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Biochemical studies on the curative efficacy of *Diabetes mellitus* with a herbal plant - *Coccinia indica* (Review)

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ABSTRACT

Coccinia indica [Ivygourd] has its place in indigenous system of medicine (Chittendon, 1992) contains pectinsugar, mucilage, coumarins, sulfur compounds, inorganic ions , flavonoids (Banergi *et al.,* 1988) and pectin, reducing sugars, amino acids as alanine, valine etc, The aqueous and ethanolic extract of *Coccinia indica* enhances the ability of glucose utilization in the body may be directly stimulating of glucose uptake or enhancing the glycogensynthetase activity or mediating insulin – like effects. Blood glucose concentrations were significantly reduced in *Coccinia indica* treated diabetic animals as compared to untreated diabetic rats.

Key words: *Diabetes mellitus, Coccinia indica.*

INTRODUCTION

Ayurvedic medicine is most preferred in certain cases to cure diseases due to its limited side effects, toxicity and economic viability than allopathic drugs (Chopra *et al.,*1958). Ayurveda (Mhaskar *et al.,* 2000) and other indigenous systems of medicine, which are claimed to be useful in the treatment of jaundice, chicken pox, sterility, cancer, diabetes mellitus, etc.,

Diabetes mellitus is one of the most common chronic diseases affecting more than 100 million people worldwide. According to World health organization (WHO) in 1980, it has been calculated that about 2.5 to 3 crore of total human population have diabetes mellitus. *Diabetes mellitus* is a group of metabolic disorders where the sugar level in the blood is high which inturn influences the fat level. Glucose (simple sugar) which is an important end product of digestion is absorbed and transported to the various cells in the body to be utilized as a fuel to provide energy. These effects of glucose are mediated by the hormone insulin produced by the β-cells of pancreas which serves as a key to open the doors of cells. When pancreas fails to perform its function or due to the lack of insulin receptors, the insufficient insulin is usable to unlock the doors of the cells to let glucose into it, which raises its level in blood. In diabetes mellitus auto oxidation of glucose and non-enzymatic protein glycation (Wolff and Dean, 1987) takes place leading to disruption of cellular function and oxidative damage to membranes such as DNA, RNA. carbohydrates, proteins and lipids (Oberley, 1985). The involvement of free radicals in diabetes, which play a vital role in membrane integrity causing a decrease insulin production, leading to impaired transport of glucose and other metabolites across cell membranes and thus hyperglycemia.

In human insulin deficiency causes a variety of diseases and administration of indigenous medicine, diabetes mellitus can be controlled as, herbal plants contain several flavonoids, metals and minerals (Rai, 1995).

Although many herbal plants like *Morus indica* (Bondada andallu 2001), *Coccinia indica, Abroma augusta* (Halim, 2003), *Caesalpinia bonducella* (Sharbana *et al.,* 2002). *Ocimum*

sanctum Linn (Hussain *et al.,* 2001). *American ginseng, Trigonella foenum greacum* (Nathan, 1997) are used in the treatment of hyperglycemia, hypertension and in digestive disorders. (Marles RJ, Farnsworth 1985) and (Voight S et al 2003), have shown that the extracts of *Coccinia indica* (Cucurbitaceae) has also got hypoglycemic properties.(Prasanna Kumar et al 2000) and (Shibib BA et al 1983).

Coccinia indica [Ivygourd] has its place in indigenous system of medicine (Chittendon, 1992) contains pectinsugar, mucilage, coumarins, sulfur compounds, inorganic ions , flavonoids (Banergi *et al.,* 1988) and pectin, reducing sugars, amino acids as alanine, valine etc, The aqueous and ethanolic extract of *Coccinia indica* enhances the ability of glucose utilization in the body may be directly stimulating of glucose uptake or enhancing the glycogensynthetase activity or mediating insulin – like effects. Blood glucose concentrations were significantly reduced in *Coccinia indica* treated diabetic animals as compared to untreated diabetic rats.

To evaluate the antidiabetic effect of *Coccinia indica* fruit extract on the biochemical changes in the tissues and circulation of experimental animals i.e., blood glucose in diabetic rats in comparison to controlled rats and to determine the effect of *Coccinia indica* fruit extract on lipid peroxidation and antioxidant status in comparison to the control rats. Thus to detect the hypoglycemic and antioxidant effect of *Coccinia indica* in Streptozotozin induced diabetes mellitus, i.e., it can directly stimulate glucose uptake or indirectly enhance insulin secretion.

