors, including the case history, lipid levels, and genetic analysis. The most frequent anomalies are mutations in the genes encoding the low-density lipoprotein receptor (LDLR), apolipoprotein B, pro-protein convertase subtilisin/kexin nine (PCSK9), and LDLR adapter supermolecule. Early patient identification and treatment, screening of families, significantly reduces the risk of developing an illness. Most anti-hypercholesterolemic medications deliver many adverse effects for patients, by that healthful plants have begun to draw attention to treating hypocholesteraemia. Aim of this study is to review the natural sources obtainable for the management of hypercholesterolemia.

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INTRODUCTION

Hypercholesterolemia is a form of Hyperlipidemia characterized by high cholesterol levels in blood. Type 2 diabetes, high blood pressure, peripheral artery disease, coronary heart disease, and stroke are all brought on by excessive cholesterol levels (1). Cardiovascular disease risk is highly associated with increased intake of diets high in cholesterol. The production of cholesterol takes place in the liver belongs to the class of lipids which helps in constructing the membranes of animal cells and is involved in the production of certain hormones (2). It is also important in the production of substances which are required for fat digestion. Cholesterol is insoluble in water that is why its transport takes place within protein particles in the blood plasma. These lipoproteins are grouped according to how dense they are, i.e. LDL and HDL are two types of lipoproteins. LDL is a detrimental lipid, that distributes cholesterol to the periphery where it blocks arterial

lumen. Since low-density lipoprotein has a high level of cholesterol, therefore, atherosclerosis and coronary heart disease are more likely to occur (3). Clinically, there are number of researches done to treat hypercholesterolemia from natural sources. There are also many alternative treatments which are being used by many people, and also there are some cholesterol-lowering supplements and natural remedies. Persons should take a diet that contains mostly unsaturated fats such as fish, nuts, seeds, avocados and vegetable oil. Garlic has been used medicinally since ancient times to lower cholesterol levels in blood. The components present in flaxseeds also have some effect on the level of blood cholesterol (4,5). HDL is a good cholesterol which clears cholesterol plaques from peripheral blood vessels, and returns to liver (6). Cholesterol contributes to the production of vitamin-D for the skin, which affects how the body processes calcium and supports the maintenance of bone density (7)

Additionally, cholesterol in the body produces bile acids, which are necessary for the breakdown of lipids in the digestive tract so they can be absorbed by the body (8).

There are many inherited forms of hypercholesterolemia that can cause many health issues like; the buildup of excessive cholesterol in many tissues. When there is an abnormal buildup of cholesterol, the formation of plaque takes place which narrows and hardens the artery wall. As plaque or clumps gets bigger, the flow of blood can be restricted which causes chest pain called angina due to which the risk of heart attack increases in the patient (9).

There are many causes of the high level of cholesterol in the body which includes; the consumption of unhealthy food that has a lot of fat in it. Saturated fat is found in dairy products, meats, fried deep-fried, and processed food that cause an increased LDL (bad) cholesterol level. HDL level can be low if there is a lack of physical activity i.e. sitting or little exercise. Another cause of Low HDL levels is smoking, but it also raises the LDL level. Many other factors such as genetic factors also cause high levels of cholesterol for example: Familial Hypercholesterolemia (FH), it is an inherited disorder, caused by a defect on chromosome 19. This defect makes the body unable to remove low-density lipoprotein (LDL), or bad cholesterol from the blood, which results in a high level of LDL in the blood. Certain medicines may also cause high cholesterol (10).

The LDL level can be lowered by many natural food sources such as: oat bran, barley, psyllium seeds, flaxseed meal, apples, grapes, strawberries, citrus fruits, lentils, niacin, garlic, ginger, beans, eggplant and okra, nuts (almonds, pistachios), soy, fatty fish and fiber supplements. It can also be managed by limiting the consumption of saturated fats and Trans fats (11).

PLANT SOURCES

GARLIC: (*ALLIUM SATIVUM)*

In most cuisines, garlic is an essential component. It has antibacterial, anti-inflammatory, and antioxidant properties. It is supposed to help lower cholesterol levels by reducing the clotting characteristics of blood (12).

