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EVALUATION OF HYPO LIPIDEMIC AND ANTIOXIDENT PROPERTIES OF METHANOLIC EXTRACT OF LEAVES OF *RUELLIATUBEROSA LINN* ON MITHIONINE AND TRITON INDUCED MODELS IN WISTER ALBINO RATS

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Abstract:

In this modern world we are exposed to various factors which disturb homeostasis of our body physiology, leads to the development of various disease as its end point. Among the various diseased conditions less percentage of diseases were cured, in case of the remaining disease conditions only their symptoms are reduced instead of complete cure. Eg:AIDS, Cancer, Diabetic mellitus, Hypertension and hytperlipidmia. Among the various dreadful diseases, Hyperlipidimia is one the major disease affecting all age of people having a mortality rate of about 5% of all human deaths and 80% diseases caused do to this hyperlipidmia. The present synthetic Anti hyperlipidimic drugs produce undesirable side effects and treatment is cost effective. The plants selection in the present study was done on basis of it easy availability and phytochemical constituents to screen their therapeutic potential. The plant Plumeria acuminata Linn contain alkaloids, flavonoids, steroids, phenol and other constituents. The Methanolic extract of Ruellia tuberosa Linn possess phytochemicals with reported antioxidant activity, the formulation was screened for anti-oxidant activity by catalase assay and has significant free radical scavenging activity. Studies lead to the conclusion that herbal extract of the whole plant Ruellia tuberosa Linn could be used for the treatment of hyperlipidemia, as they are found to be potent and safe in pre-clinical study. However elucidation of exact mechanism of action of beneficial effects of these formulations needs further investigation. More randomized controlled trials in large patient populations have to be carried out before determining the status of these drugs in the therapy of hyperlipidemia.

Keywords: *Hyperlipidimia, Plumeria acuminata, Methanolic extract, Ruellia tuberosa, Anti hyperlipidimic drugs.*

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INTRODUCTION:

Herbal Medicine sometimes referred to as Herbalism or Botanical Medicine, is the use of herbs for their therapeutic or medicinal value. An herb is a plant or plant part valued for its medicinal, aromatic quality. Herb plants produce and contain a variety of chemical substances that act upon the body. Herbalists use the leaves, flowers, stems, berries, and roots of plants to prevent, relieve, and treat illness. Many plant components are now synthesized in large laboratories for use in pharmaceutical preparations. For example, vincristine (an antitumor drug), digitalis (a heart regulator), and ephedrine (a bronchodilator used to decrease respiratory congestion) were all originally discovered through research on plants [1]. The World Health Organization (WHO) estimates that 4 billion people, 80% of the world population, presently use herbal medicine for some aspect of primary health care. Herbal medicine is a major component in all indigenous peoples' traditional medicine and a common element in Ayurveda, homeopathic, naturopathic, traditional oriental, and Native American Indian medicine. WHO notes that of 119 plant-derived pharmaceutical medicines, about 74% are used in modern medicine in ways that correlated directly with their traditional uses as plant medicines by native cultures. Major pharmaceutical companies are currently conducting extensive research on plant materials gathered from the rain forests and other places for their potential medicinal value [2].

Hyperlipidemia:

Hyperlipidemia a broad term, also called hyper lipoproteinemia, is a metabolic disorder, specifically characterized by alterations occurring in serum lipid and lipoprotein profile due to increased concentrations of Total Cholesterol (TC), Low Density Lipoprotein Cholesterol (LDL-C), Very Low Density Lipoprotein Cholesterol (VLDL-C) and Triglycerides (TG) with a concaminant decrease in the concentrations of High Density Lipoprotein Cholesterol (HDL-C) in the blood circulation. It is a common disorder in developed countries and is the major cause of coronary heart disease. It results from abnormalities in lipid metabolism or plasma lipid transport or a disorder in the synthesis and degradation of plasma lipoproteins. The term "dyslipidaemia" now a days is increasingly being used to describe abnormal changes in lipid profile, replacing the old term hyperlipidaemia. Hyperlipidemia means abnormally high levels of fats in the blood. These fats include cholesterol and triglycerides. These are important for our bodies to function but when they are high, they can cause heart disease and stroke. Hyperlipidemia is manifested as hypercholesterolemia and/or hypertriglycerolemia [4-9].

