EVALUATION OF ANTIHYPERLIPIDEMIC EFFECT OF HYDRO-ALCOHOLIC LEAF EXTRACT OF *ERIOLAENA HOOKERIANA* IN RATS

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Submitted by

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CERTIFICATES

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **EVALUATION OF ANTIHYPERLIPIDEMIC EFFECT OF HYDRO-ALCOHOLIC LEAF EXTRACT OF *ERIOLAENA HOOKERIANA* IN RATS,** submitted by the student bearing **REG.No.261725207** to "**The Tamil Nadu Dr. M.G.R. Medical University – Chennai**", in partial fulfilment for the award of Degree of **Master of Pharmacy** in **Pharmacology** was evaluated by us during the examination held on……..…….

Internal Examiner **External Examiner**

CERTIFICATE

This is to certify that the work embodied in this dissertation entitled **EVALUATION OF ANTIHYPERLIPIDEMIC EFFECT OF HYDRO-ALCOHOLIC LEAF EXTRACT OF *ERIOLAENA HOOKERIANA* IN RATS** submitted to "**The Tamil Nadu Dr.M.G.R. Medical University- Chennai**", in partial fulfilment and requirement of university rules and regulation for the award of Degree of **Master of Pharmacy** in **Pharmacology**, is a bonafide work carried out by the student bearing **REG.No.261725207** during the academic year 2018-2019, under the guidance and supervision of **Dr.Shanmuga Sundaram, Ph.D.,** Professor, Department of Pharmacology, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

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DECLARATON

I do hereby declared that the dissertation submitted to **EVALUATION OF ANTIHYPERLIPIDEMIC EFFECT OF HYDRO-ALCOHOLIC LEAF EXTRACT OF *ERIOLAENA HOOKERIANA* IN RATS'' The Tamil Nadu Dr. M.G.R Medical University - Chennai",** for the partial fulfilment of the degree of **Master of Pharmacy** in **Pharmacology,** is a bonafide research work has been carried out by me during the academic year 2018-2019, under the guidance and supervision of **Dr.Shanmuga Sundaram, Ph.D.,** Professor, Department of Pharmacology, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

I further declare that this work is original and this dissertation has not been submitted previously for the award of any other degree, diploma, associate ship and fellowship or any other similar title. The information furnished in this dissertation is genuine to the best of my knowledge.

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CONTENTS

1. INTRODUCTION

Herbal medicines are the oldest remedies known to mankind. Herbs had been used by all cultures throughout history. In the last few years, there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects when comparing other system of medicine. India being the botanical garden of the world with more than 2400 medicinal plants out of 21000 species being listed by WHO, is the largest producer of medicinal plants around the globe.

Hyperlipidemia is a disorder of lipid metabolism manifested by increase of plasma concentrations of the various lipid and lipoprotein fractions such as increase of serum total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG) concentrations, and a decrease in the high-density lipoprotein (HDL) concentration. Hyperlipidemia is the key risk factor for cardiovascular disorders and has been reported as the most common cause of death in developed as well as developing nations. Hyperlipidemia may be caused by specific genetic abnormalities called primary hyperlipidemia or may be idiopathic caused by lifestyle habits or medical diseases such as diabetes, kidney disease, pregnancy, hypothyroidism and heart disease.[1]

Hyperlipidemia prevalence continued to increase annually, requiring the development of drugs capable of lowering blood lipids to reduce mortality and morbidity due to cardiovascular complications. Although synthetic lipid-lowering drugs are useful in treating hyperlipidemia, there are number of adverse effects. So, the current interest has stimulated the search for new lipid-lowering agents with minimal side effects from natural sources.

Eriolaena hookerianais a large, evergreen tree, 10-15m in height, indigenous to the evergreen forests at altitude of 450-1,200m and cultivated throughout the hotter parts of India. Leafof this plant is straight rough whereas bark is green or black, 1.25cm thick, exuding milky latex, leaves broad obovate, elliptic, decurrent, glabrous, entire inflorescence solitary axillaries, cauliforous and ramflours on short leafy shoots. Male head is sessile or on short peduncles receptacles, sometimes born on the ultimate twing, Female head are oblong ovoid receptacle, syncarpus, cylindrics. Seeds are separated horny endocarpus enclosed by sub-gelatinous exocarpus (1mm thick)

oblong ellipsoid in nature. The sweet yellow sheaths around the seeds are about 3-5 mm thick and have a taste similar to that of pineapple, but milder and less juicy. Even though it is well known for its antibacterial, anti-inflammatory, anti-diabetic, antioxidant and immunomodulatory properties there are no evidences regarding the anti-hyperlipidaemic effect of the leafhence our study has its relevance

The biggest organ in the body is the "LIVER" and it is likewise fills in as the essential metabolic organ of the body. In spite of the fact that the liver is comprised of various cells like hepatocytes, endothelial, kupffer and stellate cells are the most dominating with critical capacities. Another most essential one of a kind component of the liver is its capacity to recover. Well grown-up liver (i.e. Grown-up) is the standard organ accountable for detoxifying andmetabolizing, exogeneous/endogenous mixes, rendering them more hydrophilic, which as often as possible impact their force and action.

Liver infections are the genuine restorative issues went up against by the people wherever all through the world. The epidemiological review demonstrates that around 20,000 passings happen reliably in light of liver issue. In Africa and Asia, the major drivers of liver maladies are contaminations by infection and parasite, while in Europe and in North America, a vital reason is liquor manhandled. Liver ailments are primarily realized by deadly chemicals, over the top affirmation of ceaseless liquor, diseases and immune syleafissue. Hepatic harm by over measurements of drug appears, from every angle, to be a run of the mill contributing component. Liver is required to do physiological limits and additionally to guarantee against the perilous of dangerous drugs and chemicals. Prescription impelled substance damage is accountable for 5% of each mending focus attestation and half of all serious liver disappointment. Over 75% of episodes of specific prescription reactions achieve liver transplantation or death.[2]

Pathophysiological Mechanisms

Pathophysiological components of hepatotoxicity are as yet being found and contain both hepatocellular/extracellular systems.

Disturbance of hepatocyte: Medications can bind to intracellular proteins by covalent tying which realize a reducing in ATP levels inciting actin intrusion. Some portion of actin fibrils at the surface of the hepatocyte causes blebs and burst of the layer.

Interruption of transport protein

Bile stream might be hindered by meds that impact transport proteins at canalicular film. Loss of villous strategies and interruption of transport pumps, for instance, multidrug resistance-related protein 3 hinder release of bilirubin realizing cholestasis

Cytolytic T-cell actuation: Co-valent binds of pharmaceutical to Cytochrom P-450 compound goes about as an immunogen enacting T-cells and cytokines and energizing multifaceted safe responses.

Apoptosis of hepatocytes: Enhancement of apoptotic pathways by tumour rot calculate alpha receptor of Fas may trigger the course of intercellular caspases, which achieve altered cell passing.

Mitochondrial disturbance: A couple of meds limit mitochondrial limit by twofold effect on both beta-oxidation vitality creations by frustrating the union of nicotinamide adenine dinucleotide and flavin adenine dinucleotide, realizing decreased ATP era.

Bile pipe damage: Dangerous metabolites discarded in bile may achieve mischief to bile course epithelium.[3]

Solution/sedate incited liver harm is a prosperity issue, and is depended upon to increase as the amount of drugs being eaten up augmentations, both remedy and non-solution, and in view of the present example of usage of pharmacologically dynamic substances in correlative and option prescription. Prescription/tranquilize incited hepatotoxicity is the most surely understood reason alluded for withdrawal of authoritatively endorsed meds from the business. It also speaks to more than 50 percent of occasions of serious liver disappointment in the United States. The positive recurrence of solution/medication incited liver harm is difficult to gage, and all things considered, concentrates going to measuring its event encounter the evil impacts of drawbacks, for instance, under-detailing and that data by expansive start from audit thinks about. Frequently, there is in like manner a non-attendance of information about self-arrangement and use of home grown item that may associate with prescription and non-doctor embraced medications4.

Despite the repeat of solution actuated liver harm being low, data from the Centre for Disease Control and Prevention in the U.S. report pretty much 1600 new extraordinary examples of liver disappointment yearly, of which Paracetamol

hepatotoxicity speaks to plus or minus 41%. Exactly when taking a sexual orientation at hospitalized patients, the rate of hostile solution reactions is assessed to be 6.7%, and deadly disagreeable medicine reactions mean 0.32%, as controlled by a meta-investigation of around 40 imminent reviews. Amid the period 1995 to 2005, the reports of horrible prescription reactions and also passing related to these, have drastically increased. Various examples of pharmaceutical activated liver harm are particular, i.e. the reaction is whimsical considering the known pharmacological properties of the medication, and from this time forward is scarcely perceptible amid preclinical periods of change. There are however studies to demonstrate that these reactions might be liable to an extended affectability of the patient to the medicine being alluded to, dependent upon such segments as other going with contaminations or other relating prescriptions. Certain innate factors, for instance, HLA-sort, can once in a while add to the affectability of a man to opposing pharmaceutical reactions. Commonly, clinically clear hostile drug reactions happen when some season of inertness, wherever in the compass going from one to 12 months (most by and large within 90 days), and about constantly vanish after departure of the solution. Pharmaceutical researched liver damage may give a couple of unmistakable clinical segments; hepatitic/hepatocellular, cholestatic or mixed.

Regardless of their etiology, solution/tranquilize prompted hepatotoxicity remains a significant issue amid medicine advancement in the pharmaceutical business, both concerning extended threat for patients encountering clinical trials, besides tolerant hazard after the acquaintance of new drug with the treatment. Moreover, because of the extended costs that takes after disappointment of a prescription to-be at a late stage in medicine improvement or after its launch.

Drug Toxicity Mechanisms

Commonplace division of pharmaceutical responses is of at the very least 2 significant events which include:

- Drugs which clearly impact liver.
- Drugs which intervene a safe response.

Characteristic/unsurprising medication responses: Drugs that has a place into this characterization cause reproducible injuries in creatures and mischief is related to measurements. Mischief can be a result of medicine itself or to its metabolite.

Acetaminophen is the most proper delineation of a known regular or obvious hepatotoxin at supertherapeutic measurements. Another outline is carbon tetrachloride.

Quirky/eccentric medication responses: These medication reactions can be portioned into those that are named excessive touchiness or immunoallergic and those that are metabolic-particular. It occurs without evident measurement reliance and in an unusual manner

Hepatotoxicity to a great extent demonstrates the compound constrained liver devastation. A few drugs when devoured in overdose and once in a while notwithstanding when taken inside suggest measurement may harm numerous inner organs. Few compound/substances involving those that are utilized as a part of research facilities (example: CCl4 and Paracetamol) and ventures (Lead, and arsenic) and characteristic mixes (microcystine and aflatoxins) and home grown treatments (cascara sagrada, ephedra) can likewise root hepatotoxicity.

Chemicals/Compounds that cause liver harm are as one marked as hepatotoxins:

- NSAIDS (acetaminophen, aspirin, ibuprofen)
- Glucocorticoids.
- Against Tubercular medication (isoniazid).
- Mechanical poisons (arsenic, carbon tetrachloride, vinyl chloride).
- Natural cures (ackee organic product, camphor, cycasin, kava leaves, valerian, and comfrey).

