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TREATMENT OF HYPERLIPIDEMIA USING NATURAL DRUGS

Pharma

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ABSTRACT

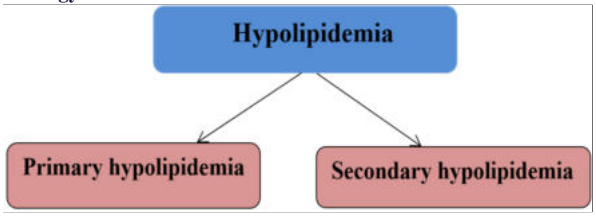
Hyperlipidemia is a condition of excess fatty substances called lipids, largely cholesterol and triglycerides in the blood. It is also called hyperlipoproteinemia because these excess lipids travel in the blood attached to proteins.There are two types of hypolipidemia I.e Primary & secondary hypolipidemia.cause of primary such as Hypobetalipoproteinemia, Chylomicron retention disease & Secondary such as Anemia Chronic inflammation Critical illnesses , Hyperthyroidism,Chronic liver disease. The plant extracts and their constituents plays the major role in traditional medicines and therapies. The present review constitutes of plants with hypolipidemic activity of various plants is used in India.

KEYWORDS

Hypolipidemic drugs, herbal plants, Death,lipoproteins.

Hypolipidemia is a decrease in plasma compound protein caused by Hereditary or factors. It's specifically characteristic & diagnosed by the mode on regular lipid test. Many clinical data show that hypolipidemia ordinary and is the highest risk for heart diseases.[2]No any worldwide laws present about lowering the value of serum cholesterol level to describe hypolipidemia. Hypolipidemia have been explained in many types of sevior anemia. Few studies have suggested that such patients have a lower incidence of cardiovascular diseases associated events. Anemia has been reported to be connected with hypolipidemia include: congenital dyserythropoietic anemia, congenital spherocytosis, sickle cell anemia, beta-thalassemia, aplastic anemia and sideroblastic anemia.[4-5]

Etiology And Classification



1. Primary Hypolipidemia

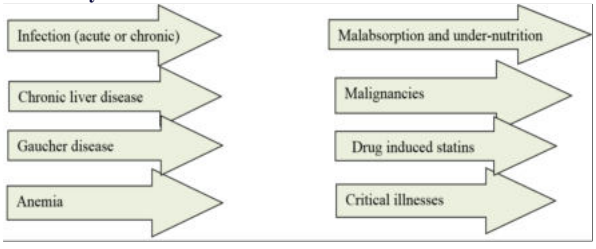
There are 3 rare special disorders of hypolipidemia in which hereditary mutations cause an production or enhanced separation of Low Density Lipoproteins (LDL) and result in lipid levels low enough to cause important consequences. These conditions are: Hypolipoproteinemia, hypolipoproteinemia and molecule.

Causes Of Hypolipidemia

Primary Disorders

- Abetalipoproteinemia Infection (acute or chronic)
- Hypobetalipoproteinemia
- Malabsorption and under-nutrition
- Chylomicron retention disease

Secondary Disorders



Secondary Hypolipidemia

Multiple mechanisms have been described in different diseases and clinical conditions that are found to be associated with hypolipidemia.

Mechanisms Of Secondary Hypolipidemia

In Chronic Illness:

- chronic exposure to IL-6 , IL-10 and TNF
- under nutrition due to anorexia

In Critically Ill Patients:

- Down regulation of hepatic synthesis, due to decreased production of cholesterol precursors.
- Dilutional effects of fluid resuscitation
- loss of lipoprotein in burns
- increased cholesterol catabolism

In Cancer Patients:

- Elevated LDL receptor activity in malignant cells
- Under-nutrition due to anorexia
- Effect of TNF

In anemia:

- Increased cholesterol requirements by the proliferating erythoid cells
- Elevated serum level of macrophage colony stimulating factor
- Auto-antibodies against LDL causing an increased LDL catabolism

In hyperthyroidism:

- Enhanced LDL receptor-mediated catabolism of LDL particles
- Increased bile excretion of cholesterol
- Increased lipoprotein lipase, which catabolizes the triglyceride-rich lipoproteins
- Increased LDL-receptor activity

Critical illness

Total cholesterol levels drop at the onset of acute illness and return to normal during recovery [6,7]. Multiple mechanisms influence hypolipidemia in critically ill patients and these include[7], probably due to decreased production of cholesterol precursors particularly lanosterol and lathosterol[8], loss of apoproteins in burns[27], and increased cholesterol catabolism.[7] Hypolipidemia have been reported in patients with acute severe pyelonephritis [10], major trauma [8], those with multiple organ dysfunction syndrome, burns, sepsis [11], and in patients undergoing surgical interventions. In meningococcal septicemia, The severity of hypolipidemia in sepsis is directly related to the severity of acute phase response [12].

