# Polyherbal drug of Cumin seeds: A future remedy for Diabetes mellitus?

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**Abstract**— In the present investigation an attempt is made to study the hypoglycemic effect of different combinations of cumin seeds in streptozotocin (STZ) induced diabetes rats. Cumin is the second most traded herb in the world. Cumin seeds are an excellent source of dietary fibre and contain many beneficial phyto-chemicals. The oral feeding of cumin extract in diabetic rats at a dosage of 250mg/kg body weight exhibited a significant reduction in fasting blood glucose level. Body weights were reduced in STZ- induced rats compared to control and only cumin extrac rats. In histology studies pancreatic cells were destroyed in diabetic treated rats, the rats fed with Cumin extract has regenerative effect on pancreatic tissue compared with control rats. In spleen, the changes caused after induction of diabetes was severe hyperemia in red pulp and sinusoids. The red pulp appeared control, which was brought back to normal after feeding with Cumin extract. While in kidney sections Diabetic rats showed degenerated glomeruli infiltrated by the inflammatory cells. Rats fed with Cumin seeds powder extracts showed features of healing i.e. normal glomeruli, absence of inflammatory cells. These results demonstrate that the combinational Cumin extract possesses a potent hypoglycemic effect in STZ- induced diabetic rats, thus supporting its traditional use in diabetes mellitus control.

**Index Terms**—Diabetes mellitus, Cumin extract, Streptozotocin (STZ), hypoglycemia.



## 1 INTRODUCTION

**Diabetes mellitus**is a group of metabolic diseases, the person has high blood glucose either because insufficient production of insulin, or because the improper response of body's cells to insulin. There are many reasons for developing diabetes mellitus, one prime factor for is an inadequate mass of β-cells in the pancreas [1].The World Health Organization (WHO) estimates that nearly 200 million people all over the world suffer from diabetes and it will be doubled by 2030. In India, there are approximately 50 million diabetics, according to the statistics of the International Diabetes Federation [2]. Diabetes is a human ailment affecting many people in different countries. In India it is provoking to be a major health issue, particularly in urban areas [3]. Chronic hyperglycemia leads to complications like diabetic nephropathy, diabetic retinopathy, diabetic neuropathy and diabetic cardiomyopathy [4&5]. There is a need for appropriate therapy to treating this disease with feasible medicine. [6]. In modern healthcare the treatment for diabetes system include insulin and oral hypoglycemic drugs [7].Due to economic constraints, it is not potential for majority of the diabetic patients to use these drugs on regular basis. Moreover synthetic antidiabetic drugs are associated with large number of adverse effects. Research investigation of traditional herbal remedies provides valuable alternative drugs and strategies [8].Herbal drugs are attaining popularity in the management of diabetic mellitus [9]. Herbal medicines are gaining higher importance because of limitations with synthetic drugs. The herbal drugs with antidiabetic activity are commercially formulated because of easy availability, affordability and minimal side effects as compared to the synthetic antidiabetic drugs. In India around 600 herbal drug manufacturers all are developing Antidiabetic herbal formulations (AHF) [10]. Spices that are used in India have been found to possess hypoglycemic activity in experimental as well as clinical studies [11 & 12]. Cumin (*Cuminum cyminum)* is the second most traded herb in the world. It is widely used as a spice in many countries. *Cuminum cyminum* L. belongs to the family Apiaceae is consumed in large quantities by Indians [13]. The seeds of Shahi Jeera (*Bunium persicum)* are longer and darker and are commonly known as black cumin. Cumin seeds are an excellent source of dietary fibre and contain many beneficial phyto-chemicals. This spice is also an excellent source for dietary minerals such as iron, copper, zinc, selenium and potassium. Several nutrients (vitamins, amino acids, protein, and minerals), starch, sugars and other carbohydrates, tannins, phytic acid and dietary fiber components have also been found in cumin seeds. [14, 15&16].Cumin has been used for centuries is many traditional medicinal systems, most disreputably in Ayurveda. Cumin is now being backed up by scientific studies that confirm the benefits of cumin in our regular diet [17]. The present study aims to evaluate the antidiabetic efficacy of variety of Cumin seeds extract was evaluated by short- term and sub-acute studies in streptozotocin- induced diabetic rats.

## 2 Materials and methods

### 2.1 Animals

Male Wistar rats (150-200gm) were used for the study. During

the experiment, rats were housed in standard housing conditions like temperature of 25 ± $1^0$C, relative humidity of 45%-55% and12 h light: 12 h dark cycle. Animals were fed with a standard pellet and water during the experiment. Animals were fasted deprived of food for 16 h but had free access to water.

## 2.2 Experimental Design

Experiment was conducted intwo ways i.e., short- term and sub-acute studies. The rats were divided into four groups comprising of six animals in each group.

