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Fructose induces Antihyperlipidemic activity of dried leaves extract of Alternanthera brasiliana L. Kuntz. in Wistar rats.

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Abstract: Objective of present study was to evaluate the Antihyperlipidemic activity of dried leaves extract of *Alternanthera brasiliana* L. Kuntz. We hypothesized that *Alternanthera brasiliana* L. kuntz dried leaves extract may benefit in diseases of hyperlipidemia. *Alternanthera brasiliana* L. Kuntz dried leaves powder was extracted using 50% ethanol + water and the extract was subjected to Antihyperlipidemic study with a view to evaluate its medicinal value against the disease.

Keywords: Alternanthera brasiliana, Antihyperlipidemic activity, Fructose, Fenofibrate

Introduction:

Hyperlipidemia is a secondary metabolic dysregulation associated with diabetes. Besides the cause effect relationship with diabetes, elevated serum level of triglycerides, cholesterol and LDL are major risk factors for the premature development of cardiovascular disease like arthrosclerosis, hypertension, coronary heart disease etc.[1] Increased plasma lipid levels mainly total cholesterol, triglycerides and LDL along with decrease in HDL are known to cause hyperlipidemia which is the reason for initiation and progression of atherosclerosis impasse.[2] Antihyperlipidemic agents having various pharmacological actions are being tested clinically.[3]

The public health burden of type 2 diabetes mellitus (T2DM) has been dramatically increased worldwide. It has been shown that the risk for developing clinical diabetes is substantially increased in the state of impaired fasting glycemia or impaired glucose tolerance. Fasting hyperglycemia is caused by unrestrained basal hepatic glucose output, primarily a consequence of hepatic resistance to insulin action. Insulin resistance not only plays an important role in T2DM but it also is an extremely common feature of a number of important human diseases including atherosclerosis, hypertension, and dyslipidemia.[4]

Alternanthera brasiliana (L.) O. kuntze, (Amaranthaceae) is an important herb found as a perennial herb, native to tropical and subtropical regions of Australia and South America; five species have been recorded from India. Through almost all of its parts are used in traditional system of medicines, leaves are the most important parts which are use medicinally.[5] It is a herb indigenous to Brazil, described as perennial, prostrate and branchy, presenting a circular to polygonal stem, long internodes and swollen nodes at which opposite leaves attach. The inflorescence is cymes, composed of hermaphrodite, actinomorphous and monocyclic flowers.[6]

Alternanthera brasiliana is a brazilin plant occurring in several regions, being known as "penicilina" or terramicina, widely used by rural communities as medicinal agent to cure different disease, such as inflammation, and dolorous or infection processes, wound healing, analgesic, antitumor activity, immunomodulator and lymphocyte proliferation. Alternanthera brasiliana focusing the influence of different kind of lights to produce compound with possible analgesic action.[7] It used against cough & diarrhoea in Brazilian popular medicine.[8]

Material & Method:

Collection and Authentication of plant materials-

The fresh leaves of Alternanthera brasiliana L. Kuntz were collected in the month of November, 2010 from the botanical garden within Ghaziabad (U.P.) India. The plant material was authenticated by Dr. H.B. Sing NISCAIR New Delhi were a voucher specimen no. NISCAIR/RHMD/Consult/-2010-11/1607/205. A specimen sample of the same was preserved in the herbarium

section of the College of Pharmacy, Teerthanker Mahaveer University, Moradabad for further reference.

Preparation of the extract:

The leaves were cleaned and shade dried in open air for 8-10 days then pulverized to dry power using electric grinder. About 400 gm of the dried leaf powder was extracted with methanol for 24 hours with each solvent, by extraction using the soxhlet apparatus at a temperature of 30 to 35˚C. The extract was concentrated by vacuum rotary evaporator and stored in a refrigerator at 4˚C.

Chemicals and Instruments-

Fenofibrate (Finolip 145), 20 mg/kg (Cipla Pvt Ltd.); Fructose, 10% w/v solution (CDH Laboratory reagent); Carboxy Methyl Cellulose, CMC (Loba chemie); Methanol extract of *Ficus infectoria*; Hydrogen peroxide, H_2O_2 (Fisher scientific); Ascorbic acid (CDH Laboratory reagent); Bio analyzer (Star 21 Plus); Vacuum Rotary Evaporator (Biogen certified); UV Spectrophotometer (Labtronicslt 2900); Glucometer (Bhat Bio-Tech India P Ltd.); Enzymatic kit (ARBA diagnostics kit).