Malignancy

Several studies suggest an inverse relationship between serum cholesterol level and cancer mortality in patients with hematological and solid organ malignancies [13]. Elevated LDL receptor activity in malignant cells may be a contributing factor to hypocholesterolemia in some cancer patients. The evidence relating hypocholesterolemia to increased risk of cancer is controversial.

Chronic liver disease because hepatocytes are the most active site of

lipid metabolism, hypolipidemia is frequently observed in severe chronic hepatic insufficiency [8]. A low serum cholesterol level is associated with a higher mortality rate in patients with liver cirrhosis [8,62]. Advanced chronic liver disease can cause a reduction in lipoprotein A and lipoprotein B levels.

Chronic inflammation changes in plasma lipid levels are a well known phenomenon in the acute phase response to inflammation. Chronic inflammation also can produce hypocholesterolemia due to the chronic effect of pro-inflammatory cytokines on lipoprotein metabolism.

Infection acute and chronic bacterial, viral, and parasitic infections all might induce hypocholesterolemia due to the chronic effect of pro-inflammatory cytokines on lipoprotein metabolism. In 1911,Since then, transient hypocholesterolemia and hyperlipidemia were frequently observed during the acute phase of bacterial infections [52].

Consequences of hypolipidemia

Effects on plasma membrane

Since about 44% of the human cell membrane is composed of lipids, they serve as a major structural component. Cell membranes are absolutely essential for the cell survival as well as for biological functions [68]. Acanthocytosis is a known clinical feature of abetalipoproteinemia and was also reported to be associated with hypolipidemia in celeriac disease.

Sepsis

Hypocholesterolemia in healthy men is reported to be associated with significantly fewer circulating lymphocytes, Harris et al reported that lipoproteins bind to and neutralize bacterial endotoxin lipopolysaccharide (LPS) [85]. Several authors report that hypocholesterolemia may be a predisposing factor to sepsis in the critically ill patient[23,30].

Intracerebral hemorrhage

Intracranial hemorrhage accounts for approximately 10% of all strokes, and carries a significantly high morbidity and mortality as the 30-day fatality rate reaches up to 50% [72]. Iribarren et al [74] described the association between low serum cholesterol level and cerebral hemorrhage in elderly men. The fundamental interaction of high diastolic blood pressure and low cholesterol levels weakens the endothelium of the intracerebral arteries [75], while another study reported platelet hypo-activity is associated with hypocholesterolemia [79], therefore affected patients may be more prone to bleeding.

Adrenal failure

Cholesterol molecules are the precursors for adrenal steroid hormones. The adrenal gland requires a continuous supplement of cholesterol for the biosynthesis of adrenal corticosteroids, which can be provide by LDL receptor-mediated consumption or through local synthesis [80]. This is likely because of the enhanced endogenous lipid analysis as a result of compensatory smooth endoplasmic reticulum hypertrophy [82,83].

Disease mortality

Studies suggest that lipoprotein play a role in the binding and neutralization of endotoxins. Hypoglycaemia is also associated with enhanced mortality in patients with tuberculosis [94]. Several epidemiological studies suggest an inverse relationship between serum cholesterol levels and cancer mortality [34]. Following a severe trauma, dying patients appear to have progressive hypocholesterolemia [24]. In conclusion, hypocholesterolemia has a statistically significant relationship to mortality in the critically ill patient and is an independent predictor of mortality in this group.

Antihyperlipidemic Activity of *Pongamia pinnata* Leaf Extracts

In this study antihyperlipidemic effect of *Pongamia pinnata* (Leguminosae) leaf extract in triton (400 mg/kg b.w.) induced hyperlipidemic rats. Petroleum ether, chloroform, ethanol and aqueous extracts of leaves were evaluated for antihyperlipidemic.Results demonstrated that chloroform extract of *P. pinnata* leaves controlled fundamental antihyperlipidemic activity hence it could be a potential herbal medicine as adjuvant with existing therapy for the treatment of hyperlipidemia.

Evaluation of Hypolipidemic Activity of *Allium schoenoprasum* in Albino Rats

This study was planned to measure the hypolipidemic action of aqueous and ethanolic extracts of leaves of *Allium schoenoprasum* in albino rats.500 g of dried leaves powder was initially soaked in 3 L of 99.9% ethanol for three days and after filtration residues was soaked in 2 L distilled water for further three days.200 mg/kg/p.o dose of ethanolic and aqueous extracts were administered to the experimental groups while Atorvastatin 10 mg/kg/p.o was given to standard control groups for 7 days. At 8th day blood sample was collected and serum samples were analyzed for biochemical parameters i.e. total serum cholesterol, serum triglycerides, HDL, LDL and VLDL level.

