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ANTI-DIABETIC PROFILE OF *CINNAMON* POWDER EXTRACT IN EXPERIMENTAL DIABETIC ANIMALS

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ABSTRACT: Objective: to investigate the anti diabetic effect of ethanolic extract of *Cinnamomum zeylanicum* on Alloxan induced diabetes in experimental animals (Rats). **Materials and Methods:** the alcohol extract of Cinnamomum *zeylanicum* was tested for its efficacy in Alloxan (150mg/kg) induced diabetic rats. The diabetic rats were divided into 5groups. Group I (control) received 2% gumacasia, group II (positive control) received standard drug Glibenclamide (10mg/kg+2%GA), group III, IV, V (T_1 T_2 T_3) were treated orally with a daily dose of 50mg/kg, 100mg, 200mg, respectively for 30 days, for all diabetic rats after giving TEST, NC, PC preparations, the blood samples were collected & the blood glucose levels determined at 0, 1…, 0 hr reading is before giving the drug & the remaining three readings after giving the drugs. 24th hr reading is considered as 0hr reading for the next day. **Results**: administration of alcohol extract of *Cinnamomum zeylanicum* produced a dose dependent decrease in blood glucose levels in Alloxan induced rats. There was significant fall in blood sugar level in High dose (200mg/kg) in comparison to low dose (50mg/kg) and median dose (100mg/kg) shown by LSD test. This is comparable to the effect of Glibenclamide. **Conclusion**: the results of this study show that chronic oral administration of an extract of *Cinnamomum zeylanicum* at an appropriate dosage may be good alternative anti diabetic agent.

INTRODUCTION: Diabetes mellitus is the world's, largest endocrine disease with deranged carbohydrate, fat and protein metabolism. The diabetes mellitus is mainly classified into two major groups, Type-1 (insulin dependent diabetes mellitus), Type-2 (non-insulin dependent diabetes mellitus. As per WHO report, approximately 150 million people have Diabetes mellitus worldwide, and this number may be doubled by the year 2025. Statistical projection suggests that the number of diabetics will rise from 15 million in the year 1995 to 57 million in 2025 in India.

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This number is making India the country with the highest number of diabetics in the world. [1] Long-term complications of diabetes are micro vascular (neuropathy, retinopathy, nephropathy) and macro vascular (heart complications) [2] diseases. The anti diabetic drugs are mainly used to replace the insulin deficiency or to enhance the action of insulin and/or decrease the insulin resistance. Although many drugs and interventions are available to manage diabetes, these are expensive for the large diabetic population of developing countries like India, apart from their inherent adverse effects. [3]

So it is necessary to look for new cheep alternatives to manage this major health problem. Different indigenous drugs are used in this subcontinent for several centuries for treatment of Diabetes mellitus with conflicting reports of their efficacy because of lack of scientific investigation in a laboratory

setting. Cinnamon is one of the oldest spices known to mankind. It is a sweet aromatic spice and the native of Sri Lanka. Cinnamon is a tropical ever green tree and the inner barks of the tree is dried and used as spice. The scientific name for Cinnamon is *Cinnamomum zeylanicum*. It is cassia-based cinnamon that is often seen on the grocery shops. *Cinnamomum zeylanic* has long been used traditionally in the treatment of Diabetes mellitus since many years [6] in South Asian countries especially in Srilanka and has rich Ayurvedic reference that made us select it for this study.

In this study, the anti diabetic potential of powder extract of *Cinnamomum zeylanicum* was screened on laboratory animal model [4, 5].

MATERIALS AND METHODS:

Before conducting this study, Institutional Animal Ethical Committee (IAEC) permission was taken. This study was conducted strictly according to CPCSEA guidelines.

Cinnamomum zeylanicum:

The powder of Cinnamomum *zeylanicum* can be used for this purpose traditionally. The Cinnamon was collected from the local market of Kurnool city and they were carefully washed to remove dust particles and other foreign materials and dried in shaded areas. The completely dried pieces were powdered with electric grinder and stored in well closed bottles. This Cinnamon powder preparation was used in the present study.

Alcohols extract preparation:

The extract is a concentrated preparation of vegetables or animal source Extract: The extract is the process or act of pulling or drawing out the active principle of a particular material like plants or animal organs. In the present study the percolation method was selected to extract the active principle of *Cinnamomum zeylanicum* powder material [6].

Cold percolation method: This is a traditional method of extraction used by the herbalists throughout the world. This is the original extraction method, and it's continuing to be the backbone of the present extracting technology. The distillation devices are "modified Soxhlet extractions" made by Eden Labs [8].

Extraction procedure:

The dried fine powder of the *Cinnamomum zeylanicum* was weighed in balance 40g and taken into the sac like cloth material and placed in the Soxhlet basket. 400ml of ethyl alcohol was taken as solvent into the Soxhlet flask. The extract laden solvent falling from the Soxhlet basket is dark in color and it becomes clearer, that indicates the extraction process is finished [9]. At the end of the extraction process the solvent is then evaporated and the remaining mass is measured.

