Review Article

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CURRENT SCENARIO OF HYPERLIPIDAEMIA AND ITS MANAGEMENT WITH DRUGS: A REVIEW

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ABSTRACT

High cholesterol and high fat are caused by fatty substances in the blood, it is an important risk factor in the development of heavy fat and lipids may rise in the body. High cholesterol levels may be caused by genetic factors or by generalized metabolic disorders like diabetes mellitus, excessive alcohol intake, hypothyroidism, or primary biliary cirrhosis. Alteration in Cholesterol, triglyceride and very low-density lipoproteins (VLDL), low-density lipoproteins (LDL) and intermediate density lipoproteins (IDL), which are different forms of lipids, responsible for possible complications in the human body such as acute pancreatitis, occlusion of blood vessels and reduced elasticity of the lumen of the artery. And there are various dosing limit are given and some synthetic drugs and herbal drugs correlated with us and describes the efficacy between synthetic drugs and herbal drugs and their mechanism are also describe and the herbal drugs which are least side effect and more efficacious used in the world population and the synthetic drugs there are more side effect such as headache acne Diarrhea nausea vomiting etc. various side effect present. The brand name of drugs synthetic drugs and herbal drugs are also described. So many of herbal drugs which can treat the hyperlipidaemia such as garlic, sugarcane, curcumin, etc. which can reduce the high cholesterol in our body.

Keywords: Cholesterol, Therapies, Dose, Diagnosis, Treatment

INTRODUCTION

The high fat is a condition of elevated lipid level in blood. The high cholesterol is atherosclerosis and dyslipidaemia related conditions. This was increased in lipids like low-density lipoproteins (LDL), cholesterol (esters derivatives) and triglycerides are mainly responsible for this condition. The lipids which were associated with blood plasma proteins and remain in the dissolved state in the blood. The first region of dyslipidaemia which was damage to lipid metabolism which is caused by the damage in lipoprotein lipase activity or absence of the surface Apo- protein C-II. Other causes of hyperlipidaemia include various genetic abnormalities and environmental factors. [1]

Hyperlipidaemia is a condition excess of fatty substances called lipids, largely cholesterol and triglycerides in the blood. It is also called hyperlipoproteinemia because these fatty substances travel in the blood attached to proteins. [2]

Hyperlipidaemia and its complications, mainly chronic heart disease. This relationship has been shown between and within cultures. The concentration of fat, triglycerides may carry lipoprotein in plasma exceeds a limit are normal. These lipoproteins deposit in the interstitial space of arteries arising from the aorta, restricting the blood supply to the heart. This phenomenon is known as atherosclerosis. Higher deposition of lipoproteins completely blocked the blood supply to the heart, and thus myocardial infarction (MI) occurs, which is commonly known as heart attack. [3]

One of the major risk factors causing cardiovascular diseases (Cardio vascular disease).Cardio vascular disease accounts for one third of total deaths around the world, it is believed that cardio vascular disease will turn out to be the main cause of death and disability worldwide by the year 2001, including triglycerides, cholesterol, cholesterol esters and phospholipids and or plasma lipoproteins including very low-density lipoprotein and low-density lipoprotein, and reduced high-density lipoprotein levels. [4]

The medical characterized by an elevation any or all lipid profile and. This medical condition or problem divided into two subtypes which are primary hyperlipidaemia and secondary hyperlipidaemia. The first stage of hypercholestrmia which usually takes place as a genetic problem such as mutation with receptors and other things underlining diseases like diabetes. Alteration and or abnormality in the metabolism of lipid and lipoproteins is a very common condition that taken place within the general population and it considers as one of the main risk factors in the incidence of cardiovascular disease due to their influence on atherosclerosis.[5]

Table 1: Lipid Profile

(a)	**LDL Cholesterol**[7]	<100	Optimal
		100-129	Near optimal/above optimal
		130-159	Borderline high
		160-189	High
		≥160-189	Very high
(b)	**Total Cholesterol**	<200	Desirable
		200-239	Borderline high
		≥ 240	High
(c)	**Total HDL**	<40	LOW
		≥60	HIGH
(d)	**Total Triglycerides**	<150	Normal
		150-199	Borderline high
		200-499	High
		≥ 500	Very high

