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Ameliorative effects of *Coccinia grandis* leaf extract on Diabetes-Induced alterations of glucose metabolism, Cox activity and histological changes in Brain of Wistar Rats

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ABSTRACT

Cocciniagrandis has been used in tribal populations of India both as food and medicine, but it has been not reported to be a neuroprotective agent yet. The present study was designed to evaluate the protective effects of *Coccinia grandis* leaf extract on diabetes induced brain damage of Wistar rats. This study reports the protective effect of methanolic leaf extract of *Coccinia grandis* against STZ induced diabetes in rats. Metformin (150mg/kg body wt.) was used as a reference drug. The enzymes of the polyol pathway and its related substrates were studied in the brain tissue. The effect of Coccinia on Cyclooxygenase (COX) and Prostaglandin peroxidise (PG) was also studied. Diabetes induced rats showed a significantly increased activity of Aldose reductase, Sorbitol dehydrogenase, Glucose-6-phosphodehydrogenase, whereas the decreased activity of Hexokinase. The content of Glucose, Sorbitol significantly increased in rat brain. Sodium potassium ATPase activity was also decreased in diabetic rats. COX, PG peroxidase was increased. Histological alternations were induced in the hippocampus of STZ treated diabetic rats. Oral administration of Coccinia leaf extract (200mg/kg) of body weight to diabetic rats for 21 days efficiently attenuated the parameters studied. A decreased activity of brain AR, sorbitol dehydrogenase, glucose-6-dehydrogenase was observed along with the increase in Hexokinase and Sodium potassium ATPase activity. It also showed decreased content of glucose and Sorbitol. Diabetes induced brain damage in the hippocampus and cerebral cortex was restored with Coccinia treatment. Decreased COX and PG peroxidase suggest its protection against inflammation. The current results suggest that *Coccinia grandis* leaf extract exerts the potential ability to reverse the progression of hyperglycemia and its concomitant induced brain damage.

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INTRODUCTION

Diabetes with longstanding hyperglycemia is considered to be a major culprit in all diabetic complications including brain damage. Hyperglycemia generates abnormally high free radicals. As a part of normal metabolism reactive oxygen species are generated continuously which sum up. This is the main cause of diabetes leading to oxidative degeneration along with protein glycation Baynes (1991) have shown that complications of diabetes are due to oxidative damage. This is the primary reason

for clinical complications in diabetes due to oxidative stress. The indirect cause for diabetic complications is because of an imbalance in oxidative stress and dysfunction of key antioxidant enzymes, along with the activation of the polyol pathway. High glucose activates alternate pathway of glycolysis i.e. polyol pathway in the brain, which is considered to be one of the factors for brain damage in long term hyperglycaemic conditions. The activated of polyol pathway will disturb the balance between antioxidant enzymes and reactive oxygen spices (Hunt *et al.*, 1988). The activated polyol pathway is responsible for the etiology of diabetic complications, which brings in changes of glucose metabolites and enzymes of polyol pathways targeting different regions of the brain (Harris, 2002). NADPH and NADH balances are disturbed as a result of a change in intermediary metabolites of the sorbitol pathway, and also depletes glutathione levels which further enhances the oxidative stress. And prolonged diabetes leads to impairment in memory, learning, and cognition in diabetic patients. This is because the major regions of the brain such as the hippocampus are subjected to morphological alteration with diabetes. This change in the hippocampus is in the form of impairment in synaptic plasticity and the CA-1 field will lead to impairment in memory, learning and cognition in diabetic patients. Even another region such as the Cerebral cortex is also subjected to histological changes such as damage in neurons, Axon, and Schwann cells (Zenker *et al.*, 2013).

Microvascular and macrovascular complications of diabetes are also directly related to oxidative stress. One of the culprits of microvascular complications is the activation of polyol pathway. The polyol pathway along with changes in its metabolites and decreased antioxidant defense leads to inflammation. Cyclooxygenase (COX) is considered to the mediatory enzyme for inflammation. This converts arachidonic acid to prostaglandins (PGs) which is a rate-limiting enzyme. Production of PGs is done by two isozymes i.e, COX-1 and COX-2. Inflammatory stimuli in peripheral nerves evoke COX-2 (Vane *et al.*, 1998) and in regions of CNS such as the hippocampus and amygdala, which is expressed in a high level in discrete layers of neurons (Yamashita *et al.*, 2007). So, COX-2 is considered to an inflammatory mediator (Vane *et al.*, 1998) as well as a neuronal modulator that affects synaptic plasticity (Kaufmann *et al.*, 1996).

