Available online at www.journalijmrr.com

INTERNATIONAL JOURNAL OF MODERN RESEARCH AND REVIEWS

ISSN: 2347-8314

Int. J. Modn. Res. Revs.
Volume 3, Issue 7, pp 721-725, July, 2015

ORIGINAL ARTICLE

HYPOLIPIDEMIC EFFICACY OF *BOERHAAVIA DIFFUSA* (LINN.) IN KIDNEY ON D-GALACTOSAMINE INDUCED FATTY LIVER IN MALE ALBINO WISTAR RATS

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Article History: *Received 15th May,2015, Accepted June 30th 2015, Published 1st July,2015*

ABSTRACT

Medicinal plants have been used in as a drug for various medical treatments since the beginning of civilization. The Medicinal plants were used by the folk to reduce high cholesterol, one of the main causes of heart disease. Hyperlipidemia stands as one of the leading health problem worldwide especially in developing countries like India. Lipids are fats in the blood stream, commonly divided in to cholesterol and triglycerides. Cholesterol circulates in the bloodstream and is involved in the structure and function of cells. Triglycerides are best viewed as energy that is either used immediately or stored in fat cells. Triglycerides are manufactured in the liver from the foods or by being absorbed from the intestine. The therapeutic potential of *Boerhaavia diffusa* was evaluated by D- Galactosamine induced hepatotoxicity in rats. Male albino wistar rats were orally treated with methanolic leaf extract of *Boerhaavia diffusa* (50, 100 and 200 mg/kg body weight) or silymarin (25 mg/kg) daily with administration of D- Galactosamine (400 mg/kg body weight- ip) only one day. D- Galactosamine induced fatty liver and significantly increased the levels of total cholesterol, free fatty acids, triglycerides and phospholipids in kidney when compared with control group. Treatment with *Boerhaavia diffusa* or silymarin consecutively for twenty eight days could significantly attenuate the levels of lipid profiles in kidney when compared with D- Galactosamine alone treated rats.

Keywords: *Boerhaavia diffusa*, lipid profiles, hepatotoxicity, D-Galactosamine, silymarin

1.INTRODUCTION

Traditional knowledge of herbal medicine can serve as a powerful approach to drug discovery. Plants are an important source of medicines for indigenous people and have a highly significant role in indigenous pharmacopoeias. These are easily available to all tribal peoples of the forest areas (Anurag *et al*., 2014). Plant drugs (Rexlin Shairibha and Rajadurai, 2012; Bailey *et al*., 1989) and herbal are frequently considered to be less toxic and free from side effects than synthetic one formulation (Mitra *et al*., 1996; Annapurna *et al*., 2001; Bhattacharya *et al*., 1997). Hepatitis is a common disease in the world especially in the developing countries. Despite, considerable progress in the treatment of liver diseases by oral hepatoprotective agents, search for newer drugs continues because the existing synthetic drugs have several limitations. Hence, there are many researchers of traditional medicines attempting to develop new drugs for hepatitis (Liu, 1989).

Galactosamine administration to rats resembles viral hepatitis both biochemically and histologically (Wojcicki *et al*., 2001) and inhibits the energy metabolism of hepatocytes (Mangeney *et al*., 1985). Moreover, Sire *et al*., (1983) showed that galactosamine injures the enzymes involved in the transport of substrates to the mitochondria and modifies the phospholipid composition of membranes. Furthermore, galactosamine is thought to induce hepatotoxicity by inhibiting the synthesis of RNA and protein through a decrease in cellular UTP concentration, which finally leads to the necrosis of liver cells which can be measured by the activities of certain liver function enzymes, such as aminotransferases (Decker and Keppler, 1974). The mechanisms responsible for galactosamine toxicity are characterized by inhibition of nuclear RNA synthesis accompanied by nuclear fragmentation or by inhibition of protein synthesis followed by accumulation of aggregates between the stacks of rough endoplasmic reticulum (Wojcicki *et al*., 2001)

Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin (Porter and Bennett, 1981). A number of therapeutic agents can adversely affect the kidney resulting in acute renal failure, chronic interstitial nephritis and nephritic syndrome because there is an increasing number of potent therapeutic drugs like aminoglycoside antibiotics, NSAID's, chemotherapeutic agents have been added to the therapeutic arsenal in recent

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years (Hoitsma *et al*., 1991). Exposure to chemical reagents like ethylene glycol, carbon tetrachloride, sodium oxalate and heavy metals such as lead, mercury, cadmium and arsenic also induces nephrotoxicity. Prompt recognition of the disease and cessation of responsible drugs are usually the only necessary therapy (Paller, 1990). Nephroprotective agents are the substances which possess protective activity against Nephrotoxicity. Medicinal plants have curative properties due to the presence of various complex chemical substances (Mohana lakshmi *et al*., 2012).

Boerhaavia diffusa, is commonly known as rakta punarnava (Kokate *et al*., 2004) of family Nyctaginaceae (Bhalla *et al*., 1971) is mainly diffused perennial herbaceous creeping weed of India (known also under its traditional name punarnava). The plant root possesses diuretic, hepatoprotective and cardiotonic (Rawat *et al*., 1997), hypotensive (Devi 1986), immunomodulating (Hansen *et al*., 1995), antioxidative (Pandey et al., 2005), antihemorrhagic (Sathees *et al*., 2004), antispasmodic (Barthwal et al., 1991), antimicrobial (Borrelli *et al*., 2006), cytotoxic (Hilou *et al*., 2006), and anticancerous (Leyon *et al*., 2005) activities. The present study was aimed to evaluate the antihyperlipidemic role of methanolic extract of *Boerhaavia diffusa* against D-Galactosamine induced renal toxicity in male albino wistar rats.

2.MATERIALS AND METHODS

Procurement and rearing of experimental animals

Adult male albino rats (Wistar strain) were collected from Central Animal House, Rajah Muthiah Medical College, Annamalai University and were used for the present study. The rats were housed in polypropylene cages at room temperature (28 ± 2°C). The animals were randomized and separated into normal and experimental groups of body weight ranging from 160-200 g. The animals received a diet of standard pellets (Hindustan Lever Ltd., Bombay). Rats were provided free access to water *ad libitum* and food through the tenure of acclimatization to the environment for a minimum period of two weeks prior to commencement of experiment. The study was approved by the Institutional Animal Ethical Committee of Rajah Muthiah Medical College (160/1999/CPCSEA, Proposal No. 1025), Annamalai University, Annamalainagar, Chidambaram.

Preparation of methanolic extract

The collected *Boerhaavia diffusa* leaves were air dried and powdered. The powdered *Boerhaavia diffusa were* kept in airtight containers in a deep freeze until the time of use. A sample containing 1 kg of *Boerhaavia diffusa* was mixed with 4000 mL of methanol and stirred magnetically overnight (12 h) at 37°C. This was repeated three consecutive times. The residue was removed by filtration and the extract evaporated to dryness at a lower temperature (<40°C) under reduced pressure in a rotary evaporator. The residual extract was dissolved in normal physiological saline and used in the study. The yield of the extract was approximately 38.55 g.

The suitable optimum dosage schedule were identified by administering the methanolic extract of *Boerhaavia diffusa* extracts at different dosages (50, 100, 200, 400 and 800 mg/kg body weight) in a day daily for twenty eight days. The optimum doses were selected as 50, 100 and 200 mg/kg body weight of the animals for twenty eight days respectively.

EXPERIMENTAL DESIGN

The animals were divided into 7 groups of 6 rats each.

Group 1: Control rats given physiological saline solution 10 mL/kg body wt..

Group 2: Rats given D-Galactosamine (400 mg/kg body wt./ip) for one day only.

Group 3: Rats given D-Galactosamine + *Boerhaavia diffusa* (50 mg/kg body wt.) administered orally using an intragastric tube.

