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ANTI HYPERGLYCEMIC AND HYPOLIPIDEMIC ACTIVITY OF *LEEA INDICA*

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Abstract: *Leea indica* (Burm.f) Merr is a well-known traditional Chinese medicine. Leaves of *Leea indica* have multiple pharmacological activities like Antitumour, Analgesic, Antiviral, Sedative and Anxiolytic and NO inhibitory activities. It has long been used as a folk medicine for the treatment of Cardiac diseases, Diabetes, Fever, headache, dizziness, soreness, eczema, sprain, leprosy, bone fracture, body pain, muscle spasms, diarrhoea and dysentery. Scientific studies are not yet carried out to prove the antihyperglycemic activity. To evaluate antihyperglycemic and hypolipidemic activity of *Leea indica* leaves in alloxan (150 mg/kg) induced diabetic rats. Alcoholic and hydroalcoholic extracts were evaluated for its toxicity (3000 mg/kg) and for antihyperglycemic activity (200 and 400 mg/kg) using glucose tolerance test and alloxan induced model for 21 days. Statistical data indicated significant decrease in blood glucose, triglycerides, total cholesterol, LDL cholesterol, VLDL cholesterol, aspartate amino transferase, alanine amino transferase, creatinine, urea and increased HDL cholesterol, liver glycogen levels when compared to standard drug glibenclamide (10 mg/kg). Hydrolcoholic extract of *Leea indica* at higher dose was found to be more effective than alcoholic extract. These results reveal that *Leea indica* has beneficial effect in reducing blood glucose and lipid levels indicating its efficient antihyperglycemic and hypolipidemic activity.

Key Words: *Leea indica*, Antihyperlipidemic, Alloxan, Antihyperglycemic, Glibenclamide.

INTRODUCTION

Plants render us broad spectrum of biologically active compounds that possess potential therapeutic effects on a myriad of diseases. *Leea indica* plant was concluded to attribute high medicinal value [1]. *Leea indica* belonging to family vitaceae [2,3] is widely distributed in India, Srilanka, Nepal, Bangladesh, Burma, Thailand, Camboida, Laos, Vietnam, China, Malasia, New guinea, North Australia, Solomon islands, Santa cruz island, New Hebrides and Fiji [4, 5, 6]. It is an evergreen large shrub or small tree growing up to 8 meters in height. Stems are glabrous to pubescent. The leaves are 1-3-pinnate bearing 7 leaflets, with petioles 7-20 cm long. Leaflets are ovate-lanceolate with crenate to serrate margins. Flowers are greenish white with 5 mm across. Fruits are purplish black, bearing six seeds with 1 cm in diameter. *Leea indica* is cultivated in parks and urban areas for the ecological services they contribute to native fauna [7]. *Leea indica* root is used as antidiarrhoeal, antidysentric, antispasmodic, sudorific, cardiac and skin diseases [8, 9]. *Leea indica* flowers were reported to possess antibacterial and antifungal activity [10]. *Leea indica* leaves were reported to possess pharmacological activities like antitumour [11], analgesic [12], antiviral [13], sedative and anxiolytic [14], phosphodiestrase inhibitory [15] and Nitric oxide inhibitory [16]. Leaf decoction is consumed by women in pregnancy and delivery for birth control and body pain [6, 17].

Dried leaves ingested as a tea beverage believed to be effective against cancer [18]. Roasted leaves relieve vertigo. Leaves (31.4%) were found to be the most frequently used plant parts in medicine preparation then fruits and roots (16.05%) [19]. Hence the present study was designed to screen the leaves for the antidibetic activity. Twenty three chemical compounds were identified from the leaves of *Leea indica* by Gc-Ms analysis, Spectroscopic techniques, and Co-TLC. Compounds identified were eleven hydrocarbons, pthalic acid, palmitic acid, 1-eicosanol, soalnesol, farneslo, three pthalic acid esters, gallic acid, lupeol, β-sitosterol and finally ursolic acid [20]. Chemical compounds have relevance in the treatment of diabetes. So the present study was taken up to evaluate the antihyperglycemic and hypolipidemic activities of *Leea indica*.

MATERIALS AND METHODS

Leea indica leaves were procured from Karthikavanam, Dhulapally forest, Kompally, Hyderabad. It was authenticated by Dr.Madhava chetty, Assistant Professor, Department of botany, Sri Venkateshwara University, Tirupathi.