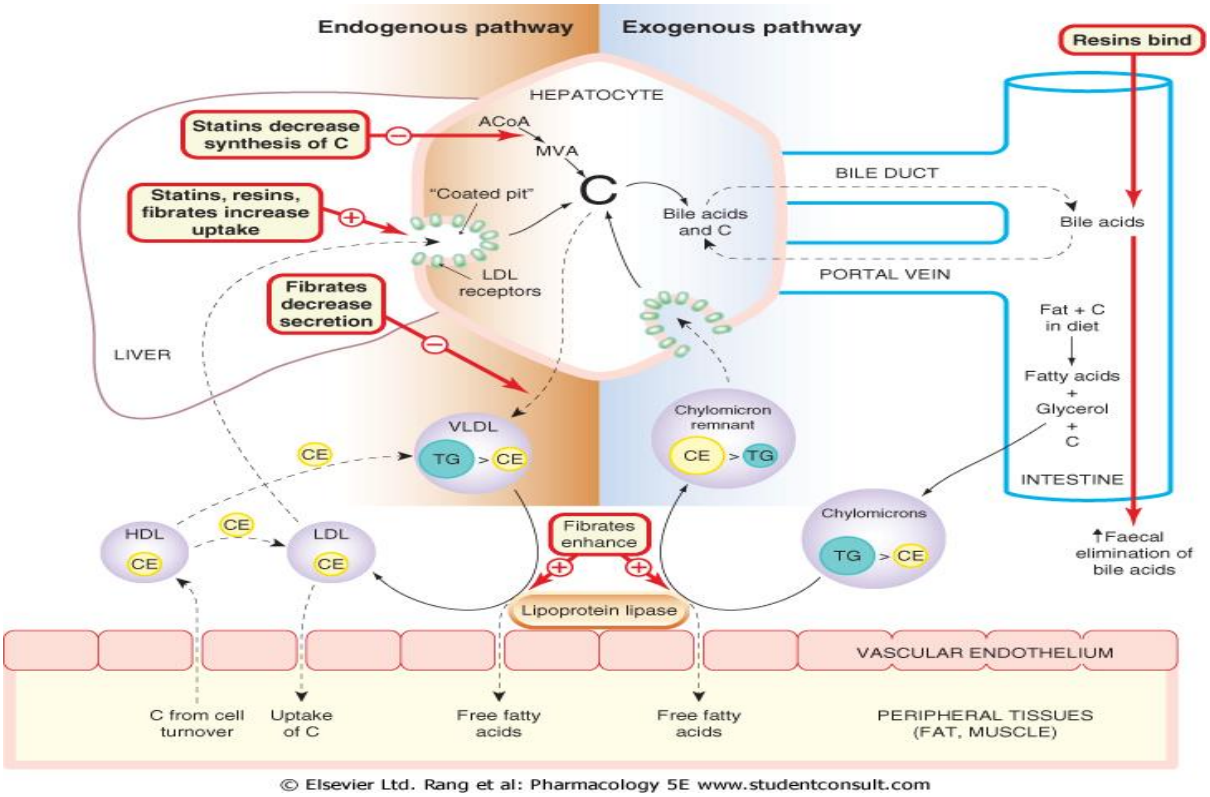

Fig 1: Schematic diagram of cholesterol transport in the tissues, with sites of action of the main drugs affecting lipoprotein metabolism

Table 1: Classification of hyperlipidemias [10]

Fredrickson classification of hyperlipidemia				
Hyperlipo Proteinemia	**Synonyms**	**Problems**	**Labs description**	**Treatment**
Type I	Burger-gruetz syndrome, Primary Hyperlipoproteinemia, or Familial Hyperchylomicronemia	Decreased lipoprotein lipase (LPL) or altered Apo	Elevated chylomicrons	Diet control
Type II a	Polygenic hypercholesterolemia or Familial hypercholesterolemia	LDL receptor deficiency	Elevated LDL only	Bile Acid, sequestrants, statins, niacin
Type II b	Combined hyperlipidemia	Decreased LDL receptor and Increased Apo-B	Elevated LDL, VLDL and Triglycerides	Statins, Niacin Gemfibrozil
Type III	Familial Dysbetalipoproteinemia	Defect in Apo-E synthesis	increased IDL	Drug of choice Gemfebrozil
Type IV	Endogenous Hyperlipidemia	Increased VLDL production and Decreased elimination	Increased VLDL	Drug of choice Niacin
Type V	Familial hypertriglyceridemia	Increased VLDL production and decreased LPL	Increased LDL and chylomicrons	Niacin Gemfebrozil

