IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Hypolipidemic And Anti-Atherogenic of Priva Cordifolia

[1,] Rani Lilhare*, [2]Rajesh Mishra

[1,2] Radha raman College of Pharmacy, Bhadbhada Road, Ratibad, Bhopal (MP) -462044

Abstract:

This article Hypolipidemic And Anti-Atherogenic looks at how certain medicinal plants can help lower high levels of fats in the blood, which is useful for treating lipid-related issues. It explains how these plants work at a biochemical level to manage fats in the body. The review also shares real-life uses of these plants and how well they work for treating high lipid levels. It includes evidence from studies done on people. For each plant, there is a detailed look at how safe it is and what possible side effects might occur. Looking ahead, the article suggests that more research is needed, including better human studies, clear dosing guidelines, and combining these plants with healthy lifestyle changes. In last few decades, WHO assembly passed several aspects in response to resurgence of interest in the study and use of traditional herbal medicines and in recognition of importance of medicinal plant to primary health care of people in many developing countries. Plants are rich source of secondary metabolites such as tannins, flavonoids, terpenoids, alkaloids etc. which have been implicated for several therapeutics activities. Now days, large number of drugs are derived from plants involving multi-disciplinary approach by combining botanical phytochemical and biological techniques. The medicinal plants have several important advantages for their therapeutic uses in a variety of ailment that is safe in addition being economical, effectiveness and ease of availability. Medicinal plants have the potential to be a natural, effective, and safer way to treat lipid problems and help with obesity around the world.

Keywords: Hyperlipidemia, Cardiovascular disease, LDL-C, HDL-C, Antihyperglycemic

INTRODUCTION

Hyperlipidemia and Cardiovascular Diseases

Hyperlipidemia is one of the most prevalent risk factors for the development of atherosclerosis and subsequent cardiovascular diseases (CVDs). It is characterized by significantly elevated levels of serum total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C). Numerous studies have consistently shown that elevated LDL-C levels contribute substantially to the formation of atherosclerotic plaques, underscoring the critical role of this lipid in the pathogenesis of CVDs. Pharmacological interventions aimed at lowering LDL-C are widely employed to prevent or treat CVDs, with statins being the most commonly prescribed drugs. While effective, statins—particularly those of synthetic origin—are associated with adverse effects that may limit their long-term use. This has spurred growing interest in natural alternatives for the management of hypercholesterolemia. Among these, lignans, a class of phenolic dimers derived from *cis-o-hydroxycinnamic acid*, have attracted considerable attention. Lignans are abundantly present in dietary sources such as flaxseeds, sesame seeds, and cruciferous vegetables. Their potential lipid-lowering, antioxidant, and cardioprotective effects make them promising candidates in the prevention and treatment of CVDs. Cardiovascular diseases remain a global health burden, accounting for nearly 31% of all deaths worldwide (Figure 1). According to the World Health Organization (WHO), CVDs have no geographic, socioeconomic, or gender boundaries, affecting populations across both developed and developing nations. It is estimated that by 2030, approximately 23.6 million people will die from CVDs, primarily heart disease and stroke, making it the leading cause of mortality worldwide. In India, which constitutes nearly one-sixth of the global population, the burden of CVD is disproportionately high compared to other ethnic groups. This alarming trend highlights the urgent need for effective, safer, and more accessible strategies to manage hyperlipidemia and reduce CVD risk.