Group I: Normal control rats
Group II: Diabetic treated rats, received STZ in single dose (i.p.)
Group III: Extract control group (Cumin extract at the dosage of (250mg/kg b.w)
Group IV: Diabetic rats treated with Cumin extract (250mg/kg b.w) for sub- acute study
Group V: Diabetic rats treated with Cumin extract (250mg/kg b.w) for short- term study

### 2.3 Preparation of Cumin extract

The three varieties of Cumin seeds (Black cumin, sweet cumin and cumin) were heated on hot pan at 60°C for couple of minutes and they were taken in the ratio of 1:3:1 to make it powder. This crude powder was extracted with water at room temperature to make aqueous extract.

*Cuminum cyminum* *Bunium persicum* *Carum carvi*

### 2.4 Streptozotocin induced diabetes

Diabetes was induced in the overnight fasted animals by a single intraperitoneal injection of freshly prepared solution ofstreptozotocin (STZ) as diabetogenic agent. Dosage of streptozotocin was selected according to [18].Streptozotocin (50 mg/kg) was dissolved in 0.1 M ice cold citrate buffer (pH 4.5).Diabetes in rats was identified by measuring fasting blood glucose levels after 48 h injection of STZ. Rats with blood glucose levels above 250 mg/dl were selected for experiments.

### 2.5 Short term studies

Four groups were maintained.Animals were fasted for 16 h prior to drug administration allowing access to only water. The diabetic rats (Group V) were fed with Cumin seeds powder at the dosage of (250mg/kg body weight). To estimate glucose levels blood samples were withdrawn from the tail vein just prior to and 1h,2h, 4h, 5h and 7h after the treatment with cumin extract. Blood glucose levels were measured using single touch glucometer (Accu-check, Roche Diagnostics, USA).

### 2.6 Sub acute studies

Sub-acute study was conducted for 15 days. The diabetic rats (Group IV) were fed with Cumin extract at the dosage of (250mg/kg body weight) for 15 days. Blood was collected from the tail vein for glucose estimation just before drug administration on the 1st day and 1 h after drug administration on days 4, 7 and 10 day.The study was performed as[19] with slight changes. In Sub-acute studies along with blood glucose levels, body weights were also measured on 1 and 15th day of treatment.

### 2.7 Body Weight:

The rats were weighed on day 0 and then on day 15 of the study period. Body weights were noted. Data were expressed as mean body weights (g) ± S.D

### 2.8 Histological study

At the end of the experiment animals were sacrificed on 16th day. Pancreas, spleen and kidney were removed, washed with cold saline and preserved in 10% formalin. Tissues were processed and embedded in paraffin. Thin sections were cut using rotary microtome and stained with hematoxilin and eosin for histomorphology evaluation.

### 2.9 Statistical Analysis

Data were expressed as the mean ± standard deviation (S.D.) of the means. For a statistical analysis of the data, group means were compared by one-way ANOVA. $P < 0.01$ was considered to be statistically significant.

## 3. Results and Discussion

### 3.1 Body Weights

During the experimental study, the animals from Group I, Group III and Group IV were healthy, active and gained body weight. Administration of streptozotocin leads to loss of body weights in STZ- induced rats. Diabetic (Group II) rats were found to have a decrease in the body weights with features of polyuria, hyperphagia and polydipsia as compared to other group rats.Table 1 shows the changes in body weights of the rats during experimental period. There was a significant reduction in body weights of the STZ- induced rats (Group II) compared with control (Group I) and STZ + cumin extract treated rats (Group IV). Rats fed with Cumin extract for 15 days shows significant increase in the body weight. The body weight was increased in the only cumin extract treated rats (Group III) compared to initial body weights. At the end of the study it was observed that the control rats (Group I) were also gained weight. A study specified that streptozotocin by producing diabetes causes reduction in the body weight of diabetic animals [20].

| Groups | INITIALBODY WEIGHTS | FINALBODY WEIGHTS |
|---|---|---|
| Group I | 182.6±2.5 | 199±4.1 |
| Group II | 184±4.1 | 172.8±2.4 |
| Group III | 181.4±3.5 | 192.4±3.5 |
| Group IV | 182±2.7 | 188.8±2.3* |

**Table 1: Effects of Cumin extract on body weight levels (g) during experimental period**

Values are expressed in Mean ± S.D. of 6 individual observations. Statistical significance * P<0.01.

### 3.2 Short term studies

The blood glucose levels were noticedat 1h, 2h, 4h, 5h and 7h of time intervals respectively in STZ along with cumin extract treated rats (Group V). Cumin extract produced significant glycaemic control effect with the dosage of 250mg/kg body weight in streptozotocin induced diabetic rats. This Cumin powder produced a maximum reduction of blood glucose levels in diabetic treated rats compared to diabetic rats. Results were shown in Figure 1. In short term studies the blood glucose levels were monitored at five intervals. The hypoglycemic effect was recorded highest at the 7 h interval with 174 mg/dL.