ACTIVE CONSTITUENTS

Fresh garlic contains 62–68% water, 26-30% carbohydrates, 1.1-3.5% organosulfur compounds, 1.5-2.1% proteins, 1.5% amino acids, and 1.5% fiber. The organic Sulphur compounds found in garlic are primarily responsible for its beneficial effects on health. Garlic contains several organosulfur compounds, including diallyl disulfide, diallyltrisulfide, methyl diallyltrisulfide, S-allyl cysteine, and alliin (13).

PREPARATION

The most often used garlic preparations are garlic powder, mature garlic extract, garlic oil, Japanese garlic powder with egg yolk, and raw garlic (14-16)

MECHANISM

When garlic was added to the diet, the hepatic activities of lipogenic and cholesterogenic enzymes such as 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase, fatty acid synthase, glucose-6 phosphate dehydrogenase, and malic enzyme were reduced. As a result, it's believed that garlic hypocholesterolemic action is partly related to a reduction in cholesterol synthesis. Indeed, garlic extracts containing various Sulfur compounds were effective at lowering blood cholesterol levels, possibly due to an inhibition of hepatic cholesterol formation (17).

SPINACH: *(SPINACIA OLERACEA)*

A lush green vegetable, spinach, originates from the Amaranth family. Spinach may help in reducing the risk of cancer and heart disease (atherosclerosis), as well as improving eye health and lowering oxidative stress levels (18).

ACTIVE CONSTITUENTS

Spinach is an excellent source of many vitamins and minerals, including iron, calcium, potassium, flavonoids, magnesium, vitamin A, vitamin C, vitamin K1, vitamin B6, vitamin B9, and vitamin E. Likewise, Lutein, nitrates of kaempferol, quercetin, and zeaxanthin are found in spinach. (19).

EFFECT ON HYPERCHOLESTEROLEMIA

The flavonoid concentration of spinach leaves (>1000 mg/kg) is equal to that of other flavonoid-rich plants (8). Spinach also includes lutein, a carotenoid antioxidant that helps to decrease harmful cholesterol levels (20).

HERBAL TEA: *(CAMELLIA SINENSIS)*

Tea includes numerous plant compounds that are healthy for heart. Traditional teas, as well as some herbal teas, include antioxidants that can help lower cholesterol levels (21).

Black tea is produced using completely fermented leaves, while green tea is produced using unfermented leaves. Tea's cholesterol-lowering impact is due to catechins, a type of antioxidant, present in the beverage (22).

Active Constituents

Catechins and quercetin are two of the most active compounds in tea.

Effect on Hypercholesterolemia

Catechins assist in the activation of nitric oxide, which is essential for maintaining healthy blood pressure. They also help to avoid blood clots by inhibiting cholesterol synthesis and absorption (23).

SOYBEANS: (*GLYCINE MAX*)

Soybeans are the top oil seeds which are produced worldwide, and are widely cultivated for their lipid content (23). In addition, because they are an incredible resource of polyunsaturated fatty acids (18%), soybeans have a high level of nutrients, high-quality protein (~40%), dietary fibers and carbohydrates, particularly glucose, sucrose, and raffinose (24).

Foods made from soybeans have long been a staple of the human diet, but nowadays soy has been given more attention due to its health benefits such as decreasing the risk of CVD (Cardio Vascular Diseases) by lowering cholesterol levels (25,26).

The substantial number of phytochemicals found in soybeans, including saponins, soluble fibers, polysaccharides, phytosterols, isoflavones, and lecithin, may work individually or in concert to promote health (27-29). For instance: saponins and soy lecithin support lipid metabolism, whereas phytosterols and linoleic acid play a significant role in showing their hypocholesterolemic activity while soy fibers

are considered valuable in terms of weight loss. Furthermore, the soy-proteins provide health benefits by reducing LDL levels as well as offering defense against renal failure, and oxidative stress, and through raising endothelial function indicators. (30).