EPIDEMIOLOGY OF HYPERLIPIDAEMIA

Epidemiological studies of hypercholesterolemia and dyslipidaemia are important for developing strategies for prevention of CHD. Unfortunately, there are limited data on population-level prevention for high cholesterol in India using lifestyle and drug therapies. The Pure study reported a very low use of secondary Hypertension drugs and healthy lifestyle practices in low income countries including India. [6]

Factors Influencing Lipid Profile

Several factors ranging from dose omission, forgetfulness, high cost and fear of side effects of some Hypolipidemic medications, to an array of difficulties encountered during filling and ingestion of prescribed medications, constitute barriers to medication adherence among patients with hyperlipidaemia. Thus, efficacy, side effects, dosing frequency monitoring requirements, quality of life implication and cost should always be considered in selecting therapeutic agents for these patients. [8] Selected lipid variables (TG, TC, LDL-C, AND HDL-C) and explanatory variables adjusted with one another (i.e., age, gender, smoking, alcohol consumption, physical activity, systolic blood pressure (SBP), diastolic blood pressure (DBP), HB, diet, and obesity[9]**.**

Risk Factors

In addition to elevated LDL levels, major risk factors associated with a higher risk of CHD include.

• The family history of premature death in the first-degree relative (male relative <55 years, female relative <65 years
• Hypertension (blood pressure ≥140/90 mm Hg or on antihypertensive medication)
• Diabetes mellitus (or impaired glucose tolerance)
• Cigarette smoking
• low HDL cholesterol (<35 mg/dl)
• Overweight or obesity
• Physical inactivity
• Increased fibrinogen pa1-1 levels
• Elevated levels of homocysteine
• Increased levels of C - reactive protein
• Increased Lp (a) level
• Role of risk factor reduction in CHD incidence reduction [10]

CURRENT MANAGEMENT TRAINED TO TREAT HYPERLIPIDEMIA

Hyperlipidaemia management at HCs must be viewed in light of concurrent changes in the treatment of these conditions. Over the past several years, national treatment guidelines have become more stringent. The 3rd report of National cholesterol education Program may evaluate the treatments and prevention diagnosis programs in human. [11]

NUTRITION THERAPY

Dietary cholesterol increases serum cholesterol approximately 10 mg/dl per 1000 kcal. Daily average cholesterol intake is higher for men (331 mg) than women (213 mg). Foods rich in cholesterol include eggs, animal, and dairy, saturated fatty acids (SFA). SFA decrease LDL receptor expression and increase LDL-C levels, whereas the long chain fatty acid, stearic acid, has little effect. The role of diet in the treatment of hypercholesterolemia has been largely neglected with the advent of the statins. The potential of diet to prevent CV disease (CVD) is often underappreciated by patients, who would rather take a pill than change ingrained habits, and by physicians. [12]

DRUGS THERAPY FOR SYNTHETIC DRUGS

HMG –Co-A – Reductase Inhibitors

Hydroxymethylglutaryl coenzyme an (HMG a) reductase inhibitors (statins). Statins are the drugs of the first choice for patients with high or less than optimal LDL-c levels. They inhibit the rate-limiting step of cholesterol synthesis, create. Transient decrease in intracellular cholesterol, increase the synthesis of the cell surface LDL receptor and accelerated the removal of LDL-c and triglyceride-rich lipoprotein. The latter accounts for the associated modest reduction in triglyceride levels that are observed with the use of these drugs, although more potent statins also inhibit VLDL synthesis a mild increase in HDL-c, also occurs.Five statins are currently approved by the FDA for cholesterol-lowering. Only three, (lovastatin, pravastatin, and simvastatin) are also approved for prevention of clinical events.

Mechanism of Statins

Statins reduce the synthesis of cholesterol in the liver by competitively inhibiting HMG reductase activity. The reduction in intracellular cholesterol concentration induces low-density lipoprotein receptor (LDLR) expression on the hepatocyte cell surface, which results in increased extraction of LDL-C from the blood and a decreased concentration of circulating LDL-C and other apo B-containing lipoproteins including TG-rich particles. [13]

The dose of Statins: Doses of statins is used 10 mg Atorvastatin 20 mg simvastatin 40 mg lovastatin/pravastatin 80 mg lovastatin.