Extraction process

Leaves were collected washed, dried under shade and powdered. Extraction process was carried out by maceration with ethanol and ethanol: water (3:1) for 3 days. Marc was pressed and filtered. Solvent

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was evaporated using Rota evaporator under reduced pressure. Percentage yield was found to be 16% and 5.6%.

Phytochemical Investigations

The preliminary photochemical screening was carried out with alcoholic and hydro alcoholic extracts of *Leea indica* for qualitative identification of phytochemical constituents employing standard methods. All the chemicals and reagents used were of analytical grade [21, 22].

Animals

Healthy Wistar rats weighing 150 -200gm b.wt were maintained under standard environmental conditions (12:12 hrs light dark cycles), standard diet (Hindustan Lever Ltd.,) and water *ad libitum*. The study was performed in accordance to the guidelines of CPCSEA, Regn No: 1662/PO/a/12/CPCSEA and Institutional Anima ethics committee (IAEC) of college, Malla Reddy Institute of Pharmaceutical Sciences, Dhulapally, Hyderabad, Andhra pradesh.

Chemicals

Alloxan monohydrate, the most widely used diabetogenic agent was procured from (Oxford laboratory reagent, Tahne). Glibenclamide, a standard antidiabetic drug was obtained from (Apollo pharmacy, Avanthi pharmaceuticals Kukatpally, Hyderabad). Glucose was obtained from qualigens fine chemicals, Mumbai.

Acute toxicity study (LD_{50})[23]

Acute toxicity study was performed according to the OECD guidelines 423, using acute toxic class method. Male rats were divided into groups containing three each. After overnight fast, alcoholic and hydroalcoholic extracts were administered at doses of 300 mg/kg and 2000 mg/kg and 3000 mg/kg b.wt. Animals were observed individually for first 30 min, periodically during first 24 hrs and daily thereafter for 14 days. At the end animals were observed for autonomic, neurological and behavioral profiles.

Antihyperglycemic activity

Assessment of plant extracts in normal rats: oral glucose tolerance test (OGTT): [24] Rats were fasted overnight. Standard drug, glibenclamide (10 mg/kg) and test extracts alcoholic (200 and 400 mg/kg b.wt), hydroalcoholic extracts (200 and 400 mg/kg b.wt) were administered orally. 30 min later glucose (3 gm/kg b.wt) was administered. Blood samples were collected before and after the administration of glucose at 0hr, 1hr, 3hr and 5 hrs.

Assessment of plant extracts in alloxan induced diabetic rats: Diabetes was induced by single intraperitoneal injection of alloxan at a dose of 150 mg/kg b.wt. Alloxan was administered by dissolving it in 0.9% w/v of Nacl. 72 hrs later blood samples were withdrawn and rats with blood glucose levels greater than 300 mg/dl were included in the experiment.

Diabetic rats were divided into seven groups of six animals each. Group I received vehicle, served as control. Group II served as diabetic control. Group III received glibenclamide (10 mg/kg), served as standard. Group IV, V, VI and VII received alcoholic and hydro alcoholic extracts each at doses of (200 and 400 mg/kg b.wt). Blood samples were withdrawn on 1, 7, 14 and 21 days for the biochemical estimation of blood glucose, triglycerides (TG), cholesterol (CH), high density lipoproteins (HDL), aspartate amino transferase (AST), alanine transaminase (ALT), creatinine, urea, and liver glycogen.

RESULTS

Table 1: Phytochemical screening of *Leea indica* leaf extract showed the presence of alkaloids, glycosides, terpenoids, flavonoids, steroids and tannins.

Phyto Constituents	Test	Alcoholic	Hydroalcoholic
Alkaloids	Mayers test	++	++
	Hagners test	++	++
	Wagners test	++	++
	Dragendroff"s test	++	++
Glycosides	Borntrager's test	--	--
Cardiac glycosides	Legal test	++	++
	Baljet test	--	++
Terpenoids	Salkowsky test	++	++
Carbohydrates	Molich test	++	++
	Fehling's test	++	++
Flavonoids	Shinoda test	++	++
Steroids	Leibermann-burchards test	++	++
Proteins	Biuret test	--	--
	Millons test	--	--
Tannins	$Fecl_3$ test	++	++
Saponins	Frothing test	++	++