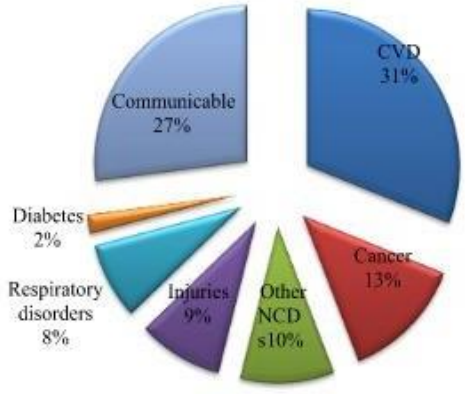

Figure 1: Worldwide role of various disorders responsible for mortality

Cardiovascular Disease and Risk Factors

Cardiovascular disease (CVD) refers to a group of disorders involving the heart and blood vessels (e.g., arteries). It is typically associated with one or more risk factors, which are defined as any attribute,

characteristic, or exposure that increases the likelihood of developing a disease or injury [1–3]. The major risk factors contributing to CVD are illustrated in Figure 2.

Among these, atherosclerosis, diabetes, dyslipidemia, and the generation of free radicals.

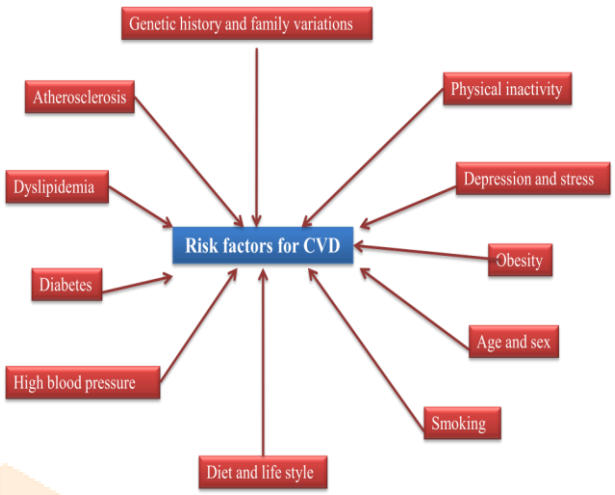

Figure 2: Various risk factor contributing to CVD[3]

play a particularly critical role in the pathogenesis of CVD [4]. Notably, the generation of free radicals or reactive oxygen species (ROS) is a common underlying mechanism that arises in nearly all the key risk factors associated with CVD [5]. Excessive ROS production leads to oxidative stress, which promotes endothelial dysfunction, lipid peroxidation, and inflammatory processes that accelerate cardiovascular damage.

Global and Indian Burden of Cardiovascular Disease

Cardiovascular disease (CVD) continues to be the leading cause of mortality worldwide, accounting for nearly one-third of all deaths, as reported by the World Health Organization (WHO) [6–7]. Several well-established factors contribute to the development of CVD, including diabetes, atherosclerosis, dyslipidemia, hypertension, obesity, and stress**.** Among these, atherosclerosis of the coronary arteries has become a particularly significant concern, with its incidence steadily increasing across the globe. In India, coronary artery disease (CAD), a major manifestation of atherosclerosis, has emerged as a growing epidemic**.** Disturbingly, it tends to affect individuals at a younger age**,** often presenting with severe, diffuse lesions and extensive angiographic involvement [8–9]. Over the past five decades, the prevalence of CAD has risen sharply in both urban and rural populations**,** and projections suggest that atherosclerosis will continue to assume epidemic proportions in the Indian subcontinent [10–11]. Another major risk factor for CVD is diabetes mellitus, the prevalence of which is escalating at an alarming rate worldwide. WHO (2010) projected that by 2030**,** the global number of adults with diabetes would nearly double—from 177 million in 2000 to 370 million. In India, the situation is particularly concerning, with more than 62 million individuals currently diagnosed with diabetes. According to the literature, the worldwide prevalence of diabetes is expected to rise from 171 million in 2000 to 366 million by 2030**,** with India contributing the largest