Antihyperlipidemic Activity of Leaf *Extracts of Leucas* aspera Linn. against Dexamethasone-induced Hyperlipidemia in Rats

This study is an attempt to investigate its antihyperlipidemic activity by *in vivo* animal model. Hyperlipidemia model can be induced by administered with dexamethasone in rats with significant increase in serum cholesterol and triglyceride (TG) levels along with increase in the atherogenic index. The ethanolic extract of leaves of *L. aspera* Linn. (200 and 400 mg/kg) treatment has shown significant inhibition against dexamethasone-induced hyperlipidemia in rats by maintaining the serum levels of cholesterol, TGs and near to the normal levels.

***In vitro* Anti-Cholesterol and Antioxidant Activity of Methanolic Extracts from Flax Seeds (*Linumusi atissimum* L.)**

In vitro anti-cholesterol activity was measured by cholesterol enzymatic endpoint method using simvastatin as positive control. The total amount of phenolic compounds was determined spectrophotometrically and the results were expressed as Gallic Acid Equivalent (GAE gG1). Antioxidant activity of flax-seeds in vitro was measured in terms of DPPH free radical scavenging and total antioxidant potential assay. The results indicated that flax-seed might reduce or control the cholesterol levels and oxidative damage and it is apparent that flax-seeds could contribute to new formulations with potential anti-cholesterol and antioxidant effects.

Antioxidant activity and Hypolipidemic effect of *Ficus carica* leaf and twig extracts in Triton WR-1339-induced hyperlipidemic mice

The hypolipidemic potential of both leaf and twig extracts of *Ficus carica* on experimental hyperlipidaemia induced by Triton WR-1339, in *Swiss albino* mice was investigated. In addition, the phenolic, flavonoid and anthocyanin contents of these extracts and their antioxidant activities were determined. These properties may have a synergistic effect on hyperlipidaemia.. The decrease rate of the lipid parameters differs significant from the leaf and twig extracts and depends also on the administered dose.

Hypolipidemic Effect of Oral Administration of Aqueous Leaf Extract of *Senna occidentalis* in Rats

This study was aimed at assessing the effect of oral administration of aqueous leaf extract of *S. occidentalis* on serum lipid profile in rats.Results of phytochemicalscreening revealed the presence of tannins,saponins, cardiac glycosides, resins, and flavonoid. It could be suggested that aqueous leaf extract of *S. occidentalis* at 500 mg/kg could cause antihyperlipidemic effect against dietary-induced hyperlipidemia.

Anti-Hyperglycemia activity of *Picrorhiza kurroa* Royle ex Benth Roots

Based on high Glycoside content in herbal plants, Picrorhiza kurroa was selected and the present study focus on the anti-hyperglycemia activity. The alcoholic,chloroform and aqueous root extracts of Picrorhiza kurroa Royle ex Benth were screened for its antihyperlipidemic activity in Triton wr- 1339 induced albino rats. Atorlip-20 was used as reference standard. The results display significant decrease in triglyceride and cholesterol level when compared with the hypolipemic groups by using different dose: low (50mg/kg), high (200mg/kg) and standard Atorlip-20(4mg/kg bw)

Hypolipidemic Potential of Herbal Drugs (Lagenaria siceraria & *Carica papaya*) and Cow Urine

We study the lipid-lowering effect of *Carica papaya, Lagenaria siceraria* and cow urine. Plants have been used by mankind as remedies from the beginning of civilization. Administration of *Carica papaya* produced a significant improvement in the lipid profile by lowering totalcholesterol, LDL and triglycerides and by increasing HDL level thus helping in retarding the secondary complications. It has anti-lipidemic and anticholesterol activities and as such could be used in the management of hyperlipidemia.

In the study we have found that cow urine consumption significantly reduced the elevated lipid profiles in human and animals.

Hypolipidemic Effect of Extracts from Abelmoschus esculentus L.(Malvaceae) on Tyloxapol-Induced Hyperlipidemia in Mice

Extracts from A. esculentus are known to ameliorate not only hyperglycemia but also hyperlipidemia in diabetic mice induced by alloxan and streptozocin. Triglyceride levels in treated groups had no significant difference as compared to simvastatin group except the AE4 treated group. Esculentus could lower cholesterol and triglyceride levels in hyperlipidemic mice.

In Vitro Hypolipidemic Activity Of Averrhoa Bilimbi Flower Extract

Averrhoa bilimbi is a traditional Medicine used as a local remedy for various ailments like hypertension, Diabetes mellitus and dyslipidemia. When used in high concentrations the fruit juice can lead to Acute renal failure due to acute tubular necrosis, The results obtained from this study indicated that Averrhoa bilimbi, has potential antioxidant and hypolipidemic activity and it may be the due to the synergistic effect of the major phyto-constituents like flavonoids, tannins, terpinoids and phenols that are highly present in the extract. But further studies are required to provide the exact mechanism of action of the reported activities by using purified fraction of the same.