Note: Present (++); Absent (--)

Table 2: Effect of *Leea indica* leaf extract on oral glucose tolerance test in normal control rat's (mean± SEM)

Group	Treatment (mg/kg body weight)	Serum glucose (mg/dl)			
		0hr	1hr	3hr	5hr
I	Normal Control	71.30±2.11	88.50±1.95	79.66±3.30	66.33±4.15
II	Control + 10 g/kg glucose	80.00±3.55	102.00±4.11*	82.83±2.73	80.16±1.52**
III	Glibenclamide(10 mg/kg)	74.66±4.1	96.33±3.10	68.16±1.95**	56.66±3.0**(41.18%)
IV	LIAE (200 mg/kg)	80.00±3.15	118.33±3.11*	81.33±2.45	70.09±2.07*(40.76%)
V	LIAE (400 mg/kg)	74.00±2.07	109.66±4.02	74.10±2.23*	62.66±1.54**(42.85%)
VI	LIHAE (200 mg/kg)	70.25±2.90	96.16±4.25	74.51±2.33*	60.83±2.00**(37.15%)
VII	LIHAE (400 mg/kg)	70.50±2.34	85.50±2.73*	65.50±1.91**	51.06±3.03**(40.28%)

n=6; Group II is compared with Group I. Groups III- VII were compared with Group II. *P<0.05. **P<0.01.

Table 3: Effect of *Leea indica* leaf extract on serum glucose levels in alloxan induced diabetic rats (mean± SEM)

Group	Treatment (mg/kg b.wt)	Serum glucose (mg/dl)			
		1st day	7th day	14th day	21st day
I	Normal Control	94.33±3.12	94.66±4.10	94.16±5.15	96.51±3.44
II	Diabetic Control	511.83±8.10	506.16±7.43**	492.83±7.19**	456.83±8.35**
III	Glibenclamide(10)	506.66±8.90	407.66±5.45**	132.33±3.11**	108.66±4.35**(78.55%)
IV	LIAE (200)	321.16±6.11	253.51±5.10**	184.50±3.12**	139.52±3.12**(56.55%)
V	LIAE (400)	404.53±5.32**	352.83±4.15**	152.83±4.10**	117.83±2.41**(70.87%)
VI	LIHAE (200)	322.00±6.15**	280.63±4.10**	150.21±3.12**	115.34±5.55**(64.18%)
VII	LIHAE (400)	420.21±5.34**	315.53±5.94**	145.63±2.19**	110.12±3.23**(73.79%)

n=6; Group II is compared with Group I. Groups III- VII were compared with Group II. *P<0.05. **P<0.01.

Table 4: Effect of *Leea indica* leaf extract on serum AST, ALT, TC, TG, HDL, LDL, VLDL levels in alloxan induced diabetic rats on 1st day (mean± SEM)

Group	Treatment (mg/kg)	AST (U/L)	ALT (U/L)	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
I	Control	39.33±2.01	51.15±2.33	80.03±4.11	87.85±3.95	44.95±4.52	33.45±1.93	17.57±0.10
II	Diabetic Control	128.67±3.12**	154.94±4.15**	136.07±2.51**	145.03±3.51**	26.63±1.07**	80.43±0.92**	29.01±0.95**
III	Glibeclamide (10)	125.09±2.91	152.90±2.45	130.97±3.10	140.87±3.51	25.03±1.03	77.76±0.85	28.17±0.43
IV	LIAE (200)	128.19±2.51	156.67±1.95	138.82±4.00	145.02±3.71	27.21±0.85	82.60±0.72	29.01±1.20
IV	LIAE (400)	129.52±3.23	158.58±2.11	141.00±3.15	141.11±3.11	28.51±0.91	83.27±0.32	29.22±0.52
V	LIAHE (200)	128.33±4.37	159.45±2.05	143.73±2.19	149.25±3.15	23.03±1.01	90.88±1.11	29.85±0.73
VI	LIHAE (400)	130.73±5.01	158.35±2.03	142.35±2.20	150.39±2.22	26.12±1.07	86.27±1.02	30.08±0.44

n=6; Group II is compared with Group I. Groups III- VII were compared with Group II. *P<0.05. **P<0.01.

