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Hypoglycaemic Activity Of *Cedrela Toona* Roxb. Leaves In Alloxan – Induced Diabetic Rats.

Shah Kinjal H[1], Dr. Patel Piyush M[2]*

[1]Research Scholar, Singhania University, Pacheri Bari, Jhunjunu, Rajasthan, India
[2]Professor, Shri B. M. Shah College Of Pharmaceutical Education And Research, Modasa, Gujarat, India
[*]**Correspondent Author:** Shah Kinjal H Research Scholar, Singhania University, Pacheri Bari, Jhunjunu, Rajasthan, India E-mail: kinjalhshah9@yahooo.co.in

Leaf extracts of Cedrela toona Roxb. were evaluated for their antidiabetic activity in Alloxan induced diabetic rats. Diabetes was induced in experimental rats by a single intraperitoneal injection of alloxan monohydrate (150 mg/kg body wt). Ethanol, Chloroform, and Aqueous extracts of Cedrela toona fruits were administered orally at a dose of 250 mg/kg body wt to diabetic rats. Blood glucose was analysed using glucose oxidase – peroxidase reactive strips. Significant antidiabetic activity was observed in ethanolic extract in terms of reduction of fasting blood glucose level in diabetic rats. After 7 hour blood glucose was depressed by 8.2% (P < 0.05) and 10.06% (P < 0.01) in alloxan – induced diabetic rats. The effect of ethanolic extract particularly at 250 mg/kg was comparable to that of standard drug Glibenclamide (1 mg/kg body wt.)

KEYWORDS: Alloxan, *Cedrela toona*, Diabetes, Leaf, Glibenclamide, Hypoglycaemic

Introduction

Diabetes mellitus is a heterogeneous metabolism disorder characterized by altered carbohydrate, lipid and protein metabolism. The incidence of diabetes is very high all over the world and particularly many Indians are suffereing from this disease and its complication in liver, heart, kidneys and lungs. Many Indian medicinal plants have been used successfully for the treatment of diabetes.

Litreture survey reveals that *Cedrela toona* Roxb. is medium sized to large deciduous tree with brown to grey scaly bark. Leaves 15 – 45 cm long usually paripinnate but sometimes with a terminal leaflet in juvenile growth, leaflets mostly 8-20, ± ovate, often falcate, 4-15 cm long, 15-50 mm wide, apex acuminate, base strongly asymmetric, margins entire, mostly glabrous, domatia present as small hair – tuffs; petiole 4-11 cm long, petiolules 5-12 mm long. Penicles 20-40 cm long. Petals 5-6 mm long, white. Capsule ellipsoid, 10-20 mm long, 6-8 mm diameter; seeds winged at both ends[1,2,3,4]. Traditionally the bark is astringent, antidysentric, antiperiodic[5]. Flowers are emmenagogue, leaf is spasmolytic, hypoglycaemic and antiprotozoal[6]. Bark and heartwood yielded tetraterpenoids, including toonacillin. Heartwood also gave a coumarin gerarnyl gernalol as its fatty esters. Toonacillin and its 6 – hydroxyl derivatives are antifeedent[5].

Phytochemical studies reported the presence of Cedrelone , isolated from the benzene extract of the heartwood of the Cedrela toona Roxb[9,10], sesquiterpene, cycloartene stigmasterol, campesterol, apotirucallene, tirucallene, catechin, proanthocynidin ,leucoanthocyanidin, toonacilin, 6-acetoxy toonacilin, toonacilid, geranyl geraniol, δ- cadinene, calamenene, α-calacorene, siderin, deoxycedrelone[18]. Cedrelone, isolated from the benzene\ extract of heartwood of *Toona ciliata*, on photooxidation yield; 3[14β,15β,22β,23β-diepoxy-6-hydroxy-6-hydroy-1,5,20(22)- meliatriene-2,7,21-trione], along with product 4[14β,15β-epoxy-6,23-dihydroxy- 1,5,20(22)-meliatriene-2,7,21-trione][11]. 12α- hydroxystigmat-4-en-3-one: a new bioactive steroid isolated from the petroleum ether extract of *Toona ciliate* (Meliaceae) along with the two known steroid and three C- methyl coumarins[12]. 5- methylcoumarins isolated from the dried and powdered stem bark of *Toona ciliata*, extracted successively with light petroleum ether (40-60°), dichloromethane and methanol in soxhlet apparatus[13]. Limonoids i.e.Toonaciliatins were reported from leaves and stem of *Toona ciliata*[14]. Siderin , a natural coumarin was isolated from the methanolic extract of the leaves of *Toona ciliata* with the help of column chromatography[15]. Toonafolin , a tetranortriterpenoid Blactone isolated from the ether extract of leaves of *Toona ciliata*. Polyynes isolated from the ethylacetate extract of the leaves of *Toona ciliata*[16]. Seven new compounds were isolated from the petrol and chloroform extract of the trees of *Toona ciliata*, and there structure were identified as 3-Acetoxy 17-furan-3- yl-1-