increase to this global burden [10–12]. Diabetes, Dyslipidemia, and Atherosclerosis in Cardiovascular Disease. Diabetes mellitus is considered a coronary heart disease (CHD)–risk equivalent, as it frequently coexists with multiple cardiovascular risk factors. Among these, dyslipidemia plays a central role in accelerating macrovascular complications of Type 2 diabetes mellitus, affecting nearly 10–73% of this population [13–14]. Notably, almost 80% of mortality in patients with diabetes can be attributed to CVD. Epidemiological data show that Asians, particularly Indians, have a higher risk of CHD compared to Caucasians [15]. Dyslipidemia in diabetes typically manifests as a lipid triad: Elevated low-density lipoprotein cholesterol (LDL-C) Reduced high-density lipoprotein cholesterol (HDL-C) Increased triglycerides (TG) Findings from the UKPDS trial confirmed that both decreased HDL-C and elevated LDL-C are strong predictors of CHD in diabetic patients [16]. Accordingly, all major international guidelines recommend aggressive lipid management in this population, with special emphasis on lowering LDL-C levels, which is proven to reduce CHD events in both primary and secondary prevention [17]. In India, diabetic dyslipidemia is considered one of the leading causes of CAD-related mortality. However, there remains a paucity of studies evaluating whether dyslipidemia is adequately controlled in Indian diabetic populations [18]. **Atherosclerosis as a Primary Driver of CVD**

The primary pathological basis of CVD is atherosclerosis, a chronic, progressive disease characterized by arterial hardening. Although its etiology is multifactorial, the initial atherogenic trigger remains elusive [19]. Diabetes is a particularly strong risk factor, conferring nearly a four-fold risk for atherosclerosis, often manifesting as intimal thickening, lipid accumulation, smooth muscle hypertrophy, extracellular matrix expansion, and inflammatory cell infiltration [20]. One mechanistic link is the presence of Amadori glucose adducts in diabetic blood, which play a vital role in vascular complications [21]. Similarly, hyperlipidemia or mixed hyperlipoproteinemia (elevated LDL-C and TG with reduced HDL-C) further accelerates atherosclerosis and enhances platelet reactivity, thereby increasing CVD risk [22].

Oxidative Stress: A Common Pathway

Atherosclerosis, dyslipidemia, and diabetes are interconnected through the generation of free radicals and oxidative stress, which contribute significantly to CVD progression [23]. Hyperglycemia promotes the formation of advanced glycation end-products (AGEs) and glycated lipoproteins, which foster vascular injury. Oxidative stress impairs endothelial function, accelerates angiopathy, and destabilizes atherosclerotic plaques, making them prone to rupture and thrombosis. Nitrosative stress (excess nitric oxide and peroxynitrite formation) further damages vascular cells, triggering inflammation and atherogenesis [24–25]. Diet-induced hypercholesterolemia worsens cardiac dysfunction by increasing peroxynitrite formation and reducing nitric oxide bioavailability [26]. Thus, the synergistic effect of dyslipidemia, diabetes, and oxidative stress greatly increases the risk of cardiovascular complications. Importantly, glycemic control remains one of the most effective strategies to prevent endothelial dysfunction, slow the progression of atherosclerosis, and reduce CVD burden in diabetic patients. The typical feature in diabetes is impaired lipid and glucose metabolism. The high glucose and lipids activate advanced formation of ROS which further

might accelerate glycation, protein kinase C, sorbitol or hexosamine pathways. These pathogenic mechanisms are interlinked to oxidative stress or damage, which have been considered as main cause in the progression of the endothelial dysfunction. [27] The relationship between oxidative stress, oxidant generation, oxidative damage and various CVD risk factors like atherosclerosis, dyslipidemia, diabetes, hypertension etc. is well known (Figure 1.3). According to literature, oxidative stress is solely used toexplain impaired ROS or RNS system which may be involved in development ofsecondary hypertension, atherosclerosis or hyperglycemia.