STRUCTURE OF STATINS [14]

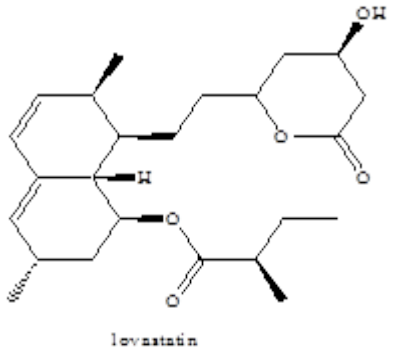


Figure 1: Levastatin

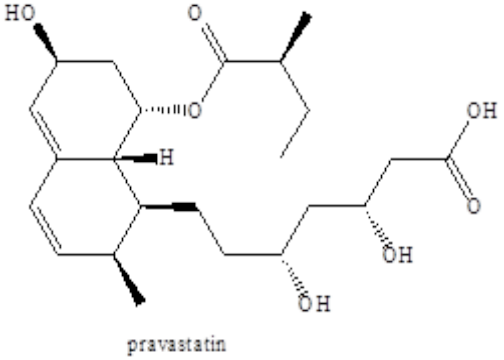


Figure 2: Pravastatin

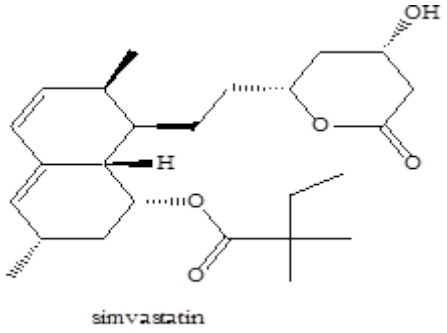


Figure 3: Simvastatin

Fibrates

Although four fibrates are available worldwide, only three fibrates are available in the United States and of these, only two (Gemfibrozil and Fenofibrate) are of any consequence. Fibrates are most effective for treating patients with hypertriglyceridemia and reduced HDL-C. The efficacy of these drugs for reducing triglyceride and increasing HDL-C is related to the magnitude of the hypertriglyceridemia. Drugs of this class reduce triglyceride and increase HDL-C by stimulating peroxisome proliferator activator receptor. The reduction in triglyceride is mediated by enhanced clearance of triglyceride-rich lipoprotein and decreased VLDL synthesis. Changes in HDL-C and the size of the LDL particles may be secondary to reduced triglyceride levels and/or to increased synthesis of Apo- protein A-I and Apo- protein A-II. In the Veterans Affairs HDL Intervention Trial (VA-HIT), the increase in HDL-C of 2 mg/dl accounted for only approximately.

Structure of Fibrates [15]

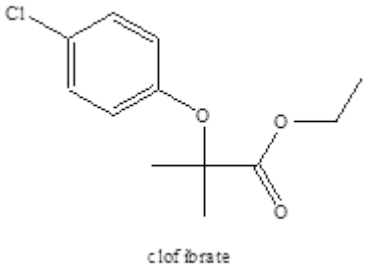


Figure 4: Clofibrate

Bile Acid Sequestrates

These agents have been available for years and in that regard is time honored. They bind bile acids in the intestine, preventing their reabsorption in the terminal ileum, and reduce the hepatic pool of bile acids that leads to increased intracellular conversion of cholesterol to bile acids in hepatocytes. This transient decrease in intracellular cholesterol leads to a compensatory increase in HMG Co-A reductase activity, increased synthesis and expression of the LDL receptor, and a subsequent increase.

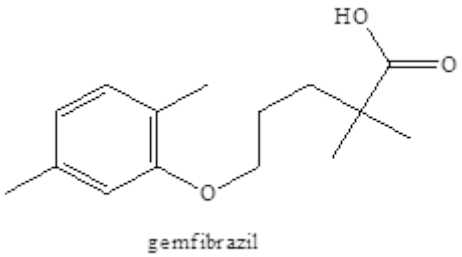
In the catabolism of LDL particles. The efficacy of this class of drugs is offset by the increase that occurs in HMG CoA reductase and in cholesterol synthesis. Bile salt binding resins are inconvenient to use because they have to be mixed with liquids or foods; however, Cholestipol is also available as a pill. Palatability and adverse gastrointestinal effects of sequestrants limit the use of large doses. The reduction in LDL-C with maximum doses is approximately30%, but a significant reduction in LDL-C, of the order of 15%, can be achieved by using two scoops per day. Sequestrants are clearly safe and effective cholesterol-lowering agents.