Plants With Anti Hyperlipidemic Activity

Plants are considered as a main source of highly effective convential drugs for treatment of Hyperlipidemia. Advantage over the hypolipidemic agents is no side effects associated with these herbal medicines. Because of the perceived effectiveness, minimal side effects in clinical experience and relatively low cost, herbal drugs are widely prescribed even when their biologically active compounds are unknown[11,12].

Plant	Family	Part	Synonyms
Coriandrum sativum	Umbelliferae	Leaves, Seeds	Coriander plant, Chinese parsley,
Trichila connaroids	Meliaceae	Leaves	Gagnep.
Curcuma longa	Zingiberaceae	Tuber	Haldi, turmeric
Nardostachys jatamansi	Valerianaceae	Whole Plant	Indianspikenard, Jataamaansii
Achyranthus aspera	Fabaceae	Aerial Parts	Burweed Chaff-flower
Cassia tora	Caesalpiniaceae	Seeds	Sickle pod
Phaseolus aconitifolius	Fabaceae	Seeds	moth bean, Vigna aconitifolia
Pterocarpus marsupium	Fabaceae	Heart wood	Malabar Kino, Benga
Adenocalymma alliaceum	Bignoniaceae	Flower	Wild garlic,
Phyllanthus niruri	Euphorbiaceae	Whole plant	Stonebreaker Nela Nelli
Terminalia arjuna	Combretaceae	Bark	Arjuna, vellamatta
Arinica montana	Compositae	Flower	Mountain flower
Inula racemosa	Arteraceae	Root	Pushkara, Pushkaramola
Averrhoa bilimbi	Oxalidaceae.	Fruit	Cucumber tree
Acacia polyantha	Mimosaceae	Heartwood	White cutch tree
Alpinia galangal	Zingiberaceae	Rhizomes	Kulanjn, Greater galangal
Argyreia nervosa	Convolvulacaae	Root	Elephant creeper
Cassia absuslinn	Caesalpiniaceae	Leaves ,seeds	Caksu bankullthi
Delphinium denudatum	Ranunculaceae	Root	Nirbisi

Fig 4: *Ruellia tuberosa* plant.

Plant Profile

Ruellia tuberosa Linn is a low-growing perennial herb with tuberous roots, growing to a height of a foot or more. Leaves are opposite, elliptic, short petioled, abruptly narrowed at the base, with undulate margins and up to 12 cm long. Flowers are showy, with funnel-shaped, 5-lobed corolla, up to 5 cm across, and mauve or light bluish purple. Fruit is a pod with 7 to 8 seeds, bursting open and hurtling the seeds when it gets wet. It is found in open waste places in the Philippines.

MATERIALS AND METHODS:

Collection of Plant Material

Leaves of the *Ruellia tuberosa* was collected near from Kondapalli in Vijayawada, Andhra Pradesh. The root was authenticated by Dr. S.Satyanarayana in Acharya Nagarjuna University, Guntur, Andhra Pradesh. The root was separated from adulterants, shade dried and powdered coarsely. It was packed in air-tight container up to the completion of study.

Extraction of Plant Material

About 80 g of air dried powdered plant materials was taken in Soxhlet apparatus and extracted with petroleum ether for up to discoloration of solution. After 72 h, the powder was taken out and dried. Then it was packed again and extracted with methanol till the colour disappeared. The methanolic extract of *Ruellia tuberosa* leavas concentrated under reduced pressure using rota-evaporator. The concentrated extract was stored in refrigerator at 10°C up to the completion of pharmacological studies.