Coccinia *grandis*, a perennial tendril climber belongs to the family Curcurbitaceae. Commonly called as ivy guard, and also known by other names like little gourd or gentleman's toes and baby watermelon. This plant is distributed throughout the tropical countries of Asia and Africa. In India, Bangladesh, and Pakistan since long before leaves and fruits of the plants are consumed as vegetables in which leaves are ascribed to hyperglycaemic as an indigenous system of medicine.

The present study was designed to investigate the enzymes of the polyol pathway (AR, SOD) and pentose phosphate pathway (glucose-6-phosphate dehydrogenase), Hexokinase, COX, PG peroxidase, Na+K+ATPase activity, and certain substrates of these enzymes such as glucose and sorbitol in the whole brain and histological analysis of amount damage to the different regions of hippocamp as well as cortex neurons.

MATERIALS AND METHODS

Chemicals and Reagents

STZ was obtained from Sigma Chemical (USA). Metformin drug procured from Hetero drugs, India. Other essential chemicals were obtained from SRL biochemical, India.

Animals

Adult male Wistar rats of 100-200g each of 11-12 weeks age were brought from National centre for Laboratory Animal Sciences (NIN), Hyderabad. They were housed in separate plastic cages with (18-22°C) controlled temperature, corn con was used as bedding material. They were maintained at 12h light/12h dark cycle and fed with standard pellet diet (NIN), water *ad libitum*. All institutional guidelines of the Institutional Animal Ethics Committee were strictly adhered to in the care and treatment of the animals used throughout the study (CPCSEA No: 383/01/a/CPCSE).

Plant collection, authentication, extraction

Large quantities of Coccinia *grandis* leaves were collected locally and were identified by the Herbarium (Voucher specimen (No.018) in Botany Department of the Osmania University, Hyderabad-500007. These were shade dried at room temperature in the laboratory and were coarsely pulverized to powered form. Powder extracted with boiling water and ethanol using a rotary evaporator and the crude extraction was used for experimentation.

Experimental design

In each group randomly selected six animals were divided into five experimental groups. Group details are as follows : Groups-I: These animals were treated with physiological saline, this group served as a control, Group-II: The animals were induced with STZ, this group served as diabetic (50mg/kg

bodyweight of rat, in citrate buffer (100mM PH 4.5), Group-III: The STZ induced diabetic animals treated with Metformin drug, this group served as Met (150mg/kg body weight in RO water), Group-IV: The STZ induced diabetic animals treated with *Cocciniagrandis* leaf extract (200mg/kg body weight in RO water), this group served as Coc+D, Group-V: Control animals treated with *Coccinia grandis* leaf extract (200mg/kg body weight in RO water), this groups served as Coc+C.

Experimental protocol

The animals were sacrificed after 21 days and polyol pathway enzymes and substrates, inflammatory mediators such as Cox and PG peroxidase were estimated in the brain.

Estimation of Cyclooxygenase

Cox activity was estimated with the method of oxygen consumption test. The preparation of microsomes and estimation of Cox was done according to Jang (2004).

Estimation of Prostaglandin peroxidase

Prostaglandins Assay was done according to Vanegas and Schaible (2001).

Biochemical estimation

Preparation of tissue extracts

All the animals were sacrificed by cervical dislocation after 21st day and Brains were carefully isolated and washed in normal saline, stored at -80 °C.

Tissue processing for all biochemical studies was done as described by Gabbay (1973).

Enzymatic Estimations

Hexokinase (EC 2.7.1.1)

Hexokinase enzyme activity was estimated according to Gumma and Mclean (1972).

Estimation of Aldose Reductase (AR, EC.1.1.1.21)

Aldose Reductase enzyme activity was estimated according to Hayman and Kinoshita (1965).

Sorbitol dehydrogenase (EC 1.1.1.14)

Sorbitol dehydrogenase enzyme activity was estimated according to Gerlach (1983).

Glucose-6-phosphate dehydrogenase (EC 1.1.1.49)

Glucose-6-phosphate dehydrogenase enzyme activity was estimated according to Baquer *et al.* (1973).

Units of Enzyme

The oxidation/reduction of one μm of NADH or NADPH per g of tissue/min is defined as one enzyme unit.