The percentage yields are calculated as mg per gm dried powder. In 400ml of alcohol, 40gms powder was suspended. 14gms (35%) of extract was obtained. The extract was suspended in 5ml of 2% Gum acacia and used for the oral administration in diabetic rats.

Animals used:

25 Rats of either sex, adult, healthy albino rats of local strain weighing between 250 to 300gms were used in this experiment. All the animals were kept in an air-conditioned animal house in the Pharmacology Department at the Kurnool Medical College, Kurnool. The rats were offered a rats pellet food and allowed tap water to drink [10].

Preparation of diabetic Rats:

The 25 rats weighing between 250-300gms were made diabetic by injecting 150 mg/kg bodyweight of alloxan monohydrate, intraperitoneally [11, 12]. Before giving Alloxan, the normal blood glucose levels of all rats were estimated. After 2hours of Alloxan injection the Dextrose (5gm) mixed with water was fed to the all-diabetic rats orally to prevent a hypoglycemic condition of rats with Alloxan [7]. After 72hours of Alloxan injection, the blood glucose levels of all surviving rats were determined by the glucose oxidase method. The rats with blood glucose levels of 220 to 500mg/dl were considered as diabetic and were employed for further study [13].

TABLE1: GROUPING OF ANIMALS (RATS)

Groups	Animals	Drug	Remarks
I	Negative control	(2% Gum Acasia)5ml	Placebo
II	Positive control	(Glibenclamide 10mg/kg+ 2% GA)5ml	Positive
III	Test (low dose 50mg/kg)	Alcohol Extract+2%GA 5ml	ExL
IV	Medium dose (100mg/kg)	Alcohol Extract+2%GA 5ml	ExM
V	High Dose (200mg/kg)	Alcohol Extract+2%GA 5ml	ExH

All Alloxan diabetic rats were randomly divided into five groups (1-5) of five animals each.

For all the diabetic rats after giving test, negative control and positive control preparations, the blood samples were collected & the blood glucose levels were estimated at 0, 1, 3 24 hrs. 0 hr reading is the one before giving the drug. 1, 3, 24 hr readings are the ones taken after giving the drug. The 24th hour reading is considered as '0'hour reading for the next day. After administration of drugs to the diabetic rats the blood was collected 1, 3 and 24-hour interval daily up to 28 days and blood glucose level was determined with the glucose oxidase method by using Glucometer for 28 days. The glucose oxidase method is more accurate, rapid and time saving method. It requires only small amount of blood. So this method is popularly used in Indian people suffering from diabetes for self-monitoring of blood glucose levels[14].

RESULTS: In the present study, alcohol extract of the *Cinnamomum zeylanicum* was assessed for its anti diabetic activity in Alloxan-induced diabetic rats. The results obtained were recorded. In **Table 2**, only weekly report was given up to 4th week (28 days).

TABLE 2: AVERAGE BLOOD GLUCOSE LEVELS OF ALL GROUPS (I TO V) BEFORE AND AFTER TREATMENT UP TO 28TH DAY

S.No.	Group – I			Group – II			Group – III			Group – IV			Group - V		
Before Alloxan	**75mg/dl**			**73 mg/dl**			**86 mg/dl**			**79 mg/dl**			**98 mg/dl**		
After Alloxan (72 Hrs.)	**288mg/dl**			**296 mg/dl**			**300 mg/dl**			**301 mg/dl**			**300 mg/dl**		
After Treatment	**0 Hr**	**1 Hr**	**3 Hr**	**0 Hr**	**1 Hr**	**3 Hr**	**0 Hr**	**1 Hr**	**3 Hr**	**0 Hr**	**1 Hr**	**3 Hr**	**0 Hr**	**1 Hr**	**3 Hr**
Day 1	288	300	301	296	280	266	300	301	310	301	293	292	300	315	316
1st week	300	277	260	259	229	240	266	255	281	266	269	275	240	233	259
2nd week	326	398	295	183	194	162	236	220	225	180	220	203	155	156	169
3rd Week	281	225	275	150	156	144	231	227	224	169	165	128	134	165	130
4th Week	211	221	230	121	136	148	181	174	196	165	141	140	125	125	133

After 28 days of treatment, there is a significant decrease in blood glucose levels was seen with the standard drug Glibenclamide and Ethanolic extract of Cinnamomum ***zeylanicum*** but there is no significant reduction in the control group treated with gum acacia.

TABLE 3: MEAN BLOOD SUGAR LEVEL OF DIFFERENT GROUPS:

Time	Group-I	Group-II	Group-III	Group-IV	Group-V
0 hr	273±10.2	113.4±2.3**	153±11.3*	156.4±3.5**	131±4.2***
1st hr	268.3±5.1	121.5±0.5***	178±15.7**	138.2±11.3***	123.5±3.6***
3rd hr	269.5±19	131.5±18.4***	198.3±19*	148±6.7***	131±18.4***

P<0.05, **P<0.01, ***P<0.001 compared to the control.

