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Preliminary evaluation of antidiabetic activity of *Chukrasia tabularis* A. Juss on streptozotocin induced male wistar rats

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ABSTRACT

This study aimed to evaluate the hypoglycemic and hypolipidemic activity of aqueous seed extract of *Chukrasia tabularis* A.Juss a wild relative of Neem. The aqueous crude seed extract was administered for 15 days in streptozotocin- induced diabetic rats. Administration of the extract at 400 mg/kg body weight significantly (P -values<0.05) decreased blood glucose levels, and improved imbalance in lipid metabolism in diabetic rats. This significant result shows the best hypoglycemic action.

Keywords: *Chukrasia tabularis* A. Juss, Aqueous seed extract, hypoglycemic activity, Hypolipidemic activity, Streptozotocin and Male wistar Rats.

INTRODUCTION

The use of medicinal plants has gained momentum with the continued search and experience of many generations of physicians and herbal practitioners. The plant products are presented in 14 of the 15 therapeutic categories of pharmaceutical preparation and they form an important role of health care system in western world [1, 2]. 25% medicine of all prescription in U.S.A is from natural products and another 25% medicines are the modification of natural products [3]. According to W.H.O 80% of World inhabitants are relied on traditional medicine for primary health care [4]. However 25% of modern medicines are derived from the plant products [5]. The pharmaceutical industries for the preparation of the drugs would depend on minerals, animals, and synthetic, microorganisms, genetic engineering and plant or plant oil. Out of the plant oil, essential oil is a good source for the drugs, which will have aroma and eco-friendly.

Diabetes mellitus is a major endocrine disorder and growing health problem in most countries [6]. It is a metabolic disease as old as mankind and its incidence is considered high all over the world [7]. Increase in sedentary lifestyle, consumption of energy-rich diets, and obesity are some of the factors causing the rise in the number of diabetics. The World Health Organization (WHO) estimated diabetes in adults to be around 173 million, and about two-thirds of these patients live in developing countries [6]. The use of natural remedies for diabetes treatment is also strengthened due to the belief that herbs can provide some benefits over allopathic medicine and allows users to feel that they have some control in their choice of medication [8].

MATERIALS AND METHODS

During Ethnobotanical and taxonomical explorations during 1997-2001 (D.M.Rao and T.Pullaiah, 2001, Flora of Eastern Ghats vol-1, Regency publication, New Delhi), authors came to know that, aboriginal tribal's in nallamalais used *Chukrasia tabularis* seeds as diabetic control agent.

Plant Description

Chukrasia tabularis A. Juss belongs to Meliaceae family and is a deciduous, monoecious, medium-sized, sometimes fairly large tree up to 30 m tall (max. 40 m); bole branchless for up to 18 m (max. 32 m), with a diameter of up to 110 cm (max. 175 cm), without buttresses; bark surface rusty brown or deep brown, deeply fissured or cracked, with lenticels, inner bark reddish. Leaves are paripinnate, with 4-6 pairs of alternate, entire, asymmetrical and acuminate leaflets (imparipinnate and lobed or incised when juvenile), glabrous or with simple hairs. Flowers unisexual, in axillary (sometimes appearing terminal) thyrses, tetramerous or pentamerous, up to 16 mm long; calyx lobed; petals free, contorted, reflexed in open flowers, white. Fruit an erect woody ovoid or ellipsoid capsule opening by 3-5 valves from the apex; valves separating to a woody outer and inner layer, apex of those in the inner layer deeply bifid; locules appearing as 1 locule due to the breaking of the septae; columella with sharp ridges. Seeds are 60-100 per locule, flat, with terminal wings arranged in layers.

Plant Material

The plant materials were collected in the vicinity of Nallamala forests. The authentication was checked by taxonomic expert from the Department of Botany, SKU, Anantapur, Specimen number is Tirumala Hills (CTR) DMR 24067. During selection, disease free seeds were selected in order to avoid unexpected results during analysis. The sundried material was stored in sterilized polythene packet and kept ready for extraction [9, 10, 11].

Procurement of animals and maintenance

Male Albino rats of body weight 150-250 gms were procured from Sri Venkateswara Enterprises, Bangalore. Animals were maintained as per guidelines of NIN animal user manual. Animals are acclimatized for 10 days to our animal house, maintained at temperature of $22^{\circ} \pm 2^{\circ}$ c. The animal was regulated by a 12 hours light, 12 hours dark schedule. Five animals are housed per cage sized 41cm length, 28 cm width and 14 cm of height. Paddy husk was used for bedding and on very alternative day bedding was changed and washed thoroughly with water along with Domex, a disinfectant and detergent. The rats were fed on a standard pellet diet purchased from Sai Durga Feeds and Foods, Bangalore.