Na^+K^+ATPase Enzyme (EC 3.6.1.3)

Na^+K^+ATPase were estimated according to Kaplay (1978).

Metabolite Estimations

Glucose

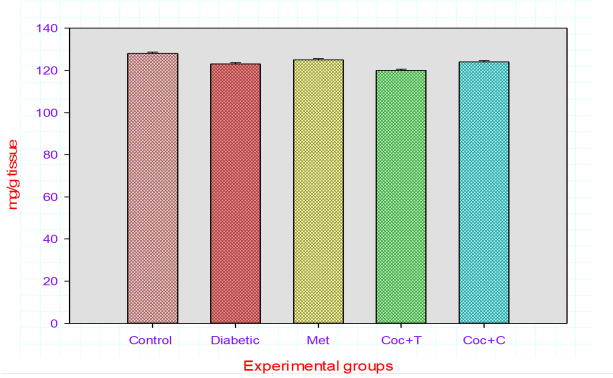
Bergmeyer *et al.* (1974) method was used for measuring Tissue Glucose.

Sorbitol

Malone *et al.* (1989) modified form of method was used for measuring Sorbitol on fluorescence spectrophotometer.

Other estimations

Protein contents in brain extracts were determined by the method of Lowry *et al.* (1951). The extent of protein oxidation was determined by measuring the protein carbonyl content of soluble protein of tissues (Brain) spectrophotometrically using 2, 4,-dinitro phenyl-hydrazine (Uchida *et al.*, 1998).

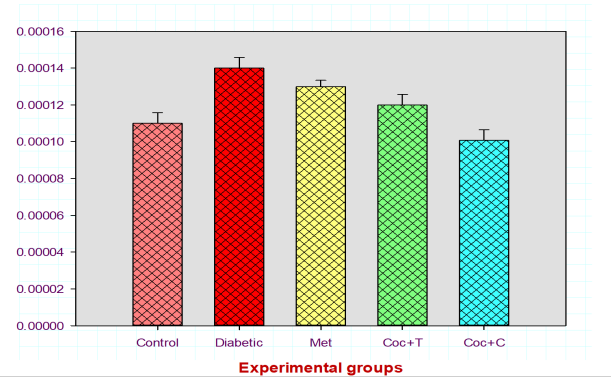


(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05. Significance)

Figure 1: Changed levels of proteins in Brain on treatment with Coccinia on 21st day. (Proteins expressed in mg/gram tissue)

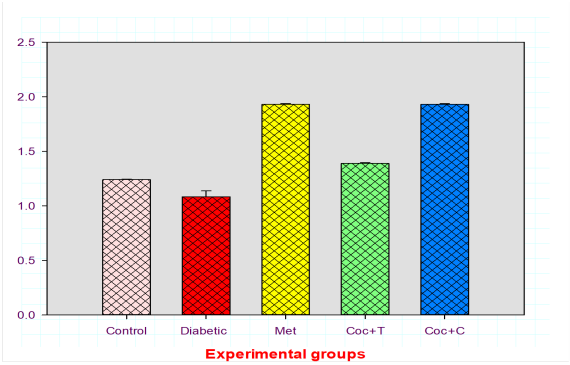
Histological processing

Brains were stored in 10% formaldehyde and later carefully hippocampus was dissected. Which was dehydrated, cleared, and embedded in paraffin? That was cut into sections with a microtome of 5 μm thicknesses, mounted on glass slides, and stained with routine hematoxylin and eosin technique (Bancroft, 2007). Morphometric analysis of the hippocamps was done by software Magnavision (2019). The hippocampus analysis was done with a rectangular shape but slightly different values. Area-1654000.00pixels, Perimeter-5308cms, Width-1000cms and Height-1654cms. The analysis was depicted as neurons degenerated in this area manually.



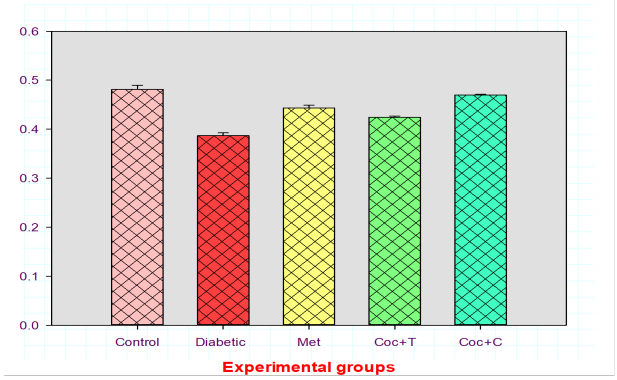
(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05. Significance)