MATERIAL AND METHODS

Coccinia indica fruits were collected, crushed and extracted with 100 mL distilled water and boiled for 30 min. The extract was filtered to get a clear solution which used as a drug in treating hyperglycemia. Streptozotocin, methanol and NADPH were purchased.

Male albino Wistar rats of body weight ranging from 175-250 g and Wateradlibitum (Hindustan Lever Ltd, Mumbai, India).

Induction of experimental diabetes mellitus

Streptozotocin (STZ) is a monofunctional nitrosurea compound, isolated from the fermentation of Streptomyces achromogenus that has been used to induce diabetes mellitus in experimental rats which causes partial destruction of pancreas resulting in hyperglycemic.(Omoruyl F, Adamson I, 1993) STZ is a highly genotoxic alkylating agent, which can cause cellular damage including DNA strand breaks and will eventually lead to cell death.

Diabetes was induced by injecting a single dose of streptozotocin monohydrate [60 mg/kg body weight] in 0.1 M-citrate buffer, pH 4.5 intrapertionally. Then the rats were tested for glucose level in urine by Benedict's qualitative method, for one week. Rats with moderate diabetes having glycosuriashow and hyperglycemia (with 200-300 mg/dl).

EXPERIMENTAL

The animals were divided into four group as Normal control rats- group I, Streptozotocin induced diabetic rats-group II, Control rats treated with *Coccinia indica* fruit extract every day by intragastric incubation for 30 days – group III and Diabetic rat treated with *Coccinia indica* fruit extract every day by intragastric incubation for 30 days – group IV.

Animals were maintained in their respective groups monitored everyday. Food consumption did not vary significantly between or within groups. Blood samples were collected every week into tubes containing potassium oxalate and sodium fluoride as anticoagulant and the glucose was estimated at the end of 30 days. Kidney, liver, heart and brain were removed, homogenized and centrifuged. The homogenate obtained was used to perform the biochemical estimations.

RESULTS AND DISCUSSION

Effect of *Coccinia indica* on body weight and blood glucose level

The weight gained by the diabetic rats (group-III) were significantly lower than those of the control animals (group-I). On treatment with *Coccinia indica* to diabetic rats (group-IV) the weight gained was significantly improved due to control the actions

of insulin and significantly reduced the blood glucose levels of administered *Coccinia indica* fruit extract rats due to inhibiting glucose - 6- phosphatase in the liver subsequently reducing the release of glucose into the blood stream. Table 1 & 2.

Effect of *Coccinia indica* on body weight and blood protein level

The total protein levels in the serum were significantly increased in diabetic rats (group – II) as compared to the control rats (group- I) ($p<0.05$). Administering *Coccinia indica* to diabetic rats significantly reduced the total protein values as compared to the untreated diabetic rats Table 3.

Effect of *Coccinia indica* on tissue lipid peroxidation

The lipid peroxidation values were significantly elevated in the liver, kidney, heart and brain of the diabetic rats ($p<0.05$) as compared to the tissues of control rats. Administering *Coccinia indica* to diabetic rats (group – II) significantly reduce the tissue lipid peroxidation values to near those control rats. The lipid peroxide mediated tissue damage has been observed in the pathogenesis of both type I and type II diabetes. It has been observed that insulin secretion is closely associated with lipoxygenase – derived peroxides. Low level of peroxides stimulate the secretion of insulin but when the concentration of endogenous peroxides increase, it may initiate uncontrolled lipid peroxidation leading to cellular infiltration and islet cell damage in type I diabetes(Hallowell et al., 1998). Table 4.

The present investigation revealed that during hyperglycemic conditions oxidative stress and poor metabolic control enhances LPO in diabetic subjects which inturn results in diabetic complications (Costagliola et al., 1998). The peroxides formed at the site is transferred to other

Table 1: Effect of *Coccinia indica* on body weight (g)

Group	Initial	Final
Control	235±19	240±17
Diabetic	170±20	190±51**
Control ±*Coccinia indica*	242±20	254±18
Diabetic ± *Coccinia indica*	210±17	235±39**

Statistically significant values are expressed as *p<0.01 by comparing group II and group IV.