Group 4: Rats given D-Galactosamine + *Boerhaavia diffusa* (100 mg/kg body wt.) administered orally using an intragastric tube.

Group 5: Rats given D-Galactosamine + *Boerhaavia diffusa* (200 mg/kg body wt.) administered orally using an intragastric tube.

Group 6: Rats given D-Galactosamine + silymarin (25 mg/kg body wt.) administered orally using an intragastric tube.

Group 7: Rats given *Boerhaavia diffusa* (200 mg/kg body wt.) alone administered orally using an intragastric tube.

At the end of the experimental period in 24 h after last treatment the animals were killed by cervical decapitation. The kidney tissues were excised immediately and washed with chilled physiological saline.

Biochemical analysis

Kidney tissues were taken into centrifuge tube with rupper caps labeled and centrifuged at 3000 rpm for 15 minutes. Lipid profiles such as cholesterol, Phospholipids, triglycerides and free fatty acids (Zlatkis *et al*., 1953; Zilvermit and Davis, 1950; Foster and Dunn, 1973; Falholt *et al*., 1973) respectively.

Statistical analysis

Statistical analysis was done by analysis of variance (ANOVA) and the groups were compared by Duncan's multiple range test (DMRT). The level of statistical significance was set at $p \leq 0.05$(Duncan, 1957).

3.RESULTS

The level of lipid profiles in kidney was estimated in normal and experimental rats. There was a significant elevation of the kidney lipid profiles in rats treated with D-Galactosamine when compared with the corresponding control rats. Administration of methanolic extracts of *Boerhaavia diffusa* 50, 100, 200 mg/kg body weight and silymarin to D-Galactosamine treated rats caused a significant reduction in kidney lipid profiles when compared with D-Galactosamine alone treated rats. No effects were observed on kidney of lipid profiles when extract alone was administered rats (Table 1).

Table 1. Renal lipid profiles in control and experimental groups

Groups	*Total cholesterol (mg/g)*	**Phospholipids (mg/g)**	**Tryglycerides (mg/g)**	**Free fatty acids (mg/g)**
Control	4.65 ± 0.35^{a}	17.32 ± 1.32^{a}	3.94 ± 0.30^{a}	6.22 ± 0.47^{a}
D-Galactosamine (400mg/kg)	11.38 ± 0.86^{e}	28.65 ± 2.18^{d}	7.56 ± 0.57^{d}	12.47 ± 0.95^{f}
D-Galactosamine + *Boerhaavia diffusa* (50 mg/kg)	10.21 ± 0.78^{d}	27.43 ± 2.08^{d}	7.10 ± 0.54^{d}	11.24 ± 0.86^{e}
D-Galactosamine + *Boerhaavia diffusa* (100 mg/kg)	8.05 ± 0.61^{c}	25.15 ± 1.91^{c}	6.24 ± 0.47^{c}	9.68 ± 0.73^{d}
D-Galactosamine + *Boerhaavia diffusa* (200 mg/kg)	5.72 ± 0.43^{b}	19.21 ± 1.46^{a}	5.46 ± 0.42^{b}	7.15 ± 0.54^{b}
D-Galactosamine + Silymarin (25 mg/kg)	7.48 ± 0.57^{c}	22.14 ± 1.68^{b}	5.95 ± 0.46^{bc}	8.36 ± 0.64^{c}
Boerhaavia diffusa (200 mg/kg) alone	4.52 ± 0.41^{a}	17.19 ± 1.31^{a}	3.89 ± 0.30^{a}	6.18 ± 0.47^{a}

All the values are mean ± SD of six observations. Values which are not sharing common superscript differ significantly at 5% level ($P < 0.05$). Duncan Multiple Range Test (DMRT).