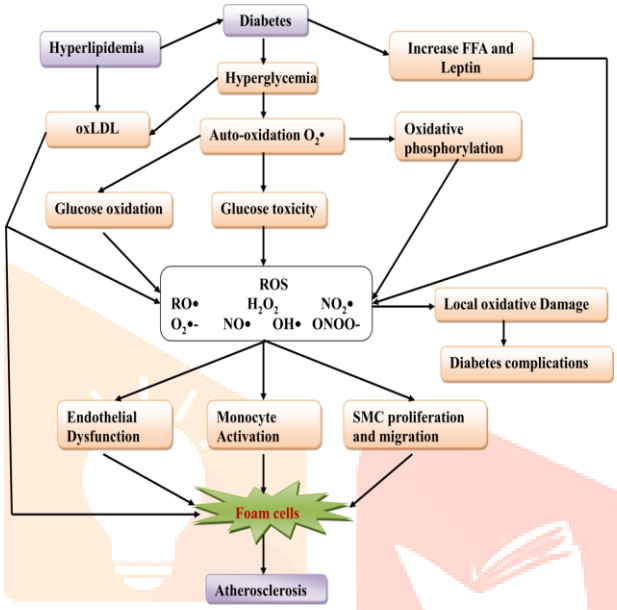

Figure 3: The relationship among oxidative stress, oxidant generation, oxidative damage and various CVD risk factors like atherosclerosis, dyslipidemia and diabetes.[26]

Management of risk factors of CVD with pharmacotherapy

It is clear that the epidemic of CVD in both developed as well as in developing countries is the common cause of death and disability. So, the management is essential to reduce the potential risk factor for cardio vascular diseases. Many patients at high risk for CHD fail to reach target lipid levels with currently available medications, and a small but clinically relevant proportion of patients experience adverse effects.[41, 42, 43] Thus, additional therapeutic strategies are required to fill these gaps in efficacy and tolerability. According to market research, 2005, Statins are the most widely used treatment for dyslipidemia, accounting for around 87% of the US market. Statins can inhibit HMG-CoA (3-hydroxy-3-methylglutaryl coenzyme A reductase) a rate-limiting step in biosynthesis of cholesterol. Depletion of hepatic cholesterol stores increases LDL-R expression, resulting in enhanced clearance of plasma LDL particles. Although statins are generally well-tolerated, about 10% of patients experience side effects, mainlymuscle aches, while a much smaller proportion will experience elevations in serum creatine kinase and transaminases.[45] An extremely rare adverse effect happening in about 1/100,000 prescriptions is rhabdomyolysis, which can typically be detected early by monitoring of patient symptoms and serum creatine kinase levels, with discontinuation of the statin as appropriate. Also, a significant proportion of