Maintenance of animals and approval of protocol-

30 Wistar albino rats of either sex weighing between 150 and 200 g were used in this study. These rats were procured from the Central Animal House Facility, Teerthanker Mahaveer University, Moradabad. They were housed in well ventilated stainless-steel cages at room temperature (24 ± 2) ºC in hygienic condition under natural light and dark schedule and were fed on standard laboratory diet. Food and water were given ad libitium. Permission for the use of animal and animal protocol was obtained from the Institutional Animal Ethical Committee (IAEC) of Committee for the Purpose of Control and Supervision of Experiments on Animals (Reg. No. 1205/c/08/CPCSEA, Dated:-21/4/2008).

Fructose induced hyperlipidemia-

Fructose induced hyperlipidemia of *Ficus infectoria* leaf and bark extract was determined by method as reported by Omprakash N et.al. (2010).[9] Wistar rats weighing between 125-200 gm were divided into five groups of six animals each. The animals of the control group had free access to tap water while other groups were fed with food pellet and water ad libitum. 10%

fructose was used as inducing agent for hyperlipidemia.

Group I- served as control group received vehicle (saline) daily for 20 days.

Group II- served as toxic control received 10% fructose solution for 20 days

Group III- served as standard received Fenofibrate at a dose of 20 mg/kg along with 10% fructose solution for 20 days.

Group IV- served as test-I received leaf and bark methanolic extract at a dose of 200 mg/kg along with 10% fructose solution for 20 days.

Group V- served as test-II received leaf and bark methanolic extract at a dose of 400 mg/kg along with 10% fructose solution for 20 days.

All the animals were fasted for half an hour prior to drug administrations. On day 21, these animals were anaesthetized with "diethyl ether". The blood was collected by retro orbital puncture and the serum was separated for estimation of total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) and very low density lipoprotein (VLDL) levels.

For estimation of triglycerides, cholesterol and HDL, kits (ARBA diagnostics kit, India) were used. All the estimations were carried out as per the instruction provided by the kit manufacturers. VLDL and LDL were calculated as per Friedewalds equation (mg/dl).[10]

VLDL = TG/5.0

LDL = TC - HDL - VLDL

Statistical analysis-

The statistical significance was assessed using one-way analysis of variance (ANOVA) followed by Bonferroni Multiple Comparisons Test by using Graph Pad InStat (File version 3.0.10.0). The values were expressed as mean ± Standard Error Mean (SEM) for six rats in each group and $P<0.05$ were considered significant.

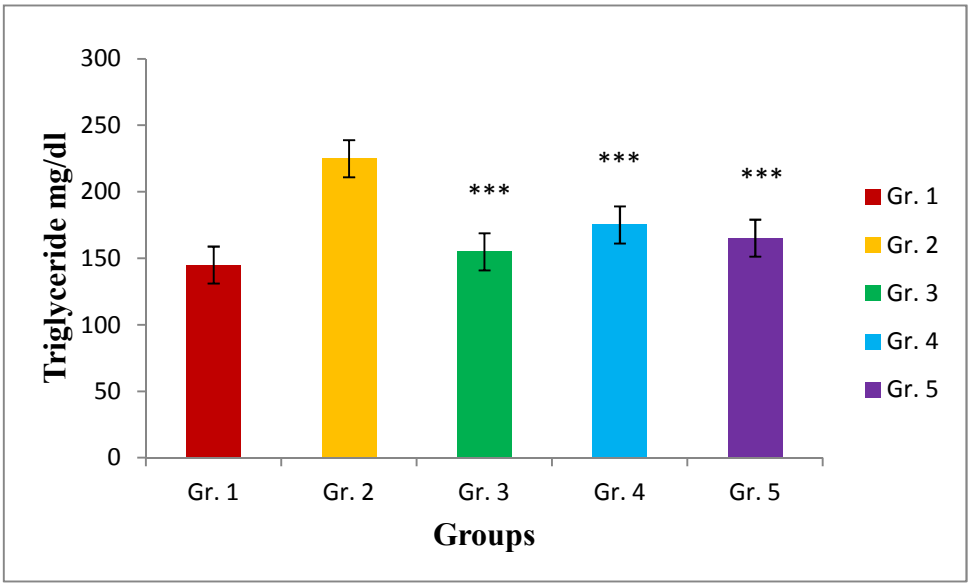
Result & Discussion:

The Antihyperlipidemic activity of *Alternanthera brasiliana* L. Kuntz leaves extract was determined by estimating the suppression of lipid profile (triglyceride, total cholesterol, LDL, VLDL) in Wistar rats of different groups.

