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Hypolipidemic effect of *Asteracantha longifolia* L. (Nees.) in kidney on Thioacetamide induced Fatty liver in Rats

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Abstract

Plants have been considered as wellsprings of therapeutic specialists for the treatment of numerous sicknesses. The therapeutic potential of *Asteracantha longifolia* L. (Nees) was evaluated by thioacetamide induced fatty liver in rats. Male albino wistar rats were orally treated with *Asteracantha longifolia* (50, 100 and 200 mg/kg body weight) or silymarin (25 mg/kg) daily with administration of Thioacetamide (100 mg/kg body weight- s.c) only one day. Thioacetamide induced fatty liver and significantly increased the levels of total cholesterol, free fatty acids, triglycerides and phospholipids in kidney as compared with control group. Treatment with *Asteracantha longifolia* or silymarin successively for twenty eight days could notably decrease the levels of renal lipid profiles in kidney when compared with Thioacetamide only treated rats. Thus, our results indicate that the administration of 200 mg/kg BW *Asteracantha longifolia* extract restores near normal lipid profile in thioacetamide-diabetic rats.

The lipids are huge biomolecules. Cholesterol is an essential part of the human cell membrane, and they are significant antecedent to steroid chemicals and bile acids. Indeed, even triglyceroids play a critical capacity in communicating energy from food to body cells. Any overabundance biomolecule isn't ideal for human wellbeing[12,23]. Hyperlipidemia is one of the significant danger variables of atherosclerosis illnesses[32]. Hyperlipidemia contributes essentially in the appearance and improvement of atherosclerosis and coronary heart illnesses (CHD). Atherosclerosis is the most well-known reason for mortality and horribleness around the world. Albeit a few elements, for example, diet high in immersed fats and cholesterol, age, family ancestry, hypertension, and way of life, assume a critical

part in causing cardiovascular breakdown, the undeniable degrees of cholesterol, especially total cholesterol (TC), fatty oil (TG), and low-density lipoprotein (LDL) cholesterol, are mostly answerable for the beginning of CHDs. About 20% decrease of blood cholesterol level can diminish about 31% of CHD occurrence and 33% of its death rate[38]. It characterized as the rise of serum TC, TG, VLDL, LDL and HDL, which are answerable for different confusions like heart assault, coronary conduit condition, stroke, atherosclerosis, myocardial dead tissue and pancreatitis[5].

The movement of diabetes has been expanding internationally from 108 million (1980) to 463 million (2019) with 1.6 million passings in 2016 credited to them around the world, assessed to ascend to 578 million (10.2%) by 2030 and 700 million by 2045. As indicated by the WHO, about 80% of the population is utilizing natural drugs in the point of treating a few sicknesses and acquiring developing consideration in worldwide medical care discussions[7,18,29,39].

Ayurveda has been the first to give an intricate depiction of this sickness, its clinical highlights and the examples and its administration by home grown or herbomineral drugs. Plant drugs are regularly viewed as less harmful and liberated from results than manufactured ones[30]. As of late, plant-based meds have pulled in the consideration of mainstream researchers as novel defensive and even helpful systems for the administration of a few illnesses, particularly weight, because of their bioactive segments. The ethnobotanical and ethnopharmacological approaches used to assess the remedial significance of plants give a strong premise to add to the choice of the plants to be additionally evaluated to create novel phytotherapeutic meds[14]. In this specific situation, *Asteracantha longifolia*, superb helpful worth plant.

Asteracantha longifolia L. (Nees.) (synonym: *Hygrophila auriculata* (K. Schum) Heine *H. schulli* (Ham.) MR and SM Almeida, *H. spinosa* T. Anders. *Barleria auriculata* Schum and *B. longifolia* L.) has a place with family Acanthaceae[33]. *Asteracantha longifolia* (*Kokilaksha*) is a yearly spice having great therapeutic worth generally appropriated in India, Sri Lanka, Malaysia and Nepal and widely utilized in diuretics, jaundice, kidney stone, stiffness, liver brokenness, urinogenital issues, and so on. It is rich with steroids, alkaloids, butelin, lupeol and unsaturated fats additionally utilized in diabetes and diarrhea[19]. *Kokilaksha* is a yearly spice that grows up to the stature of 60 cms normally known as *Neermulli, Talmakhana, Kokilaksha* and *Iksura* is a typical plant filling in mucky and water logged territories[8]. *Asteracantha longifolia* has been reported to have hypoglycemic movement in human subjects[16], hepatoprotective action against paracetamol and thioacetamide intoxification in rodents[36] and CCl_4-actuated liver dysfunctions[34], antitumor[25], antidiabetic action[27]. *Hygrophila auriculata* seeds have been accounted for to enhance the exercises of activities of antioxidant enzymes glutathione peroxidase (GPx) and catalase (CAT) in hepatocarcinoma[1].

However there are no reports regarding the lipid profiles in kidney of methanolic extract of *Asteracantha longifolia* to thioacetamide

induced fatty liver. The present study was aimed to evaluate hypolipidemic role of *Asteracantha longifolia* against thioacetamide induced fatty liver in rats.