hydroxy-1,4,4,10,13-penta-methyl-12-oxo-tetradecahydro-16,20-dioxacyclopropa[14,15]cyclopenta[alpha]phenanthrene-7- carboxylic acid methyl ester, beta sitosterol, stigmasterol, n-C35H72, palmitinic acid, n-C20H42,3-(3-Propyl-{1,1_,3_,1_]tercyclohexan-3-yl)-propan-1-ol[17]. 9,10dihydrophenanthrenes isolated from the dichloromethane extract of the root of *Toona cilita*[18]. One new limonoid, toonaciliatone A, and one new tirucallane type triterpenoid, toonaciliatine A, along with three known compounds, methyl – 3b-acetoxy-1-oxomelic-14(15)-enate, perforin A, and cholest-14-ene-3,7,24,25-tetrol-21,23-epoxy-21-methoxy-4,4,8-trimethyl-3-(3-methyl-2-butenoate), were isolated from the leaves of *Toona ciliata*[19,20].

Plant also possess antioxidant[21,22], Antiulcer[23,24], Analgesic[25], Antifungal[26], Antimicrobial[27,28], Anti feedant, Anti tumor[29] activity and cytotoxicity[29]. The present study is designed to explore the anti diabetic effect of various extracts of leaves of the plant *Cedrela toona* Roxb. belonging to Family Meliaceae.

Materials and Methods

Plant Material

The leaves of the plant were collected from the Paritosh Herbals, Dehradun in the month of October 2011. The plant was identified and authentified as *Cedrela toona* Roxb. (Family: Meliaceae) by Dr. M. S. Jangid, Department of Botany at Sir P. T. Science College, Modasa, Gujarat, India where a voucher specimen has been deposited.

Preparation of plant powder and extracts

Aqueous, ethanol and chloroform extracts of fruits were prepared following standard procedures. Matured unripe fruits were dried in an incubator for two days at 40^0C, crushed in a mechanical grinder into fine powder. The powder (500 g) was extracted sequentially with 2.5 litres of 60% chloroform in a soxhlet apparatus at 65^0C until the powder became exhausted totally. The resulting extracts were filtered, concentrated and dried in vacuo (yield 7.60, 8.25 and 8.75% w/w, respectively). The extracts were stored in desiccators for use in subsequent experiments.

Phytochemical analysis

Preliminary phytochemical analysis was done following the metod of Harbone[30].

Animals

Healthy adult wistar albino rats weighing 180 – 240 g were used for this study. Animals were allowed to acclimize for a period of 15 days in the laboratory environment prior to the experiment. Rats were housed in standard polypropylene cages (three animals per cage), maintained under standard laboratory conditions (i.e. 12:12 h light and dark cycle, at an ambient temperature of 25 ± 5^0C; 35 – 60% of relative humidity)[31]; the animals were fed with standard rat pellet diet (Hindustan Lever Ltd., Mumbai) and water *ad libitum*. Animal House of B. Pharmacy College, Rampura – Kakanpur, Gujarat, India was used for the study after prior scrutinization and approval from Institutional Animal Ethical Committee. (IAEC/RAMPH/04/2011-12).

Chemicals

Alloxan monohydrate was procured from Loba Chemie, Mumbai. Other reagents used in the experiment were of analytical grade. Glibenclamide (Batch No. 029057) a standard antidiabetic agent, was purchased from Aventis Pharma Ltd, Goa.