4.DISCUSSION

For the past two decades, there has been an increasing interest in the investigation of medicinal plants as potential sources of new therapeutic agents (Feroz *et al.*, 2013). Study of herbal drugs is gaining more attention due to their ameliorating effect on acute and chronic disease conditions. The plant extracts have been used in traditional medicines for centuries, since they act as a source of antioxidants and efficient pharmacophores (Rajamurugan *et al.*, 2012). Galactosamine produces liver damage, with histopathological changes resembling human viral hepatitis (Thakur, 2002). Galactosamine administration in rats produced cholestasis, due to inhibition of the synthesis of bile acids and also their conjugation with proteins or to damage in the biliary system (Pradhan and Girish, 2006).

Cholesterol, triglycerides, and high-density lipoproteins are important constituents of the lipid fraction of the human body. Cholesterol is an unsaturated alcohol of the steroid family of compounds; it is essential for the normal function of all animal cells and is a fundamental element of their cell membranes. It is also a precursor of various critical substances such as adrenal and gonadal steroid hormones and bile acids. Triglycerides are fatty acid esters of glycerol and represent the main lipid component of dietary fat and fat depots of animals. Cholesterol and triglycerides, being non polar lipid substances (insoluble in water), need to be transported in the plasma associated with various lipoprotein particles (Rafael *et al.*,1990). Phospholipids are vital components of biomembrane.

The increased concentration of free fatty acids in liver and kidney may be due to lipid breakdown and this may cause increased generation of NADPH, which results in the activation of NADPH dependent microsomal lipid peroxidation. Phospholipids is present in cell membrane and make up vast majority of the surface lipoprotein forming a lipid bilayer that acts as an interface with both polar plasma environment and non-polar lipoprotein of lipoprotein core (Cohn and Roth 1996). The increased concentration of cholesterol could result in a relative molecular ordering of the residual phospholipids resulting in a decrease in membrane fluidity (Dario *et al.*, 1996). Phospholipids are vital part of biomembrane rich in PUFA, which are susceptible substrate for free radicals such as O2 •- and OH• radicals (Ahmed *et al.*, 2001). These phospholipids are important for the maintenance of cellular integrity, microviscosity and survival (Sailaja *et al.*, 2004).

In the present investigation, oral administration of methanolic extract of *Boerhaavia diffusa* 50, 100, 200 mg/kg and silymarin to D-Galactosamine treated rats showed that decrease the enhanced levels of cholesterol, phospholipids, triglycerides and free fatty acids in kidney when compared with D-Galactosamine alone treated rats. Simillarly oral administration of extracts of *Astracantha longifolia* on carbon tetrachloride treated rats shows minimize the lipid profiles in kidney (Muthulingam, 2002). Dried flowers of *Adenocalymma alliaceum* when fed at 2% level for 6 weeks to hypercholesterolaemic rats, lowered serum cholesterol levels significantly, lowering the absorption of dietary cholesterol from the intestines (Srinivasan *et al.*, 1995). *Curcuma xanthorrhiza* reduced serum triglycerides (Yasni *et al.*, 1993). *Ocimum sanctum* powder supplementation reduced serum triglycerides (Rai *et al.*, 1997). Ginger (*Zingiber officinale*) reduced serum and tissue triglycerides (Murugaiah *et al.*, 1999). Saraswat *et al.*, (1995) reported that the significant anticholestatic effect of silymarin in comparison to andrographolide. *Semecarpus anacardium* (Bhallatak, nut shell) extract also exhibited hypocholesterolemic action and prevented cholesterol induced atheroma in hypercholesterolaemic rabbits (Sharma *et al.*, 1995). *Terminalia belerica* reduced the levels of lipids in experimentally induced hypercholesterolaemia in rabbits. There was also a significant decrease in liver and heart lipids (Shaila *et al.*, 1995). Administration of ethanolic extract of *Plumbago zeylanica* root, alone and in combination with vitamin E, significantly reduced serum total cholesterol, LDL cholesterol and triglyceride levels in experimentally induced hyperlipidaemic rabbits (Ram, 1996). Administration of cell culture extract of *Hemidesmus indicus* in rats also receiving an atherogenic diet prevented hypercholesterolaemia (Bopanna *et al.*, 1997). Roots of winter cherry (*Winthania somnifera*) significantly decreased serum triglycerides in humans (Andallu *et al.*, 2000). *Allium victorialis* decreased serum total triglycerides in rabbits and mouse (Kim *et al.*, 2000). Administration of 100 and 200 mg/kg per day of aqueous extract of *Eclipta prostrate* showed statistically significant decrease in total cholesterol and triglyceride level as compared to hyperlipidemic animals (Dhandapani, 2007). Administration of methanolic and aqueous leaf extract of *Psidium guajava* (200 mg/kg, and 400 mg/kg) to hyperlipidemic rats shows that significantly decrease in serum