Mechanism

Fat is synthesized from the liver by bile acids. The bile acids are released into the intestinal lumen, but most of the bile acid is returned to the liver from the terminal ileum via active absorption. Two older drugs presented here such as cholestyramine and Cholestipol, are both bile acid-binding changing from resins. Currently, Colesevelam has been introduced into the market. The bile acid sequestrants altered by digestive enzymes. Therefore, the beneficial clinical effects are indirect. The binding the bile acids, drugs inhibit the action of bile acid into the blood and remove the bile portion.

Acids from the enter hepatic circulation. The liver, depleted of bile, synthesizes more from hepatic stores of cholesterol. The decrease in bile acid returned to the liver leads to up-regulation of key enzymes responsible for bile acid synthesis from cholesterol, particularly CYP7A1. The rise in fat catabolism to bile acids results the rise in liver LDLR activity, Clearing LDL-C from the circulation and thus reducing LDL-C levels. And also this agent decline glucose levels in hyperglycaemic patients. .

STRUCTURE [16]



gemfibrazil

Figure 5: Gemfibrazil

Cholesterol Absorption Inhibitors

The first drug of this class was approved by the FDA in November 2002. It interferes with the absorption of cholesterol, and when used as mono therapy, reduces LDL-C by 15–20%. It is effective in patients on a low SFA, low cholesterol diet because it blocks reabsorption of cholesterol secreted into bile and the enterohepatic circulation of endogenously produced cholesterol. Endogenous cholesterol synthesis is approximately 900 mg/d, several times greater than cholesterol intake. The reduction in LDL-C is due to increased endogenous catabolism of LDL. Its effects on triglyceride and HDL-C levels are trivial.

Mechanism

Ezetimibe is the first lipid-lowering drug that inhibits intestinal uptake of dietary and biliary cholesterol without affecting the absorption of fat-soluble nutrients. By inhibiting cholesterol absorption at the level of the brush border of the intestine(most probably by interacting with the NPC1L1 protein), Ezetimibe reduces the amount of lipoprotein cholesterol circulated to the liver. In response to reduced cholesterol delivery, the liver reacts by up-regulating LDLR, which in turn leads to increased clearance of LDL from the blood.

DOSE OF C_AI

GD-The recommended dose of Ezetimibe of 10 mg/day can be administered in the morning or evening without regard to food intake.

Nicotinic Acid

Niacin is a drug that reduces Lp(a), LDL-C, and triglyceride and increases HDL-C and LDL particle size, all desirable ant atherosclerotic changes Large doses must be used, which has adverse effects preventing the use of niacin for some patients or requiring the use of lower total daily doses for others. It is available in immediate-release and delayed-release preparations. Its major adverse effects are hot flashes, pruritus, gastric irritation, hepatotoxicity, and precipitation or worsening of glucose metabolism. Niacin also increases serum homocysteine and uric acid levels. Nicotinamide, although well tolerated, cannot be substituted because it has no lipid-lowering properties. Some patients tolerate the immediate-release preparations (approximately 50%), and a greater percentage (85%) tolerate the delayed-release preparations.

Mechanism

Nicotinic acid has broad lipid-modulating action, raising HDL-C in a dose-dependent manner by 25%, and decline LDL-C, 15–18 percent and TG by 20–40 percent at the 2 gram per day dose. It is firstly used in subjects with low HDL-C levels atypical of mixed hyperlipidaemia. Nicotinic acid may be used in combination with statins.

The dose of Nicotinic Acid

The maximum dose of extended-release niacin should not exceed 2000 mg/d, to avoid hepatotoxicity, and doses of 1000–1500 mg/d are most reasonable, particularly because its role is to supplement or amplify therapy with an LDL-C lowering agent.

Mixed

The target LDL level is reached and very high risk of proportion subjects, patients link with mono therapy and gives additional treatments. There are also patients who are statin intolerant or are not able to tolerate higher statin doses. In these cases, combination therapy should be considered.

Statins and Bile Acid Sequestrants

Combination of a statin and cholestyramine, Cholestipol, or colesevelam could be useful in achieving LDL-C goals. The bile acid sequestrants to a statin reduce LDL-C further by 10–20 percent. Bile acid sequestrants or colesevelam in combination with different drugs. The results have been found to reduce atherosclerosis, as evaluated by coronary angiography.

Statins and Cholesterol Absorption Inhibitors

Both Ezetimibe with a statin decline LDL-C by additional 15–25 percent. The results of the Ezetimibe, simvastatin administered concomitantly reduce the incidence of ischaemic cardiovascular disease but not events related to aortic valve stenosis. Currently, the data of the fasted trial were presented with positive results.