Liquor Hepatotoxicity

Liquor is one of the key inducer of end-stage liver harm far and wide. In the United States, alcoholic liver malady is the second most normal reason behind liver transplantation. The Dionysos Study, an accomplice examination of the transcendence of unending liver malady in an Italian people, showed that 21% of the masses considered were at peril for making liver harm. Of these, only 5.5% of the general population at peril implied at genuine liver harm. Around 50 years earlier it was acknowledged that liquor in itself was not destructive, rather that the dietary deficiencies every now and again running as an inseparable unit with it were the genuine purposes behind liver damage. Regardless, it was demonstrated by Lieber and

De Carli that in rats, alcoholic liver harm made despite satisfactory sustenance. The lethality of liquor was later on exhibited to be related to its absorption framework by liquor dehydrogenases (ADHs) moreover to the assimilation framework by CYP2E1. There is also a piece of assimilation framework by catalase. The basic pathway for ethanol (EtOH) oxidation in the liver is by method for ADH to acetaldehyde, which is associated with the diminishment of NAD to NADH. NADH in this way constructs xanthine oxidase activity, which rises era of superoxide. Metabolic arrangement of EtOH by liquor dehydrogenase impacts the redox status of the liver in like manner in various ways. Lifted acetaldehyde creation after EtOH digestion syleafdecreases hepatic glutathione (GSH) content. The reducing in GSH is both on account of an extended disaster, and furthermore a lower rate of blend

Ethanol prompts number of harmful metabolic changes in liver. Admission of ethanol for long time prompts to advancement of steatosis, alcoholic hepatitis and cirrhosis bringing about weight and volume changes. Around 80% of overwhelming consumers had been accounted for to create steatosis, 10-35% alcoholic hepatitis and roughly 10% liver cirrhosis7.

Ethanol-induced hepatotoxicity

Liquor utilization brings about increment in arrival of endotoxin from gut microbes and layer porousness of gut to endotoxin or both. Females are all the more frequently touchy to these progressions. Blood endotoxin is lifted and enters liver where it is overwhelmed by Kupffer cells that get to be distinctly actuated discharging TNF-alpha, PGE2 and free radical. Prostaglandins increment oxygen take-up and are in charge of hypermetabolic state in liver. Increment in oxygen request prompts to hypoxia of liver and on reperfusion alpha - hydroxyethyl free radicals are framed that prompts to tissue harm in oxygen poor pericentral districts of liver lobule. Obstructing of these occasions should be possible by sanitization of gut utilizing anti-infection agents or decimation of Kupffer cells with Gdcl3 and in this manner averts liver injury8.

Symptoms of Hepatotoxicity

Signs and side effects delineated in different foundations for Hepatotoxicity incorporate 15 side effects as recorded below:[9]

- Sickness
- Regurgitating
- Stomach torment
- Loss of hunger
- Looseness of the bowels
- Tiredness
- Shortcoming
- Jaundice
- Yellow eyes
- Yellow skin
- Hepatomegaly
- Irregular liver capacity test comes about
- Swelling in feet
- Weight increase because of water maintenance
- Delayed draining time.

Treatment for Hepatotoxicity

The rundown of medications specified in different hotspots for hepatotoxicity incorporates the accompanying. Continuously take after expert restorative guidance about any treatment or change in treatment arranges. Treatment of hepatotoxicity is relies on causative operator, level of liver brokenness and age and general strength of patient.

Medicines for hepatotoxicity include:

Withdrawal of causative solution or expulsion from introduction to causative specialist.

General checking of patient and survey of liver capacity – where liver brokenness is mellow to direct and liver capacity is moving forward.

Finish shirking of liquor and drug that may add to further liver harm.

N-Acetylcysteine is utilized for paracetamol harmfulness.

Administration of indications of liver harm.

- Nutrition – with vitamin supplementation as required
- Regular practice with a specific end goal to keep up bulk.
- Ursodeoxycholic corrosive.

- Administration of pruritus
- Cholestyramine
- Antihistamines.

Administration of ascites

- Low sodium eat less carbs.
- Diuretics – furosemide, spironolactone.
- Removal of liquid through a needle in the stomach area – Paracentesis.
- Portosystemic shunting.

Administration of entry hypertension

- Beta – blockers
- Oesophagealvariceal banding
- Portocaval shunt
- Administration of intense liver disappointment because of hepatotoxicity
- Supportive care dependably in emergency unit aviation route assurance, liquid and electrolyte administration.
- Management of intricacies, for example, draining issues and hepatic encephalopathy.
- Liver transplantation – for intense fulminant liver disappointment or end organize cirrhosis.

1.7.1 Present day Medicines for Treatment of Liver Diseases

Liver illnesses can be dealt with utilizing allopathic and in addition by utilizing home grown medications.

Hepatoprotective Allopathic Treatment

Couple of present day drugs are accessible for treating liver illnesses that incorporates:

Ursodeoxycholic corrosive (Ursodiol): Ursodiol diminishes intestinal retention and stifles hepatic union and capacity of cholesterol. It is predominantly utilized as a part of administration of constant hepatic ailments in people.

Penicillamine: Penicillamine chelates a few metals like copper, iron, lead and mercury shaping stable water dissolvable edifices which are renally discharged.

Different medications

Antiviral pharmaceutical, for example, alpha interferon, ribavirin, steroids, anti-infection agents and so on are additionally utilized as a part of liver ailments. Drugs like tricholinecitrate, trithioparamethoxy phenyl propane, basic phospholipids, blend of medications, for example, L-ornithine, L-aspartate and pancreatin, silymarin and Ursodeoxycholic corrosive are generally recommended for hepatitis, cirrhosis and other liver sicknesses. N-acetylcysteine is utilized as a part of early periods of acetaminophen harmfulness. L-carnitine is conceivably significant amid valproate poisonous quality. Cholestyramine can be utilized to mitigate pruritus.

Inconveniences of allopathic medications

Symptoms of numerous cutting edge medications are generally disturbing. Collaborations, contra-cooperations, reactions and danger of engineered pharmaceutical shift from gentle to extreme that incorporates sleep deprivation, regurgitating, weariness, dry mouth, looseness of the bowels, blockage, tipsiness, self-destructive thought, despondency, seizures, pallor, male pattern baldness, high glucose, swelling, impotency, perplexity, blacking out lastly passing. Anti-microbials more often than not bring about stomach furious or unfavorably susceptible responses. Interferon indicates symptoms as influenza like ailment with fever and body throbs.

Natural Hepatoprotective Drug Treatment

Various polyherbal arrangements have been utilized as a part of treating different liver issue since ages. Some natural definitions include:

Constraints of natural arrangements

Natural based arrangements for treating liver issue has been utilized as a part of India for long time and has been promoted worldwide by selling pharmaceuticals. Regardless of prevalence of home grown prescriptions for liver illnesses specifically, are still inadmissible treatment modalities for liver sicknesses. Constraining variables include:

- Lack of institutionalization syleavesof home grown arrangements.
- Lack of recognizable proof of dynamic parts and standards.
- Lack of randomized controlled clinical trials (RCTs).

- Lack of toxicological evaluation.
- Poor solvency.
- Poor bioavailability.
- Poor hepatic cell recovery.

Hepatoprotective Mono-Herbal Medicines

Restorative plants are critical wellsprings of hepatoprotective medications. Very nearly 160 phytoconstituents from 101plants have been guaranteed by Pharmacopeia Foundation to have hepatoprotective action. Home grown medications are most generally utilized than allopathic medications as hepatoprotectives in light of the fact that these are normally cheap, better social adequacy, enhanced similarity with human body and insignificant symptoms. Different classes of phytoconstituents like flavonoids, triterpenes, lignans, steroids, glycosides, polyphenols, saponins, coumarins and unpredictable oils and so forth gangs hepatoprotective action.

Basically diabetes is characterized by hyperglycemia, a condition of lack of insulin and development of complications in nephrons of kidney, peripheral nerves and retinal damages. Considerable effect on heart has also be the problem of developing further complications leading to atherosclerotic threats to brain, myocardium and lower extremities. Hyperglycemia causes various kind of injury to vascular regions viz, increased pace of high glucose flux, intracellular production of advanced glycation products, activation of protein kinase and abnormal hexoseamine pathway. The increased mitochondrial reactive oxygen species (ROS) would lead to microvascular changes heart and other vital functions of organs and their complex pathways. The damage breaks out by ROS production both mitochondrial and non-mitochondrial results in, tumor formation, age-related degeneration, inflammatory conditions and diabetes mellitus. Better understanding of ROS production and its intervention strategies leading to solution to this problem with newer technologies. In this context major factor for onset of diabetes has been evidenced due to ROS generation. Further various animal studies confirm that embryos are more vulnerable to the oxidative stress especially in type 2 diabetes. Maternal abnormalities were developed and observed to be more prominent in heart and reduction in pregnancy of the animals has been notified.The existing methods of treating diabetes do not combat diabetic complications, so there is an increased need for effective treatment, which is

essential to fight with diabetic complications in relation to considerable reduction of ROS by using various technology and herbal drugs.

Consequences for Insulin Resistance and ROS production

In a condition pertaining to the high plasma levels of glucose and free fatty acids leads to increased production of reactive oxygen species (ROS) and to a least of reactive nitrogen species (RNS). In turn the initiation of various kinases starts occurring; proceed to phosphorylation of the insulin receptor and nitric oxide generation. Both the aforementioned pathways cause the signalling of insulin and suppress it drastically. Cascading reactions lends increased insulin resistance in liver, skeletal muscle and adipose tissues.As shown in the Fig 1. Increased free fatty acid level and lipid content are the prime factor for insulin resistant type2 diabetes. Besides, the production of ROS could be more due to free fatty acids are common and mitochondrial how ROS is produced is still not understood and yet to be explored.

ROS and associated Hypertension

The considerate onset of hypertension is due to the non-phagocytic NAD(P)H oxidase (Nox1, Nox 2 and Nox 4), apart from other factors for increased diabetic and hypertensive complications such as mitochondrial generation, inflammation, hypertrophy apoptosis, fibrosis, angiogenesis and rarefaction. Miscellaneous occurrence for ROS bounds to xanthine oxidase, cyclooxygenase, lipoxygenase and nitric oxide synthase..

Normal physiological processes affected by ROS are immunity, endocrine functions, embryogenesis and signal transduction at cellular level [13]. The intervention has given a tool to effectively control the ROS generation by antioxidants or nitric oxide production, to minimize the vascular injury, renal dysfunction and prevent target organ damage in diabetes and hypertension

Delayed Wound Healing Pattern – Increased ROS

Scoring up of ROS generation would lead to delayed wound healing, as it is the significant clinical problem to deal with to treat with different approach. Antioxidants have forecasted evidence for healing process to be very effective if it is provided. a study has provided robust substantiation in cultured fibroblast, a diabetic

phenotype and IGF1, which promotes wound healing on exposure to antioxidants. Pre-treatment of antioxidants increased the IGF1 has brought down diabetic complication and accelerate wound healing.