triglycerides, total cholesterol and LDL-Cholesterol levels as well as significant decrease in Atherogenic index value (Shinde *et al*., 2013; Venu gopalarao *et al*., 2013). Oral administration of methanolic and n-Hexane extract of *Boswellia ovalifoliolata* to D- Galactosamine / Lipopolysaccharide treated rat's shows that increase the levels of HDL and decrease the levels of cholesterol, triglycerides, LDL and VLDL cholesterol when compared with D- Galactosamine / Lipopolysaccharide alone treated rats (Kadam *et al*., 2015). The administration of ethanolic extract of leaves of *Portulaca oleracea* (200 and 400 mg/kg) to dexamethasone induced hyperlipidemia rats showed significant inhibition against dexamethasone induced hyperlipidemia in rats by maintaining the serum levels of cholesterol, triglycerides and near to the normal levels (Pragda et al., 2012). Annie Felicia (2013) reported that methanolic extract of *Indigofera tinctoria* reduced the cholesterol, phospholipids, triglycerides and free fatty acids in the kidney of paracetamol treated rats.

5.CONCLUSION

It is concluded that treatment with methanolic extract of *Boerhaavia diffusa* decreases the D-Galactosamine induced toxicity and renal lipid profiles. These findings suggest that the methanolic extract of *Boerhaavia diffusa* was reduce the cholesterol, phospholipids, triglycerides and free fatty acids in kidney. Reduction of renal lipid profile may be the action of flavanoids and β- sitosterol were present in the plant, *Boerhaavia diffusa*.

6.ACKNOWLEDGEMENT

The author thankful to DST- SERB (File No.SR/FT/LS-142/2011) for financial support, Dr. N. Indra, Professor and Head, Department of Zoology, Dr. S. Sethupathy, Professor and Head, Department of Biochemistry, Rajah Muthiah Medical College and Hospital and Authorities of Annamalai University for providing facilities.

7.REFERENCES

Ahmed, M., Shikha, H.A., Sadhu, S.K., Rahman, M.T and Datta, B.K., 2001. Diuretic, and anti-inflammatory principle from *Scoparia dulcis*. *Pharmazie*., 56:657-660.

Andallu, B and Radhika, B., 2000. Hypoglycemic, diuretic and hypocholesterolemic effect of winter cherry (*Withania somnifera*, Dunal) root. *Ind. J. Expe. Bio*. 38:607-609

Annapurna A, Kanaka R, Mahalakshmi D, Murali Krishna K., 2001. Antidiabetic activity of a polyherbal preparation (tincture of punchparna) in normal and diabetic rats. *Indian J Exp Biol*., 39:500-502.

Annie Felicia, F., 2013. Antihepatotoxic efficacy of *Indigofera tinctoria* (Linn.) on paracetamol induced liver damage in rats. Ph.D Thesis, Annamalai University, Chidambaram, India.

Anurag, S., Shivendra, S., Gopal, K and Ajai Kumar, P., 2014. Traditional Knowledge and Ethnopharmacological Perspectives of Herbal Medicine in India: A Review, *Journal of Medicinal Plants Studies,* 2(1): 89-96.

Bailey CJ, Day C. Traditional treatments for diabetes. *Diab Care*. 1989; 12:553-564.