RESULTS:

Table 2: Priliminary phyto chemical analysis Methonalic extract of *Ruellia tuberosa* leaves

S.No.	Phytochemical constituents	Methonalic extract of *Ruellia tuberosa*
1.	Carbohydrates	+ve
2.	Alkaloids	+ve
3.	Steroids & sterols	+ve
4.	Glycosides	+ve
5.	Saponins	+ve
6.	Flavanoids	+ve
7.	Tannins	+ve
8.	Proteins & amino acids	+ve
9.	Phenols	+ve
10.	Terpenoids	-ve

Table 3: Effect of Methanolic extract of *Ruellia tuberosa* on acute toxicity in mice

S.N	Response	Head		Body		Tail	
		Before	After	Before	After	Before	After
1	Alertness	Normal	Normal	Normal	Normal	Normal	Normal
2	Grooming	Absent	Absent	Absent	Absent	Absent	Absent
3	Touch response	Absent	Absent	Absent	Absent	Absent	Absent
4	Torch response	Normal	Normal	Normal	Normal	Normal	Normal
5	Pain response	Normal	Normal	Normal	Normal	Normal	Normal
6	Tremors	Absent	Absent	Absent	Absent	Absent	Absent
7	Convulsion	Absent	Absent	Absent	Absent	Absent	Absent
8	Righting reflux	Normal	Normal	Normal	Normal	Normal	Normal
9	Gripping strength	Normal	Normal	Normal	Normal	Normal	Normal
10	Pinna reflux	Present	Present	Present	Present	Present	Present
11	Corneal reflux	Present	Present	Present	Present	Present	Present
12	Writhing	Absent	Absent	Absent	Absent	Absent	Absent
13	Pupils	Normal	Normal	Normal	Normal	Normal	Normal
14	Urination	Normal	Normal	Normal	Normal	Normal	Normal
15	Salivation	Normal	Normal	Normal	Normal	Normal	Normal
6	Skin colour	Normal	Normal	Normal	Normal	Normal	Normal
17	Lacrimation	Normal	Normal	Normal	Normal	Normal	Normal

Table 4: Effect of Methonalic extract of *Ruellia tuberosa* lipid profiles in Methionine induced hyperlipidemic animals.

Group	Dose (mg/kg)	TC (mg/dl)		TG (mg/dl)		HDL (mg/dl)		LDL (mg/dl)		VLDL (mg/dl)		Atherogenic index	
		15 D	30 D	15 D	30 D	15 D	30 D	15 D	30 D	15 D	30 D	15 D	30 D
Normal control	Saline (5ml/kg))	59.60 ± 0.99	82.51 ± 0.34	30.75 ± 2.52	119.91 ± 0.85	41.17 ± 0.47	37.01 ± 0.57	13.61 ± 0.67	6.33 ± 1.76	6.27 ± 0.98	23.87 ± 0.17	0.20 ± 0.03	0.50 ± 0.01
Hyperlipidemic control	Saline (5ml/kg)	96.6 ± 3.80^{a}	113.51 ± 0.59^{a}	62.27 ±1.21^{a}	173.90 ±1.22^{a}	36.33 ±1.48^{a}	26.07 ±0.61^{a}	45.79 ±4.54^{a}	52.60 ± 0.88^{a}	12.91 ± 0.17^{a}	34.67 ±0.2^{a}	0.21 ±0.09^{a}	0.84 ±0.01^{a}
METHANOLIC EXTRACT OF TECTONA GRANDIS	100	56.38 ±0.88^{b,e}	84.22 ±0.52^{b,e}	47.46 ±0.59^{c}	145.00 ± 1.52^{b}	53.21 ±0.68^{b}	43.00 ±1.15^{b}	14.12 ±0.02^{b}	14.00 ±0.57^{b,g}	9.67 ± 0.08^{b}	29.00 ±0.3^{b}	0.05 ±0.09^{b}	0.52 ±0.08^{b}
METHANOLIC EXTRACT OF TECTONA GRANDIS	200	47.46 ±0.5^{b,f,h}	82.79 ±0.91^{b,j}	54.38 ±0.90^{c}	131.30 ±0.91^{b,h}	54.67 ±0.88^{b}	41.27 ±0.73^{b}	6.43 ±1.24^{b}	15.67 ±0.88$^{b.h}$	11.67 ±0.08^{ns}	26.27 ±0.17^{b}	0.02 ±0.01^{b}	0.48 ±0.12^{b}
Atrovastatin	10	74.07 ± 1.71^{b}	94.61 ± 2.56^{b}	34.08 ±1.6^{b}	134.8 ± 1.08^{b}	55.00 ± 0.9^{b}	42.63 ±0.56^{b}	24.36 ±0.15^{b}	25.33 ± 1.85^{b}	7.23 ±0.31^{b}	26.87 ±0.2a^{b}	-0.17 ±0.02^{b}	0.50 ±0.08^{b}