Antihyperlipidemic activity of Chloroxylon swietenia in triton WR1339 induced hyperlipidemia

Medicinal herbs are beneficial and effective either in the management and prevention of several metabolic disorders, associated with hyperlipidemia, hypertension and insulin resistance which increases the cardio-metabolic risk and demands for the life time therapy. Current allopathic medicines are expensive and reported with several adverse effects and hence, finding of a suitable herbal medicine for hyperlipidemic disorders is very important. Both the aqueous and ethanolic extract groups significantly reduced the TG and VLDL levels. The extracts exhibited remarkable activity on one or either parameter of the lipid profile. It could be due to the presence of alkaloids, steroids, flavonoids, coumarins and phenols in the extracts.

List of Herbal Drugs having Hypolipidemic Activity

S.N.	PLANT NAME	BIOLOGICAL SOURCE/FAMILY	PART OF PLANT USED	RESEARCH EVIDENCE
1.	Basil leaves	Ocimum sanctum linn./Lamiaceae	Leaves	Reff. 81
2.	Celery	Apium graveolens/Apiaceae	Plant	Reff. 82
3.	Dandelion	Taraxacum officinale/Asteraceae	Plant	Reff. 83
4.	Clove (Eugenol)	Syzygium aromaticam/ Myrtaceae	Flower bud	Reff. 84
5.	Evening Primrose	Oenothera biennis/ onagraceae	Flower	Reff. 85
6.	Methi	Trigonella foenum graecum/ Fabaceae	Fruit	Reff. 86
7.	Ginger	Zingiber officinale roscoe/ Zingiberaceae	Root Extract	Reff. 87
8.	Ginseng	Panax ginseng/ Araliaceae	Root Extract	Reff. 88
9.	Grape	Vitis vinifera/ Vitaceae	Fruit	Reff. 89
10.	Green Tea	Camellia sinensis/ Theaceae	Leaves	Reff. 90
11.	Fennel	Nigella sativa/ Ranunculaceae	Seeds	Reff. 91
12.	Psyllium	Plantago ovata/ Plantaginaceae	Fruits	Reff. 92
13.	Hing	Ferula asafoetida/ Umbellifetrae	Rhizome	Reff. 93
14.	Garlic	Allium sativum/Amaryllidaceae	Fruit bulb	Reff. 94
15.	Turmeric	Curcuma longa/Zingiberaceae	Rhizome	Reff. 95
16.	Mastic tree	Pistacia lentiscus var.chia/ Anacardiaceae	Gum resin	Reff. 96
17.	Artichoke	Cynara cardunculus var.scolymus/Asteraceae	Flower bud	Reff. 97
18.	Red yeast rice	Monascus purpureus/Monascaceae		Reff. 98
19.	Oleo leaf	Olea europaea/ Oleaceae	Leaves	Reff. 99
20.	Tulsi	Ocimum tenuiflorum/ Lamiaceae	Leaves	Reff. 100
21.	Spikenard	Nardostachys jatamansi/ Caprifoliaceae	Flower	Reff. 101
22.	Black tea	Camellia sinensis	Leaves	Reff. 102
23.	Guggul	Commiphora wightii/ Burseraceae	Gum resin	Reff. 103
24.	Ashwagandha	Withania somnifera / Solanaceae	Bark	Reff. 104
25.	Daruharidra	Berberis aristata/ Bererdaceae	Bark	Reff. 105