Barthwal, M and Srivastva, K., 1991. Management of IUD associated menorrhagia in female rhesus monkeys (*Macaca mulatta*). *Adv. Contracept*. 7(1): 67–76.

Bhalla, T.N., Gupta, M.B and Bhargava, K.P., 1971. Antiinflammatory activity of *Boerhaavia diffusa*. *Journal of Research in India Medicine*. 6: 11-15.

Bhattacharya, S.K., Satyan, K.S and Chakrbarti, A., 1997. Effect of Trasina, an Ayurvedic herbal formulation, on pancreatic islet superoxide dismutase activity in hyperglycaemic rats. *Indian J Exp Biol*. 35:297-299

Bopanna, K.N., Bhagyalakshmi, N and Rathod, S.P., 1997. Cell culture derived Hemidesmus indicus in the prevention of hypercholesterolemia in normal and hyperlipidemic rats. *Indian J Pharmacol*, 29:105-109.

Borrelli, F, Ascione, V., Capasso, R., Izzo, A. A., Fattorusso, E and Taglialatela-Scafati, O., 2006. Spasmolytic effects of nonprenylatedrotenoid constituents of *Boerhaavia diffusa* roots. *J. Nat. Prod*. 69: 903-906.

Cohn, R.M and Roth, K.S., 1996. Lipid and lipoprotein metabolism. In *Biochemistry and disease* Williams and Wilkins Publishers, *Baltimore*; 280-283.

Dario, G., Antonio, C and Giuseppe, P., 1996. Oxidative stress and diabetic complications. *Diabetes Care*., 19:257-267.

Decker, K and Keppler, D., 1974. Galactosamine hepatitis: Key role of the nucleotide deficiency period in the pathogenesis of cell injury and cell death. *Rev. Physiol. Biochem. Pharmacol*. 71: 77-106.

Devi, M.V., 1986. Effect of *Phyllanthus niruri* on the diuretic activity of punarnava Tablets. *Res. Educ. Ind. Med*. 5: 11-12.

Dhandapani, R., 2007. Hypolipidemic activity of *Eclipta prostrata* (L.) L. leaf extract in atherogenic diet induced hyperlipidemic rats. *Indian Journal of Experimental Biology*, 45: 617-619.

Duncan, B.D., 1957. Multiple range tests for correlated and heteroscedastic means. *Biometrics*, 13: 359-364.

Falholt K, Falholt W, Lund, B., 1973. An easy colorimetric method for routine determination of | free fatty acids in plasma. *Clin Chim Acta*, 46:105-111.

Foster, L.B. and Dunn, R.T., 1973. Stable reagents for determination of serum triglycerides by a colorimetric Hantzsch condensation method. *Clin. Chem*., 19: 338-340.

Feroz, Z, Khan, R.A., Amber and Mahayrookh, 2013. Impact of herbal drug combination on lipid profile, renal and cardiac parameters. *Pak J Pharm Sci.*, ;26(4):819-22.

Hansen, K., Nyman, U., Smitt, U.W., Adsersen, A., Gudiksen, L., Rajasekharan, S and Pushpangadan, P., 1995. In vitro screening of traditional medicines for anti-hypertensive effect based on inhibition of the angiotensin converting enzyme (ACE). *Journal of Ethanopharmacology*.48: 43-51.

Hilou, A., Nacoulma, O.G and Guiguemde, T.R., 2006. In vivo antimalarial activities of extracts from *Amaranthus spinosus* L. and *Boerhaavia erecta* L. in mice. *J. Ethanopharmacol*.103: 236-240.

Hoitsma, A.J., Wetzels, J.F and Koene, R.A., 1991. Drug induced nephrotoxicity. Aetiology, clinical features and management, *Drug Saf*, 6 (2): 131-147.

Kadam, S.D., Sreedhar, C and Chandrasekha, K.B., 2015. D-Galactosamine / Lipopolysaccharide induced hepatoprotective activity of *Boswellia ovalifoliolata, Journal of Academia and Industrial Research,* 3(8): 348-354.