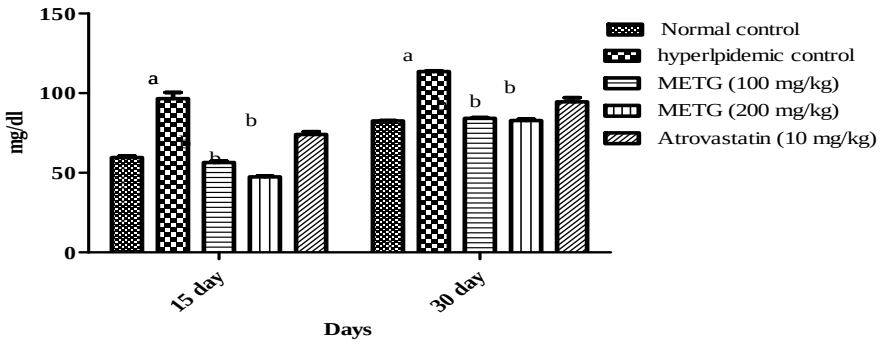

Fig 2: Effect of Methonalic extract of *Ruellia tuberosa* ON TC level in Methonine induced animals.

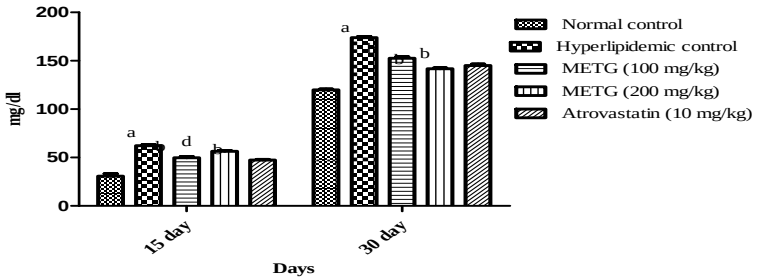

Fig 3: Effect of Methonalic extract of *Ruellia tuberosa* ON TG level in Methonine induced animals.

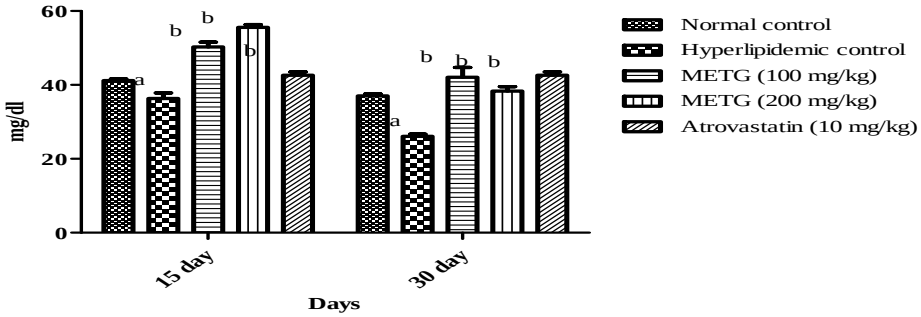

Fig 4: Effect of Methonalic extract of *Ruellia tuberosa* HDL level in Methonine induced animals.