patients on statins do not reach stringent LDL-C targets. [28] The next category is bile acids sequestrants (BAS) (colestipol, cholestyramine) are amphiphilic molecules synthesized from cholesterol that facilitate intestinal absorption of dietary fat. BAS deplete the endogenous bile acid pool (about 40%), stimulate an increment in bile acid synthesis from hepatic cholesterol centre and increase LDL-R expression that results in enhanced LDL particle clearance and lowering of plasma LDL-C by approximately 15%.[47] Unfortunately, BAS are associated with increased plasma triglyceride level and can also alter the absorption of medicationssuch as levothyroxine or warfarin. Furthermore, BAS use is complicated byconstipation and flatulence, reducing patient compliance. Newer BAS, such as colesevelam, have greater affinity for binding bile acids, with fewer side effects. Moreover, colesevelam has been shown to decrease C-reactive protein. [29] Fibrates are weak peroxisome proliferator activated receptor (PPAR-α) agonists which decrease TG levels up to 50%. Their effects on LDL and HDL are more variable,with a decrease and increase of around 10% and 10%, respectively. Fibrates downregulate apo C-III expression, resulting in increased VLDL clearance, and upregulate apoA-I, SR-BI and ABCA1 expression, not increasing reverse cholesterol transport. The most common side effects of fibrates include myalgias, increased serumcreatinine, cholelithiasis and increased. Niacin is an effective broad-spectrum antidyslipidemic drug, which is associatedwith HDL-C and increases up to 30% as well as reduction in total cholesterol, triglyceride, LDL-C and lipoprotein by 20-40%. Side effects from niacin use may include insulin resistance, gout, or gastritis. However, the most limiting side effect fromniacin use has been skin flushing and related vasodilatory symptoms. Probucol (lipophilic antioxidant) act by taking LDL particle and endothelial cells. They inhibit oxidation of LDL and prevent ingestion by macrophage foam cells. Also, decreases HDL production. [31] Currently available hypolipidemic drugs have been associated with a number of side effects. Statins are universally well tolerated among individuals. However, significant increment in alanine aminotransferase (ALT) and aspartate transaminase (AST) levels has been observed in 1% of the patients.[53] Although statin therapy is contraindicated in liver disease, but no any evidence of aggravation of liver function hasnot found in individuals having fatty liver, primary biliary cirrhosis or chronic hepatitis C. Patients on treatment with crystalline niacin or extended-release niacin showed significant elevation in ALT. As well as, slow release niacin has greater risk risk of hepatotoxicity. After starting statin or niacin therapy, the measurement of ALT levels is recommended at the 0 and between 1-3 months. The level of plasma creatinine is increased in fibrate-treated patients and increment is more significant in renal disease patients. [32] Moreover, oral hypoglycemic agents are associated with common side effects related to their pharmacokinetic actions, hypoglycemia, secondary failure rates, skin reactions, gastrointestinal disturbances, hematological disorders, rise in hepatic enzyme levels etc [33] Due to the adverse or side effects and lack of the curative value in modern (allophatic) medicines, the interest and approach in the natural/herbal remedies is increased. Herbs can be used as medicinal or functional food and researcher has focusedtheir interest on various plants that have antidyslipidemic or antihyperglycemic potential that may be used as adjunct therapy inreduce CVD risks.[34]

Herbal approach

Plants are basic source of life on earth and central to people's livelihood. They are potential source of drugs and being used from the ancient period as herbal remedies for the prevention and cure of various disease and ailments. [35] As per WHO survey it was suggested that about 80% of populations relies on the traditional or herbal system of medicine, as its major source of medicinal products. In last few decades, WHO assembly passed several aspects in response to resurgence of interest in the study and use of traditional herbal medicines and in recognition of importance of medicinal plant to primary health care of people in many developing countries.[36] Plants are rich source of secondary metabolites such as tannins, flavonoids, terpenoids, alkaloids etc. which have been implicated for several therapeutics activities. Now a days, large number of drugs are derived from plants involving multi-disciplinary approach by combining botanical phytochemical and biological techniques. The medicinal plants have several important advantages for their therapeutic uses in a variety of ailment that is safe in addition being economical, effectiveness and ease of availability. Also, due to these advantages the herbals are widely used by the traditional medical practitioner in their practice. [37] Today herbal drugs symbolize safety and economic as compared to synthetic drugs which regards as risky to individuals as well as to environment. According to a estimation, plant constitute as much as 25% of the total drugs in developed countries such as United States. Traditional medicine occupies a share of US $ 250 billion in global market and estimated to be expanding at 20% annually. There are about 25,000 herbal formulations/products which are used in traditional medicine and rural communities of India. [38] Ayurveda is oldest medicinal system which is well developed and widely practiced. The literal meaning of Ayurveda is "Ancient science of life". Indian herbal medicinal industries have about Rs. 2,300 crores annual turnover against the Pharmaceutical industry's turnover of Rs. 14,500 crores and with a effective growth rate (15%) annually.[72] In India, export of herbs/medicinal plants has been found fairlyextensive within last years. India become the second largest producer of castor seed throughout the world and produce about 1,25000 tonnes/annum. At present, it is reported that India consume around $1billion in herbal drug market and the requirementof medicinal plants is rising exponentially and pharmaceutical companies are presently conducting extensive research on herbals for their potential medicinal value. [39] The increased use of medicinal plants has the potential of improving and lowering the health care cost. Herbs are rich source of medicinal drugs. So, there are necessities of research for the discovery of efficacious, cheap and safe medicinal product from the natural sources. There are a variety of herbs which successfully attenuated cholesterol levels without any adverse/side effects. Moreover, numerouschemical and drugs originated from plants lowered blood lipid, glucose and atherogenesis. So, there is a need to substantial attention to re-establish traditional claims with scientific interest. [40]