Kim, T. G., Kim, S.H., Kang, S.Y., Jung, K.K., Choi, D.H., Park, Y.B., Ryu, J.H and Han, H.M., 2000. Antiatherogenic effect of the extract of *Allium victorialis*

on the experimental atherosclerosis in the rabbit and transgenic mouse. *Kor. J. Pharm*. 31:149-156.

Kokate, C.K., Purohit, A.P and Gokhale, S.B., 2004. Pharmacognosy edition 13 Nirali Prakashan Pune. 593-597.

Leyon, P.V, Lini, C.C and Kuttan, G., 2005. Inhibitory effect of *Boerhaavia diffusa* on experimental metastasis by B16F10 melanoma in C57BL/6 mice. *Life Sci*.76: 1339- 1349.

Mangeney, M., Sire, O., Montagne, J and Nordmann, J., 1985. Effect of D-galactosamine in vitro on [U-14 C] palmitate oxidation, triacylglycerol synthesis and secretion in isolated hepatocytes. *Biochem. Biophys. Acta*. 833: 119-127.

Mitra, S.K., Gopumadhavan, S., Muralidhar, T.S., Anturlikar, S.D and Sujatha, M.B., 1996. Effect of a herbomineral preparation D-400 in streptozotocin induced diabetic rats. *J Ethnopharmacol*. 54: 41-46.

Mohana lakshmi, S., Usher, K.R and Tand Sandhya Rani, K.S., 2012. A review on medicinal plants for nephroprotective activity, *Asian J Pharm Clin Res*, 5 (4): 8-14.

Murugaiah, J. S., Nalini, N., Menon, V.P and Namasivayam, N., 1999. Effect of ginger (*Zingiber officinale* R.) on lipids in rats fed atherogenic diet. *J. Clin. Bio. Nutr*. 27:79-87.

Muthulingam, M. 2002. Studies on the curative efficacy of *Astercantha longifolia* on carbon tetrachloride induced hepatotoxicity in rats. *Ph.D. Thesis*, Annamalai University.

Paller, M.S., 1990. Drug induced nephropathies *Med Clin North Am*, 74 (4):909-917.

Pandey R, Maurya R, Singh G, Sathiamoorthy B and Naik S (2005) Immunosuppressive properties of flavonoids isolated from *Boerhaavia diffusa* Linn. *Immuno pharmacology*. 5: 541-553.

Porter, G.A and Bennett, W.M., 1981. Nephrotoxic acute renal failure due to common drugs *American journal of Physiology*, 241(7): F1-F8.

Pradhan, S.C and Girish, C., 2006. Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine, *Indian J Med Res* 124 : 491-504.

Pragda, S., Kuppast, I.J., Mankani, K.L and Ramesh, L., 2012. Evaluation of antihyperlipidemic activity of leaves of *Portulaca oleracea* Linn against Dexamethasone induced hyperlipidemia in rats. *Int J Pharm Pharm Sci*, 4 (4) : 279-283.

Rafael, A., Cox and Mario, R., 1990. Garcia-Palmieri Laboratory31 Cholesterol, Triglycerides, and Associated Lipoproteins, II. The cardiovascular system, Physical, and Laboratory Examinations**,** Clinical Methods, 3rd edition The History, 53-160.

Rai, V., Mani, U.V and Iyer, U.M., 1997. Effect of *Ocimum sanctum* leaf powder on blood lipoproteins, glycated proteins and total amino acids in patients with non-insulin-dependent diabetes mellitus. *J. Nut. Env. Med*. 7:113-118.

Rajamurugan, R., Suyavaran, A., Selvaganabathy, N., Ramamurthy, C.H., Pramodh Reddy, G., Sujatha, V and Thirunavukkarasu, C., 2012. Brassica nigra plays a remedy role in hepatic and renal damage. Pharmaceutical Biology, 50(12): 1-10.