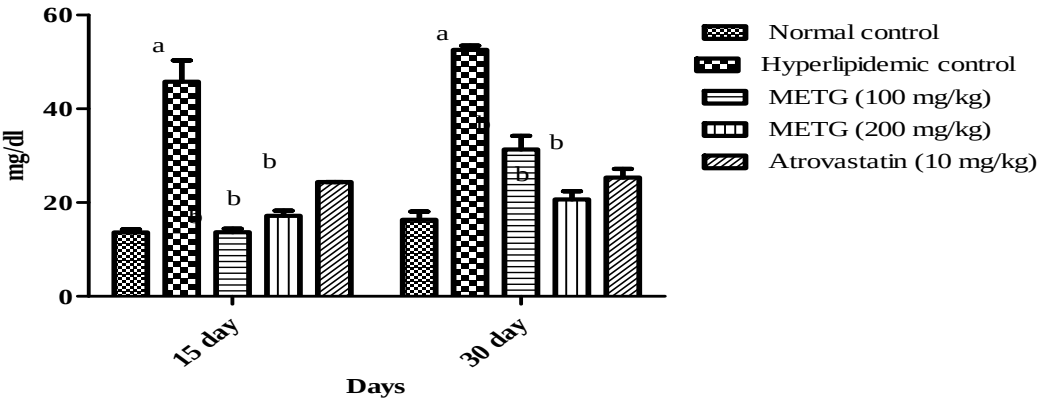

Fig 5: Effect of Methonalic extract of *Ruellia tuberosa* LDL levels in Methonine induced animals.

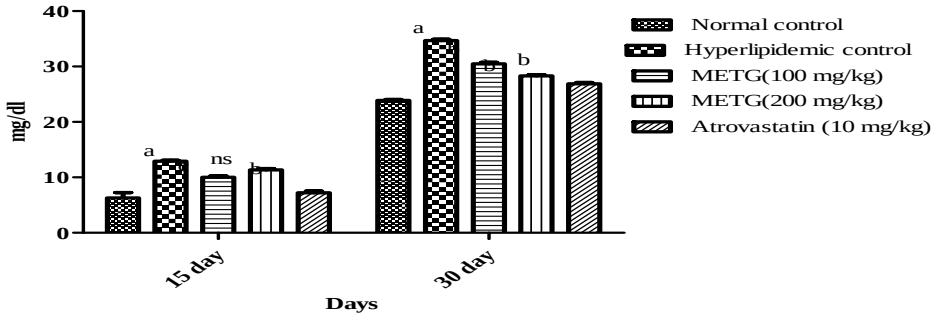

Fig 6: Effect of Methonalic extract of *Ruellia tuberosa* VLDL level in Methonine induced animals

Table 5: Effect of Methonalic extract of *Ruellia tuberosa* SGOT level in Methonine induced animals

GROUPS (n=6)	Control	Hyperlipidic control	Methonalic extract of *Ruellia tuberosa* 100mg/kg	Methonalic extract of *Ruellia tuberosa* 200mg/kg	Atrovastatin 10mg/kg
SGOT(U/L)	76.33± 7.965	133.7± 5.667	113.0± 24.00 ns	98.67± 14.67 ns	182.7± 11.33 ns

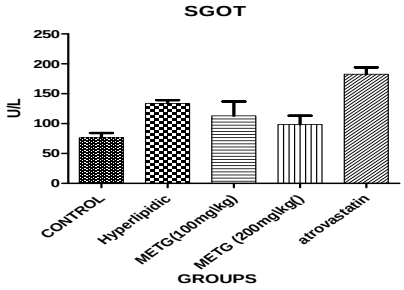

Fig 6: Effect of Methonalic extract of *Ruellia tuberosa* SGOT level in Methonine induced animals

Table 6: Effect of Methonalic extract of *Ruellia tuberosa* in Methonine induced animals SGPT level

GROUPS (n=6)	Control	HYPERLIPIDIC MODEL	Methonalic extract of Methonalic extract of *Ruellia tuberosa* 100 mg/kg	Methonalic extract of Methonalic extract of *Ruellia tuberosa* 200mg/kg	Atrovastatin 10mg/kg
SGPT(U/L)	74.00± 2.082	83.33± 6.173[a]	45.33± 2.028[b]	44.00± 1.155[b]	87.33± 6.642 ns

Fig 7: Effect of Methonalic extract of *Ruellia tuberosa* SGPT level in Methonine induced animals

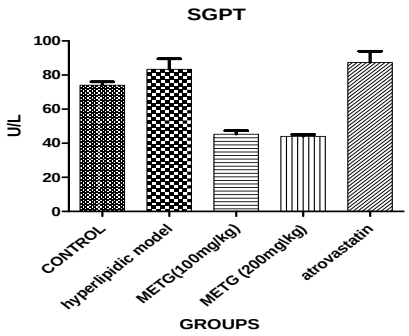

Table 7:.Effect of Methonalic extract of *Ruellia tuberosa* Methonine induced animals Creatinine level