REFERENCES

1) Elmehdawi, RR. *Hypolipidemia: A Word of Caution. Libyan Journal of Medicine,*2008;*3:84– 90.*
2) Runmei Yang, Xinxin Chu1, Le Sun, Zhuoying Kang, *et al*. Hypolipidemic activity and mechanisms of the total phenylpropanoid glycosides from Ligustrum robustum (Roxb.) December 2017.
3) Mathur N et al. International Journal of Advances in Medicine Int J Adv Med. 2021;8(2):183-185
4) Hartman C, Tamary H, Tamir A, Shabad E, Levine C, Koren A, Shamir R. Hypocholesterolemia in children and adolescents with beta-thalassemia intermedia. J Pediatr. 2002; 141(4):543-7.
5) Shalev H, Kapelushnik J, Moser A, Knobler H, Tamary H. Hypocholesterolemia in chronic anemias with increased erythropoietic activity. Am J Hematol. 2007; 82(3):199-202.
6) Marik PE. Dyslipidemia in the critically ill. Crit Care Clin. 2006; 22(1):151-9.
7) Dunham CM, Fealk MH, Sever WE. Following severe injury, hypocholesterolemia improves with convalescence but persists with organ failure or onset of infection. Crit Care. 2003; 7(6):R145-53.
8) Bakalar B, Hyspler R, Pachl J, Zadak Z. Changes in cholesterol and its precursors during the first days after major trauma. Wien Klin Wochenschr. 2003,28; 115(21-22):775-9.
9) Bonville DA, *et.al*. The relationships of hypocholesterolemia to cytokine concentrations and mortality in critically ill patients with systemic inflammatory response syndrome. Surg Infect. 2004; 5(1):39-49.
10) Zissin R, Osadchy A, Gayer G, Kitay-Cohen Y. Extrarenal manifestations of severe acute pyelonephritis: CT findings in 21 cases. Emerg Radiol. 2006; 13(2):73-7.
11) Vermont CL, *et.al*. Serum lipids and disease severity in children with severe meningococcal sepsis. Crit Care Med. 2005; 33(7):1610-5.
12) Chiarla C, Giovannini I, Siegel JH. The relationship between plasma cholesterol, amino acids and acute phase proteins in sepsis. Amino Acids. 2004; 27(1):97-100.
13) Tomiki Y, *et.al*. Reduced low-density-lipoprotein cholesterol causing low serum cholesterol levels in gastrointestinal cancer: a case control study. J Exp Clin Cancer Res. 2004; 23(2):233-40.
14) Shepherd J, *et al*. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomized controlled trial. Lancet 2002; 360:1623-30.
15) Badiaga S, *et.al*. Contribution of nonspecific laboratory test to the diagnosis of malaria in febrile travelers returning from endemic areas: value of hypocholesterolemia. J Travel Med. 2002; 9(3):117-21.
16) Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005; 366:1267-78.
17) Brar P, Kwon GY, Holleran S, Bai D, Tall AR, Ramakrishnan R, Green PH. Change in lipid profile in celiac disease: beneficial effect of gluten-free diet. Am J Med. 2006; 119(9):786-90.
18) Siagris D, *et.al*. Serum lipid pattern in chronic hepatitis C: histological and virological correlations. J Viral Hepat. 2006; 13(1):56-61.
19) Petit JM, Benichou M, Duvillard L, Jooste V, Bour JB, Minello A, Verges B, Brun JM, Gambert P, Hillon P. Hepatitis C virusassociated hypobetalipoproteinemia is correlated