TABLE 4: MEAN BLOOD GLUCOSE LEVELS (MEAN±SEM) AT 28TH DAY.

Animals	Control	Glibenclamide	Ex-L	Ex-M	Ex-H
R1	-11.14	-78.66	-58.11	-80.51	-156.45
R2	-366.56	-65.31	-39.65	-58.19	-68.28
R3	-11.38	-69.69	-77.61	-73.33	-89.05
R4	-58.10	-121.48	-8.04	-54.83	-161.05
R5	4.65	-62.11	-77.62	-78.79	-58.22
Variation	NS	Sig	Sig	Less sig	Sig

DISCUSSION: In the present study, alcohol extract of powder of the *Cinnamomum zeylanicum* was assessed for its anti diabetic activity in Alloxan-induced diabetic rats. The results obtained were recorded. A placebo-controlled sub-acute study was conducted on 5 groups of 5-diabetic rat models to show the hypoglycemic effect of 3 increasing doses (50mg/ kg, 100mg / kg and 200mg / kg body weight) of the alcohol extract of *Cinnamomum zeylanicum* suspended in gum acacia. The result was compared with the established anti-diabetic drug Glibenclamide in the dose of 10mg/Kg body weight. Gum acacia was taken as the placebo in this study.

The blood sugar level was recorded daily by Glucometer for 28 days but in the above table only weekly report was given. The decrease in the blood sugar level was recorded daily from the initial value and was shown in the above table (**Table 2**). Here the blood sugar levels were highly decreased after treatment with high dose of extract. The blood sugar levels came down to almost normal levels. The high dose effect of extract is almost similar to Glibenclamide effect after 28 days of treatment. The fall in the blood sugar level was summarized in **Table 1** to **4** and ANOVA tests were done. There was significant variation in the decrease of blood sugar among the diabetic rat models in each group except in dose of 200mg / Kg body weight. (**Table 3**)

Overall comparison between different groups of rats:

The fall in the blood sugar was compared among the groups of animals with ANOVA. It was found that there was significant variation ($P < 0.01$) among the groups.

Multiple comparison tests were performed to find out the differences between the groups:

Comparison with Control:

The Dennett's test was conducted between the control group and the groups that were given Glibenclamide and the extracts in 3 increasing doses. As expected the fall in the blood sugar level was significant ($P < 0.05$) in the Glibenclamide group. There was no significant difference in the fall in the blood sugar levels with ExL, ExM in comparison with the control but there was significant ($P < 0.05$) fall in blood sugar level in ExH group.

Comparison with Glibenclamide:

The effect of Extract in all the 3 doses in lowering blood sugar level showed no statistically significant difference with that of Glibenclamide in the doses used in this study. This result was checked by two post-ANOVA multiple comparison tests like LSD test of Fisher (accommodates a lot of Type I error) and FSD test of Scheffe (accommodates a lot of Type II error). Both the tests gave an identical result. It gave a strong hint that the Extracts of *Cinnamomum zeylanicum* were as efficient as Glibenclamide in lowering the blood sugar in diabetic rats and that was achieved in a broad range of doses ranging from 50mg/ Kg to 200 mg / Kg, so it might be much a safer alternative to the established drugs.

Comparison between different doses of the Extract:

There was significant fall in blood sugar level in ExH dose in comparison to ExL and ExH dose in comparison with ExM as shown by LSD test. But such difference was not found in with Scheffe's test. The present study, the hypoglycemic effect of *Cinnamomum zeylanicum* extract was compared with Glibenclamide. Similar studies by Akhtar MS et al, in 1981 and Biyani MK et al (2003) the acute hypoglycemic effect was compared with sulphonylureas and concluded positive effect. So the present study showed the hypoglycemic effect of alcoholic extract of *Cinnamomum zeylanicum* in the dose ranging from 50mg/kg, 100mg/kg, 200mg/kg.body weight of diabetic rats given orally. The hypoglycemic effect was comparable to that of the standard anti-diabetic drug Glibenclamide in the dose of 10mg/Kg body weight of rats. The broad dose range of hypoglycemic effect of *Cinnamomum zeylanicum* may be an interesting finding which may prove it safer in comparison to the established hypoglycemic drugs.

CONCLUSION: *Cinnamomum zeylanicum* was taken traditionally for control of diabetics in India and in other countries for long time. Three doses of alcoholic extract of the powder of *Cinnamomum zeylanicum* were taken to study the hypoglycemic

effect of in 5 groups of Alloxan-induced diabetic in Rats. It was a placebo-controlled open study where blood sugar levels were recorded daily for 4 weeks. The study showed hypoglycemic effect of the extract in the oral dose range of 50mg/kg to 200mg/ kg body weight of rats. The hypoglycemic effect was comparable to that of established anti-diabetic drug Glibenclamide in the dose of 10mg / Kg. The broad dose range of the extract producing hypoglycemic effect in diabetic rats was an interesting observation, which requires further study.

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