GROUPS (n=6)	Control	HYPERLIPIDIC MODEL	Methonalic extract of Methonalic extract of *Ruellia tuberosa* 100mg/kg	Methonalic extract of Methonalic extract of *Ruellia tuberosa* 200mg/kg	Atrovastatin 10mg/kg
SGPT(U/L)	0.5333± 0.03333	0.5333± 0.03333a	0.6000± 0.0 ns	0.5333± 0.03333 ns	0.4667± 0.03333 ns

Fig 8: Effect of Methonalic extract of *Ruellia tuberose* Creatinine level in Methonine induced animals

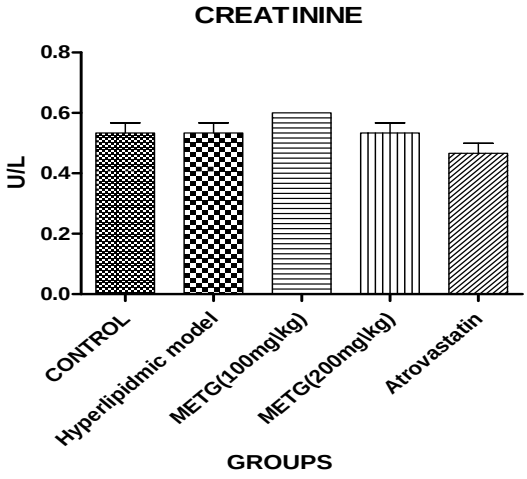

Table 8: Effect of Methonalic extract of *Ruellia tuberosa* in Methonine induced animals ALP level

GROUPS (n=6)	Control	HYPERLIPIDIC MODEL	Methonalic extract of Methonalic extract of *Ruellia tuberosa* 100mg/kg	Methonalic extract of Methonalic extract of *Ruellia tuberosa* 200mg/kg	Atrvostatin 10mg/kg
ALP(U/L)	16.7± 3.480	176.0± 27.50[a]	89.00± 8.737[b]	88.33± 8.570[b]	99.33± 8.950[c]

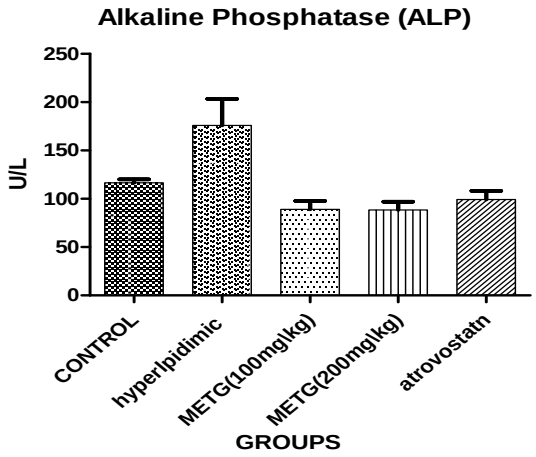

Fig 9: Effect of Methonalic extract of *Ruellia tuberosa* ALP level in Methonine induced animals

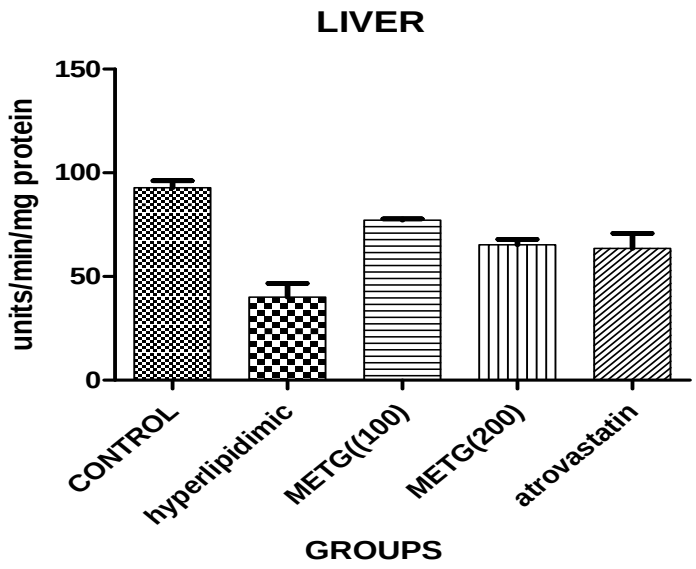

Fig 10: Effect of Methonalic extract of *Ruellia tuberosa* SOD level in Methonine induced animals

