Summary

Cardiovascular diseases (CVD) are reckoned amongst the top reasons for early deaths. Hyperlipidemia is a predominant risk factor for atherosclerosis and associated cardiovascular diseases. It leads to various cardiovascular disorders like angina pectoris, hypertension, atherosclerosis, myocardial infraction, congestive heart failure (Grundy, 1986). About 17 million people around the world die because of cardiovascular diseases every year (WHO, 2004). 30% global deaths are due to cardiovascular disease of global deaths in which 80% deaths occur in low and middle income countries. Coronary vascular diseases (CVD) are the number one cause of death globally, more people die annually from CVDs than from any other cause. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths, of these deaths, an estimated 7.3 million were due to coronary heart disease. Low and middle-income countries are disproportionately affected, over 80% of CVD deaths take place in low and middle income countries and occur almost equally in men and women. The number of people, who die from CVDs, mainly from heart disease and stroke, will increase to reach 23.3 million by 2030 (Global status report WHO, 2011, Mathers and Loncar, 2006). This estimate is likely to be even higher taking into consideration population growth, ageing, urbanization, declining levels of physical activity, with unbalanced diet.

Anti hyperlipidaemic therapy involves non pharmacological and pharmacological therapy. Non pharmacologic approaches include dietary modifications, weight loss or control, aerobic exercise, reduction in alcohol consumption and smoking cessation and physical activity (Chase, 2002, Krauss, 2000). Pharmacological intervention of hyperlipidemia with lipid lowering drugs, include bile acid sequestrants, niacin,
fibric acid derivatives and statins. Besides they have undesirable side effects. For instance, rhabdomyolysis; psychiatric adverse reactions include depression, memory loss, confusion aggressive reactions (Jan Fedacko, 2010).

This emphasizes the urgent need for a more effective and safer treatment of hyperlipidaemia and related cardiovascular disorders. Compared to synthetic drugs, herbal preparations are frequently considered to be less toxic with fewer side effects. Herbal medicine is a major component in almost all indigenous systems. Plant stanols/sterols, flavonoids and other polyphenols have been shown its beneficial effect in controlling hyperlipidemia. Thus, herbal medicines have been given a valuable status by WHO and has endorsed their safe and effective use (WHO Research Guidelines, 1993, Mahmood et al., 2010). In the way of making these systems globally acceptable is the lacks of standardized products are in need of phytochemical, pharmacological evidences (Suresh Baburaj, 2007). Hence to provide systematic scientific evidence for this plant, we made an effort to standardize the plant M. azedarach and to carry out its evaluation for the lipid lowering activity.

The pharmacognostical study not only gives the authentication but also ensures quality, purity and standard of the plant drug. According to WHO (WHO guidelines 2007) the macroscopical and microscopical description of a medicinal plant is the first step towards establishing the identity and the degree of purity of such material. The pharmacognostical parameters are major reliable and inexpensive criteria for confirmation of the crude drugs. Phytochemical screening to identify the presence of various phytochemical constituents such as alkaloids, amino acids, carbohydrates, fixed oils, flavonoids, glycosides, phenols, proteins, saponins, sterols and tannins. Estimations of phytoconstituents such as total phenolic content,
flavonoid content and tannin contents were also estimated. Investigation of natural raw materials in accordance with pharmacognostical principles is carried out by using methods of thin layer chromatography. Few marker compounds such as β sitosterol, lupeol, rutin quercetin and gallic acid were also identified and quantified in different extracts.

Oxidation and production of free radicals are an integral part of normal cell metabolism. An imbalance between reactive oxygen species (ROS) and endogenous antioxidant defense mechanisms (Enzymatic and non-enzymatic) of a cell leads to excessive production of reactive oxygen metabolites, creating a condition frequently termed as “oxidative stress”. Excessive oxidative stress has been implicated in the pathology and complications of CVD.

Prepared extracts of plant were screened for their scavenging activity using different in vitro methods such as 2,2-diphenyl-1-picryl hydrazyl (DPPH), scavenging of 2,2'-azino-bis (3-ethylbenz-thiazoline-6-sulfonic acid) diammonium salt (ABTS) radical cation assay, o-phenanthroline, reducing power methods. Further, total antioxidant capacities extracts were determined.

The most of the extract such as CHLMA, EAMA, MEMA and AQMA showed comparable free radical scavenging ability. However, EAMA, MEMA, CHLMA predominantly showed more potent scavenging of different free radicals as compared to other extracts.

Several authors have reported flavonoids, phenolics, sterols, terpenoids and coumarins as bioactive compounds (Samudram et al., 2008, Cavoski et al., 2012). We also quantified the amount of β sitosterol, lupeol, rutin quercetin and gallic acid were also identified and quantified in different extracts by using methods of thin layer chromatography (HPTLC)
Based on the estimations of the phytochemicals and \textit{in vitro antioxidant} studies extracts were screened for the lipid lowering activities in acute and chronic hyperlipidemic models. The results suggest that AQMA and MEMA extracts may have therapeutical potential in hyperlipidemic conditions.

These flavonoids and other polyphenolics have a role in hypocholesterolemic and hypolipidemic effects (Monfort \textit{et al.}, 1995; Son and Lewis, 2002). Tannins enhance the increase in activity of the endothelium bound lipoprotein lipase activity, which hydrolyzes triglycerides. Plant sterols decrease cholesterol absorption and increase excretion. Phytosterols compete with dietary and biliary cholesterol for incorporation into mixed mesicles in the intestinal lumen thus inhibiting their uptake. Observed antioxidant and hypolipidemic activity of \textit{Melia azedarach} may be attributed to these constituents identified from these sources. It could also result from synergizing action of a combination of several components.

We have synthesized few quercetin analogues characterized and screened for their lipid lowering activity, results obtained from these agents are comparable with extracts of \textit{Melia azedarach}.

Major outcome of the present study is this plant represents an important source of flavonoid, phenolic compounds. Experimental results suggest that \textit{M. azedarach} has the potential to be a candidate as a lipid lowering agent. However, mechanism of action needs to established, thus providing ample scope for further research on this plant.
References


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2. Vijaya Kumar S, Dhirendra B. Sanghai, Mallikarjuna Rao C., Shreedhara C.S.
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Other publications during tenure as Research Scholar
1. Jothi Varghese, Vijay Kumar Tumkur, Vasudev Ballal, Giliyar Subraya Bhat,
4. Prashanth Kumar S, Vijaya Kumar S, Dhirendra B Sanghai, C. S.
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Presentations

1. C S Shreedhara, S Vijaya Kumar, Dhirendra B Sanghai, Mallikarjuna Rao, N. Gopalan Kutty Simultaneous estimation of Quercetin and Gallic acid in *Melia azedarach* L. by Planar Chromatography, DUPHAT