FENUGREEK SEEDS: (*TRIGONELLA FOENUM-GRAECUM*)

There are a number of abnormalities that are associated with lipid metabolism, diabetes mellitus, dyslipidemia, cardiac diseases, inflammation, and many other disorders (31). Currently, there are various modern anti-hyperlipidemic medications available to treat obesity, cardiac diseases, etc. However, they have various unfavorable effects and also impact financial strain (32). In order to overcome this problem, researchers discovered various medicinal plants such as fenugreek which contains anti-hyperlipidemic properties and somewhat controls both obesity and dyslipidemia (33). An annual plant belonging to the Fabaceae family, fenugreek (Methi, Trigonellafoenum-graecum) is widely known for its pharmacological properties. Consuming fenugreek seeds lowers blood and liver cholesterol levels and is an excellent source of soluble dietary fiber (34). Fenugreek seed powder for oral use has also shown its antihyperlipidemic properties in experimental animals (35). The real factor responsible for this anti-hyperlipidemic activity has not been established yet but it might have been considered that increasing the excretion of salts and bile acids as well as inhibitors of hepatic cholesterol biosynthesis produced by bacteria present in the lower part of the large intestine involved in the fermentation of soluble dietary fibers, total dietary fiber may have contributed to lowering cholesterol levels (36).Fenugreek seeds contain amino acids mainly 4-hydroxyisoleucine and phenolic compounds mainly flavonoids. The hypolipidemic activity of fenugreek is mainly due to 4-hydroxy isoleucine, which is a typical branched amino acid (37,38). Fenugreek's impact on adipocytes and liver cells causes a decrease in the production of cholesterol and triglycerides, which enhances the LDL levels, this is the reason behind the lowering of lipid levels by fenugreek (39).

OLIVE *(OLEA EUROPAEA)* AND SESAME OIL *(SESAMUM INDICUM L.)*:

The olive and sesame oil are of great therapeutic value in lowering cholesterol levels. Sesame oil is considered great for its lipid metabolism (40). On the other hand, olive oil is of great value in lipid profile balance. Olive oil is quite common in the human diet and is considered beneficial for its effects such as preventing various degenerative diseases as well as coronary heart diseases, skin and blood cancers, etc. Olive oil contains oleic acid, squalene, and phenolic compounds which contribute to its health benefits (41). On the other hand, sesame oil is also known for its various benefits and therapeutic uses like anti-cancer, anti-hyperlipidemic, and anti-hypertensive. It induces the aldehyde dehydrogenase expression, it's an alcohol metabolizing enzyme. At the mRNA level, sesamin controls lipid metabolism, xenobiotics, and alcohol (42,43). As a result, we can say that both oils have shown the same effects and there is no difference between them. A study showed that the Everyday intake of olive oil at a dose of 25 can improve heart health, minimize cholesterol levels, and improved glutathione antioxidant status (44).

SUGARCANE: *(SACCHARUM OFFICINARUM)*

Sugarcane contains a chemical called policosanol, a mixture of long-chain primary alcohols, which is used as a supplement for

lowering the levels of cholesterol in the body. It is either used alone or in combination with other supplements. Studies have shown that policosanol can impede the body's production of cholesterol and the daily consumption of this dietary supplement has been demonstrated to lower the body's levels of both LDL and total cholesterol. Thus, it is helpful in treating cholesterol in patients suffering from mild to moderate hypercholesterolemia (45,46).

NUTS

Nuts contain lots of fiber, protein, vitamins, nutrients, antioxidants, and healthy monosaturated fats. Many studies have shown that nuts contain the cholesterol-lowering abilities in the body. Nuts such as pistachios, almonds, walnuts, etc, help reduce the body's triglyceride levels and are good for people suffering from hypercholesterolemia. The body's triglyceride levels are reduced by omega-3 fatty acids, which are found in walnuts (47). Almonds are also very helpful in lowering cholesterol level and studies have shown that almond decreases the LDL-cholesterol and the total plasma cholesterol levels in the body (48).