Basis for Diabetic and ROS

Long term diabetic causes are

i. Excess nourishment (Food)
ii. sedentary life style
iii. genetic or miscellaneous factors

All the above conditions leads to glucose and fatty acid overload, in addition the reaction of glucose with plasma proteins forms glycation end products and ROS. The ROS which in turn causes increased non-availability of nitric oxide, increased inflammatory mediators and modification of lipoproteins in atherosclerotic condition.

Common complications of diabetes due to ROS are

i. development of insulin resistance
ii. β- cell dysfunction
iii. type 2 diabetes
iv. increased glucose tolerance

Diabetic Nephropathy and ROS

ROS play an important role in commencement and progression of diabetic nephropathy. The roles of oxidative stress in pathogenesis of diabetes complications are evidenced. Vulnerability to glomeruli and retina is observed in patients with insulin resistance diabetes. A ROS-regulated signalling pathway leads to extracellular matrix (ECM) deposition in diabetic kidney was evidenced. ROS are increased in the glomeruli isolated from streptozotocin diabetic rats, providing a direct evidence of increased ROS in diabetic glomeruli.

An approach positively controls the nephritic damages are the treatment with antioxidants. As Antioxidants effectively inhibit high glucose and H_2O_2 induced activation in case of diabetic nephropathy, which would favor patients. The effect of antioxidant therapy is well documented in cell and animal studies, although convincing evidence for clinical efficacy is still lacking.

Exhaustive glycemic control and inhibition of angiotensin II delay the onset and progression of diabetic nephropathy, in part, through prevention of overproduction of

ROS. Antioxidants have been shown to prevent or delay the onset of diabetic nephropathy and its progression.

Role of ROS in insulin resistant type 2 diabetes

Receptor level binding of insulin at cell surface leads to the phosphorylation and various signaling pathways, which has been affected by ROS with increased insulin resistance and pancreatic cell dysfunction. Therapy with antioxidants like N-acetyl-L-cystine and taurine prevents the hyperglycemia induced by insulin resistance. In patients with type 2 diabetes, acute and chronic administration of lipoic acid, antioxidant, improved insulin resistance.

Role of Herbal antioxidants in ROS

The damaging effects of ROS is tackled effectively by antioxidants, normally superoxide and hydrogen peroxide are produced in the body. If excess quantities of generation leads to pathological ROS production. Many herbs has the potential to compromise ROS such as green tea, grape seed, ginseng and *Scutellariabaicalensis*. Long while herbal medicines used for the diabetes has been in existence. Current pre-clinical and clinical studies have demonstrated that many of them exhibit potent anti- inflammatory and anti-oxidative properties, and have also identified the active phytochemicals responsible for their activities.The herbal medicines and nutraceuticals, as well as their bioactive components, which exhibit anti-inflammatory and anti-oxidative properties, provide a promising approach for the prevention and treatment of diabetic complications. The etiology of diabetes and its complications are because of free radicals and for the reason herbs with antioxidant properties are believed to possess faith in controlling and minimizing the damage due the reactions. The list of some herbs used for diabetes and its complications are given in Nearly 400 herbs are accounting for diabetes treatment worldwide.

Acacia arabica (Babhul*)* has got anti-diabetic agent shown to have hypoglycemic effect. *Aegle marmelos* (Bengal Quince) which improves digestion and reduces blood glucose, urea and serum cholesterol level. *Allium cepa* (Onion) is a potential antioxidant, anti hyperglycemic and anti hyperlipedemic activity. *Allium sativum* (Garlic) has been used to increases insulin secretion and controls lipid peroxidation. *Aloe vera* stimulates β cell to secrete insulin, Anti-inflammatory and wound healing. *Azadirachtaindica (Neem) evidenced usinganti-hyperglycemic,*

hepatoprotective and antioxidant activities. Eugenia jambolana (Jamun) is a viable anti-hyperglycemic agent. *Mangiferaindica* (Mango*)* is a anti-diabetic agent, reduces intestinal glucose uptake. *Momordicacharantia* (Bitter gourd)is utilized as antidiabetic and antihyperglycemic Agent. *Ocimum Sanctum* (Holy basil) cause glucose level decline in fasting condition, triglyceride and total lipid content. *Phyllanthusamarus* (Bhuiawala) is aantinflammatory, anticancer, antioxidant and antidiarrhoeal. Certain formulations available for the diabetic treatments are given table 2

Bao et al studied icariin, a flavonoid of *Epimediumpubescens* known to have considerable antioxidant activity. They demonstrated cardiac functions and mitochondrial oxidative stress in streptomycin induced diabetic rats. The observations are in favor of controlling oxidative stress of cardiac complications in diabetes induced animal. An 8 weeks of administration markedly improved cardiac function and ROS has been proved effectively.

The nanotechnology is facing expansions in all dimensions for serving mankind, that almost all the countries are striving to explore for the social well-being and economy of the country. Nanoparticles are known to have tremendous applications in the field of diagnosis and theraphy. Such imperative nanoparticles have very great trait to carry and serve like an antioxidant, antihyperglycemic and ROS interfering action. Treatment of antidiabetic potent nanoparticle with plants would have therapeutic value do create a new platform for herbal medicines in nanoscience for drug delivery. Intentions of few antidiabetic nanoparticles of herbal origin are discussed.

Hyperlipidaemia mainly increased level of cholesterol or low-density lipoprotein cholesterol (LDL-C) contributes significantly to the manifestation and development of atherosclerosis and coronary heart diseases (CHDs). Cardiovascular diseases, including atherosclerosis, are the most common causes of mortality and morbidity worldwide. Approximately 12 million people reportedly die of cardiovascular disease each yearworld-wide. Although several factors such as diet high in saturated fats and cholesterol, age, family history, hypertension, and lifestyle play a significant role in causing heart failure, the high level of cholesterol, particularly LDL-C is mainly responsible for the onset of CHDs. The lowering of lipids and cholesterol levels by drug or dietary interventions could reduce the risk of CHDs. The known lipid-lowering drugs (fibrates, statins, bile acid sequestrants, etc.)

regulate the lipid metabolism by different mechanisms, but they also have many side effects.Therefore, the development of lipid-lowering drugs from natural sources is the best option and is in great demand. Medicinal plants continue to provide valuable therapeutic agents, both in modern medicine and in traditional systems.

Plants and many plant derived preparations have long been used as traditional remedies and in folklore medicine for the treatment of hyperlipidaemias in many parts of the world. There are many plants and their products that have been reputedly and repeatedly used in Indian traditional syleafof medicine**.** Recently, the search for appropriate antihyperlipidemic agents have been again focused on plants because of less toxicity, easy availability and easy absorption in the body that may be better treatment than currently used drugs. Plants that were once considered of no value are now being investigated, evaluated and developed in to drugs with no side effects. One of such plant is *S.hispida*Linn commonly known as *'Shaggi'* button weed' belongs tothe family *Rubiaceae* and is widely distributed throughout the world as a useful medicinal plant. The seeds of plants as confection are cooling demulcent and given in diarrhoea and dysentery. Seeds have been recommended as a substitute for coffee. Seeds are crushed in to paste and taken orally to treat stomach problems. According to some studies, *S. hispida*Linn has also anti-hypertensive activity. The plant has been extensively studied for its phytochemical composition and a large number of active ingredients such as, Borreline, β-sitosterol, Ursolic acid and Isorhmnatin. Recently, pharmacological studies have shown that *S.hispida*seeds exhibit antidiabetic properties in rats. Hence, in the present study, the ethanolic extract of *S. Hispida*seeds was investigated for Antihyperlipidaemic activity intriton WR-1339 induced hyperlipidaemic rats.

Feng Lin *et al.*, have demonstrated the preparation of nanosuspension of Cuscutachinensis, since its principles are majorly flavonoids which has got poor solubility. It drives them to make it more soluble formulation. The prepared formulations are tested with acetaminophen induced hepatotoxic rats. As the flavonoids are known to have antioxidant which has the caliber to control oxidative stress these components (flavonoids) are taken into account in this study. They observed only 50mg/kg of body weight of nanosuspension containing Cuscutachinensis, effective than 125mg/kg weight administered from ethanolic extract of same drug. In this context suggestions are given to increase the tough molecules solubility enhancement through nanotechnology

High antioxidant activity of *Dalbergiasissoo* (Indian Rosewood)

Nayan Roy *et al*., studied extracts of the plant leafbark, they intervened to extend they work towards invitro antioxidant determination by chemical method, using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity. In their experimentation of aqueous and methanolic extract they found aqueous extact has greater activity. They concluded that plant has high antioxidant activity and it may find it very useful in the treatment of diseases and complications caused by oxidative stress.

Nanoencapsulation of *Albiziachinensis*

Avneshkumar *et al.,* explained the nanoencapsulation of the herb having potential antioxidant activity of its content quercitrin. The polymer poly-D,L-lactide (PLA) is used to encapsulate the material and solvent evaporation technique was deployed to prepare the nanodimensions of the drug. The drug quercitin was made to encapsulate to increase the solubility, permeability and stability of the molecule. Moreover, the properties of nanomedcine has provided a new potential use of less useful highly active antioxidant molecule towards the development of oxidative stress related inflammation and its related complication profiles.

Antioxidant enriched Siylmarin Nanoparticles

Xia cao *et al.,* ventured in developing the porous silica nanoparticles of silymarin to increase the solubility as it has the considerable antioxidant activity. The silymarinnanoparitcles were prepared by porous microemulsion and ultrasonic corrosion methods. The results are bioavailability of silymarin was considerably increased despite the drugs basic poor solubility nature. The evidences are strong that herbal components are appropriate option for oxidative stress management in excessive ROS generation.

Metal andioxidant nanoparticle

As antioxidants have significant role in influencing ROS, such antioxidant nanoparticles are prepared from metals such as gold, silver and so on. These methods of producing metal antioxidant nanoparticle using plant extracts are extremely biosynthesized. Kannan et al explored syhthesis of gold nanoparticles using leaf extracts of *Coleus amboinicus*. The prepared nanoparticles are characterized by UV-

vis spectroscopy, XRD, TEM and SAED analyses. This method utilizes cheap production of nanoparticles with non-toxic nature. Praveenkumar et al studied gold nanoparticle synthesis using *Zingiberofficinale* extract. They got nanoparticles of size range 5 to 15 nm, and *Zingiberofficinale* as stabilizing and reducing agent which is more potent than asprin. Characterization was done by Dynamic Light scattering (DLS), TEM and UV-Vis Spectroscopy. The produced nanopartcles are biocompatible with the blood has been observed [35].

Diabetic treatment channelizing to the effective control of glucose level and specific strategy to target the ROS generating pathway curbing, do produce better results and compliments each other beneficially. Biologicalantioxidants capable of restraining oxidative stress mediated diabetic complication in due course of hyperglycemia are still mandatory to foresee better clinical improvements. The antioxidant enriched herbal components is the viable tool to cope with oxidative stress condition in diseased condition especially, the diabetes. Secondly, evidences are there that such components of antioxidant, antidiabetic and hypoglycemic herbs are tailored to nanotization for the maximum benefit. Provided with the strong scientific back up evidences, the clinical implications of nanotechnology based herbal constituents such as antioxidants are in great need to the mankind, to fight with oxidative stress related complications in diabetes and related ailments.