Other Combinations

In high-risk patients such as those with FH, or in cases of statin intolerance, other combinations may be considered. Co-administration of Ezetimibe and bile acid sequestrants (colesevelam, Cholestipol, or cholestyramine) resulted in an additional reduction of LDL-C levels without any additional adverse effects when compared with the stable bile acid sequestrants regimen alone. Both Ezetimibe to nicotinic acid decrease LDL-C and without effect nicotinic by HDL increase. Also, triple therapy (bile acid sequestrants, statin, and Ezetimibe or nicotinic acid) will further reduce LDL-C. The Clinical results found with these combinations have not been performed.

Table 2: Dosing Schedule

S.No	Drug	Dose Forms	Daily Dose	Maximum Dose	Brand Name
1	Atorvastatin	10 mg tab	10 mg	80mg	Lipitor, Atorva
2	lovastatin	20-40 mg tab	20-40 mg	80 mg	Mevacor
3	Pravastatin	20-40 mg tab	20-40	40 mg	Pravachol
4	Clofibrate	500mg cap	1 g bid	2g	Atromid- s
5	Fenofibrate	43,67,87,134,-200mg	54-67mg	201 mg	Tricor
6	Gemfibrozil	600 mg cap	600 mg cap BID	1-2 g	Lopid
7	Cholestyramine	Bulk powder 4g part.	8 g tid		
8	Cholestipol HCL	bulk powder 5g pct.	10 g tid		
9	Ezetimibe	10 mg tab	10 mg tab	10 mg tab	Vytorin
10	Fenugreek	25-50gm	25-50gm	50gm	Biotrex fenugreek, Ryal fenugreek seed oil Bioorganic
11	Garlic	600mg	1000mg	32 g	Questran
12	Liquorice	150mg	300mg	30g	colestid
13	Red yeast rice	2.4gm	0.8 gm	4g	Grunions red yeast rice, juvenile phyto red yeast rice
14	Sugarcane	20mg	20mg	180mg	policosanol

DRUGS THERAPY FOR HERBAL DRUGS

Garlic (*Allium sativum)*

The taxonomic position of garlic and related genera had been a matter of controversy for long period of time. The most recent classification scheme of garlic was class Liliopsida, subclass Liliidae, superorder Liliianae, order Amaryllidales, family Alliaceae, subfamily Allioideae; tribe Allieae. Garlic can rightfully be called one of nature's wonderful plants with healing power. It can destroy and inhibit bacteria, fungi, decrease B.P Blood Pressure, blood cholesterol, and blood sugar, may inhibit coagulation of blood, and contains anti-tumor activity. It can also boost the immune system to fight off potential disease and maintain health. It has the ability to stimulate the lymphatic system which expedites the removal of waste products from the body. [17]

Constituent's Formulations for Garlic

Garlic contains at least 33 sulphur compounds, several enzymes and the minerals germanium, calcium, copper, iron, potassium, magnesium, selenium and zinc; vitamins A, B1, and C, fibre and water. It also contains 17 amino acids to be found in garlic: lysine, histidine, arginine, aspartic acid threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan, and phenylalanine it has a higher concentration of sulphur compounds. It is well reported to scavenge oxidants, increase superoxide dismutase, catalase, glutathione peroxidase, glutathione levels, inhibit lipid peroxidation as well as it reduces cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl-COA. It has been shown to reduce platelet aggregation, arterial plaque formation, decrease homocysteine, lower blood pressure, and increase microcirculation.

Fenugreek *(Trigonella foenum-graecum* L.*)*

Fenugreek is a medicinal plant that uses in disease some therapy. And fenugreek which is used for blood cholestol decrease and blood sugar can also decrease for diabetic and non-diabetic patients. It contains active chemical constituents such as Saponin alkaloids steroids etc. It plant. It has been most widely used as a traditional drugs and food. Fenugreek is known to have hypoglycaemic, and hypocholesterolaemic. [18]

Constituents' Formulation

The fenugreek seeds contain the phenolic compounds, mainly flavonoids. An amino acid compound, 4- hydroxyl isoleucine, was identified in the fenugreek the hypolipidemic effect of the fenugreek seeds could be attributed to the presence of 4-hydroxy isoleucine, an atypical, branched chain amino acid. The lipid lowering effect of fenugreek is due to its action on the adipocytes and the liver cells, which leads to decreased triglycerides and cholesterol synthesis in addition to an enhanced low density lipoprotein (LDL) Receptor mediated LDL uptake. [19]