REFERENCE

1. Takei A, Huang Y, Lopes-Virella F. Intercellular adhesion molecule-1 (ICAM- 1) expression induced by oxLDL on human umbilical vein endothelial cells (HUVEC) depends on the stage of LDL oxidation. Diabetes. 1998; 47:A115- A115.
2. Leopold JA, Loscalzo J. Oxidative risk for atherothrombotic cardiovascular disease. Free Radic Biol Med. 2009; 47:1673-1706.
3. Nishikawa T, Edelstein D, Du XL, Yamagishi S, Matsumura T, Kaneda Y, et al. Normalizing mitochondrial superoxide production blocks three pathways ofhyperglycemic damage. Nature. 2000; 404:787-790.
4. Wolff SP. Diabetes mellitus and free radicals. Free radicals, transition metals and oxidative stress in the aetiology of diabetes mellitus and complications. Br Med Bull. 1993; 49:642-652.
5. Baynes JW, Thorpe SR. Role of oxidative stress in diabetic complications: a new perspective on an old paradigm. Diabetes. 1999; 48:1-9.
6. Ahn SC. Neuromuscular complications of statins. Phys Med Rehabil Clin North Am. 2008;19:47-59
7. Sueta CA, Massing MW, Chowdhury M. Undertreatment of hyperlipidemia in patients with coronary artery disease and heart failure. J Card Fail. 2003;9:36- 41
8. Einarsson K, Ericsson S, Ewerth S. Bile acid sequestrants: mechanisms of action on bile acid and cholesterol metabolism. Eur J Clin Pharmacol. 1991; 40 (Suppl 1):S53-8.
9. Bays HE, Davidson M, Jones MR. Effects of colesevelam hydrochloride on low-density lipoprotein cholesterol and high-sensitivity C-reactive protein when added to statins in patients with hypercholesterolemia. Am J Cardiol. 2006; 97:1198-205.
10. Hoogt CCV, Haan W, Westerterp M, Hoekstra M, Dallinga-Thie GM, Romijn JA, et al. Fenofibrate increases HDL-cholesterol by reducing cholesteryl ester transfer protein expression. J Lipid Res. 2007;48:1763-71.
11. Alsheikh-Ali AA, Kuvin JT, Karas RH. "Risk of adverse events with fibrates." Am J Cardiol. 2004; 94:935-8.
12. Malik S, Kashyap ML. Niacin, lipids, and heart disease. Curr Cardiol Rep. 2003;5:470-6.
13. Asmis R, Jelk J. Vitamin E supplementation of human macrophages prevents neither foam cell formation nor increased susceptibility of foam cells to lysis by oxidized LDL. Atherosclerosis and Lipoproteins. Arteriosclero Thromb Vasc Biol. 2000; 20:2078-86.
14. Farmer JA, Torre-Amione G. Comparative tolerability of the HMG-CoA reductase inhibitors. Drug Saf. 2000; 23:197-213.
15. Chalasani N. Statins and hepatotoxicity: Focus on patients with fatty liver. Hepatol. 2005; 41:690-5.
16. Rakesh Tiwle, A Review On Senegalia Catechu (Acacia Catechu Willd) International Journal Of Phytopharmacy Research, Vol 5 | Issue 4 | 2015 | XXX-XXX.