Table 1: The list of some herbs for diabetes and its complications

S.No	Botanical name	Common/Vernacular Name
1.	*Eugenia Jambolana*	Indian Gooseberry
2.	*Momordicacharantia*	Bitter gourd
3.	*Ocimum sanctum*	Holy Basil
4.	*Phyllanthusamarus*	Bhuiawala
5.	*Pterocarpus marsupium*	benga
6.	*Tinosporacordifolia*	*Guduchi*
7.	*Trigonellafoenum*	Fenugreek
8.	*Withaniasomnifera*	Ashwagandha
9.	*Allium sativum*	Garlic

Table 2: The list of herbs and its intention to intend

Name of Herb	Common/Vernacular	Intention/purpose
Acacia arabica	Babhul	Anti-diabetic agent shown to have hypoglycemic effect.
Aegle marmelos	Bengal Quince	Improves digestion and reduces blood glucose, urea and serum cholesterol level
Allium cepa	Onion	Antioxidant, anti-hyperglycemic and anti hyperlipedemic activity
Allium sativum	Garlic	Increases insulin secretion and controls lipid peroxidation
Aloe vera	Kathalai	Stimulates β cell to secrete insulin, Anti-inflammatory and wound healing
Azadirachtaindica	*Neem*	*Anti-hyperglycemic, hepatoprotective and antioxidant activity*
Eugenia jambolana	Jamun	Anti-hyperglycemic
Mangiferaindica	Mango	Anti-diabetic agent reduces intestinal glucose uptake.
Momordicacharantia	Bitter gourd	Antidiabeticand Antihyperglycemic Agent
Ocimum Sanctum	Holy basil	Glucose level decline in fasting condition, triglyceride and total lipid content
Phyllanthusamarus	Bhuiawala	Antiinflammatory, anticancer, antioxidant and antidiarrhoeal

Eriolaena hookeriana is one of the most significant trees in tropical homegardens and perhaps the most widespread and useful tree in the important genus *Lantana* . It is a medium-size evergreen tree typically reaching 8–25 m (26–82 ft) in height that is easily recognized by its fruit, the largest among cultivated plants. The succulent, aromatic, and flavorful fruit is eaten fresh or preserved in myriad ways. The nutritious seeds are boiled or roasted and eaten like chestnuts, added to flour for baking, or cooked in dishes. It is also known for its remarkable, durable timber, which ages to an orange or red-brown color. The leaves and fruit waste provide valuable fodder for cattle, pigs, and goats. Many parts of the plant includingthe bark, roots,

leaves, and fruit are attributed with medicinal properties. Wood chips yield a dye used to give the famous orange-red color to the robes of Buddhist priests. The tree can provide many environmental services. It is highly wind tolerant and therefore makes a good component in a windbreak or border planting. Growing in pastures, it can provide fallen fruit for livestock, shade, and long-term timber. In homegardens, the dense canopy can provide a visual screen and is very ornamental. Introduced to most Pacific islands after European contact, the tree can be found throughout the Pacific, mainly in homegardens, where it finds a place among other favorite multipurpose plants. It is easy to grow and more adaptable than some of the other common *Lantana* species such as breadfruit (*A. altilis*). It is not considered to be an invasive species.

2. LITERATURE REVIEW

Ganeshkumaret al., (2011)[34]explained in his study used aqueous extract from *Eriolaena hookeriana* leaves to evaluated for its hypocholesterolaemic and hypotriglyceridemic activities. The animals were divided into Normal (CG), Triton treated group (T), Triton plus Atorvastatin, Triton plus herb extract 200 mg/kg, Triton plus herb extract 400 mg/kg, treated groups. Oral administration of *Eriolaena hookeriana leaf* extract (200 mg/kg and 400 mg/kg) in both groups At 24 hrs after treatment with TRITON WR 1339 caused a significant decrease in serum lipid parameters like Triglycerides (TG), Cholesterol (CH), LDL- cholesterol, Atherogenic index (AI), LDL/HDL Ratio and Total proteins as like in atorvastatin treated groups. The both extract treated groups and atorvastatin treated group bought about a significant increase in HDL-Cholesterol levels levels.

Georgetaet al., (2013)[35] *studied the* wound healing activity of the leaves of *Eriolaena hookeriana* (moraceae) on ex-vivo porcine skin wound healing model and found that that the ethyl acetate extract of the leaves possesses potential wound healing activity.

Gómez-Pérez, et al., (2008)[36] examined the antioxidative, hypoglycemic, and hypolipidemic activities of *Eriolaena hookeriana* (jack fruit) leaf extracts. Various extracts like 70% ethanol n-butanol, water, chloroform, and ethyl acetate extracts are examined. The administration of 70% ethanol extract or n-butanol extract to streptozotocin (STZ)-diabetic rats significantly reduced fasting blood glucose (FBG) from 200 to 56 and 79 mg%, respectively; elevated insulin from 10.8 to 19.5 and 15.1

µU/ml, respectively; decreased lipid peroxides from 7.3 to 5.4 and 5.9 nmol/ml, respectively; decreased %glycosylated hemoglobin A1C (%HbA1C) from 6.8 to 4.5 and 5.0%, respectively; and increased total protein content from 2.5 to 6.3 and 5.7 mg%, respectively. Triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), VLDL-C, and LDL/HDL ratio significantly declined by -37, -19, -23, -37, and -39%, respectively, in the case of 70% ethanol extract; and by -31, -14, -17, -31, and -25%, respectively, in the case of n-butanol extract; as compared to diabetic rats. HDL-C increased by +37% (70% ethanol extract) and by +11% (n-butanol extract). Both JFEE and JFBE have shown appreciable results in decreasing FBG, lipid peroxides, %HbA1C, TC, LDL-C, and TG levels, and increasing insulin, HDL-C, and protein content.

Goyal et al. (2010)[37] investigated and evaluated the antimicrobial and phytochemical properties of *Eriolaena hookeriana* in leaf and leafbark extracts Hexane, dichloromethane and ethanol were used as extraction solvents and test organisms were Escherichia coli, Micrococcus luteus, *Aspergillus niger* and *Trichoderma sp.* A disc diffusion test was adopted to test the susceptibility of the selected microbes to the extracts while Minimum inhibitory concentration (MIC) was determined using serial dilution of extracts. Ethanolic leafbark extracts (30mg/ml) of *A.heterophyllus* exibi ts significant antibacterial activity against *Escherichia coli* with 9.50 ± 0.44 inhibition zone radii. Dichloromethane extracts of leaf and leaf bark showed lesser antibacterial activity against both of the bacteria with inhibition zones of 3.00 ± 0.34 mm to 5.66 ± 0.16 mm while hexane extracts did not show any antibacterial activity. Antifungal activity on the other hand was not detected in any of the extracts. Phytochemical screening confirmed the presence of phytosterols, anthraquinone, terpenoids, phenols, glycosides, flavonoids and diterpenes.

Gomez, et al., (2007)[38] herbal remedies have evolved with enormous impending of alleviate. Herbal medicine progress against the non-communicable disease like diabetes is one of the propel area of research in the field of worldwide medicine. Hyperlipidemia is a disorder of lipid metabolism manifested by increase of plasma concentrations of the assortment of lipid and lipoprotein fractions. Hyperlipidemia has been one of the maximum risk factors contributing to the occurrence and relentlessness of coronary heart diseases. HMG Co A reductase is a key enzyme involving in rate limiting step of cholesterol biosynthesis. Conservative anti-hyperlipidemic drugs have restricted efficacies and vital side effects, so that alternative lipid lowering agents are required. This review explains the plants possessing significant anti-hyperlipidemic activity with their botanical name, family, part used, extract used and inducing agent of hyperlipidemia

Gregersenet al., (2004)[39]in his study investigates the hypoglycemic and hypolipidemic effects of an ethylacetate (EA) fraction of the mature leaves of *A. heterophyllus* in a streptozotocin (STZ) induced diabetic rat model. In normoglycemic rats, administration of a single dose (20 mg/kg) of the EA fraction resulted in a significant ($P < 0.05$) reduction in the fasting blood glucose concentration and a significant improvement in glucose tolerance ($P < 0.05$), compared to the controls. In STZ-induced diabetic rats, chronic administration of the EA fraction of *A. Heterophyllus* leaves daily for 5 weeks resulted in a significant lowering of serum

glucose, cholesterol and triglyceride (TG) levels. Compared to control diabetic rats, the extract-treated rats had 39% less serum glucose, 23% lower serum total cholesterol and 40% lower serum TG levels and 11% higher body weight at the end of the fifth week.

Haraguchiet al., (2002)[40] in his study "Antidiabetic activity of *Eriolaena hookeriana rag* extract studied in high fat fed- low dose STZ induced experimental type 2 diabetic rats" reports that *Eriolaena hookeriana rag* possess antibacterial, anti-inflammatory, antioxidant and immunomodulatory properties. In the study Diabetic rats were treated with *Eriolaena hookeriana rag* extract at a dosage of 300 mg/kg b.w daily for 30 days. Metformin (200 mg/kg. b.w) was used as a reference drug and fasting blood glucose, plasma insulin and HbA1c were the parameters under consideration. The extract supplementation attenuated the elevated levels of glucose, glycosylated hemoglobin, AST, ALT and ALP. The insulin level was improved with an improvement in hepatic glycogen content of insulin resistant diabetic rats. The altered activities of glycogen metabolizing enzymes were normalized upon extract treatment. Also the extract improves insulin sensitivity which is evident from intraperitoneal insulin tolerance test. The results show that the rags of *Eriolaena hookeriana* is non-toxic and possess significant antidiabetic properties.

Heim et al., (2002)[41] Increasing drug resistance of pathogens and negative consequences of antibiotic usage has led to the search for alternative medicines from nature. Many plants have been exploited to cure infectious diseases from time immemorial. The present investigation evaluated the antimicrobial and phytochemical properties of *Eriolaena hookeriana i.e.* Jack fruit (Kos in Sinhala) and *Lantana altilis*

i.e. Bread fruit (Dhel in Sinhala) leaf and leaf bark extracts. Hexane, dichloromethane and ethanol were used as extraction solvents and test organisms were *Escherichia coli*, *Micrococcus luteus*, *Aspergillus niger* and *Trichoderma* sp. A disc diffusion test was adopted to test the susceptibility of the selected microbes to the extracts while Minimum inhibitory concentration (MIC) was determined using serial dilution of extracts. Phytochemical screening was carried out by specific chemical identification tests. Bioassay data were statistically analyzed using two-way ANOVA (SPSS 20 at 95% confidence level). Ethanolic leafbark extracts (30mg/ml) of *A.heterophyllus* and *A.altilis* possessed significant antibacterial activity against *Escherichia coli* with 9.50

± 0.44 mm and 7.49 ± 0.28 mm inhibition zone radii respectively. Dichloromethane extracts of leaf and leaf bark showed lesser antibacterial activity against both of the bacteria with inhibition zones of 3.00 ± 0.34 mm to 5.66 ± 0.16 mm while hexane extracts did not show any antibacterial activity. Antifungal activity on the other hand was not detected in any of the extracts. Bacterial antibiotic tetracycline and fungal antibiotic ketoconazole which were used as positive controls were more effective even at 1/10 concentration compared to all the plant extracts tested. Phytochemical screening confirmed the presence of phytosterols, anthraquinone, terpenoids, phenols, glycosides, flavonoids and diterpenes in both of the trees. These results confirm the potential antibacterial activity of *A.heterophyllus* and *A.altilis*

Hi Bahl et al., (2003)[42]studied Mangiferaindica L., known as mango (Family; *Anacardiaceae*), commonly used herb in ayurvedic medicine, traditionally used for their antidiabetic, anti-oxidant, anti-viral, cardiotonic, hypotensive, anti-inflammatory properties, antibacterial, anti-fungal, anthelmintic, anti-parasitic, anti-tumor, anti HIV, antibone resorption, antispasmodic, antipyretic, antidiarrhoeal, antiallergic, immunomodulation, hypolipidemic, anti-microbial, hepatoprotective, gastroprotectiveeffects. To investigate effect of aqueous extract of *Mangifera indica* leaf on high cholesterol fed diet rats. High cholesterol fed diet rats exhibited significant increase in total serum cholesterol, triglycerides, low density lipoprotein, very low density lipoprotein and significant decrease in high density lipoproteins. Treatment with aqueous extract of Mangifera indica leaves significantly decreased total serum cholesterol, triglycerides, low density lipoprotein, very low density lipoprotein and increased in high density lipoproteins rats. Hypolipidemic activity of *M. indica* may be attributed due to presence of flavonoids, Saponins, glycosides, tannins, phenolics.