Fenugreek contains saponins that are transformed in the gastrointestinal tract into saponins. The very important saponin plant of Diosgenin. Fenugreek seeds contain 50-percent fibre (30-per-cent soluble fibre and 20-percent insoluble fibre) that can slow the rate of postprandial glucose absorption. Fenugreek seeds contain oils, alkaloids, amino acids (lysine, arginine, tryptophan, threonin, valyn and methionin) and mucilage that in this plant is most famous galactomannan, too are contain vitamins A, C, D, B1 and, minerals calcium, iron, and zinc. [20]

Red Yeast Rice *(Monascus purpureus)*

Red yeast rice is used as food or food additives. It contains rice starch, protein, fibre, sterols, and fatty acids, red yeast rice effective active constituents, Nacolin K including. Researchers have determined that one of the ingredients in red yeast rice, called monocline K, inhibits the production of cholesterol by stopping the action of a key Enzyme The HMG Co- Reductase is responsible for cholestol process. It is an Asian dietary. It is an Asian dietary made yeast on rice fastly gaining recognition as fat lowering agent. It is used as colouring and flavouring agents and also reduces total cholesterol, hyperlipidaemia. The red yeast rice are discovered recent that lovastatin and others statins drugs are useful treatment of cancers and other Alzimer's and stroke disease dementias, and macular degeneration. [21]

Turmeric *(Curcuma longa* L.*)*

The drugs as well as curcumin, to decrease the uptake of fat from the gut and rise the high-density lipids (HDL) fat and reduce low-density lipids (LDL. It can also inhibit the peroxidation of serum LDLthe main chemical components. Curcumin (60%), desmethoxycurcumin, monodemethoxycurcumin, bi desmethoxycurcumin, dihydrocurcumin and cyclo curcumin. By the oxidation of curcumin vanillin can be yielded. [22] Curcumin (di feruloylmethane), a major component of turmeric, is a yellow

pigment obtained from rhizomes of Curcuma longa and commonly used in Indian cuisine as a spice and food-colouring**.** [23] It is very helpful in converting the blockage the arteries such as heart attack or stroke in one of two ways. Turmeric reduce the cholestol level with inhabit the bad cholestol LDL. Oxidized LDL deposits in the walls of blood vessels and develop of fatty plaque. It prevents platelet build up along the walls of an injured blood vessel. The platelets which are a damaged blood vessel cause blood clots to form seal the arteries and veins. [24]

Sugar Cane *(Saccharum officinarum* L.*)*

Sugar cane extract (*Saccharum officinarum* L.) has been researched in Cuba in all populations for its cholesterol-lowering properties. The serum lipid and sugar cane reduce the LDL level and LDL oxidation and reduce the platelet aggregation and decrease smooth muscles and tissue proliferation. Side effects are virtually non-existent. The clinical indications which are describes in hypercholestrmia .and cardio vascular disease. . It is well known fact that elevated total cholesterol and low density lipoprotein cholesterol (LDL-c) levels promote atherosclerosis and cardiovascular complications. Oxidative modification of low density lipoprotein cholesterol (LDL-c) appears to have an important role in initiation and progression of atherogenic changes in aorta.Its effect on hepatic cholesterol biosynthesis from [$^{1\ 4C}$] - acetate. They also suggest that this effect is not elicited by a direct action of policosanol on HMG-coa reductase. Further research on the effect of policosanol on the cholesterol biosynthetic pathway is required to determine the primary site of action of policosanol oral administration of policosanol, demonstrating that policosanol orally administered for one month inhibits hepatic Cholesterol biosynthesis from titrated water in normal cholesterol emic rats. These results Agree with previous studies in this species, where an inhibition of cholesterol biosynthesis from $^{1\ 4\ C}$ - acetate was observed. Its represents from the waxy coating. Chemically, policosanol is a mixture of very long chain of Alcohol,

APPROACHES OF HYPERLIPIDEMIA

This review will discuss recent statin trial data in a variety of high-risk patient populations, as well as identifying remaining uncertainties within the management of Hyperlipidaemia.