Table 5: Effect of *Leea indica* leaf extract on serum AST, ALT, TC, TG, HDL, LDL, VLDL levels in alloxan induced diabetic rats on 21st day (mean± SEM)

Group	Treatment (mg/kg)	AST (U/L)	ALT (U/L)	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
I	Control	40.97±3.21	50.05±4.14	82.33±3.10	90.17±5.40	45.040±2.51	19.25±1.53	18.04±1.25
II	Diabetic Control	135.44±5.32**	168.87±4.11**	149.23±2.10**	163.06±3.91**	20.15±2.00**	96.47±3.02**	32.61±1.2**
III	Glibeclamide (10)	55.53±2.45** (55.60%)	53.05±3.13** (65.30%)	84.79±4.14** (35.25%)	91.17±2.97** (35.28%)	46.83±4.01** (87.09%)	19.73±1.55** (74.62%)	18.23±1.7** (35.28%)
IV	LIAE (200)	88.55±3.01** (30.92%)	82.83±3.02** (47.13%)	120.59±2.15** (13.13%)	125.03±3.90** (13.78%)	35.75±2.27** (31.38%)	59.83±2.33** (27.56%)	25.01±1.9** (13.78%)
IV	LIAE (400)	66.45±3.55** (48.69%)	55.66±2.73** (64.90%)	87.00±2.75** (38.34%)	94.70±4.44** (32.35%)	49.19±3.10** (72.53%)	18.87±1.02** (77.33%)	18.94±2.0** (35.18%)
V	LIAHE (200)	82.51±4.32** (35.70%)	85.32±3.75** (46.49%)	120.55±2.01** (16.12%)	125.62±2.02** (15.83%)	33.97±2.01**(47.50%)	61.46±1.37** (32.37%)	25.12±1.5** (15.84%)
VI	LIHAE (400)	70.32±1.01** (46.20%)	60.95±2.02** (61.50%)	85.30±3.12** (40.07%)	97.70±4.15**(35.03%)	45.21±1.05** (73.08%)	20.55±1.05** (76.17%)	19.54±1.3** (35.03%)

n=6; Group II is compared with Group I. Groups III- VII were compared with Group II. *P<0.05. **P<0.01

Table 6: Effect of *Leea indica* leaf extract on serum creatinine and serum urea levels in alloxan induced diabetic rats on 21st day (mean± SEM)

Group	Treatment	Serum Creatinine (mg/dl)	Serum Urea(mg/dl)
I	Control	0.54±0.07	30.26±1.32
II	Diabetic Control	1.20±0.01**	40.53±1.97**
III	Glibenclamide (10 mg/kg)	0.59±0.03** (50.83%)	33.71±1.53** (16.82%)
IV	LIAE (200 mg/kg)	0.71±0.01** (40.83%)	34.32±1.67* (15.32%)
V	LIAE (400 mg/kg)	0.60±0.02** (50.00%)	32.89±1.05** (18.85%)
VI	LIHAE (200 mg/kg)	0.71±0.05** (40.83%)	37.63±1.04 (7.15%)
VII	LIHAE (400 mg/kg)	0.65±0.07** (40.83%)	35.03±1.02*(13.57%)

n=6; Group II is compared with Group I. Groups III- VII were compared with Group II. *P<0.05. **P<0.01.

Table 7: Effect of *Leea indica* leaf extract on liver glycogen levels in alloxan induced diabetic rat's on 21st day

Group	Treatment	Liver glycogen levels (mg/gm) of wet tissue (mean± SEM)
I	Control	50.12±3.12
II	Diabetic Control	22.56±2.15**
III	Glibenclamide (10 mg/kg)	47.83±4.01** (52.83%)
IV	LIAE (200 mg/kg)	42.65±2.71** (47.10%)
V	LIAE (400 mg/kg)	46.54±4.53** (51.52%)
VI	LIHAE (200 mg/kg)	42.71±3.27** (47.17%)
VII	LIHAE (400 mg/kg)	45.91±2.95** (50.86%)

n=6; Group II is compared with Group I. Groups III- VII were compared with Group II. *P<0.05. **P<0.01.