Antihyperglycaemic studies

Induction of diabetes, hyperglycaemia was induced in overnight fasted adult rats weighing 180 – 240 g by a single intraperitoneal injection of freshly prepared alloxan monohydrate in normal saline (150 mg/kg body wt) in a volume of 2ml/kg body wt[32]. Hyperglycaemia was confirmed by the elevated glucose level in

plasma determined at 48 hr after injection[33]. The hyperglycaemic rats were used for antihyperglycaemic study.

Experimental design

Animals were divided into six groups of six rats per groups. Test groups were administered aqueous, ethanol and chloroform extracts at a dose of 250 mg/kg body wt, respectively by oral route. Positive control group animals were treated with standard drug Glibenclamide at an oral dose of 1 mg/kg body wt. All doses were started 48 h after alloxan injection.

The experimental designs were as follows:

Group I : Control (2 ml/kg body wt)
Group II : Diabetic + Alloxan (2 ml/kg body wt)
Group III : Diabetic + aqueous extract of *Cedrela toona* leaf (250 mg/kg body wt)
Group IV : Diabetic + ethanol extract of *Cedrela toona* leaf (250 mg/kg body wt)
Group V : Diabetic + chloroform extract of *Cedrela toona* leaf (250 mg/kg body wt)
Group VI : Diabetic + Glibenclamide (1 mg/kg body wt).

Fasting blood glucose levels were estimated at 1, 3, 5 and 7 h after administration of treated and control drugs.

Collection of blood and determination of serum glucose

Blood was withdrawn from the tail vein and glucose levels were estimated using glucose oxidase – peroxidase reactive strips and a glucometer (Ascensia Entrust, Bayer Health Care, USA).

Statistical analysis

Data were statistically analysed using one – way ANOVA and expressed as mean ± S.E.M. followed by Dunnett's t – test using computerized Graph pad instate version 3.05, Graph pad software, U.S.A.

Results And Discussion

Alloxan (β – cytotoxin chemical) induced diabetes in a wide variety of animal species including rats, damaged the insulin – secreting β – cells. In the present study, hypoglycaemic activity of *Cedrela toona* leaf extracts was evaluated in alloxan – induced diabetic rats. The preliminary phytochemical analysis revealed the presence of alkaloids, tannins, flavonoids and triterpenoids. The effect of chloroform, ethanol and aqueous extract of leaves on blood glucose levels of alloxan – induced diabetic rats are shown in Table 1. The blood glucose level was reduced maximum in ethanol extract at 5^{th} and 7^{th} h after treatment. Blood glucose was depressed by 8.2% *(P<0.05)* and 10.06% *(P<0.01)* in alloxan – induced diabetic rats after treatment which was comparable to the standard drug, Glibenclamide. This may be due to the activation of the existing pancreatic cells in diabetic rats by the ethanolic extract. Futher, comparative studies of alloxan induced results with Streptozotocin induced diabetic rats with respect to leaves and other parts of the plant are to be taken up by us.

Table 1 – Effect of *Cedrela toona* on blood glucose level of alloxan – induced diabetic albino rats

Group	Dose	Blood glucose level (mg/100 ml) (mean ± SEM)				
		Initial	1 h	3 h	5 h	7 h
I	2 ml saline	98.56 ± 0.874	99.32 ± 0.866	99.4 ± 0.950	99.91 ± 1.288	99.74 ± 1.133
II	2ml saline 150 mg/kg b. wt.	203.6 ± 3.850	208.3 ± 4.485	213.0 ± 3.83	217.8 ± 4.03	222.0 ± 4.058
III	250 mg/kg b. wt.	204.6 ± 4.162	203.0 ± 4.239	200.0 ± 4.167	196.1 ± 3.953	191.7 ± 4.009
IV	250 mg/kg b. wt.	203.3 ±	202.4 ±	199.2 ±	193.2 ±	184.8 ±

		3.697	3.382	3.401	3.158	3.818
V	250 mg/kg b. wt.	205.7 ± 3.042	203.5 ± 3.201	200.0 ± 3.282	198.5 ± 2.571	195.0 ± 2.897
VI	1 mg/kg b. wt.	286.33 ± 10.84	217.67 ± 7.68	197.83 ± 7.77	189.5 ± 8.73	146.67 ± 6.48

Conclusion

The present study suggested that the ethanolic extract of *Cedrela toona* leaf possesses hypoglycaemic activity and therefore further studies can be taken up for drug discovery.

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