ARTICHOKE: *(CYNARA CARDUNCULUS VAR. SCOLYMUS)*

Another natural treatment for decreasing cholesterol is the leaf extract of Cynarascolymus, sometimes referred to as artichoke thistle. In addition to lowering blood glucose and cholesterol, C. cardunculus leaf extract also treats damaged and compromised kidneys. These findings are relevant because HC is connected to conditions that can be treated with artichoke, including diabetes and kidney impairment
(49)].Inhibiting the enzyme HMG-
CoA reductase, which decreases blood chol esterol levels and enhances lipid profiles, is one of the artichoke's anti-hypercholesterolemia qualities(50).

RED YEAST RICE: *(MONASCUSPURPUREUS)*

Red yeast rice is a rice product found in China and is used as traditional medicine (51,52).

It contains monacolins, phytosterols, pigments, polyketides, unsaturated fatty acids, and phytosterols (52,53). By blocking 5-hydroxy—methyl-glutaryl-coenzyme A (HMG-CoA) reductase, a rate-limiting step in the manufacture of cholesterol in the liver, it reduces cholesterol levels. The substance is comparable to lovastatin (a medication used to treat hypercholesterolemia), especially monacolins. (52,54).

OAT: *(AVENA SATIVA)*

Oats, being a high-fiber cereal with a variety of nutritious qualities, can help lower cholesterol levels in the blood (55). Individuals with hyperlipidemia who ate oats saw lower cholesterol and low-density lipoprotein levels. It has also been reported that the antioxidant capabilities of oats reduce the oxidation of low-density lipoproteins in a dose-dependent manner. The recommended dosage for people with hyperlipidemia is 28 g/day (56).

MINERAL AND VITAMIN SOURCES*:*

VITAMIN B3: (NIACIN)

The oldest lipid-lowering drug used to treat hyperlipidemia is niacin, a water-soluble vitamin of type B that has been shown to decrease cardiovascular illness and overall death rate. Triglycerides, LDL cholesterol, and total cholesterol are all decreased.

Furthermore, when taken at a daily dose of 1 gm,
Niacin is the most successful treatment for l ow HDL values (57).

VITAMIN B5: (PANTOTHENIC ACID)

Vitamin B5 is also known as pantothenic acid, a water-soluble vitamin. It is necessary

for coenzyme synthesis. In addition to lowering LDL metabolism and lowering triglycerides (58,59).

VITAMIN C: (ASCORBIC ACID)

Vitamin C is a water-soluble water-soluble vitamin necessary for the productio n of enzymes and tissue repair. It helps some individuals' lipid metab olism, shields LDL from oxidation, and redu ces lipoprotein and atherosclerosis (60,61).

VITAMIN D: (CALCIFEROL)

Vitamin D is a fat-soluble vitamin with numerous functions in the body, including calcium homeostasis and the suppression of foam cell formation, which reduces the risk of arterial blockage and thus the problems associated with cardiovascular diseases (62,63).

CHOLINE

Choline controls lipoprotein and HDL metab olism through the enzyme lecithin cholester ol acyltransferase (64,65).

ANIMAL SOURCES; MEATS WITH LOW CHOLESTEROL LEVEL

The saturated and trans fats in beef may cause our bodies to produce more cholesterol. As a result, people should try to consume lean meat which contains as little fat as possible.

Here are some general guidelines for consuming meats low in cholesterol. Staying away from meat cuts with a lot of visible fat. Choose extra-lean or lean beef. Remove any fat that is visible before cooking.Removing any meat's skin before cooking. After cooking, remove extra fat from the meat by wiping it off or squeezing it out.

Using a grill, broiler rack, or any cooking technique that allows fat to drain off of the meat. (66, 67)

FISH

There are a number of fish that are naturally low in saturated fat. Some people choose tuna steaks over traditional steaks because they are higher in unsaturated fats and omega-3 fatty acids, or they try a salmon patty over a burger. Fatty fish like salmon, herring, tuna, or mackerel should be substituted with fatty chicken parts like beef, pork, veal, and lamb because they contain omega-3 fatty acids, an anti-inflammatory fat that helps to lower LDL. Your total lipid profile is getting better, according to Zumpano. "When you swap out the fat in meat with fish fat (68, 69).