Hideaki Kaneto et al., (2010)[43]detailed the hyperlipidemia plays an important role in the development of atherosclerosis, the main cause of death in the world. In this study, the lipid-lowering effect of *Carica papaya* leaf in rats fed with a high cholesterol diet was evaluated. Daily doses of *C. papaya* extract 0, 31, 62 or 125 mg/kg body weight were orally administered in 300µl polyethylene glycol to hypercholesterolemic rats; it was also administered 62 mg/kg body weight of the extract to rats with normal diet. After a 20-day treatment, the animals were sacrificed; blood and liver were analyzed. Hypercholesterolemic rats showed an increased serum and liver cholesterol, triacylglycerols, and atherogenic index. The *C.papaya* extract

produced a significant decrease of serum and liver cholesterol concentrations in hypercholesterolemic rats, but did not modify serum or liver triacylglycerols; however, the extract reduced the atherogenic index in a dose-dependent manner. *C. papaya* treatment decreased LDL-C and increased HDL-C in serum significantly. When the oxygen consumption was evaluated in phosphorylating and resting states, the respiratory control in hypercholesterolemic rats mitochondria was lower than in normal diet rats. However, a higher respiratory control in hypercho- lesterolemic rats mitochondria was observed after *C papaya* treatment. The liver morphological data are in accordance with serum and liver biochemical values. Our data support that *C. papaya* has a significant hypocholesterolemic action and HDL-C raising effect on rats fed with a cholesterol- rich diet, however, the precise metabolites responsible of this effect remain unknown**.**

Hirosumiet al., (2002)[44]The present study examines the antioxidative, hypoglycemic, and hypolipidemicactivities of *Eriolaena hookeriana* (jack fruit) leaf extracts (JFEs). The 70% ethanol(JFEE), n-butanol (JFBE), water (JFWE), chloroform (JFCE), and ethyl acetate (JFEAE)extracts were obtained. Both JFEE and JFBE markedly scavenge diphenylpicrylhydrazylradical and chelate Fe+2 *in vitro*. A compound was isolated from JFBE and identifiedusing 1D and 2D 1H- and 13C-NMR. The administration of JFEE or JFBE to Streptozotocin (STZ)-diabetic rats significantly reduced fasting blood glucose (FBG) from 200 to 56 and 79 mg%, respectively; elevated insulin from 10.8 to 19.5 and 15.1 μU/ml, respectively; decreased lipid peroxides from 7.3 to 5.4 and 5.9 nmol/ml, respectively; decreased %glycosylated hemoglobin A1C (%HbA1C) from 6.8 to 4.5 and 5.0%, respectively; and increased total protein content from 2.5 to 6.3 and 5.7 mg%, respectively. Triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), VLDL-C, and LDL/HDL ratio significantly declined by -37, -19, -23, -37, and -39%, respectively, in the case of JFEE; and by -31, -14, -17, -31, and -25%, respectively, in the case of JFBE; as compared to diabetic rats. HDL-C increased by +37% (JFEE) and by +11% (JFBE). Both JFEE and JFBE have shown appreciable results in decreasing FBG, lipid peroxides, %HbA1C, TC, LDL-C, and TG levels, and increasing insulin, HDL-C, and protein content. The spectrometric analysis confirmed that the flavonoid isolated from JFBE was isoquercitrin. We can conclude from this study that JFEE and JFBE exert hypoglycemic and hypolipidemic effects in STZ-diabetic rats through an antioxidative pathway that might be referred to their

flavonoid contents.

Hollman et al., (1999)[45]Herbal medicines have good curative effect on certain diseases especially for diabetes mellitus which needs continuous medication throughout the life. Present day allopathic medicines are costlier and having more side effects which could cause severe damages to the vital organs. Hence, finding a suitable herbal medicine for diabetes mellitus is very important in the current situation. In this present study, the fruit extract of *Helicteresisora* was used to evaluate the antihyperlipidemic activity in streptozotocin induced diabetic rats. Powdered fruits of *Helicteres isora* were extracted in ethanol and the crude extract was used for the treatment of diabetic rats. Streptozotocin was used to induce the diabetic condition in wistar rats. For the treatment, the drug glibenclamide also used to treat the diabetic rats to compare the efficacy of the herbal extract. After 45 days of treatment, the animals were sacrificed and lipid profiles were estimated in the serum and liver. The serum and liver lipid levels were abnormal in streptozotocin induced diabetic rats than in the control rats. Total cholesterol, triglycerides, phospholipids, LDL and VLDL were elevated and the HDL level was significantly decreased in diabetic rats. After treated with *Helicteres isora* fruit extract (HiFE), the lipid levels of diabetic rats were restored to near normal level. HiFE has the potential of antihyperlipidemic activity which was proved by the above results. It is suggested that HiFE may have the similar action mechanism of glibenclamide.

Hunjoo et al., (2008)[46]The anti-hyperlipidemic effect of methanolic extract of whole plant of *Rhinacanthus nasutus*(RNM) was tested in Triton and fat diet induced hyperlipidemic rat models. Here, Acute hyperlipidemia was induced by administration of single dose of Triton X 100 (400 mg/kg,i.p) and Chronic hyperlipidemia was induced by feeding fat diet for 21 days to rats. Treatment with RNM (200 and 400 mg/kg, p.o) significantly reduced the hyperlipidemia i.e., decreased levels of serum Total Cholesterol, Triglycerides, Low Density Lipoprotein Cholesterol (LDL-C), Very Low Density Lipoprotein Cholesterol (VLDL-C) , and increase of serum High Density Lipoprotein Cholesterol (HDL-C) when compared to vehicle control and standard drug Atorvastatin (10 mg/kg). The results demonstrated that methanolic extract of whole plant of *Rhinacanthus nasutus* possessed significant antihyperlipidemic activity.

Ibrahim et al., (2011)[47] designed to perform preliminary phytochemical screening, acute oral toxicity and to evaluate antihyperglycemic activity of whole

plant of *Glycosmis pentaphyla* ethanolic extract. .*Glycosmis pentaphylla,*whole plant vwas extracted using ethanol as solvent by soxhlet apparatus. The extract was subjected to preliminary phytochemical screening. Acute oral toxicity studies were performed to determine test dose. The evaluation of antihyperlipidemic activity was done using Triton X 100 and High Fat Diet induced hyperlipidemia models in Wistar albino rats. Preliminary phytochemical screening revealed the presence of alkaloids, carbohydrates, glycosides, saponins, tannins, flavonoids, proteins, and amino acids. Doses up to 2000mg/kg were found to be safe after acute toxicity tests. Cholesterol, triglycerides, HDL, LDL, VLDL, SGOT, SGPT, Total protein and glucose were measured. The results suggested that EGP (ethanolic extract.*Glycosmis pentaphylla*) possess antihyper lipidemic activity against hyper lipidemia induced by Triton X 100 and also High Fat Diet induced experimental models

InduBarwalet al., (2013)[48] were greatest risk factor of coronary heart disease. Currently available hypolipidaemic drugs have been associated with number of side effects. Herbal treatment for hyperlipidaemia has no side effects and is relatively cheap and locally available. Literature claims that Saponins are able to reduce hyperlipidemia. Based on high saponin content in herbal plants, *Spermacoce hispida* (*S.hispida*) was selected and the present study focus on the antihyperlipidaemic activity of ethanolic seed extract of *S. Hispida* against triton-WR-1339 induced hyperlipidaemia in rats. Hyperlipidaemia was induced in Wistar rats by intraperitoneal (i.p) injections of Triton WR-1339 at a dose of 400 mg/kg body weight. *S. Hispida* was administered orally at a dose of 200 mg/kg to triton WR-1339 induced hyperlipidaemic rats. After administration of *S. Hispida* shows a significant decrease in the levels of cholesterol, phospholipids, triglycerides, LDL, VLDL and significant increase in the level of HDL in serum and liver tissues against triton induced hyperlipidaemic in rats. Therefore it effectively suppressed the triton induced hyperlipidemia in rats, suggesting the potential protective role in Coronary heart disease.

Jacob et al., (1999)[49]Phytochemical investigation of the leaves of *Eriolaena hookeriana* furnished six compounds from different combinations of petroleum ether, chloroform and methanol. Structures of these compounds were elucidated and established by standard spectroscopic methods. Isolated compounds are n-Octadec-9-enoyl α-L-rhamnopyranoside(1), n-octadec-9,12-dienoyl-α-L- rhamnopyranoside (2), n-octadec-9,12-dienoyl-β-D-glucopyranoside (3), n-octadec-9-

enoyl-β-D-glucopyranoside (4), n-octadec-9-enoyl-β-D-arabinopyranoside (5) and n-octadec-9-enoyl-α-D-xylopyranoside (6) respectively. The structures of all the phytoconstituents are elucidated on the basis of spectral data analyses and chemical reactions.

3. AIM, OBJECTIVES AND PLAN OF THE WORK

The aim of the study is to evaluate the antihyperlipidemic activity of *Eriolaena hookeriana* leaf hydroalcoholic extract onhigh fat diet-induced hypercholesterolemia model in rats.