with plasma viral load, steatosis, and liver fibrosis. Am J Gastroenterol. 2003; 98(5):1150-4.
20) Yamaguchi A, Tazuma S, Nihioka T, Ohishi W, Hyogo H, Nomura S, *et al* . Hepatitis C virus core protein modulates fatty acid metabolism and thereby causes lipid accumulation in the liver. Dig Dis Sci 2005; 50:1361-71.
21) Mathur M, Mathur N. *et.al*. Stroke: Risk factors evaluation in patients attending a tertiary health care institute of Rajasthan. Paripex. Indian J res. 2017;6:1-3.
22) Elmehdawi RR. Hypolipidemia: a word of caution. Libyan J Med. 2008;3:84-90.
23) Mathur M, Mathur N, *et al*. Demographic characters and factors favouring emergence of diabetes mellitus type two. Int J Res Med Sci. 2018;6:950-4.
24) Yokoyama M, Suto Y, Sato H, Arai K, Waga S, Kitazawa J et al. Low serum lipids suggest severe bone marrowfailure in children with aplastic anemia. Pediatr Int. 2000;42:613-9.
25) Takeuchi, K., & Reue, K. Biochemistry, physiology, and genetics of GPAT, AGPAT, and lipin enzymes in triglyceride synthesis. American Journal of Physiology. Endocrinology and Metabolism, 2009;296, 1195–1209.
26) Santini, A., & Novellino, E. Nutraceuticals in hypercholesterolaemia: An overview. British Journal of Pharmacology, 2017; 174, 1450–1463.
27) Merkel, M., Eckel, R. H., & Goldberg, I. J. Lipoprotein lipase: Genetics, lipid uptake, and regulation. Journal of Lipid Research,2002; 43, 1997–2006.
28) Ballantyne, C. Arroll, B., & Shepherd, J. Lipids and CVD management: Towards a global consensus. European Heart Journal,2005; 26, 2224–2231.
29) Kahn, B. B., Alquier, T., Carling, D., & Hardie, D. G. AMP-activated protein kinase: Ancient energy gauge provides clues to modern understanding of metabolism. Cell Metabolism, 2005;1, 15–25.
30) Zhang, J. J., Pan, L. T., Yang, L. Y., & Mo, Y. Z. The preliminary study on pharmacological effect of Ligustrum robustum Blume. Chinese Journal of Ethnomedicine and Ethnopharmacy,2004; 4, 241–243
31) Ghule BV, Ghante MH, Saoji AN, Yeole PGHypolipidemic and antihyperlipidemic effects of *Lagenaria siceraria* (Mol.) fruit extracts, Indian J Exp Biol 2006;44, 905-909.
32) Pari L, Latha M, Effect of *Cassia auriculata* flowers on blood sugar levels, serum and tissue lipids in streptozotocin diabetic rats, Singapore Med J 43, 2002, 617-621.
33) Saravana K, Mazumder A, Saravanan VS, Antihyperlipidemic activity of *Camellia sinensis* leaves in triton WR-1339 induced albino rats, Phcog Mag 4, 2008 60-64.
34) Manoharan S, Punitha R, Antihyperglycemic and antilipidperoxidative effects of *Pongamia pinnata* (Linn.) Pierre flowers in alloxan induced diabetic rats, J Ethnopharmacol 105, 2006 39-46.
35) Ministry of Health (India), Pharmacopoeia of India, Government of India,1982 p 650-948.
36) Pande VV, Dubey Sonal, Antihyperlipidemic activity of *Sphaeranthus indicus* onatherogenic diet-induced hyperlipidemia in rats, Int J Green Pharm 3(2), 2009 159-161.
37) Nishi AA,Kumar P. Hypolipidemic effect of chlorogenic acid in a hypercholesterolemic rat model. Int J Pharm Bio Sci. 2013; 4(1):582-586.
38) Eddouks M, Lemhadri A, Michel JB. Hypolipidemic activity of aqueous extract of *Capparis spinosa* L. in normal and diabetic rats. J of ethnopharmacol. 2005; 98(3):345-350.
39) Sowmya A, Ananthi T. Hypolipidemic activity of *Mimosa pudica* Linn. on butter induced hyperlipidemia in rats. Asian J. Res. Pharm. Sci. 2011;1(4):123-126.
40) Saravanakumar A, *et.al*. Hypolipidemic activity of *Sesbania grandiflora* in triton wr-1339 induced hyperlipidemic rats. Int J of Phytomedicine. 2010;2(1).
41) Sudha S, Karthic R, Naveen JR. Anti hyperlipidemic activity of *Spirulina platensis* in Triton X-100 induced hyperlipidemic rats. Hygeia: J Drugs Med. 2011;3:32-37.
42) Banu S. Hepatoprotective and antioxidant activity of *Leucas aspera* against D-galactosamine induced liver damage in rats. Pharm Biol 2012;50:1592-5.
43) Reddy MK, *et.al*. Anti-ulcer activity of *Leucas aspera* spreng. Anc Sci Life 1992;XII:257-60.
44) Evans WC. An overview of drugs having antihepatotoxic and oral hypoglycaemic activities. In: Trease and Evans, Pharmacognosy. 14th ed. UK: Sanders Company Ltd.; 1996. p. 119-59.
45) Haughton PJ, Raman A. Laboratory Handbook for the Fractionation of Natural Extracts. 1st ed. USA: Chapman and Hall; 1998. p. 22-52.
46) Adisakwattana, S.J. *et al*. Lipid-Lowering mechanisms of grape seed extract (*Vitis vinifera* L.) and its antihyperlidemic activity. J. Med. Plant 2015 Res., 4: 2113-2120.
47) Baskaran,G.,S. *et.al*. HMG-CoA reductase inhibitory activity and phytocomponent investigation of *Basella alba* leaf extract as a treatment for hypercholesterolemia. Drug Des. Dev. Therapy, 2015 9: 509-517.