The results obtained were as depicted in Table no. 1, 2, 3, 4, 5 and Fig. no. 1, 2, 3, 4, 5.

Table no. 1: Variation in the Triglycerides level

Group	Treatment	Dose (mg/kg)	Triglycerides mg/dl
I	Normal Control	-	145.13 ± 1.32
II	Fructose control	10% Fructose	225.34 ± 1.29
III	Fenofibrate	20	155.22± 1.75***
IV	*Alternanthera brasiliana* extract	200	175.26 ± 1.35***
V	*Alternanthera brasiliana* extract	400	165.28 ± 1.47***



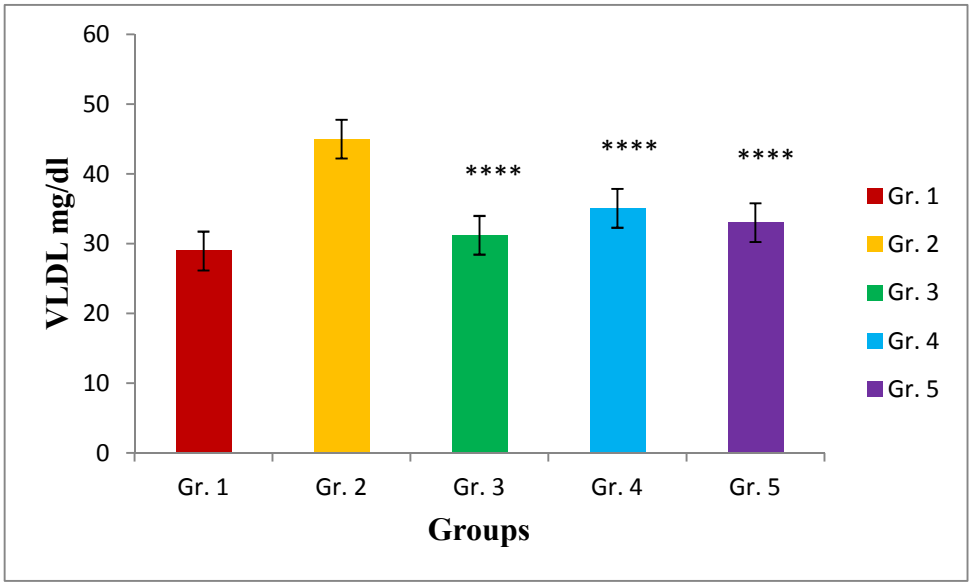
*****P<0.001 compared to Group II, The results expressed as mean±S.E.**

Fig no. 1 Graph showing variation in Triglyceride level

The study concluded that *Alternanthera brasiliana* L. Kuntz leaves extract (200 mg/kg and 400 mg/kg) and Fenofibrate (20 mg/kg) showed significant decrease in Triglyceride level, as compared to Fructose control group.

Table 2: Variation of Very low density lipoprotein (VLDL) level

Group	Treatment	Dose (mg/kg)	VLDL mg/dl
I	Normal Control	-	28.97± 0.24
II	Fructose control	10% Fructose	45.00 ± 0.25
III	Fenofibrate	20	31.22 ±0.32****
IV	*Alternanthera brasiliana* extract	200	35.08 ±0.294****
V	*Alternanthera brasiliana* extract	400	33.03 ±0.294****