Animal ethical clearance

Local Institutional Animal ethical committee of our university obtained ethical clearance for conducting experiments on animals from committee for the purpose of control and supervision of experiments on animals (CPCSEA) (Regd.no. 470/01/a/CPCSEA, dt 24th Aug 2001). The present work was carried out with a prior permission from Local Institutional Animal ethical committee.

Animals used

25 Albino male wistar rats weighing 200-250gms were used in the experiment. Then they were grouped into five groups of each containing 5 as Normal control, Normal Treated, Diabetic control, Diabetic Treated (Test) and Diabetic Treated (Standard). The rats were trained to remain quiet in restraint cage.

Extract used

The aqueous seed extract of *Chukrasia tabularis* was used. Weighed amount of the dried extract was suspended in 1% W/V SCMC solution and administered through orally to rats at a dose of 400mg/kg body weight.

Test Drug

STZ was used for this study, at 60 mg/kg by i.p. route.

Standard Drug

Glibenclamide was used for this study as a standard drug.

Experimental Design

Thirty male Wister rats were used in this study. The rats were randomized and divided into the following five groups of five animals each.

- Group I : Normal Control rats, received citrate buffer (0.01M, pH 4.5)
 Group II : Normal treated rats, receiving Aqueous extract of *Chukrasia tabularis* (400mg/kg body weight) orally for 15 days.
 Group III : Diabetic controls, received STZ (60 mg/kg body weight, i.p.) once.
 Group IV : Diabetic test treated rats, receiving aqueous seed extract of *Chukrasia tabularis* (400 mg/kg body weight) orally for 15 days.
 Group V : Diabetic standard treated rats, receiving 0.5 mg/kg body weight of glybenclamide orally for 15 days.

Collection of blood sample

Blood samples were collected by end tail vein cutting method for blood glucose level was determination. At the end of the experiment, after fasting for 16 hours, blood was collected through ocular puncture to separate serum for various biochemical estimations.

Measurement of blood glucose level

The blood glucose level was measured for 7days by using single touch glucometer (ACCU CHECK ACTIVE).

Serum Triglyceride

Serum triglyceride was measured by using kit (Ebra Mannheim). The absorbance was noted at 540/670nm. The value was expressed in the unit of mg/dL.

Serum Total Cholesterol

Serum total cholesterol (TC) was quantified by spectrophotometric method by the addition of enzyme present in reagent kit (Ebra Mannheim). The absorbance of red quinoneimine complex was determined at 505/670nm. The value of TC present in serum was expressed in mg/dL

Serum HDL-cholesterol

Serum HDL was measured by using kit (Ebra Mannheim). The absorbance was noted at 540/670nm. The value was expressed in the unit of mg/dL.

Serum low density lipoprotein (LDL)

Low density lipoprotein (LDL) was calculated as per Friedevald's equation:

$$\text{LDL} = \text{Total cholesterol} - \frac{\text{Total triglycerides}}{5} - \text{HDL}$$

Table 1: Glucose level values

Animal Groups	INITIAL	DAY1	DAY3	DAY5	DAY8	DAY10	DAY15
GROUP I (n=5)	89.2 ± 1.393	89 ± 0.7071	90.2 ± 1.393	90.4 ± 1.030	91 ± 1.049	90.8 ± 1.068	90.2 ± 0.7848
GROUP II (n=5)	96.7 ± 3.513*	97.2 ± 2.289*	100 ± 2.646*	101.3 ± 1.860*	101.6 ± 1.530*	101.2 ± 1.020*	98.5 ± 2.694*
GROUP III (n=5)	278.5 ± 3.007*	279.85 ± 4.339*	281.42 ± 5.051*	289.71 ± 5.511*	290.14 ± 5.812*	290.71 ± 5.571*	290.28 ± 5.870*
GROUP IV (n=5)	258.28 ± 4.04*	209.14 ± 3.305*	173.42 ± 3.605*	151 ± 2.828*	133 ± 3.147*	109.5 ± 2.852*	108.85 ± 3.355*
GROUP V (n=5)	252.8 ± 3.426*	206.4 ± 1.806*	169.8 ± 2.905*	141.6 ± 2.015*	123.8 ± 1.463*	112.2 ± 1.393*	99.8 ± 1.241*

The values are expressed as mean ± SEM.; n= number of animals in each group.

Statistical significant test for comparison was done by ANOVA, followed by Dunnet's –'t' test.

The values of 1st and 3rd days are compared with intial values. *- Significant

Statistical analysis

Statistical evolution of data was performed by using one-way analysis of variance (ANOVA) followed by Dunnet's t-test. P-values<0.05 were considered as significant.