Figure 2: Changed levels of protein carbonyls in Brain on treatment with Coccinia on 21st day. (Proteins expressed in ng/gram tissue)



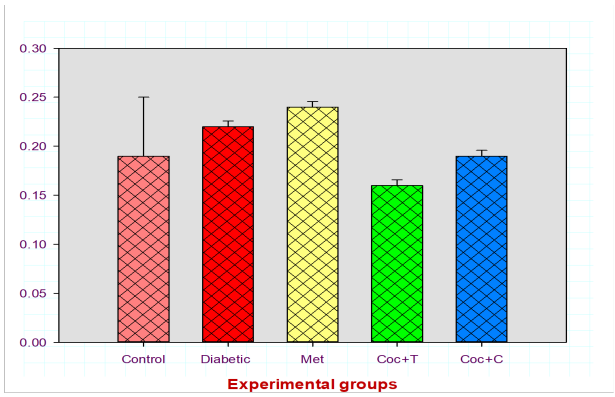
(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05. Significance Control Vs Met+D is < 0.1, Control Vs Cur+D is < 0.5 ,Diabetes Vs Met+D is< 0.009, Diabetes Vs Cur+D is < 0.002, Met+D Vs Cur+C is < 0.1, Met+D Vs Cur+D is < 0.4, Cur+D Vs Cur+C is < 0.5 respectively)

Figure 3: Effect of Coccinia on Hexokinase activity of Brain in Control and other Experimental Rats on 21st day. (Expressed as μ moles of NADPH oxidized/ hour/100 mg of protein)



(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05Significance Control Vs Cur+C is < 0.5, Diabetes Vs Cur+D is < 0.04, Met+D Vs Cur+D is < 0.01 respectively)

Figure 4: Effect of Coccinia on G-6-PDH activity of Brainin Control and Experimental groups of Rats on 21st day. (Expressed as μ moles of NADPH oxidized/ hour/100 mg of protein)



(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05Significance Diabetes vs Cur+C is<0.2 respectively)

Figure 5: Effect of Coccinia on AR activity of Brain in Control and Experimental group of Rats on 21st day. (Expressed as μ moles of NADPH oxidized/ hour/100 mg of protein)

Statistical Analysis

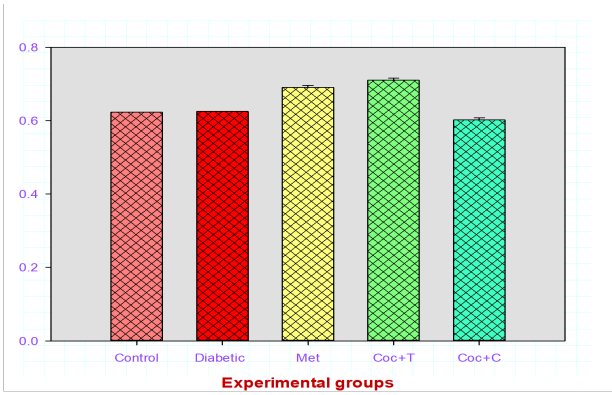
Results are presented as mean ± S.E., six in each group. Statistical difference between control and various groups was determined by one-way ANOVA, followed by post Hoc test (Multiple comparisons). *p*-values less than 0.05 were considered significant.

RESULTS AND DISCUSSION

The total protein levels and protein carbonyls of total brain tissue are shown in Figure 1 and Figure 2. Diabetic rats showed decreased protein quantity (-3.90%) and protein carbonyls increase as compared to the control and other treated groups. Protein carbonyls in diabetic rats caused a 27% increase in comparison to the control group which was restored to 12% in Metformin treated animal and an almost similar trend was shown when treated with Coccinia.