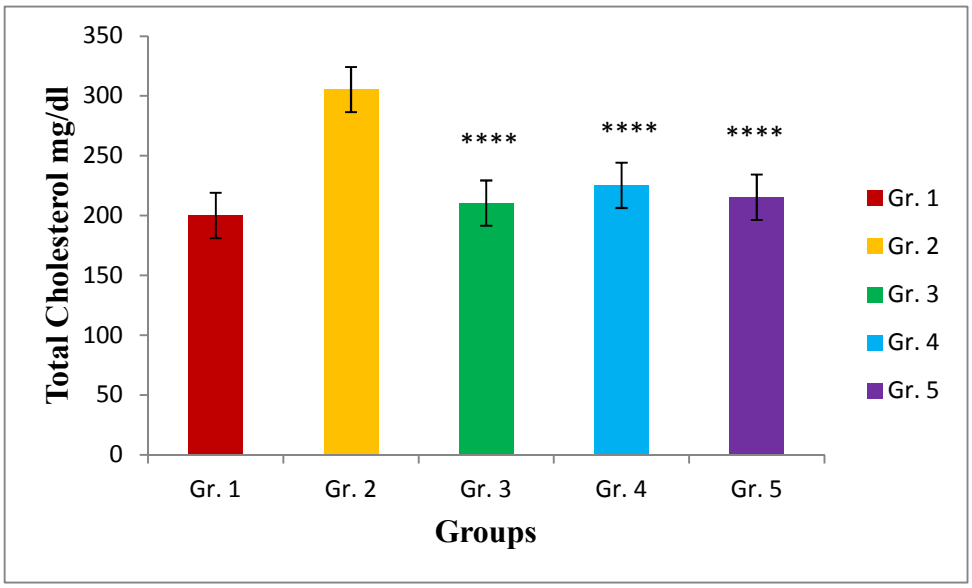
******p<0.0001 compared to Group II, **P<0.01 compared to Group III with Group V, ***P<0.001 compared to Group IV with Group V; the results expressed as mean±S.E.**

Fig no. 2 Graph showing variation in Very low density lipoprotein (VLDL)

The study concluded that *Alternanthera brasiliana* L. Kuntz leaves extract (200 mg/kg and 400 mg/kg) and Fenofibrate (20 mg/kg) showed significant decrease in Very low density lipoprotein (VLDL) level, as compared to Fructose control group.

Table 3: Variation of Total cholesterol level

Group	Treatment	Dose (mg/kg)	Total Cholesterol mg/dl
I	Normal Control	-	200.0 ± 2.66
II	Fructose control	10% Fructose	305.0 ± 1.47
III	Fenofibrate	20	210.0 ± 1.64****
IV	*Alternanthera brasiliana* extract	200	225.3 ± 1.32****
V	*Alternanthera brasiliana* extract	400	215.3 ±0.442****



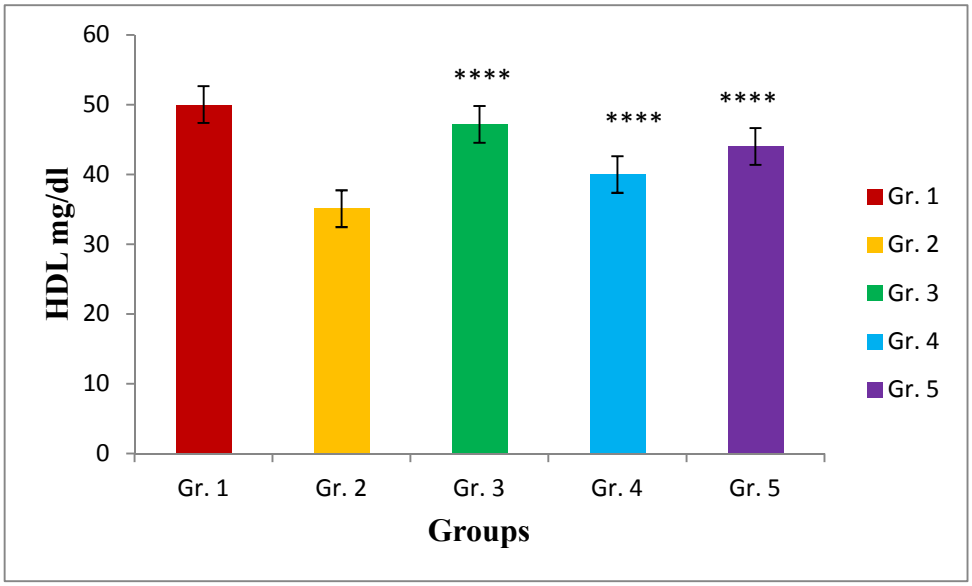
******p<0.0001 compared to Group II, **P<0.01 compared to Group IV with Group V; The results expressed as mean±S.E.**

Fig no. 3 Graph showing variation in Total cholesterol levels

The study concluded that *Alternanthera brasiliana* L. Kuntz leaves extract (200 mg/kg and 400 mg/kg) and Fenofibrate (20 mg/kg) showed significant decrease in Total cholesterol level, as compared to Fructose control group.