Table 2:Effect of *Coccinia indica* on blood glucose levels in control and experimental rats (Mg/dl)

Group	Liver	Heart	Kidney	Brain
Control	106.80±15.60	26.60±10.40	51.60±23.60	68.20±3.40
Diabetic	290±20.80	92.70±24.70	113.60±12.50	380±11.43
Control +*Coccinia indica*	126±22.10	82.60±23.40	74.60±40.60	66.20±4.10
Diabetic + *Coccinia indica*	125±10.40*	57.60±13.10*	82.10±18.50*	230±9.80

Values are mean + SD of 6 rats from each group. Statistically significant values are expressed as *p<0.05 by comparing group II and group IV.

Table 3: Effect of *Coccinia indica* on Blood protein level in control and experimental rats Mg/dl)

Group	Liver	Heart	Kidney	Brain
Control	58.90±22.50	24.20±10.20	60.10±10.40	9.01±6.01
Diabetic	78.40±38.40	28.60±12.90	78.30±13.90	82.10±7.04
Control ±*Coccinia indica*	60±28.10	30.10±10.20	67.10±10.20	77.07±5.12
Diabetic ± *Coccinia indica*	64.80±22.10*	14.70±6.57*	49.50±11.30	64.20±5.07*

Protein values are expressed as mg/dl. Statistically significant values are expressed as *p<0.01 by comparing group II and group IV.

organs and tissues which inturn damage the organs (Hiram et al., 1976). On supplementing *Coccinia indica* fruit extract to diabetic rats, significantly decreased levels of TBARS and hydroperoxides.

Effect of *Coccinia indica* on the enzymic and non-enzymic antioxidants

The activities of SOD, CAT, GPX and GSH enzymes were significantly increased in the liver, kidney, heart and brain of the diabetic rats as (group –II) as compared to those of control rats(group-I). On administering *Coccinia indica* to diabetic rats (group-III) the levels of these enzymes were significantly decreased in the liver, kidney, heart and brain as compared to the untreated diabetic rats (group-II). The reduced activities of SOD and CAT in the tissues may result in a number of deleterious defects due to accumulation of superoxide radicals (O_2) and hydrogen peroxide which are cause marked injuries to the surrounding tissues and organs. (Searle et al., 1980 and Halliwell et al., 1998) Table 5-6.

The GPX and GSH enzymes were protecting cells against cytotoxic chemicals by scavenging reactive oxygen species. These enzymes have lower activity and catalyses the reduction of hydrogen peroxide and lipid

Table 4: Effect of *Coccinia indica* on Tissue lipid peroxidation (TBARS) in control and experimental rats (M/g tissue)

Group	Liver	Heart	Kidney	Brain
Control	0.59±0.16	0.40±0.23	0.46±0.27	0.44±0.26
Diabetic	0.37±0.12	0.25±0.08	0.46±0.15	0.37±0.23
Control ±*Coccinia indica*	0.44±0.17	0.41±0.15	0.42±0.21	0.38±0.13
Diabetic ± *Coccinia indica*	0.36±0.20*	0.2±0.16	0.31±0.13*	0.30±0.20

Values are expressed as m/g tissue. Statistically significant values are expressed as *p<0.01 by comparing group II and group IV.

Table 5: Effect of *Coccinia indica* on tissue antioxidant - SOD in control and experimental rats)

Group	Liver	Heart	Kidney	Brain
Control	9.10±1.19	10.9±0.97	12.10±1.21	5.14±0.41
Diabetic	11.21±2.02	10.71±1.82	15.02±2.07	7.48±0.49
Control ±*Coccinia indica*	9.01±0.92	17.90±1.87	13.02±2.01	4.21±0.32
Diabetic ± *Coccinia indica*	10.10±1.19*	9.01±0.87*	10.01±1.01	6.04±0.21*

Statistically significant values are expressed as *p<0.001 by comparing group II and group IV.

Table 6: Effect of *Coccinia indica* on tissue catalase in control and experimental rats

Group	Liver	Heart	Kidney	Brain
Control	64.8±8.20	6.68±6.03	21.2±1.90	2.05±0.03
Diabetic	92.41±72.39	11.04±3.01	54.9±6.15	124.73±2.88
Control ±*Coccinia indica*	50.69±9.08	11.7±1.62	41.4±1.09	5.29±1.02
Diabetic ± *Coccinia indica*	50.20±0.07	9.90±1.08*	35.01±0.08	10.01±0.08

Catalase- The enzyme activity is expressed as µ moles of hydrogen peroxide. Statistically significant values are expressed as *p<0.001 by comparing group II and group IV.