Procurement and rearing of experimental animals :

Adult albino rats of both sexes weighing between 160-220 g were purchased from Biogen lab, Bengaluru. The animals were acclimatized for period of two weeks under ambient environmental conditions. They were allowed free access to grower's mash (Vital feeds) and water *ad libitum*. The investigation was endorsed by the Institutional Animal Ethical Committee of Rajah Muthiah Medical College and Hospital (160/1999/CPCSEA, Proposal No. 1168), Annamalai University, Annamalainagar, Chidambaram.

Preparation of Methanolic Extract :

The collected *Asteracantha longifolia* leaves were air dried and powdered. The powdered *Asteracantha longifolia* were kept in airtight containers in a deep freeze until the time of use. A sample containing 1 kg of *Asteracantha longifolia* was mixed with 4000 mL of methanol and stirred magnetically overnight (12 h) at 3oC. This was repeated three consecutive times. The residue was removed by filtration and the extract evaporated to dryness at a lower temperature (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 g. The optimum doses were selected methanolic extract of *Asteracantha longifolia* 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 Thioacetamide (100mg/ kg body wt./s.c) for one day only.

Group 3: Rats given Thioacetamide + *Asteracantha longifolia* (50 mg/kg body wt.) administered orally using an intragastric tube.

Group 4: Rats given Thioacetamide + *Asteracantha longifolia* (100 mg/kg body wt.) administered orally using an intragastric tube.

Group 5: Rats given Thioacetamide + *Asteracantha longifolia* (200 mg/kg body wt.) administered orally using an intragastric tube.

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

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

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[15,17,41] respectively.

Statistical analysis :

Statistical analysis was done by analysis of variance (ANOVA) and the groups

were compared by Duncan's multiple range test (DMRT)[13]. The level of statistical significance was set at $p \leq 0.05$.

The level of total cholesterol, phospholipids, triglycerides and free fatty acids were estimated in normal and experimental rats. There was a significant elevation of the kidney lipid profiles in rats treated with thioacetamide when compared with the corresponding control rats. Administration of methanolic extracts of *Asteracantha longifolia* 50, 100, 200 mg/kg body weight and silymarin to Thioacetamide treated rats caused a significant reduction in kidney lipid profiles when compared with thioacetamide alone treated rats. No effects were observed on kidney of lipid profiles when extract alone was administered rats (Table-1).

Table-1. Kidney lipid profiles in control and experimental groups

Groups	Total cholesterol (mg/g)	Phospholipids (mg/g)	Tryglycerides (mg/g)	Free fatty acids (mg/g)
Control	5.49 ± 0.33^{a}	18.26 ± 1.30^{a}	4.89 ± 0.29^{a}	7.18 ± 0.45^{a}
Thioacetamide (100 mg/kg)	13.72 ± 0.91^{e}	31.16 ± 2.23^{d}	9.35 ± 0.61^{d}	14.55 ± 0.98^{f}
Thioacetamide + *Astracantha longifolia* (50 mg/kg)	11.54 ± 0.75^{d}	27.22 ± 2.03^{d}	8.48 ± 0.55^{d}	12.64 ± 0.89^{e}
Thioacetamide + *Astracantha longifolia* (100 mg/kg)	9.18 ± 0.67^{c}	26.37 ± 1.88^{c}	7.54 ± 0.49^{c}	10.75 ± 0.78^{d}
Thioacetamide + *Astracantha longifolia* (200 mg/kg)	6.61 ± 0.40^{b}	19.76 ± 1.43^{a}	6.25 ± 0.40^{b}	8.21 ± 0.57^{b}
Thioacetamide + Silymarin (25 mg/kg)	8.53 ± 0.57^{c}	23.10 ± 1.65^{b}	6.91 ± 0.44^{bc}	9.39 ± 0.67^{c}
Astracantha longifolia (200 mg/kg) alone	5.51 ± 0.35^{a}	18.21 ± 1.31^{a}	4.86 ± 0.28^{a}	7.15 ± 0.44^{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).

For as far back as twenty years, there has been expanding revenue in the examination of restorative plants as likely wellsprings of new helpful specialists. Investigation of home grown medications is acquiring consideration because of their improving impact on intense and ongoing sickness conditions. The plant removes have been utilized in conventional meds for quite a long time, since they go about as a wellspring of cell reinforcements and productive pharmacophores[6]. Lipid profiles are hazard pointers of coronary illness. Adjustments in lipids and lipoprotein levels, particularly hypercholesterolemia, bring about an assortment of chronis confusions like coronary heart illnesses and atherosclerosis[4]. In most of all around created nations, cardiovascular infections are the main source of death. The most well-known reason for cardiovascular infections is atherosclerosis, which keeps on creating from youth in patients with lipid issues[10,20].

The kidney is an imperative organ to actualize significant jobs like a discharge of harmful substances and metabolites, and homeostasis upkeep. The kidney is a significant objective organ for poisonous elements. Internationally, renal (kidney) dysfunctions are considered as a significant medical condition. Intense renal injury is identified with various causes like synthetic poisonousness, consumes, stun, sepsis, injury and serious looseness of the bowels, at whatever stage in life[28].