48) Ferreira, E.A. *et.al*. 2',4',6'-trihydroxyacetophenone isolated from *Myrcia multiflora* has antiobesity and mixed hypolipidemic effects with the reduction of lipid intestinal absorption. Planta Med., 77: 1569-1574.
49) Hor, S.Y.*et.al*. Lipid-lowering effects of *Coriolus versicolor* extract in poloxamer 407-induced hypercholesterolaemic rats and high cholesterol-fed rats. J. Med. Plants 2011 Res., 5: 2261-2266.
50) Makni, M., *et al*., 2008. Hypolipidemic and hepatoprotective effects of flax and pumpkin seed mixture rich in ω-3 and ω-6 fatty acids in hypercholesterolemic rats. Food Chem. Toxicol., 46: 3714-3720.
51) Adeneye AA,*et.al* Anti-obesity and antihyperlipidaemic effect Hunteria umbellata seed extract in experimental hyperlipidaemia. Journal of Ethnopharmacology. 2010;130:307-14.
52) Ahmed I,*et.al* Hypotriglyceridemic and hypocholesterolemic effects of anti-diabetic Momordica charantia (karela) fruit extract in streptozotocin-induced diabetic rats. Diabetes Research and Clinical Practice. 2001;51:155-61.
53) Banerjee A, Vaghasiya R, Shrivastava N, Padh H, Nivsarkar M. Anti-hyperlipidemic effect of carcia papaya L in sprague dawley rats. Nigerian Journal of Natural Products and Medicine. 2006;10:69-72.
54) Khanna A, Rizvi F, Chander R. Lipid lowering activity of Phyllanthus niruri in hyperlipemic rats. Journal of Ethnopharmacology. 2002;82:19-22.
55) Girija K, Lakshman K, Udaya C, Sachi GS, Divya T. Anti–diabetic and anti–cholesterolemic activity of methanol extracts of three species of Amaranthus. Asian Pacifific Journal of Tropical Biomedicine. 2011;1:133-8.
56) Zulet MA, Barber A, Garchin H, Higueret P, Martnez JA. Alterations in Carbohydrate and Lipid metabolism induced by a diet rich in coconut oil and cholesterol in a rat model. J Am Coll Nutr 1999;18:1:36-42.
57) WHO. Legal status of traditional medicines and complementary/ Alternative medicine. A worldwide review. WHO Publishing; 2001.
58) National Research Council. 2011. Guide for the Care and Use of Laboratory Animals. 8th ed. Washington, DC: The National Academies Press; 2011.
59) YokozawaT. The protective role of chinese prescription kangen-karyu extract on diet-induced hypercholesterolemia in rats. Bio Pharm Bull 2006;29:760-5.
60) Panwala. P. T, Naik S. R and D'mello. P. M. 'Indian Drugs', Antihyperlipidemic and antioxidant activity of Syzgium cumini,2004 41(6): pp -345-49.
61) Saravana kumar A., Mazumder Avijit, Saravana kumar S. 'PHCOG MAG', Antihyperlipidemic activity of camellia sinensis leaves in Triton WR-1339 induced albino rats. vol-4, Issue-13.2008 ISSN 0973-1296.
62) R. N. Chopra, S. L. Nayar, I. C. Chopra. 'Glossary of Indian Medicinal Plants',2002 .192
63) S. L. Brown. Lowered serum cholesterol and low mood. Br. Med. J.1996 313: 637- 638.
64) J. A. Berliner and J. W. Heinecke . The role of oxidized lipoprotein in atherogenesis. Free. Radic. Biol. Med. 20: 707- 727(1996).
65) T. Suzuki and Y. Suzuki. Current topics of lipid dynamics and pathobiology in membrane lipid rafts. Biol .Pharm. Bull. 29(8)1538-1541(2006).
66) Pankaj G. Jain.et.al" a review of Indian medicinal plants with hypolipidemic activity and their medicinal importance "world journal of pharmacy and pharmaceutical sciences, Volume 4, Issue 03, 2015, 1477- 1493.
70) Ghule BV, et.al Hypolipidemic and antihyperlipidemic effects of *Lagenaria siceraria* (Mol.) fruit extracts. Indian J Exp Biol. 44, 2006, 905–9.
71) Morou CO, Basile G. Hyperlipidemia and medicinal plants. Fitoterapia 71, 2000, S73 S82.
72) Seidell J.C et.al Assessing hyperlipidemia: Classification and epidemiology. British Medical Bulletin 53,1997 238–252.
73) Francisco J. et. al. Effect of *Hibiscus sabdariffa* on hyperlipidemia in MSG mice Journal of Ethnopharmacology 114, 2007, 66–71.
74) Saojia A.N et al. Antihyperlipidemic effect of the methanolic extract from *Lagenaria siceraria* Stand. fruit in hyperlipidemic rats, Journal of Ethno pharmacology 2009, 124, 333-337.
75) Yamini Dixit et al, *Lagenaria siceraria* Peel Extract in the Regulation of Hyperthyroidism, Hyperglycemia and Lipid Peroxidation in Mice, International Journal of Biomedical and Pharmaceutical Sciences. 2, 2008, 79-83.
76) William Charles Evans. Trease & EvansPharmacognosy.15th edition. Savnders; 2013, 2-3.
77) Bakul G et.al Acute oxalate nephropathy due to Averrhoa bilimbi fruit juice ingestion Indian journal of Nephrol. 2013, 297-300.