17. Gibson K, Rindone JP. Experience with statin use in patients with chronic hepatitis C infection. Am J Cardiol. 2005; 96:1278-9.
18. Ritzel U, Leonhardt U, Näther M, Schäfer G, Armstrong VW, Ramadori G. Simvastatin in primary biliary cirrhosis: Effects on serum lipids and distinct disease markers. J Hepatol. 2002;36:454-8.
19. McKenney JM, Proctor JD, Harris S, Chinchili VM. A comparison of the efficacy and toxic effects of sustained- VS immediate-release niacin in hypercholesterolemic patients. JAMA. 1994; 271:672-7.
20. Ellen RL, McPherson R. Long-term efficacy and safety of fenofibrate and a statin in the treatment of combined hyperlipidemia. Am J Cardiol. 1998;81:60B-5B
21. Rakesh Tiwle, Importance Of Village Plant Rhubarb: Review. Int J Pharma Res Health Sci. 2016; 4 (6): 1438-1443
22. Lipscombe J, Lewis GF, Cattran D, Bargman JM. Deterioration in renal function associated with fibrate therapy. Clin Nephrol. 2001;55:39-44.
23. Rout SP, Chowdary KA, Kar DM, Das L. Plants as source of novel anti- diabetic drug: present scenario and future perspectives. Curr Trends Biotechnol Pharm. 2009;3:37-55
24. Farnsworth NR. Screening plants for new medicines. In Biodiversity (Wilson EO, ed.), National Academic Press, 1988; 83-97.
25. Cordell G. Biodiversity and drug discovery: A symbiotic relationship. Phytochem. 2000; 55:463-80.
26. Kalia AN. Text book of industrial pharmacognosy. Oscar Publication, New Delhi, India 2005.
27. Pradhan P, Joseph L, Gupta V, Chulet R, Arya H. *Saraca asoca* (Ashoka): A Review. J Chem Pharma Res. 2009;1(1):62-71.
28. Timothy O, Idu M, Falodun A, Oronsaye FE. Preliminary phytochemistry and antimicrobial screening of methanol extract of *Baissea axillaris* Hau. leaf. J Biomed Sci. 2008;8:239-41.
29. Rakesh Tiwle, A Multi Use Full Plant Of Cinnamon: A Pharmacological Review International Journal Of Phytopharmacy And Research, Vol 6 | Issue 1 | 2015 | 16-20.
30. Meena AK, Rao MM, Ajit K, Sannd R, Kiran, Niranjan U, Yadav AK. Standardisation of *Desmodium gangeticum*- A tradition ayurvedic plant. Drug Invention Today. 2010;2(2):182-4.
31. Joy PP, Thomas J, Samuel M, Skaria BP. Medicinal Plants. Aromatic and Medicinal Plant Research Station, Kerala, India 1998.
32. Perumalsamy R, Gopalakrishnakone P. Current status of herbal and their future perspectives. Nat Precedings. 2007; 1176:1-13.
33. Verma S, Singh SP. Current and future status of herbal medicines. Veterinary World. 2008;1:347-350.
34. Kamboj VP. Herbal medicine. Curr Sci. 2000; 78:35-9.
35. Shah Biren. Textbook of Pharmacognosy and Phytochemistry. Published by Elsevier Health Sciences 2009.

36. Tandon V, Kapoor B, Gupta BM. Herbal drug research in India: A trend analysis using IJP as a marker (1995-2003). Ind J Pharmacol. 2004;36(2):99- 100.
37. Bounda GA, Feng YU. Review of clinical studies of *Polygonum multiflorum* Thunb. and its isolated bioactive compounds. Pharmacognosy Res. 2015;7(3):225-36.
38. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, et al. ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the american college of cardiology foundation/american heart association task force on practice guidelines. J Am Coll Cardiol. 2010;56(25):e50-e103
39. Van De Graaff: Human Anatomy. Circulatory system. Sixth Edition, The McGraw-Hill Companies; 2001.chapter 16. p.595.
40. Gotlieb AI, Silver MD. Atherosclerosis: Morphology and Pathogenesis in Cardiovascular Pathology. Silver MD, Gotlieb AI, Schoen FJ, editors New