Thioacetamide (TAA; CH_3CSNH_2), an organosulfur compound, is commonly used as a fungicide owing to its generation of sulfide ions that prevent the germination of fungal spores. TAA is also widely used as an in situ source of sulfide ions in qualitative inorganic analysis to replace hydrogen sulfide in the pharmaceutical and chemical industries. The routes of human exposure to TAA include the generation of toxic fumes inhaled/ingested or absorbed through the skin. TAA is a model toxicant of choice due to its water-soluble nature and remarkable ability to induce assault. TAA belongs to the class 2B-type carcinogens and results in acute liver and cytomegaly. Acute exposure to TAA leads to necrosis as well as changes in chronic calcium permeability to the membrane due to an imbalance in calcium uptake, leading to apoptosis in the liver tissue. TAA affects the ending of the proximal renal tubule by causing cell death. When TAA is bioactivated, thioacetamide S-oxide is formed which leads to the generation of peroxide radicals further leading to the generation of reactive oxygen species (ROS). ROS initiates oxidation reactions such as lipid peroxidation to unsaturated lipids or triggers other reactions with sulfhydryl compounds, leading to liver injury[40]. Additionally, it has been accounted for that TAA can likewise harm distinctive organ frameworks other than liver, including lungs, digestive tract, kidneys, spleen, thymus and pancreas subsequently can change amine lipids and proteins prompting further fundamental oxidative stress, cytokine discharge, and

altered kidney function that remain poorly understood[2].

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. Phospholipids are vital components of biomembrane[31].

The impacts of methanolic concentrate of *Asteracantha longifolia* on the degrees of all out cholesterol, Triglycerides (TG) and FFA in kidney tissues of control and exploratory rodents are appeared in Figure. These outcomes uphold the theory that cholesterol stores in the lipid drops of the fat tissue cells is delivered into plasma and is the central wellspring of the hypercholesterolemia saw during pressure. Our outcomes showed expanded degrees of tissue cholesterol, fatty substances, FFA in thioacetamide-actuated rodents and this was for the most part because of an expanded esterified cholesterol division. The increment in serum complete cholesterol levels might be because of the blockage of the liver bile conduits, which decreases or stops cholesterol discharge into the duodenum[22]. Methanolic concentrate of *Asteracantha longifolia* co-controlled rodents essentially diminished these lipids levels in thioacetamide-incited rodents, in this way uncovering the hepatoprotective impact of methanolic impact of *Asteracantha longifolia*. Simillarly oral organization of concentrates of *Astracantha longifolia* on carbon tetrachloride treated rodents shows limit the lipid profiles in kidney[26].

Thioacetamide actuates changes in the quality articulation of some hepatic proteins. Therefore, level of cholesterol was expanded in blood and furthermore fringe tissues[37]. Expanded cholesterol (Hypercholesterolemia) is a significant danger of Coronary Heart Diseases (CHD). Concentrate of *Asteracantha longifolia* leaves fundamentally decreased the cholesterol level which demonstrated the hypo cholesterolemic action of leaves separate. The impact of plant extricate on cholesterol level was like standard medication impact. No critical contrast was seen in charge and plant removes treated rodents.

Cholestasis is brought about by a decrease in bile stream; it significantly expands the corrosive degrees of both the liver and serum bile and from that point may prompt intense liver harmfulness, multiplication of bile channels, and inevitable cirrhosis[9,21] announced that organization of oil ether concentrate of *Opuntia dillenii* against CCl_4 treated rodents showed lessen the complete cholesterol when contrasted and CCl_4 alone treated rodents. Organization of methanolic concentrate of *Asteracantha longifolia* (AL) seeds to APAP treated rodents showed diminished the absolute cholesterol, fatty substances, Free unsaturated fats expanded when contrasted

and APAP alone treated rodents [35].

Roots of winter cherry (*Winthania somnifera*) altogether diminished serum fatty oils in people[3]. *Allium victorialis* diminished serum complete fatty substances in bunnies and mouse[24]. Organization of 100 and 200 mg/kg each day of watery concentrate of *Eclipta prostrate* showed measurably critical decline in complete cholesterol and fatty substance level when contrasted with hyperlipidemic creatures[11].

In the present study administration of Thioacetamide treated rats showed an increase in the level of total cholesterol, phospholipids, triglycerides and free fatty acids tissues (Kidney) when compared with control rats. Oral administration of methanolic extract of *Asteracantha longifolia* (50, 100 and 200 mg/kg body weight) and silymarin to Thioacetamide treated rats showed reverse trends when compared with Thioacetamide alone treated rats.

It is concluded that treatment with methanolic extract of *Asteracantha longifolia* decreases the thioacetamide induced toxicity and renal lipid profiles. These findings suggest that the methanolic extract of *Asteracantha longifolia* was reduce the cholesterol, phospholipids, triglycerides and free fatty acids in kidney. The study demonstrates that, methanolic extract of *Asteracantha longifolia* have a potential hypolipidemic properties in rats.

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Conflict of interest :

The authors declare that there is no conflict of interest regarding this study.

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