Ram, A., 1996. Effect of *Plumbago zeylanica* in hyperlipidaemic rabbits and its modification by vitamin E. *Indian J Pharmacol*, 28:161-166.

Rawat, A.K.S., Mehrotra, S., Triphati, S.K and Sharma, U., 1997. Hepatoprotective activity in Punarnava- a popular Indian ethno medicine. *Journal of Ethnopharmacology*. 56(1): 61-68.

Rexlin Shairibha, S.M and M. Rajadurai, 2012. Effect of Glymin, a Polyherbal formulation on lipid profile and histopathological examination in streptozotocin-induced diabetic rats. *International Journal of Pharmaceutical Sciences and Drug Research*, 4(1): 49-55.

Sailaja, Y.R., Baskar, R., Srinivas Rao, C.S and Saralakumari, D., 2004. Membrane lipids and protein-bound carbohydrates status during the maturation of reticulocytes to erythrocytes in type 2 diabetes. *Clin Chim Acta*, 341:185-192.

Saraswat, B., Visen, P.K.S., Patnaik, G.K and Dhawan, B.N., 1995. Effect of andrographolide against galactosamine-induced hepatotoxicity. *Fitoterapia*. 66 : 415-20.

Satheesh, M.A and Pari, L., 2004. Antioxidant effect of *Boerhavia diffusa* L. in tissues of alloxan induced diabetic rats. *Indian J Exp Biol*. 42: 989-992.

Shaila, H.P., Udupa, A.L and Udupa, S.L., 1995. Preventive actions of *Terminalia belerica* in experimentally induced atherosclerosis. *Int J Cardiol*, 49:101-106.

Sharma, A., Mathur, R and Dixit, V.P., 1995. Hypocholesterolemic activity of nut shell extract of *Semecarpus anacardium* (Bhilawa) in cholesterol fed rabbits. Indian J Exp Biol, 3:444- 448.

Shinde, S., Chivate, N., Kulkarni, P and Naikwade, N., 2013. Hypolipidemic activity of *Psidium guajava* Linn leaves extracts in hyperlipidemic rats. *Int J Pharm Pharm Sci*.,, 5(1): 70- 72.

Sire, O., Mangeney, M., Montagne, J., Nordmann, R and Nordmann, J., 1983. Carnitine palmitoyltransferase I. Inhibition by D-galactosamine and role of phospholipids. *Eur. J. Biochem*. 136: 371-375.

Srinivasan, M.R and Srinivasan, K., 1995. Hypocholesterolemic efficacy of garlic-smelling flower *Adenocalymma alliaceum* Miers. in experimental rats. *Indian J Exp Biol*, 33:64-6.

Thakur, S.K., 2002. Silymarin- A hepatoprotective agent. *Gastroenterol Today*, 6 : 78-82.

Venu gopala rao, K., Madhavi, E., Ruckmani, A and Venkataramana, Y., 2013. A review on medicinal plants with potential hypolipidemic activity, *Int J Pharm Bio Sci*, 4(4): 729 – 740.

Wojcicki, J., Samochowiec, L and Hinek, A., 2001. The effect of cernitin on galactosamine-induced hepatic injury in rat. *Int. Pharmacol. Toxicol*. 72: 70-111.

Yasni, S., Imaizumi, K., Nakamura, M., Aimoto, J and Sugano, M., 1993. Effects of *Curcuma xanthorrhiza* Roxb. and curcuminoids on the level of serum and liver lipids, serum apolipoprotein A-I and lipogenic enzymes in rats. *Food. Chem. Toxico*. 31:213-218.

Zilversmit, B.B. and Davis, A.K., 1950. Micro determination of plasma phospholipids by TCA Precipitation. *J. Lab. Clin. Med*., 35: 155-160.

Zlatkis, A., Zak, B and Boyle, A.J., 1953. A new method for the direct determination of serum cholesterol. *J. Lab. Clin. Med*., 41: 486-492.

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