- ✓ Collection and authenticate of *Eriolaena hookeriana* leaves.
- ✓ Extraction of the dried leaf of *Eriolaena hookeriana* using hydroalcholic solvent.
- ✓ Pharmacological screening for antihyperlipidemic activity in rats using
  - High-cholesterol diet induced rat model.
- ✓ Blood collection and fat measurement
  - At the end of the study, the animals will be sacrificed and blood will be collected through the brachial plexus and centrifuged. Abdominal fat will be determined as follows: after opening the peritonium and removing the viscera, abdominal fat will be carefully dissected and weighed.
- Biochemical determinations
  - Triglycerides and cholesterol were measured with enzymatic Trinder kits (Labtest, Belo Horizonte, MG, Brazil). HDL-cholesterol was determined after precipitation of VLDL and LDL with phosphotungstenic acid and magnesium chloride. The VLDL- and LDL-cholesterol concentrations
- ✓ Statistical analysis
  - Data were expressed as mean ± standard deviation. In order to compare the groups, analysis of variance (ANOVA) was used. $P < 0.05$ values were considered to be statistically significant

IV.PLANT PROFILE

Plant:Eriolaena hookeriana

Family:*Sterculiaceae*

Vernacular name: Dindivase

Habit: Tree

Distribution: Mysore

Shrub or small tree up to 6 m high.Bark smooth, mottled grey and brown; young branches stellate hairy. Leaves simple, more or less broadly ovate, up to 14 cm long, 3-5-veined from the base, stellate hairy only when young; margins coarsely crenate.; petiole 3-7 cm long; stipules paired, linear, 10-15 mm long. Inflorescences lax, terminal or axillary, sparsely-branched; peduncles up to 10 cm long.Flowers c.3 cm in diameter, bright yellow. Fruit a globose woody capsule, c. 15 mm in diameter, ribbed, dehiscent. *Eriolaena hookeriana* is a species of flowering plant in the family *Sterculiaceae.* It is found only in Andhra Pradesh and Tamil Nadu in India. It is threatened by habitat loss.

Fig 1.*Eriolaena hookeriana leaves*

Eriolaena hookeriana is an endemic and threatened medium-sized deciduous tree species. The flowering is very brief and occurs during the early wet season. The flowers are solitary, remain within the foliage and attract a few bee foragers only in the presence. It exhibit gregarious flowering and attract a wide array of insects. In *E. hookeriana*, the floral characteristics suggest entomophily but it is exclusively melittophilous involving *Apis*,*Trigona* and *Xylocopa*bees in the study area. The hermaphroditic flowers with the stigmatosestyle beyond the height of

stamens and the sticky pollen grains do not facilitate autogamy but promote out-crossing. The study showed that pollinator limitation is responsible for the low fruit set but it is, however, compensated by multi-seeded fruits. Anther predation by a beetle also affects the reproductive success. Explosive fruit dehiscence and anemochory are special characteristics but these events are not effective during the wet season. The locals exploit the plant for treating snake bites, scorpion sting, making ropes and fuel wood. Therefore, the pollinator limitation, ineffective anemochory, seedling establishment problems and local uses largely contribute to the endemic and endangered status of *E. hookeriana*.

5. MATERIALS AND METHODS

a) Plant collection

The flower part of plant was collected from less rain fall irrigation hills and which authenticated by recognized plant survey office.

b) Extraction procedure by Cold maceration

The 1000g of coarse powder of plants, mixed with 2000ml of hydroalcoholicsolvent in round bottom flask, which kept for 15days and shaken regularly 2 times per day and decanted. The extracts are dried under reduced pressure and stored in a desiccator.

c) Preliminary Phytochemical screening

1. Test for Carbohydrate

Molisch's test

To 2-3 ml of extract, added few drops of α-naphthol solution in alcohol, shake and added concentrated H_2SO_4 from sides of the test tube to form violet ring at the junction of two liquids.

Benedict's test – Test solution was mixed with few drops of Benedict's reagent (alkaline solution containing cupric citrate complex) and boiled in water bath.

2. Test for Proteins

Biuret Test – Test solution was treated with 10% sodium hydroxide solution and two drops of 0.1% copper sulphate solution and observed for the formation of violet/pink color.

3. Test for Free Amino Acids

Ninhydrin Test – Test solution when boiled with 0.2%solution of Ninhydrin, would result in the formation of purple color.

4. Test for Steroids and Triterpenoids

Liebermann Burchard test - Crude extract was mixed with few drops of acetic anhydride, boiled and cooled. Concentrated sulphuric acid was then added from the sides of the test tube and observed for the formation of a brown ring at the junction of two layers.

5. Test for Glycosides

Keller Killiani Test – Test solution was treated with few drops of glacial acetic acid and Ferric chloride solution and mixed. Concentrated sulphuric acid was added, andobserved for the formation of two layers.

Bromine water test - Test solution was dissolved in bromine water and observed for the formation of yellow precipitate to show a positive result for the presence of glycosides.

6. Test for Saponins:

Foam Test – Test solution was mixed with water and shaken and observed for the formation of froth, which are stable for15 minutes for a positive result.

7. Test for Alkaloids:

Hager's Test – Test solution was treated with few drops of Hager's reagent (saturated picric acid solution). Formation of yellow precipitate.

8. Test for Flavonoids:

a) Ferric chloride Test: Test solution when treated with few drops of Ferric chloride solution would result in the formation of blackish red color.

b) Alkaline Reagent Test: Extracts were treated with few drops of sodium hydroxide solution. Formation of intense yellow colour, which becomes colourless on addition of dilute acid.

c) Lead acetate Test:Extracts were treated with few drops of lead acetate solution. Formation of yellow colour precipitate.

d) Alkaline reagent Test: Test solution when treated with sodium hydroxide solution, shows increase in the intensity of yellow color which would become colorless on addition of few drops of dilute Hydrochloric acid, acetate solution Test – Test solution when treated with few drops of lead acetate (10%) solution.

Animals:

A Wistar rat ranges from150 – 180 g& Sprague–Dawley rats weighing 200- 250 g, of either sex were obtained from Central animal house, J.K.K.Nattraja College of Pharmacy. Animals were maintained under standard laboratory conditions at an ambient temperature of 25°C. Animals had free access to food and water with a natural light and dark cycle. Animals were acclimatized for at least 5 days before behavioral experiments. The study

protocol was approved by Institutional Animal Ethics Committee (IAEC) of the college and the experiments were carried out as per CPCSEA guidelines No: 887/PO/Re/S/2005/CPCSEA

Groups:

Group I – Control- Fed with Standard Diet

Group II – High Cholesterol Diet-Fed

GROUP III – Hydroalcoholic extract of *Eriolaena hookeriana* (HAEEH)400 mg/kg

Group IV – Standard (Atrovastatin 15 mg/kg)

Animals and diet for inducing hypercholesterolemia:

Wistar rats weighing 200- 250 m, were divided into 4 groups of 6 animals each randomly.

Group I served as normal control.

Group II was administered with groundnut oil (10 ml/kg) and

Group III was treated with cholesterol at the dose of 500 mg/kg and cholic acid at the dose of 50 mg/kg in groundnut oil

Group IV was administered with hydro-alcoholic extract of *Eriolaena hookeriana* (HAEEH 500 mg/kg p.o.) + atorvastatin at 10 mg/kg and

Group V was treated with atorvastatin at 10 mg/kg rat body weight.

Demineralized water was used as a vehicle for administration of reference standards and test substance. All the treatments were given daily by oral gavage for 42 days.
Individual animal body weight was recorded at initiation of the study and mean group body weights were calculated thereafter weekly, until the end of the experiment.

Plasma levels of cholesterol and triglycerides were estimated at weekly intervals, till the end of the study period.The fifth group was treated with atorvastatin suspension prepared with 0.5% CMC (10mg/kg; p.o.), once a day for 30 days. After 30 days blood was collected by retro orbital sinus puncture, under mild ether anaesthesia. The collected samples were centrifuged for 10 minutes at 2000 r.p.m. and serum samples so collected

were used for various biochemical tests The animals were then sacrificed and the liver collected.

Acute toxicity study

Acute oral toxicity test was performed as per OECD-423 guidelines. Healthy adult female rats, acclimatized to laboratory conditions for 1 week before dosing, were used in this study. Animals were randomly assigned to the cages, and the individual animal was fur marked with picric acid. The females were nulliparous and not pregnant. The rats were deprived of feed overnight before and 3 h after the administration of the test substance. Water was not withheld during this period. The test substance, solubilized in demineralized water, was administered by gavage to rats for 14 days using an intubation needle of appropriate size fitted into a syringe

6. RESULTS AND DISCUSSION

Table 3: Preliminary Phytochemical studies of hydro-alcoholic extract of *Eriolaena hookeriana* (HAEEH)

Class of compounds	Tests performed	Results
Carbohydrates	Molisch's test	+
	Fehling's test	+
Phenols	Phosphomolybdic acid test	+
Flavonoids	Shinoda test	+
	Lead acetate test	
Alkaloids	Wagner's	+
	Mayer's	
	Draggendrof's test	
Glycosides	Legal's test	+
	Brontranger's test	
Saponins	Foam test	-
Sterols	Salkowski's test	+
Amino acids	Ninhydrin test	+
Terpenoids	Lieberman Burchardt test	+
Gums and Mucilage	**Alcoholic precipitation**	-

+ =Present; - =Absent

The phytochemical studies results revealed that the Molisch's test no characteristic observation indicated the presence of carbohydrates in both extract. Green color formed indicated the presence of phenols in both extracts. Pink or red coloration of the solution indicated the presence of flavonoids in both. Orange coloration of the spot indicated the presence of alkaloids Yellow or reddish brown precipitation precipitation indicated the presence of alkaloids in both. Pink to red color solution indicates the presence of glycosides in both extract. No layer of foam formation indicates the absence of saponins in both extracts. Pink and red color observed indicated presence steroids in both extract. Violet precipitation formed in the presence of amino acids in both . Red coloration of the solution formation indicated s

Observations of clinical signs were made at 10 min, 30 min, 1 h, 2 h, 4 h, and 6 h after dosing on day 0 and once daily thereafter for 14 days at approximately same time. Cage-side observations included changes in the skin, fur, eyes, and mucous membrane. It also included respiratory, circulatory, autonomic and central nervous system, and somato motor activity and behavioral pattern. Particular attention was directed to the observation of tremors, convulsion, salivation, diarrhea, lethargy, sleep, and coma.

In acute oral toxicity studies, the test animals did not show any significant physical changes and behavioral patterns. There was no mortality even after 14 days observation, and there were no abnormalities found in the organs after the sacrifice of animals when compared to the control at the end of 14 days of general observation.

Eriolaena hookeriana has been reported to possess antidiabetic and hypolipidemic activities. Phytochemical analysis of leaves of *Eriolaena hookeriana* has shown the presence of many bioactive compounds such as flavonoids and phenolics. In the present *in vivo* study, the hydro-alcoholic extract of leaves of *Eriolaena hookeriana* (HAEEA) has shown a significant reduction in serum cholesterol level in albino Wistar rats. The dose of 500 mg/kg body weight was chosen to consider the human dose of 1.0 g/day. This study has shown reduction of 14% serum cholesterol level. In case of triglycerides, the reduction due to extract was 31%. It may be concluded that *Eriolaena hookeriana* may lower the lipid profile by acting as HMG-CoA reductase inhibitor (STs) by blocking the HMG-CoA reductase enzyme, which catalyzes the rate-limiting step in de novo cholesterol synthesis. The results of the present study have shown that extract treated groups had significantly reduced the levels of cholesterol, and the activity was comparable with the activity of standards used in the study. The chemical constituents present in the extract have shown hypocholesterol activity by different mechanisms. The water-soluble flavonoids present in the extract might be contributing for HMG-CoA reductase inhibition,[35] whereas the nonpolar sterol like 3β-taraxerol present in the extract might be competing with cholesterol for absorption. Thereby, the different constituents present in the extract could contribute to the reduction of cholesterol and triglycerides level in the study.