### 3.3 Sub-acute studies

The blood glucose levels were markedly raised in the STZ-induced rats (Group II) as compared to control rats (Group I). Treatment with Cumin extract to STZ-induced rats for 15 days produced a substantial reduction in blood glucose levels (Figure 2).Blood glucose levels were noticed on the days of 1, 4, 7, 11 and 15 day of treatment. The reduction was significant after the treatment for one week. At the end of second week Cumin extract (250mg/kg b.w.) produced considerable blood glucose reduction. In sub-acute study treatment with cumin extract 250 mg/kg b.w. in STZ-induced diabetic rats, stated reducing blood glucose levels after 4 days and made them completely normoglycemic after 15 days with 121.3mg/dL.

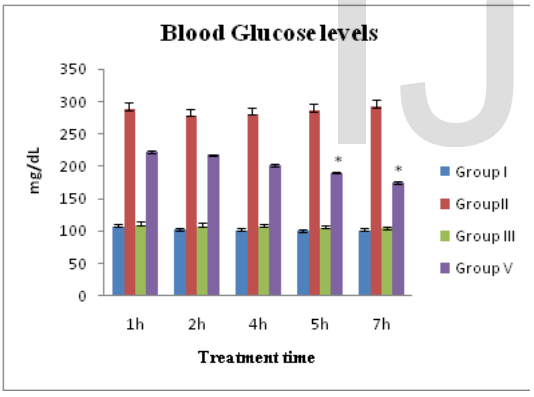


**Figure 1: Effect of Cumin extract on Blood glucose levels (mg/dL) during Short term study** Values are mean±SD; n=6 in each group. Significant difference from control group, *p<0.05

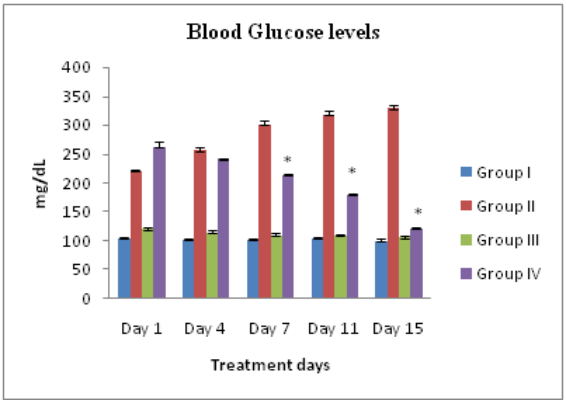


**Figure 2: Effect of Cumin extract on Blood glucose levels (mg/dL) during sub-acute study.** Values are mean±SD; n=6 in each group. Significant difference from control group, *p<0.01

### 3.4 Histological study

The microscopical histological observation of pancreas, kidney and spleen shows that

**Pancreas**

Pancreatic section in control rats showed normal acini and normal cells of islets of langerhans (3A). The pancreatic cells were destroyed with the induction of streptozotocin, which is clear from the slide (3B) of the STZ- induced rats shows severe necrotic changes of pancreatic islets. Rats treated/fed with Cumin extract (3C) was very similar to normal section of pancreas without any changes. Rats treated/fed with Cumin extract (3D) have regenerative effect on normal cellular size of islets of pancreatic tissue, when compared to diabetic rats.

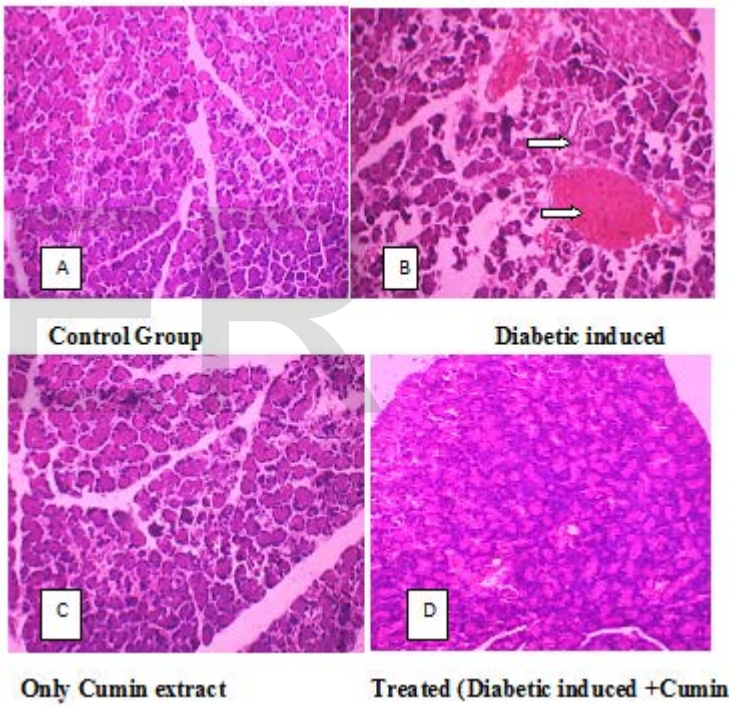


**Figure 3: Histological studies of Pancreas,** Sections of Pancreas (H&E 10X objective). Arrow showing in fig B showing necrotic changes of pancreatic islets.