Hexokinase

The Hexokinase activity in the Brain (-12%) was significantly (P<0.05) decreased in STZ induced diabetic rats on the 21st day compared to control animals (Figure 3). The Hexokinase activity in the brain



(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05)

Figure 6: Effect of Coccinia on Sorbitol dehydrogenase activity of Brain in Control and Experimental group of Rats on 21st day. (Expressed as μ moles of NADPH oxidized/ hour/100 mg of protein)

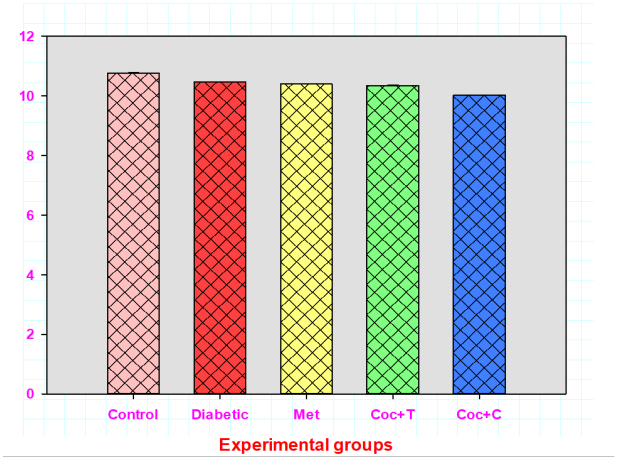


Figure 7: Effect of Coccinia on Sodium potassium ATPase enzyme of Brain in Control and Experimental Rats on 21st day. (Expressed as μ moles of pi/ hour/mg wt. of tissue)

(55%) was markedly recovered on 21st day after treatment with Metformin in STZ induced diabetic rats, whereas the brain has shown a reversal in Hexokinase activity (12.09%) after treatment of diabetic rats with Coccinia. Controls animals treated with Coccinia have shown 55.64% Hexokinase activity in Brain.

Glucose 6-phosphate dehydrogenase

Glucose-6-phosphate dehydrogenase (G-6-PDH) activity was significantly (p<0.05) decreased in the Brain on the 21st day by -19.65% in STZ induced diabetic rats when compared to control (Figure 4). After treatment of diabetic rats with Metformin decrease of G-6-PDH activity in the Brain was

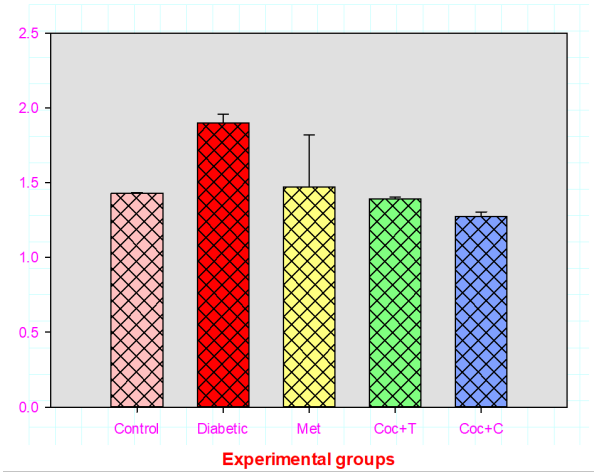


Figure 8: Effect of Coccinia on glucose of Brain in Control and Experimental Rats on 21st day. (Expressed as μ moles/gm tissue)

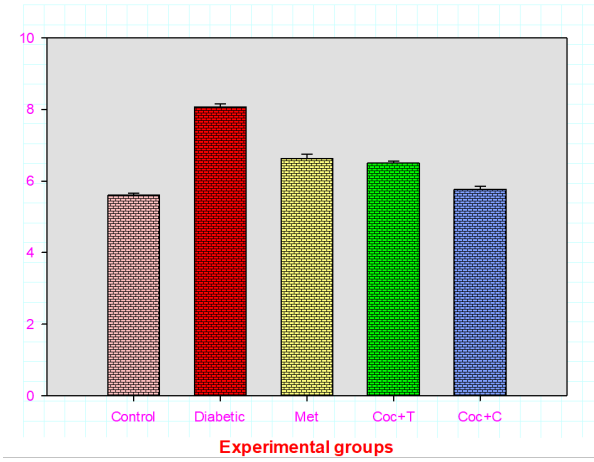
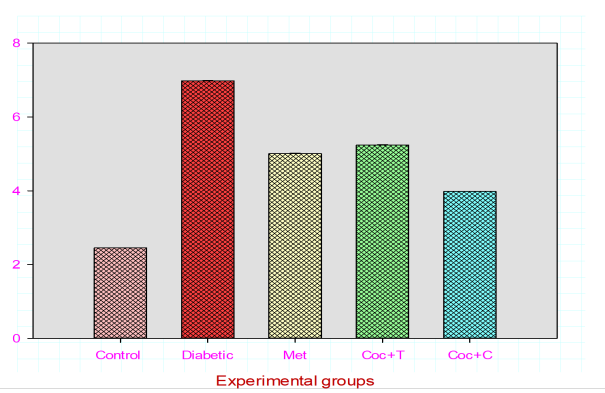
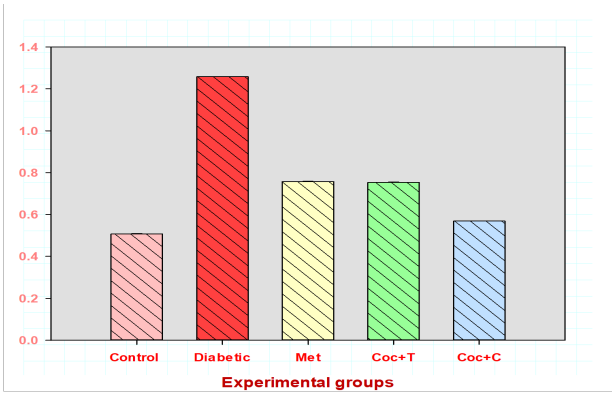