The nontoxic nature of hydro-alcoholic extract of *Eriolaena hookeriana* was confirmed from the acute oral toxicity study as per Organisation for Economic Co-operation and Development (OECD) guidelines. The results indicated that the methanol extract of *M. indica* is nontoxic at the dose of 5000 mg/kg body weight of animal and test animals have shown normal behavior during a period of 14 days.

Acute oral toxicity studies:

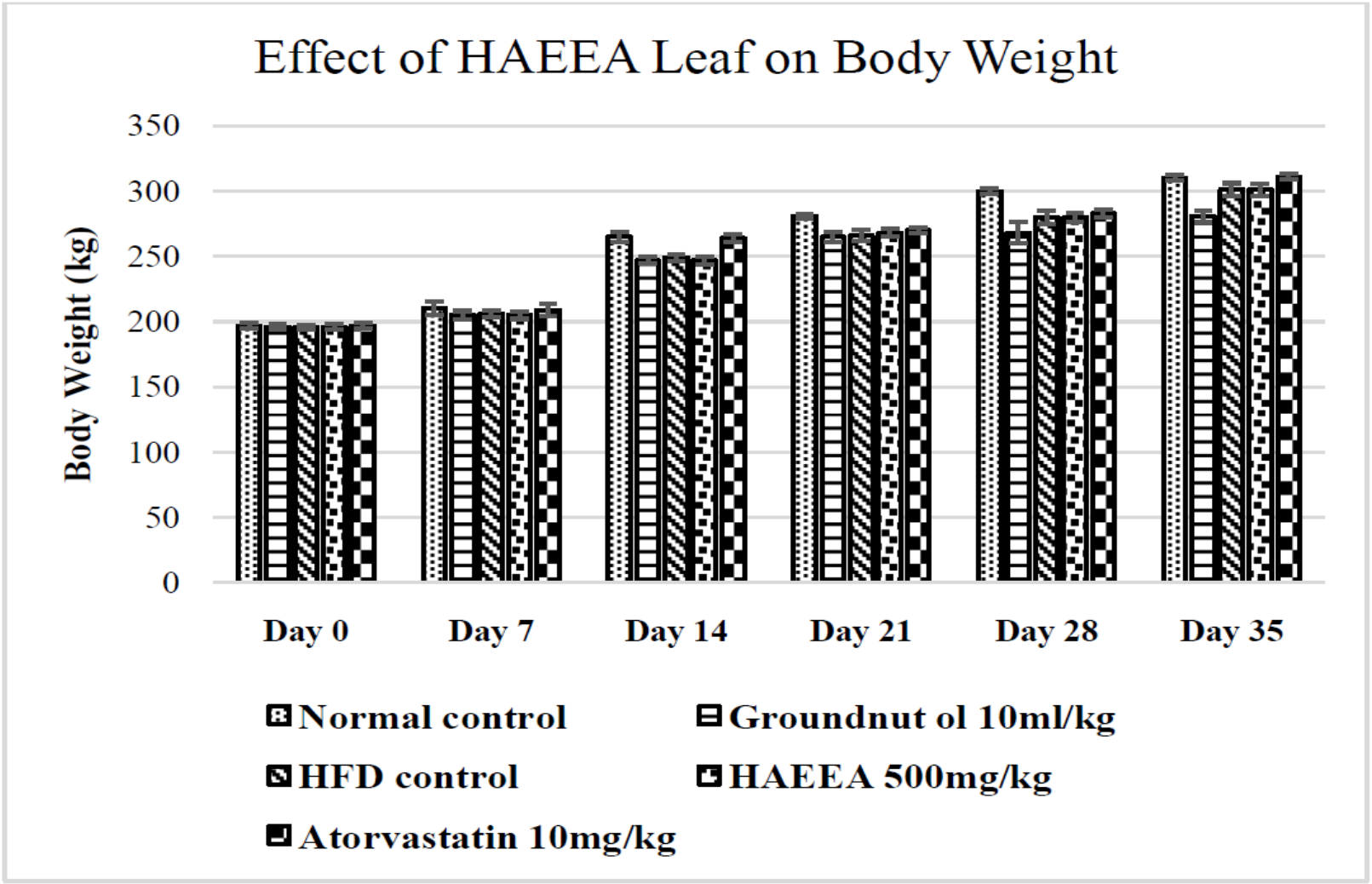
In acute oral toxicity studies, the test animals did not show any significant physical changes and behavioral patterns. There was no mortality even after 14 days observation, and there were no abnormalities found in the organs after the sacrifice of animals when compared to the control at the end of 14 days of general observation.

Measurements on changes in body weight:

The mean body weight of experimental rats at weekly intervals is represented in Table 4 and Figure 2. On day 0, no significant difference in body weight was observed in all the groups. There was no significant difference in body weight observed in cholesterol control rats when compared to vehicle control rats on different weekly time intervals of the study period.

Table 4 - Effect of HAEEA Leaf on Body Weight

Groups	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35
Normal control	197±2.1	210±5.2	265± 3.8	281±1.82	300±2.01	310±2.12
Groundnut oil 10ml/kg	196±1.8	205±3.1	247±2.5	265±3.7	268±8.02	281±4.31
HFD control	196±1.7	206±2.8	249±2.3	266±4.1	280±2.08	301±5.03
HAEEA 500mg/kg	196±2.1	205±2.9	247±3.1	268±2.9	280±3.24	301±4.92
Atorvastatin 10mg/kg	197±1.9	209±4.9	264±3.2	270±1.91	283±3.01	311±2.11

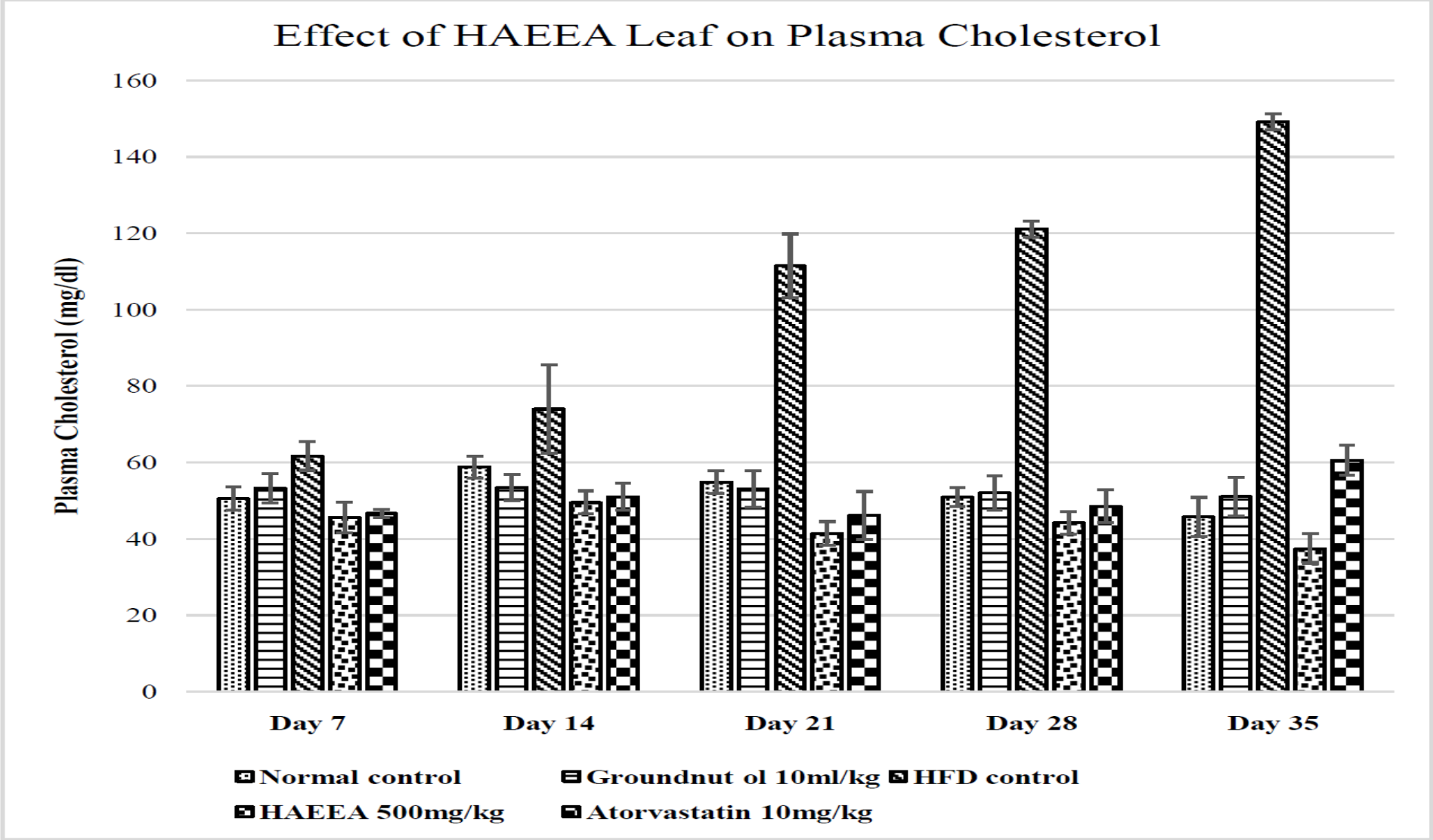

Effect of HAEEA Leaf on Body Weight
Body Weight (kg)
350
300
250
200
150
100
50
0
Day 0
Day 7
Day 14
Day 21
Day 28
Day 35
Normal control
Groundnut ol 10ml/kg
HFD control
HAEEA 500mg/kg
Atorvastatin 10mg/kg

Total cholesterol, HDL-, LDL- and VLDL-c and triglycerides:

The mean plasma cholesterol levels at weekly intervals are presented in Table 5 and Figure 3. The plasma cholesterol was significantly increased in cholesterol control from day 21 to day 42 with a nonsignificant increase observed during day 7 to day 14 when compared to vehicle control. A significant decrease in plasma cholesterol was observed on treatment with an extract of HAEEA and all other substances from day 21 to day 42 as compared to cholesterol control rats.