**Kidney**

Kidney tissues in the control rats (4A) revealed normal glomeruli surrounded by the Bowman's capsule, proximal and distal convoluted tubules without any changes. Diabetic rats (4B) showed degenerated glomeruli infiltrated by the inflammatory cells and thickening of the basement membrane. Rats treated/fed with Cumin extract (4C) have normal structures. Rats fed with Cumin extract (4D) showed topographies of healing with normal glomeruli, absence of inflammatory cells, normal basement membrane, capillaries, decrease in the mucopolysaccharide and hyaline deposit. The tissue necrosis was also lessened in the group treated with cumin extract.

**Spleen**

Spleen in control rats (5A) showed normal structures of red pulp. In diabetic control rats (5B) revealed severe hyperemia in the red pulps and sinusoids with distorted atrophy. Rats treated/fed with Cumin extract (5C) almost very similar to control sections, no detectable changes seen. In diabetic rats treated/fed with cumin extract (5D) spleen section no changes have been found. Cumin extract restore the changes induced by STZ.

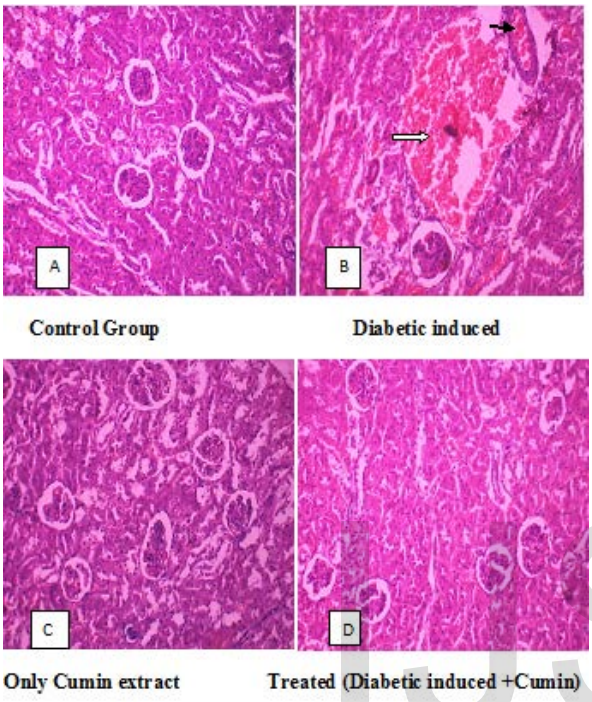


**Figure 4: Histological studies of Kidney,** Kidney sections (H&E 10X objective). White arrow in fig B showing lobultion of some glomeruli, thin black arrows showing thickening of Bowman's capsule.

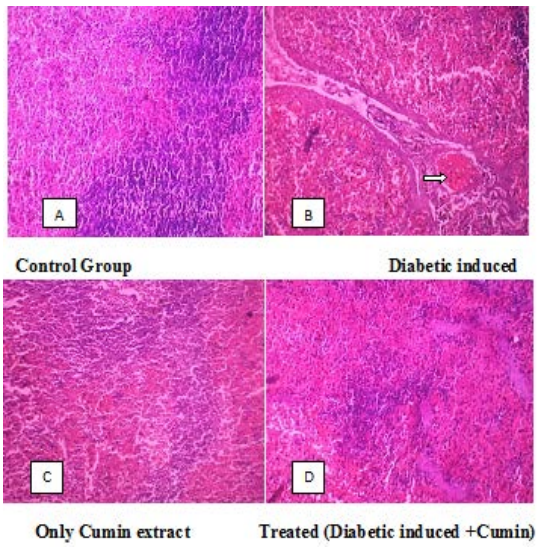


**Figure 5: Histological studies of Spleen,** Spleen sections (H&E 10X objective). Arrow indicates in fig B showing severe hyperemia in the red pulps and sinusoids.

## 4 Conclusion

Our results indicated aneffective action in short term studies and sub-acute study and this could be due to active principles possessed by the different combinations of cumin seeds. Histology studies showed clear justification of folklore use of cumin seeds as an antidiabetic agent. This study shows a new alternative approach for the clinical management of diabetes. Although the exact chemical compounds responsible for the hypoglycemic effects are unknown.Further investigation needed for the evaluation of the compounds and the mechanisms involved in it.

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