Table 4: Variation in High density lipoprotein (HDL) levels

Group	Treatment	Dose (mg/kg)	HDL mg/dl
I	Normal Control	-	50.00 ± 0.79
II	Fructose control	10% Fructose	35.08 ± 0.65
III	Fenofibrate	20	47.17 ± 0.55****
IV	*Alternanthera brasiliana* extract	200	39.98 ± 0.34****
V	*Alternanthera brasiliana* extract	400	44.00 ± 0.48****



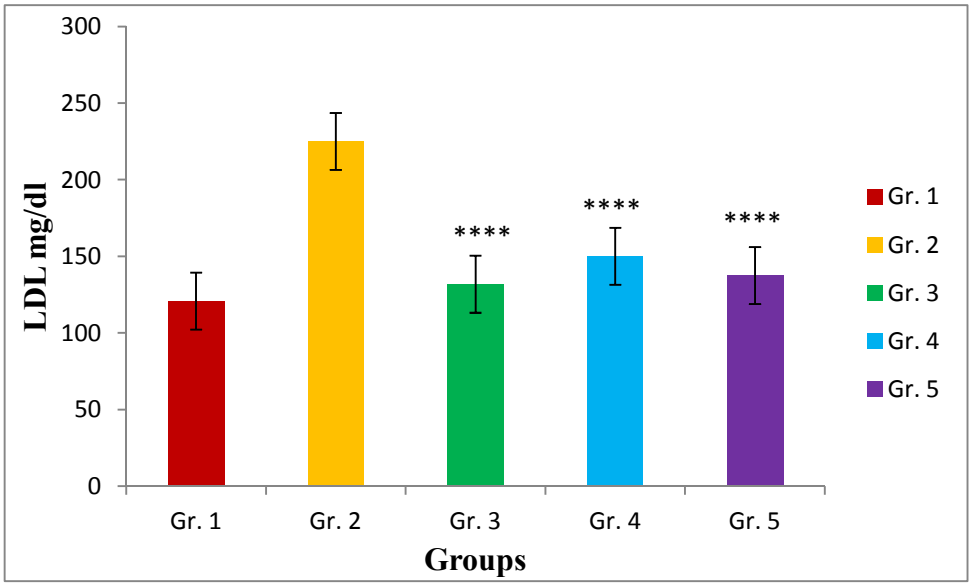
******P<0.0001 compared to Group II, **P<0.01 compared to Group III with Group V; The results expressed as mean±S.E.**

Fig no. 4 Graph showing variation in High density lipoprotein (HDL) levels

The study concluded that *Alternanthera brasiliana* L. Kuntz leaves extract (200 mg/kg and 400 mg/kg) and Fenofibrate (20 mg/kg) showed significant increased in High density lipoprotein (HDL) level, as compared to Fructose control group.

Table 5: Variation in Low density lipoprotein (LDL) levels

Group	Treatment	Dose (mg/kg)	LDL mg/dl
I	Normal Control	-	121.0 ± 2.80
II	Fructose control	10% Fructose	225.2 ± 1.91
III	Fenofibrate	20	132.0 ± 1.62****
IV	*Alternanthera brasiliana* extract	200	150.3 ± 1.76****
V	*Alternanthera brasiliana* extract	400	137.7 ± 0.59****



******P<0.0001 compared to Group II, ***P<0.001 compared to Group IV with Group V; The results expressed as mean±S.E.**

Fig no. 5 Graph showing variation in low density lipoprotein (LDL) levels

Conclusion:

Alternanthera brasiliana L. Kuntz leaves extract exhibited Antihyperlipidemic activity when subjected to the tests like Fructose induced hyperlipidemia and estimation of Low density lipoprotein (LDL), Triglyceride, High density lipoprotein (HDL), Very low density lipoprotein (VLDL) and Total cholesterol. The obtained results for Antihyperlipidemic activity of Alternanthera brasiliana L. Kuntz leaves extract (200mg/kg and 400mg/kg) dose were Low density lipoprotein (LDL) level (150.3 ± 1.76 and 137.7 ±0.59), Very low density lipoprotein (VLDL) level (35.06 ± 0.294 and 33.03 ± 0.294), Triglyceride level (175.26 ± 1.35 and 165.28 ± 1.47), Total cholesterol level (225.3 ± 1.32 and 215.3 ± 0.442) and High density lipoprotein (HDL) level (39.98 ± 0.34 and 44.00 ± 0.48).

The study concluded that *Alternanthera brasiliana* L. Kuntz leaves extract (200 mg/kg and 400 mg/kg) and Fenofibrate (20 mg/kg) showed significant decrease in low density lipoprotein (LDL) level, as compared to Fructose control group.

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