RESULTS

Acute toxicity studies have shown that both alcoholic and hydroalcoholic extracts of *Leea indica* were safe up to a dose of 3000 mg/kg b.wt. No toxicity was observed. So the doses selected were 200 and 400 mg/kg b.wt. Table 1 results have shown the phyto-constituents that were present in *Leea indica* alcoholic extract and hydroalcoholic extract. In the preliminary study of oral glucose tolerance test LIAE and LIHAE at doses of 200 and 400 mg/kg b.wt significantly lowered fasting serum glucose levels in a dose dependent manner (Table 2). LIAE at a dose of 400 mg/kg was found to be more effective than LIHAE at a dose of 400 mg/kg. Oral treatment with LIAE and LIHAE (200 mg/kg & 400 mg/kg) for 21 days significantly and dose dependently reduced the serum glucose (Table 3), triglycerides, cholesterol, low density lipoproteins and very low density lipoproteins, alanine transaminase and aspartate aminotransferase (Table 4 & Table 5) and elevated HDL levels. The extract was also found to decrease serum creatinine and urea levels and increase liver glycogen (Table 6, Table 7). These results indicated that LIHAE at a dose of 400 mg/kg b.wt was more effective than LIAE at a dose of 400 mg/kg and the obtained values are comparatively equal to that of standard, glibenclamide (10 mg/kg).

DISSCUSSION AND CONCLUSION

Results have shown more hypoglycemic and antidiabetic effects of LIHAE in alloxan induced diabetic rats than LIAE treated rats despite of equal doses administered. Presence of the components like terpenoids (ursolic acid) and (tannins) might have induced the observed effect. It is well established that alloxan administration selectively leads to pancreatic β cell membrane disruption by intracellular accumulation leading to insulin deficiency [25]. Insulin deficiency leads to various metabolic aberrations which include increased blood glucose level [26], increased levels of cholesterol and triglycerides [27, 28]. Previous literature reports identified ursolic acid and gallic acid from the leaves of *Leea indica* [21]. Ursolic acid, recently reported as an effective insulin-mimetic agent, which stimulates glucose uptake and enhances insulin receptor phosphorylation [29]. Gallic acid reported to be an insulin-secretagogue, antihyperlipidemic an antioxidant [30]. Thus the reported active principles might be responsible for the observed pharmacological effects. All the obtained results indicated that LIHAE at a dose 400 mg/kg b. wt produces a significant decrease in serum glucose levels, decrease in serum triglyceride levels, decrease in cholesterol levels, decrease in ALT levels, decrease in AST levels and increase in HDL levels and Liver glycogen levels in alloxan induced diabetic rats confirming the traditional indication of *Leea indica* for the treatment of diabetes. It is suggested that the antihyperglycemic and hypolipidemic properties of *Leea indica* could be mainly due to presence of its major compounds like ursolic acid (an effective insulinomimetic), gallic acid (insulin secretagogue). Further studies are required to prove the mechanism of the hypoglycemic action of *Leea indica*

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REFERENCES

1. Sourvh Bias, A phytopharmacological review on an important medicinal plant: *Leea indica*, Inventi Rapid: Ethanopharmacology, 2013, vol (1):1-4.

2. Stevens PF, 2001 onwards, Angiosperm phylogeny website, Version 9, June 2008 (and more or less continuously updated since), http://www.org/MOBOT/research/APweb/ (Accessed on 31 Dec.2009).

3. Angiosperm phylogeny Group (APG), An update of the Angiosperm phylogeny Group classification for the orders and families of flowering plants: APG II, Botanical Journal of the Linnean Society, 2003, 141(4):399-436.

4. Ridsdale CE, A revision of the family Leeaceae, Blumea, 1974, 22(1):57-100.

5. Ridsdale CE. Leeaceae. Flora Malesiana. Series1, 1976, 7, pg 775-782.

6. Saralamp P. Medicinal plants in Thailand. Department of Pharmaceutical Botany, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand, 1997, vol (2).

7. Alvin Francis SL. Lok WF Ang, Ng B.Y.Q, Suen SM, Yeo CK and Hugh TW Tan Leea L, (vitaceae) of Singapore, Nature on Singapore, 2011, vol (4), pg 55-71

8. Srinivasan GV, Sharanappa P and Vijayan KK, International Journal of Biomedical Research and analysis, 2010, vol (1), 92-95.

9. Dhar M L, Dhar M M, Dhawan B N, Mehrotra B N and Ray C, Indian Journal of Experimental Biology, 1968, 6(4), pg 232-247.