- Statin therapy in patients with normal cholesterol levels.
  The Heart Protection Study (HPS) enrolled a wide range of patients, aged 40–80 years, who were considered to be at substantial 5-year risk of death from CHD. Patients with total cholesterol levels of z135 mg/dl (z3.5 mmol/l) were randomized to 40 mg simvastatin daily or placebo.
- Statin therapy in the elderly until recently, there was little evidence that lipid-lowering may reduce the risk of CHD in individuals older than 70 years of age. The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trial was the first study to examine the effects of statin therapy in an entirely elderly population (70–82 years at trial onset).
- Treating the patient with diabetes and dyslipidaemia
  The best agent for diabetic patients with dyslipidaemia remains unclear. The key atherogenic features of diabetic dyslipidaemia are elevated levels of serum triglycerides, low levels of high-density lipoprotein (HDL) cholesterol, and the preponderance of small, dense LDL. [2]

Table 3: Drugs Mechanism of Action

Drug	Drugs Mechanism of Action	Use	Effect On Lipoproteins	Adverse Effects
Statins	By inhibiting on version of 3-hydroxy-3-methylglutarylcoenzyme A-CoA to mevalonate.	Type IIa	LDL decreases 18-55%	SGOT, SGPT, Myositis
Atorvastatin (10-80 mg)	By inhibiting on version of 3-hydroxy-3-methylglutarylcoenzyme A-CoA to mevalonate.			GI complaints, Increase liver
Fluvastatin (20-80 mg)	By inhibiting on version of 3-hydroxy-3-methylglutarylcoenzyme A-CoA to mevalonate.			Enzymes Rhabdomyolysis Impaired cognitive function
Bile acid sequestrants Cholestyramine (4-16 g)	By interrupting enterohepatic recycling of bile acids. FXR mediated CYP7A repression	Type IIa	LDL decreases 15-30% HDL increases 3-5%	Constipation and bloating, Haemorrhoidal bleeding
Cholestipol (5-20 g)	By interrupting enterohepatic recycling of bile acids. FXR mediated CYP7A repression		TG no change or increases	Dry flaking skin Gallstone
Fabric acid derivatives Gemfibrozil (600 mg)	Increase lipolysis of triglycerides via lipoprotein lipase. Act as agonist for PPAR-a, resulting in increased expression of lipoprotein lipase and inhibition of Apo lipoprotein-C-III gene transcription	Types III and IV	LDL5-20% HDL increases 10-20%	SGOT, SGPT, Myositis, Gallstone Arrhythmias
Nicotinic acid Immediate release (1.5-3 g) Extended release (1-2 g)	By decreasing flux of FFA to the liver. Through GI coupled receptor (GPR109A, PUMA-G, HM74) By non-competitive blocking of DGAT2	Types IIa and IV	LDL decreases 5-25% HDL increases 15-35% TG decreases 20-50%	Flushing, SGOT, SGPT Tachycardia, Pruritus Glucose intolerance Hyperuricemia, Nausea diarrhoea Hepatotoxicity [26]

Garlic	The effect of garlic on cholesterol suggests garlic to be effective in reducing total serum cholesterol by 17 6 mg/dL and LDL cholesterol by 96 mg/dL in individuals with elevated total cholesterol levels (>200 mg/dl), provided garlic is taken for more than 2 months. HDL cholesterol levels improved slightly, by 1.5 1.3 mg/dL		Elevated HDL 10-15% decreasing the LDL 10-20%	Garlic to cause harmful interactions if taken in addition, To blood-thinning, blood-sugar-regulating, or anti-inflammatory Medications [27].
Fenugreek				Slightly stomach irritation and allergic reaction, bloating gas, Diarrhoea
Liquorice				normal constipation ocular effect, hypersenstiity, Hypokalaemia.
Red yeast rice	Red yeast rice is a consequence of an inhibitory effect on cholesterol biosynthesis in hepatic cells.3 It is unclear whether the lipid-lowering effect		Total cholesterol, LDL cholesterol, and triglycerides Dropped by 23, 31, and 34 percent, respectively. Serum HDL levels increased by 20 percent	Toxicity evaluations of red yeast rice in animals for as long as four months have shown no toxicity.1 Human trials have not shown elevations of liver enzymes or renal impairment.2,5 Side effects have been limited to headaches and gastrointestinal Discomfort.