Table 7: Effect of Coccinia indica on tissue Glutathione peroxidase in control and experimental rats

Group	Liver	Heart	Kidney	Brain
Control	12.0±5.85	100.8±92.20	9.6±3.72	9.06±3.72
Diabetic	87.6±8.26	64.8±6.44	30.4±9.84	10.2±7.08
Control ±*Coccinia indica*	55.2±23.52	84±24.80	60±21.68	72±22.31
Diabetic ± *Coccinia indica*	73.6±9.80*	33.6±3.92*	216.544*	79.2±6.40*

GPX - The enzyme activity is expressed as µm or m/g of tissue. Statistically significant values are expressed as *p<0.001 by comparing group II and group IV.

Table 8: Effect of *Coccinia indica* on tissue reduced glutathione in control and experimental rats

Group	Liver	Heart	Kidney	Brain
Control	26.0±2.10	7.82±2.82	20.0±3.54	10.40±2.90
Diabetic	3.75±5.65	11.22±2.52	221±5.23	13.65±2.52
Control ±*Coccinia indica*	34.58±2.92	33.74±2.08	22.4±3.17	15.83±2.14
Diabetic ± *Coccinia indica*	25.82±3.74*	7.4±1.57*	13.74±4.67*	7.92±4.67*

GPX - reduced glutathione activity is expressed as µm or m/g of tissue. Statistically significant values are expressed as *p<0.001 by comparing group II and group IV.

Table 9: Effect of *Coccinia indica* on tissue non-enzymic antioxidant Vitamin-A in control and experimental rats

Group	Liver	Heart	Kidney	Brain
Control	1.52±0.14	1.41±0.21	0.64±0.13	3.70±32
Diabetic	9.04±0.32	9.51±0.52	10.60±2.60	8.66±1.36
Control ±*Coccinia indica*	1.04±0.12	10.00±0.73	9.22±0.31	3.42±0.31
Diabetic ± *Coccinia indica*	8.20±0.82*	8.24±0.60*	8.88±0.36*	8.08±9.07*

Vitamin-A values are expressed as µg/mg of tissue. Statistically significant values are expressed as *p<0.001 by comparing group II and group IV.

Table 10: Effect of *Coccinia indica* on tissue non-enzymic antioxidant Vitamin-E in control and experimental rats

Group	Liver	Heart	Kidney	Brain
Control	3.20±0.10	1.32±1.20	0.40±0.90	4.70±1.40
Diabetic	3.90±0.71	2.12±1.32	1.71±1.21	3.11±0.96
Control ±*Coccinia indica*	2.30±1.00	1.48±1.09	0.81±1.71	3.21±0.71
Diabetic ± *Coccinia indica*	2.10±0.12*	1.304±0.90*	0.91±0.31*	2.10.17S*

Vitamin-E values are expressed as µg/mg of tissue. Statistically significant values are expressed as *p<0.001 by comparing group II and group IV.

hydroperoxides (LO_2H) (Little and Briem, 1968) in diabetes mellitus may induce various injuries to the surrounding organs leading to some clinical disorders. Table 7-8.

The non-enzymic antioxidants like Vitamin A, C, E and GSH have a significant role in hyperglycemic conditions. These enzymes protect lipids against peroxidation by quenching free radicals of O_2^- and OH^- and neutralizing their toxic effects. *Coccinia indica* feeding to diabetic rats elevated the Vitamin A, C and E levels and may be the cause for the decreased oxidative stress. Table 9-10.

CONCLUSION

The biochemical changes, enzymic antioxidants like SOD,GPX, CAT and non-enzymic antioxidants like vitamin A, C, E and GSH including blood glucose and protein levels were studied in various organs. *Coccinia indica* fruit extract therapy to diabetic rats significantly controlled hyperglycemic lowered tissue lipid peroxidation and significantly elevated the tissue peroxidation, tissue enzymic(SOD,CAT,GPX) and non-enzymic antioxidant (vitamin A.E,C and GSH) levels as compared to the untreated diabetic rats. Thus the significant protective effect of *Coccinia indica* fruit extract in streptozotocin induced diabetic rats.

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