Table 2: Results of Triglycerides, Total Cholesterol, HDL, LDL

Animal Groups	TRIGLYCERIDES	TOTAL CHOLESTROL	HDL	LDL
GROUP I (n=5)	79.45±0.8156	127.114±0.8297	49.494±0.3819	61.726±0.7017*
GROUP II (n=5)	78.62±1.246*	123.234±0.3488*	54.006±0.3717*	53.5±0.6284*
GROUP III (n=5)	185.98±0.899*	237.676±0.8384*	24.406±0.3304*	176.068±0.7782*
GROUP IV (n=5)	84.57±0.3727*	139.693±0.2676*	39.976±0.2553*	82.8±0.2543*
GROUP V (n=5)	74.5±0.3784*	133.9±0.4581*	44.992±0.3656*	74.004±0.7*

The values are expressed as mean ± SEM; n= number of animals in each group.

Statistical significant test for comparison was done by ANOVA, followed by Dunnett's – 't' test.

The values of 1st and 3rd days are compared with initial values. *- Significant

DISCUSSION

The present study is assessment of antihyperglycemic activity of alcoholic extract of seeds of *Chukrasia tabularis* on male wistar rats. STZ is toxic to pancreatic β -cells and is thus widely used for induction of experimental diabetes mellitus in animals, resulting in the production of ROS [12]. STZ causes a significant elivaton in the level of blood glucose in rats [13, 14]. Administration of 400 mg/kg body weight of alcoholic extract of *Chukrasia tabularis* seed powder significantly decreased the blood glucose level in these rats suggesting that it has hypoglycemic properties (Table-1).

The decreased body weight in diabetic rats is due to excessive breakdown of tissue proteins. Treatment with *Chukrasia tabularis* improved body weight significantly in a dose dependent manner, indicating prevention of muscle wasting due to hyperglycemic condition. The rise in blood sugar is accompanied with the increase in TC, LDL-c, TG and fall of HDL-c [12]. Diabetes is also known to be associated with an increase in the synthesis of cholesterol, which may be due to the increased activity of HMG CoA reductase [15, 16]. Increased LDL-cholesterol may arise from gylcosylation of the lysyl residues of apoprotien B as well as from decreasing affinity for the LDL receptor and hence, decreased metabolism (Table-2).

A number of observations indicate that plasma HDL cholesterol is low in untreated insulin-deficient diabetics, which was associated with a decline in HDL-turnover rate [17, 18]. Further the HDL-cholesterol levels correlate with lipoprotiene lipase levels in IDDM patients. Hypertriglyceridemia is a common finding in patients with diabetes mellitus and is responsible for vascular complications. It has been reported deficiency of lipoprotein lipase (LPL) activity may contribute significantly to the elevation of triglycerides in diabetes (Table-2). However, oral administration of EESC exhibited hypocholesterolemic and hypotriglyceridemic effects while at the same time increasing HDL-c, possibly by controlling the hydrolysis of certain lipoproteins and their selective uptake and metabolism by different tissues. This implies that EESC can prevent or be helpful in reducing the complications of lipid profile seen in some diabetics in whom hyperglycaemia and hypercholesteromia coexist quite often. Induction of diabetes in rats with STZ uniformly results in an increase in lipid peroxidation (TBARS), an indirect evidence of intensified free radical production. Most of the tissue damage is considered to be mediated by these free radicals by attacking membranes through peroxidation of unsaturated fatty acids. The concentration of lipid peroxidation products may reflect the degree of oxidative stress in diabetes. In the present study the concentrations of lipid peroxides and hydroperoxides were significantly increased in liver of diabetic rats, indicating an increase in the generation of free radicals. An observed increase in the level of TBARS in liver may be due to increased susceptibility of the tissue of diabetic rats to lipid peroxidation. Administration with *C.tabularis* protects the cells through attenuation of lipid peroxidation and decreased the production of free radical derivatives, as evident from the decreased levels of liver MDA and hydroperoxides.

This suggests protective role of EESC, which could be due to the antioxidative effect of polyphenols present in the seed extract, which may act as strong superoxide radical and singlet oxygen quenchers. Reduced activities of SOD and CAT in liver of diabetic rats have been observed in our study. The decreased activities of SOD and CAT in liver during diabetes may be due to increased production of reactive oxygen radicals that can themselves reduce the activity of these enzymes. SOD is an important defense enzyme which converts super oxide radicals to hydrogen peroxide. Increase in SOD activity could be due to its indication by increased production of superoxide, which has been implicated in cell disfunction. H_2O_2 has been reported to act as an inducer of tissue SOD. CAT is a hemeprotien, which decomposes hydrogen peroxide and protects the tissues from highly reactive hydroxyl radicals. The reduction in the activity of these enzymes may result in a number of deleterious effects.

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