Co-Relation between Synthetic Drugs

The efficacy of herbal drugs which are comparative character presents in the following synthetic drugs

- **Statins-** lower rates of CAD and total motility in highest risk patient marked lowering of LDL-c (20-35%) and increase HDL-c (5-7)%
- **Fibrates -**Lower CADin primary prevention trial benefits in men with LDL-c/HDL-c Ratio is greater than 5.0and triglycerides is greater the 200mg/dl drug choice foe triglyceride is greater the 800 percent prevent precaution
- **Resins**–lower rates of total non-fatal CAD moderate lowering of LDL-c (10-20 %)
- **Nicotinic Acid-** Reduction in total mortality and CV end points best drug to raise HDL-c up to 30 %

Toxicity

Statins –Liver enzymes myositis (rare**)**
Fibrates- Small risk gall stone long term data for men and women and no clinical trial data in women
Nicotinic Acid-Gout, diabetes, acanthuses
Resins- Not absorbed bind with other drugs ex-digoxin, antibiotics thyroid agent raise try glyceride level [28]

Co-Relation between Herbal Drugs

Currently study survey which have found and identified the 10 widely used herbal drugs s and found that 18.9% of the adult population reported the use of an herb to treat a medical illness within the past year.

However, many different side effects to herbs have been reported and recently reviewed, including effects from biologically active constituents from herbs, side effects caused by contaminants, and herb–drug interactions. Case reports of nephropathy caused by the use of certain Chinese herbs are common. A particularly morbid case series describes 105 patients in Belgium who had been taking a Chinese herbal product for weight loss and developed nephropathy caused by the herb Aristo lochia fang chi. Forty-three patients developed end-stage renal failure and had prophylactic kidney removal. 18 of these patients were found to have urothelial carcinoma, which was shown to be related to the formation of adducts of DNA from the aristolochic acid in this herb and the other widely toxicity to herbal drugs involves pyrrolizidine alkaloids, which are complexmolecules found in certain plants that may be used or inadvertently added to herbal medicines [29]

Potential Interaction of Herbal Drugs

Table 4: Drugs Interaction

Drugs	Interaction
Garlic	Increased risk of bleeding with anti-coagulants, Decreased serum levels of drugs metabolized via the cytochrome P450 system, Increased hepatotoxicity with acetaminophen, Decreased effectiveness of antacids, Increased effect of hypotensive, Hypoglycaemia with anti-diabetics, Increased chronographic and inotropic, effects with isoprenaline
Panax ginseng	Increased effects of anti-hypertensive drugs, Additive effects with benzodiazepines, Increased effect of cardiac glycosides, Decreased effect of immunosuppressant's, Increased effect of anti-diabetic drugs, Potentiation of adverse effects of MAO inhibitors, Increased effectiveness of kanamycin and Neomycin additive effects with stimulant [31]

Herbs	Percent Use	Common Treatment	Scientific Evidence	Safety
Garlic	3.4	Claudication hypercholesterolemia	Likely effective	Mild GI side, effect garlic odour cause bleeding
Chamomile	1.5	Hypercholestrmia, GI problems	Effective, no high quality data	Rare allergic reaction[30]

CONCLUSION

In this study which are the herbal drugs and synthetic drugs are pharmacologically active and there are least side effect in compare to synthetic drugs but the herbal drugs which are used in the Population. There least side effect in the herbal drugs compares to synthetics drugs. And there are some diseases which are developed from Hyperlipidaemia causes are below the paragraph.

The dyslipidaemia is related to myocardial infarction, ischemic stroke CAD etc. Complications of Hyperlipidaemia Myocardial Infarction. It was a condition which occurs when blood and oxygen supplies are partially or completely blocked from flowing in one or more cardiac arteries, resulting in defect or death of heart cells. The occlusion may be due to ruptured atherosclerotic plaque. The studies show that about one-fourth of survivors of myocardial infarction were hyperlipidaemia**.**

Ischemic stroke: stroke is the chronic reason for death. Usually strokes occur due to blockage of an artery by a blood clot or a piece of atherosclerotic plaque that breaks loose in a small vessel within the brain. Many clinical trials revealed that lowering of low-density lipoprotein and total cholesterol by 15% significantly reduced the risk of the first stroke.

Coronary Artery Disease (CAD): dyslipidaemia the major cause of coronary artery disease, characterized by the accumulation of lipid and the formation of fibrous plaques within the wall of the arteries resulting in narrowing of the arteries that supply blood to the myocardium, and results in limiting blood flow and insufficient amounts of oxygen to meet the needs of the heart. Rise and increase lipid profile has been linked to the development of coronary atherosclerosis.

Atherosclerosis: It is a pathologic process characterized by which the accumulation of lipids, fat and calcium and the development of fibrous plaques with in the walls of large and medium arteries.

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