10. Srinivasan GV, Sharanappa P, Leela N K, Sadashiva C T and Vijayan K K, Natural product radiance, 2009, vol8(5), pg 448-493.

11. Obayed Raihan Md, Mohammed Tareq Syed, Mohammed, Afrina Brishti, Kursad Alam Md, Haque Anamul, Sekendar Ali Md, American Journal of Biomedical sciences, 2012, vol 4(2), pg143-152.

12. Talha Bio Emran, Atiar Rahman Md, Zahid Hose S.M and Mominur Rahman Md.et al, Phytopharmacology, 2012, vol 3(1), pg 150-157.

13. Abdul manaf Ali, Muhammad mukram mackeen, Saleh H, El-sharkawy, Junainah A. Hamid, NOR HADIANI Ismail, Faujan B. H, Ahmad and Nordin H.Lajis, Antiviral and cytotoxic activities of some plants used in Malaysian indigenous medicine, Pertanika J.Trop.Agric.Sci, 1996,19(2/3), pg 129-136.

14. Obayed Raihan Md, Mohammed Tareq Syed, Afrina Brishti, Kursad Alam Md, Haque Anamul, Sekendar Ali Md, Drug discoveries and Therapeutics, 2011, vol 5(4), pg 185-189.

15. Prapapan Temkitthawan, Jarupa Viyoch, Nanteetip limpeanchub,wittaya pongamornkul, chawlada sirikul, Anchana Kumpila, Khanit suwanborirux, Kornkanok ingkaninan, Journal of Ethanopharmacology, 2008, vol 119 (2), pg 214-217.

16. Saha K, Lajis NH, Israf DA, Hamzah AS, Khoziroh S, Khamis S, Syahida A, Evaluation of antioxidant and nitric oxide inhibitory activities of selected Malaysian medicinal plants, Journal of Ethanopharmacology, 2004, vol 92 (2-3), pg 263-267.

17. Graham JG, Quinn, M L, Fabricant, D S and Fransworth, N R, Journal of Ethanopharmacology, 2000, vol 73(3), pg 347-377.

18. Bourdy, G and Walter, A, Journal of Ethanopharmacology, 1992, 37(3), pg 179-196.

19. Shanmugan S, Annadurai M and Rajendran K, Ethano medicinal plants used to cure diarrhoea and dysentery in pachalur hills of dindigul district in Tamilnadu, Southern India, India Journal of Apllied Pharmaceutical Science, 2011, Vol 01(08), pg 94-97.

20. Govindarajapuram varadarajan, Srinivasan, choorikkat Ranjith, Kochukaratu Krishnan Vijayan, Identification of chemical compounds from the leaves of *Leea indica*, Acta pharm, 2008, vol (58), pg 207-214.

21. Kokate CK, Practical Pharmacognosy, New Delhi: Vallabh Prakashan 1994, vol 4, pg 110-111.

22. Khandelwal Kr, Practical Pharmacognosy, techniques and experiments, Pune: Nirali prakashan, 2000, vol 2, pg 149-155.

23. OECD 17th December 2001, OECD guidelines for testing of chemicals, Acute oral toxicity- Acute toxic class method, No: 423.

24. Devigneaud V, Karr V, J Biol chem, 1985, pg 66-281.

25. Shafrir E. In: porte D, Sherwin Rs, editors, Ellenberg and Rifkins diabetes mellitus, Connecticut: Appleton and Lange, 1997, pg 301.

26. Chude MA, Orisakwe Oe, Afonne OJ, Gamenial KS, Vantau OH, obi E, Indian J Pharmacol, 2001, vol 33, pg 215.

27. Ribes G, Dacosta C, Loubatieres-Mariani MM, Phys Res, 1987, vol 1, pg 38.

28. Venkateshwarlu V, Kokate CK, Rambhau D, Veerashame, Planta Med, 1993, vol 59, pg 391.

29. Jung SH, Ha YJ, Shim EK, Choi SY, Jin JL, Yun-Choi HS, et al, Biochem J. 2007, pg 403:243.

30. Cecily Rosemary Latha. R, Daisy.P, Insulin secretagogue, antihyperlipidemic and other protective effects of gallic acid isolated from Terminalia bellerica Roxb. in streptozotocin-induced diabetic rats, Chemico-biological Interactions, 2011, vol 189, issue 1-2, pg 112-118.

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