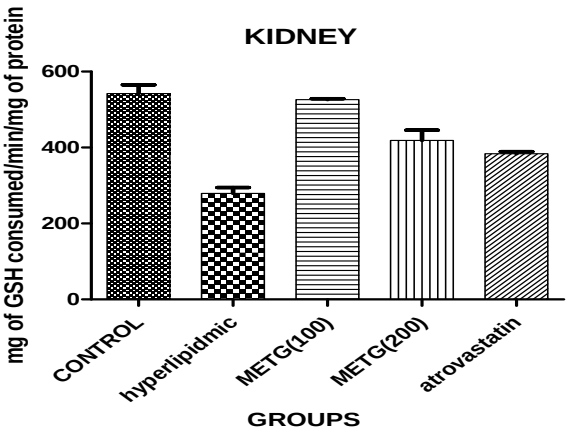

Fig 11: Effect of Methonalic extract of *Ruellia tuberosa* GPX level in Methonine induced animals

Table 9: Effect of total cholesterol in Triton Induced model on triglycerides

Normal	65.51±1.26
Hyperlipidemic	98.72±2.28[a]
Atorvastatin	39±1.09[b]
Methonalic extract of *Ruellia tuberosa s*100mg	39.6±1.08[b]
Methonalic extract of *Ruellia tuberosa* 200mg	36.7±1.4[b]

Table 10: Effect of total cholesterol in Triton Induced model on HDL

Normal	21.28±1.42
Hyperlipidemic	43.56±1.0[a]
Atorvastatin	29.3±1.13[b]
Methonalic extract of *Ruellia tuberosa* 100mg	34.58±1.29[b]
Methonalic extract of *Ruellia tuberosa* 500mg	30.31±1.17[b]

Table 11: Effect of total cholesterol in Triton Induced model on LDL

Normal	36.12±1.0
Hyperlipidemic	97.21±1.52[a]
Atorvastatin	52.71±1.18[b]
Methonalic extract of *Ruellia tuberosa s*100mg	67.91±2.0[b]
Methonalic extract of *Ruellia tuberosa* 200mg	53.52±1.19[b]

CONCLUSION:

The Methanolic herbal extract at two different doses was evaluated for antihyperlipidemic activity, in the present study. The Methanolic extract of *Ruellia tuberosa* whole leaves was subjected to phytochemical screening to find the chemical constituents present. The extract revealed the presence of carbohydrates, alkaloids, phytosterols, proteins & aminoacids, tannin, saponins and flavonoids. The extract was also studied for anti-hyperlipidemic activity with Methionine induced hyperlipidimic model and Triton X 100 induced hyperlipidemic model which mimics hyperlipidemia in experimental animals. The effect of the Methanolic extract of the *Ruellia tuberosa* on total cholesterol, triglycerides, LDL, HDL and VLDL levels were studied. Both the dose levels of Methanolic extract of *Ruellia tuberosa* showed significant anti hyperlipidemic activity as compared to the control group. The herbal extracts at dose level of 100 mg/kg b.w and 200 mg/kg b.w reduced the blood lipids level significantly. The 200 mg/kg was found to be more potent than lower dose in reducing lipid levels. The Methanol extract reduced the total Cholesterol, Triglycerides, LDL, and increased Body weight level in hyperlipidemia induced rats which are less significant compared to the standard and more significant compared to positive control.

The Methanolic extract of *Ruellia tuberosa Linn* possess phytochemicals with reported antioxidant activity, the formulation was screened for anti-oxidant activity by catalase assay and has significant free radical scavenging activity. Studies lead to the conclusion that herbal extract of the whole plant *Ruellia tuberosa Linn* could be used for the treatment of hyperlipidemia, as they are found to be potent and safe in pre-clinical study. However elucidation of exact mechanism of action of beneficial effects of these formulations needs further investigation. More randomized controlled trials in large patient populations have to be carried out before determining the status of these drugs in the therapy of hyperlipidemia.

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