78) Kumar G et.al The hypolipidemic activity of Ayurvedic medicine, Arogyavardhini vati in Triton WR-1339-induced hyperlipidemic rats: a comparison with fenofibrate. Journal of Ayurveda and integrative medicine. 2013 Jul;4(3):165.
79) Mishra R et.al Antihyperlipidemic activity of alcoholic extracts of trichosanthes anguina in triton WR 1339 induced hyperlipidemic rats. IJPSR. 2014;5(10):4269-74.
80) Pasha SR. Evaluation of hypolipidemic activity of methanolic extract of ficus dalhousiaemiq. on triton-x and high fat diet induced hyperlipidemia in albino rats EJPMR. 2014;1(1):183-91.
81) Nisya Ayu Rachmawati ***et al shows the study of*** Basil Leaves *(Ocimum sanctum linn.)* Extract Decreases Total Cholesterol Levels in Hypercholesterolemia Sprague Dawley Rats Model. 2019.
82) D.Tsi,BKH Tan shows the Effects of Celery extract and 3-N-Butylphthalide on lipid levels in genetically Hypercholesterolaemic (RICO) Rats ;Mar.1996.
83) Ung-Kyu Choi, *et al* study shows Hypolipidemic and antioxidant effects of Dandelion(*Taraxacum officinale*) root and leaf on cholestrol-rabbits ;Jan 2010.
84) Amani A.harb *et al* shows Eugenol reduces LDL Cholesterol and Hepatic steatosis in Hypercholesterolemic Rats by Modulating TRPV1Receptor ; Sep 2019.
85) Noha M Abo-Gresha *et al* study shows Evening primrose oil ameliorates platelet aggregation and improves cardiac recovery in myocardial-infract hypercholesterolemic rats ; Mar 2014.
86) Megh Shyam Sharma *et al* shows Hypolipiemic effect of fenugreek seeds and its comparison with atorvastatin on experimentally induced hyperlipidemia ; Aug 2014
87) Ahmad sameer al-noory *et al* shows Antihyperlipidemic effects of ginger extreacts in alloxan-induced diabetes and propylthiouracil-induced hypothyroidism in (rats); Sep 2013.
88) Yi-Seong Kwak *et al* shows the study Anti-hyperlipidemic effects of Red Ginseng acidic polysaccharide from Korean red ginseng ; Oct 2010.
89) Emilia Yasuko Ismimoto *et al* shows Hypolipidemic and antioxidant effects of grape processing by-products in high-fat/cholesterol diet-induced hyperlipidemic hamsters ; sep 2010
90) Xin-Xin Zheng *et al* study shows that Green tea intake lowers fasting serum total and LDL cholesterol in adults:a meta-analysis of 14 randomized controlled trials ; Jun 2011
91) Sedigheh Asgary *et al* shows Nigella sativa L.improves lipid profile and prevents atherosclerosis:evidence from an experimental study on Hypercholesterolemic rabbits ; Jan 2013.
92) James W Anderson *et al* shows Long-term cholesterol - lowring effects of psyllium as an adjunct to diet therapy in the treatment of Hypercholesterolemia ; June 2000.
93) Ebrahim Latifi *et al* shows Antidiabetic and antihyperlipidemic effects of ethanolic ferula assa-foetida oleo-gum-resin extract in streptozotocin-induced diabetic wistar rats ; Feb 2019.
94) Yue-E-Sun *et al* shows Anti-hyperlipidemia of garlic by reducing the level of total cholesterol and low-density lipoprotein ; May 2014.
95) Yunes Panahi *et al* study shows Curcumin as a potential candidate for treating hyperlipidemia:A review of cellular and metabolic mechanism ; Jan 2018.
96) Athanasios Katalis *et al* shows the Effects of chios mastic gum on cholesterol and glucose levels of healthy volunteers:a prospective,randomized,placebo-controlled,piot study (CHIOS-MASTIHA) ;Aug 2020.
97) Amirhossein Sahebkar *et al* study shows Lipid-lowering activity of artichoke extracts:A systematic review and meta-analysis ; Aug 2017.
98) Aeeigo F.G Cicero *et al* shows Red Yeast Rice for Hypercholesterolemia ; Sep 2019.
99) Ercument Olmez et al shows Olive leaf extract improves the Atherogenic lipid profile in rats fed a high cholesterol diet ; Aug 2015.
100) Thamolwan Suanarunswat *et al* shows Lipid-lowering and antioxidative activitiesof Aqueous extracts od Ocimum sanctum linn Leaves in rats fed with a high-cholesterol diet ; Sep 2011.
101) R Subashini *et al* shows the study of biochemical stiudy on the protective potential of Nardostachys jatamansi extract on lipid profile and lipid metabolizing enzyme in doxorubicin ; May 2007.
102) Ali imran *et al* shows that Exploring the potential of Black tea based Flavonoids against hyperlipidemia related disorders ; Mar 2018.
103) Philippe O Szapary *et al* shows that Guggulipid for the treatment of hypercholesterolemia:a randomized Controlled trial : Aug 2003.
104) Nishant P Visavadiya *et al* shows that Hypercholesteremic and antioxidant effects of *Withania somnifera* (Dunal) in hypercholesteremic Rats ; Feb 2007.
105) Faiza Abdul Razzaq *et al* study shows Effects of *Berberis aristata* on lipid profile and coagulation parameters ; July 2011.