Table - 5 Effect of HAEEA Leaf on Plasma Cholesterol

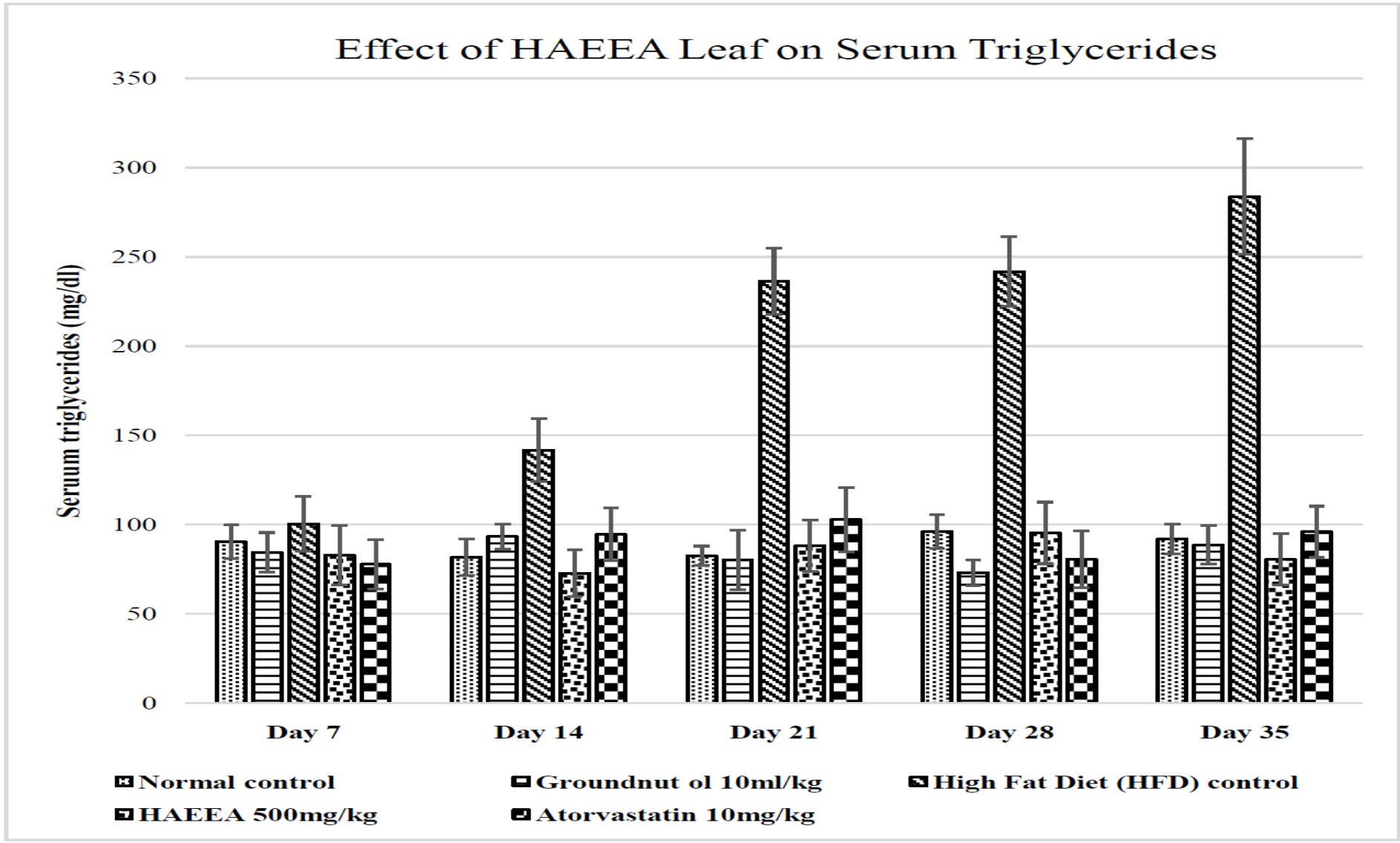
Groups	Day 7	Day 14	Day 21	Day 28	Day 35
Normal control	50.52±3.04	58.83±2.84	54.86±2.96	50.93±2.48	45.74±5.13
Groundnut oil 10ml/kg	53.32±3.8	53.48±3.49	53.02±4.79	52.04±4.43	51.06±5.03
HFD control	61.74±3.79	74.00±11.52	111.52±8.35	121.17±2.12	149.22±2.04
HAEEA 500mg/kg	45.65±4.00	49.55±3.05	41.46±3.11	44.21±2.91	37.52±3.84
Atorvastatin 10mg/kg	46.67±0.99	51.02±3.53	46.15±6.25	48.56±4.27	60.64±3.97


Effect of HAEEA Leaf on Plasma Cholesterol
Plasma Cholesterol (mg/dl)
160
140
120
100
80
60
40
20
0
Day 7
Day 14
Day 21
Day 28
Day 35
Normal control
Groundnut ol 10ml/kg
HFD control
HAEEA 500mg/kg
Atorvastatin 10mg/kg

Oral administration of hydro-alcoholic extract of *Eriolaena hookeriana* (HAEEA) at the dose of 500 mg/kg to HFD- induced hyperlipidemic rats, significantly reduced the serum and liver cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C) and VLDL-cholesterol levels. Levels of serum and liver HDL-cholesterol were significantly increased in rats treated with has compared to HFD treated rats presented in table 7 and figure 5.

Table - 6 Effect of HAEEA Leaf on Serum Triglycerides

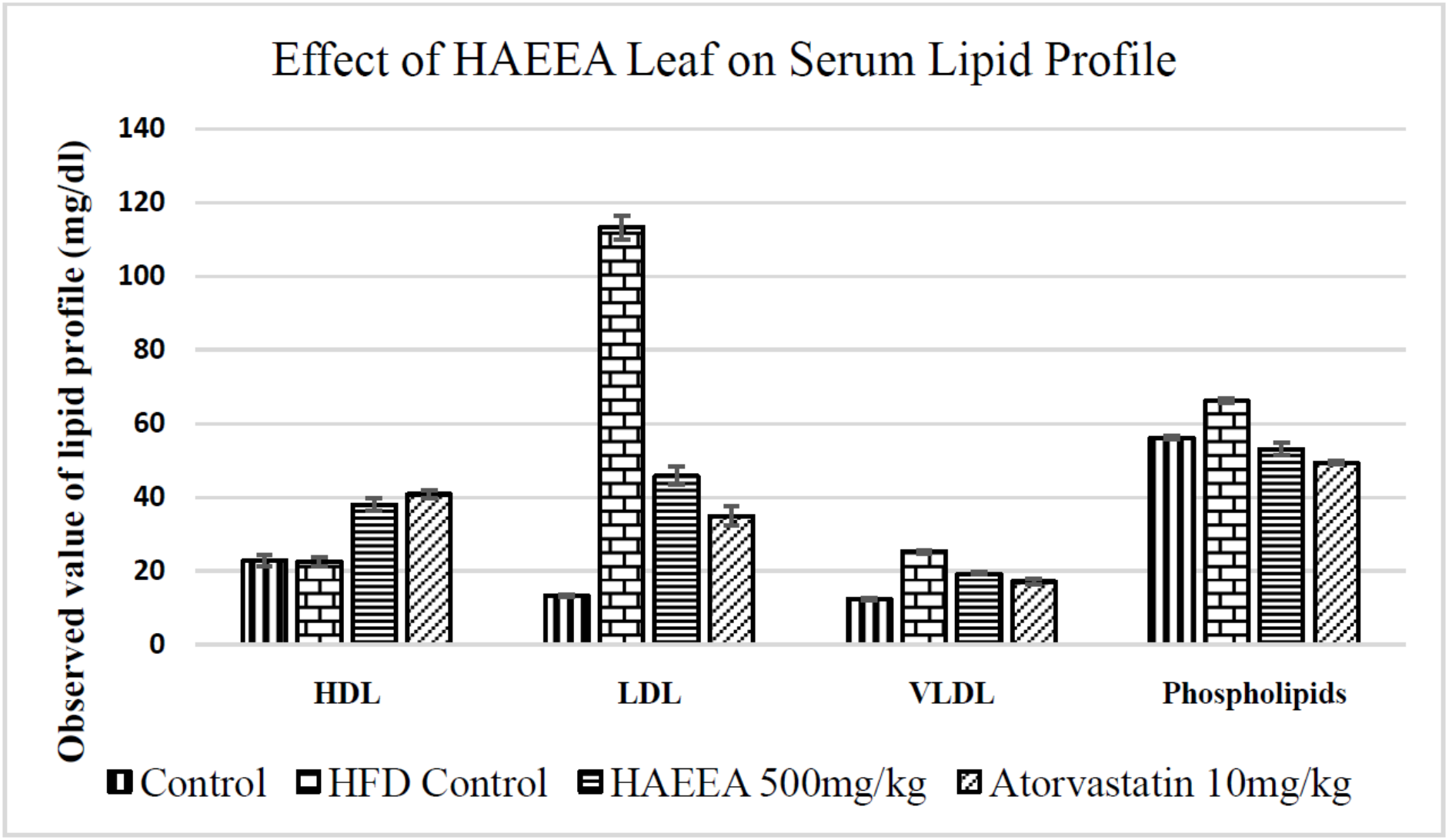
Groups	**Day 7**	**Day 14**	**Day 21**	**Day 28**	**Day 35**
Normal control	90.46±9.52	81.7±10.32	82.55±5.42	96.08±9.34	91.96±8.27
Groundnut oil 10ml/kg	84.44±11.09	93.35±7.03	80.12±16.61	73.00±7.21	88.58±10.78
HFD control	100.47±15.35	141.76±17.51	236.3±18.49	241.7±19.5	283.76±32.38
HAEEA 500mg/kg	82.82±16.77	72.78±13.00	88.12±14.28	95.36±17.24	80.44±14.41
Atorvastatin 10mg/kg	77.75±13.8	94.5±14.74	102.8±18.06	80.68±15.93	95.96±14.36


Effect of HAEEA Leaf on Serum Triglycerides
Seruum triglycerides (mg/dl)
350
300
250
200
150
100
50
0
Day 7
Day 14
Day 21
Day 28
Day 35
Normal control
Groundnut ol 10ml/kg
High Fat Diet (HFD) control
HAEEA 500mg/kg
Atorvastatin 10mg/kg

The mean plasma triglycerides levels at different time intervals are presented in Table 7 and Figure 4. The plasma triglyceride was significantly increased in cholesterol control rats from day 21 to day 42 as compared to vehicle control rats. A significant decrease in plasma triglycerides was observed on treatment with an extract of HAEEA and all other substances from day 21 to day 42 as compared to cholesterol control rats.

Table – 7 Effect of HAEEA Leaf on Serum Lipid Profile

Groups	**HDL**	**LDL**	**VLDL**	**Phospholipids**
Control	22.68±1.51	13.12±0.42	12.27±0.32	56.00±0.45
HFD Control	22.45±1.24	113.18±3.19	25.12±0.42	66.00±0.58
HAEEA 500mg/kg	37.92±1.59	45.7±2.44	19.19±0.29	53.00±1.62
Atorvastatin 10mg/kg	40.7±1.12	34.86±2.51	16.99±0.68	49.2±0.45


Effect of HAEEA Leaf on Serum Lipid Profile
Observed value of lipid profile (mg/dl)
140
120
100
80
60
40
20
0
HDL
LDL
VLDL
Phospholipids
Control
HFD Control
HAEEA 500mg/kg
Atorvastatin 10mg/kg

VII. SUMMARY & CONCLUSION

The present was undertaken to evaluate the anti hyperlipidemic activity of hydro-alcoholic leaf extract of *Eriolaena hookeriana* in high fat diet-induced model using rats. The hydro-alcoholic extract of *Eriolaena hookeriana* showed a significant cholesterol-lowering activity at 500 mg/kg from day 21 to day 42 of 6 weeks treatment period, and a significant decrease in plasma triglycerides was also observed on treatment with extract. The hydroalcoholic extract of *Eriolaena hookeriana* leaf was found to be safe after oral administration of single dose of 5000 mg/kg body weight to Wistar rats.

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