Little total and saturated fat is found in shellfish. On a TLC diet, you can occasionally enjoy shrimp as long as your daily cholesterol intake is less than 200mg. For example, 3 ounces of steamed shrimp, for instance, contains 167 mg of cholesterol. (70)

According to the USDA Trusted Source, 100 g of baked salmon contains:

•calories:160
•protein:25.8g
•fat:5.5g
•carbohydrates:0.1g
•fiber:0g
• sugars: 0.04 g(71)

STEAK

Lean cuts of steak, like sirloin or round slices, are preferable for people controlling their cholesterol. Also, think twice before consuming “prime” or “select” portions of beef. The USDA states that some beef grades have a significant amount of marbling or fat content. Considering that "select" cuts are slimmer, they might be a better choice. Aim for a 95% lean hamburger or even more lean cuts of beef. A top beefsteak is an example of a lean beef cut. 100 g of broiled top beefsteak, based on the USDA Trusted Source, contains

•calories:188
•protein:30.3g
•fat:6.5g
•carbohydrates:0g

•fiber:0g
• sugars: 0 g (72)
The types of ingredients that they add along with the exact nutritional content may vary by the manufacturer.

POULTRY

Select low-fat options like turkey or chicken breast. By selecting breast meat, one might be capable of removing the skin and most of the fat. The U.S. Department of Agriculture's (USDA) Trusted Source estimates that 100 grams (g) of grilled skinless malformation includes the following components:
calories: 151
protein: 30.5 g
fat: 3.2 g
carbohydrates: 0 g
fiber: 0 g
sugars: 0 g(73)

TOFU:

A versatile meat substitute prepared from mashed soybean curd is tofu. According to the USDA Trusted Source, 100 g of tofu has the following components:
calories: 144
protein: 17.3 g
fat: 8.7 g
carbohydrates: 2.8 g
fiber: 2.3 g
sugars: N/A (74, 75)

CONCLUSION

High levels of cholesterol can be a result of your diet and lifestyle, genetics, or some of both. Because high cholesterol doesn't generate any symptoms, it might be challenging to determine if you have it. If your cholesterol levels are high, you have a higher risk of having a heart attack, a stroke, and other illnesses.

Waxy substances called phytosterols derived from plants. They inhibit cholesterol from being absorbed by your intestines. They can be found in whole rains, nuts and vegetables in their natural state.

It has been suggested during the past several decades that increasing the amount of fibre, particularly β-glucans, in the diet lowers cholesterol levels. The precise mechanism behind this response is still not known, though. Garlic supposed to reduce the blood's tendency to clot and assist lower cholesterol levels. Spinach might help in the prevention of cancer and heart disease (atherosclerosis). Herbal tea includes antioxidants that can help lower cholesterol levels. Soybean has been given more attention due to its beneficial effects on health, such as reducing cholesterol to reduce the risk of CVD. Fenugreek Seeds and Nuts contain the cholesterol-lowering abilities. Olive and Sesame oil are of great therapeutic value in lowering cholesterol levels. Sugarcane contains a chemical called policosanol, used in lowering the levels of cholesterol. Artichokes and Oats can also be helpful in reducing blood cholesterol levels.

Vitamins that are helpful in the management of hypercholesterolemia includes vitamin B3, B5, Vitamin C and D by either lowering LDL or by reducing the risk of arterial blockage and thus the problems associated with cardiovascular diseases.

A diet rich in high-fibre foods like fruits, vegetables, whole grains, lentils, and beans combined with unsaturated fats found in foods such as olive oil, some nuts, and fatty fish can lower LDL and safeguard your heart. Choose unflavored milk, yoghurt and cheese. If you have high cholesterol or heart problems, choose low-fat products. Make sure there is no added sugar by checking the labels. Non-dairy milks and yogurts are also acceptable to consume; just make sure they have calcium added and no additional sugar. The primary goal of treating familial hypercholesterolemia is to lower the abnormally high LDL (bad) cholesterol

levels. By doing so, the risks of death and heart attack is reduced.

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