Figure 9: Effect of Coccinia on Sorbital of Brain in Control and Experimental Rats on 21st day. (Expressed as μ moles/gm tissue)



(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05)

Figure 10: Effect of Coccinia on Cyclooxygenase (COX) activity in Brain on 21st day. (Expressed as μM Oxygen Consumption/min/100mg protein/ 1ml)



(Values are given as mean ± S.E for groups of six animals each. Values are statistically significant at p<0.05)

Figure 11: Effect of methanolic leaf extract on Prostaglandin Peroxidase (PG peroxidase) activity in Brain of rats treated with Coccinia *grandis* on 21st day

-7.89%. However, the G-6-PDH activity in the Brain is partially regained by -11.82 % when diabetic animals treated with Coccinia. Control animals treated with Coccinia have shown decreased -2.34% of the G-6-PDH activity in the Brain compared to control animals.

Aldose reductase

There was a significant increase in Aldose reductase enzyme activity in the Brain of diabetic animals (+11.67%) as compared to normal animals. Diabetic rats treated with Coccinia showed a decrease in Aldose reductase activity by 18% (Figure 5). The percentage of variation of Metformin treated diabetic was 18% and that of control animals treated with Coccinia was - 12%.

Sorbitol dehydrogenase

The Sorbitol dehydrogenase activity in the Brain (+18.39%) was significantly (P<0.005) increased in STZ induced diabetic rats on the 21^{st} day (Figure 6). After simultaneous treatment of Metformin in STZ induced diabetic rat (Met), the Sorbitol dehydrogenase activity was markedly reversed in the Brain on the 21^{st} day (+4.01%). Coccinia treatment has shown a marginal reversal as compared to the Metformin group by +7%. Control animals treated with Coccinia have shown the Sorbitol dehydrogenase activity in the Brain is -4.01%.

Sodium potassium ATPase enzyme

The tissue levels of this enzyme of all the experimental groups are shown in Figure 7. STZ-induced diabetes in rats caused -2.78% decreased activity in comparison to the control group almost trend was shown (-2%) in Metformin treated animals and -1.85% in Coccinia treated animals.

Substrates

Tissue Glucose

The tissue glucose levels of all the experimental groups are shown in Figure 8. STZ-induced diabetes in rats caused a 32.86% increase in the glucose levels in comparison to the control group which was restored to 2% in Metformin treated animals and 0.96% in Coccinia treated animals.

Sorbitol

A spontaneous increase in Sorbitol level was observed (+44.05%) in the Brain on the 21^{st} day in the STZ induced diabetic rats group when compared to control (Figure 9). The Sorbitol content in the Brain after treatment with Metformin of STZ induced diabetic rats was gradually recovered on 21st day by +18%. After Coccinia treatment, Sorbitol content was recovered in Brain with +16% when compared to control.

Cyclooxygenase

The Cyclooxygenase (COX) activity in the Brain of control and experimental animals is presented in Figure 10. In STZ induced diabetic rats a significant (p<0.05) increase in Cyclooxygenase (COX) activity was observed in the Brain +184.89% on the 21^{st} day when compared to the control group. The Cyclooxygenase (COX) activity was predominantly recovered in the Brain (+104.48%) when diabetic animals which were treated with Metformin. Coccinia treatment of diabetic rats has shown a gradual recovery of Cyclooxygenase (COX) activity in the Brain (+109.84%).

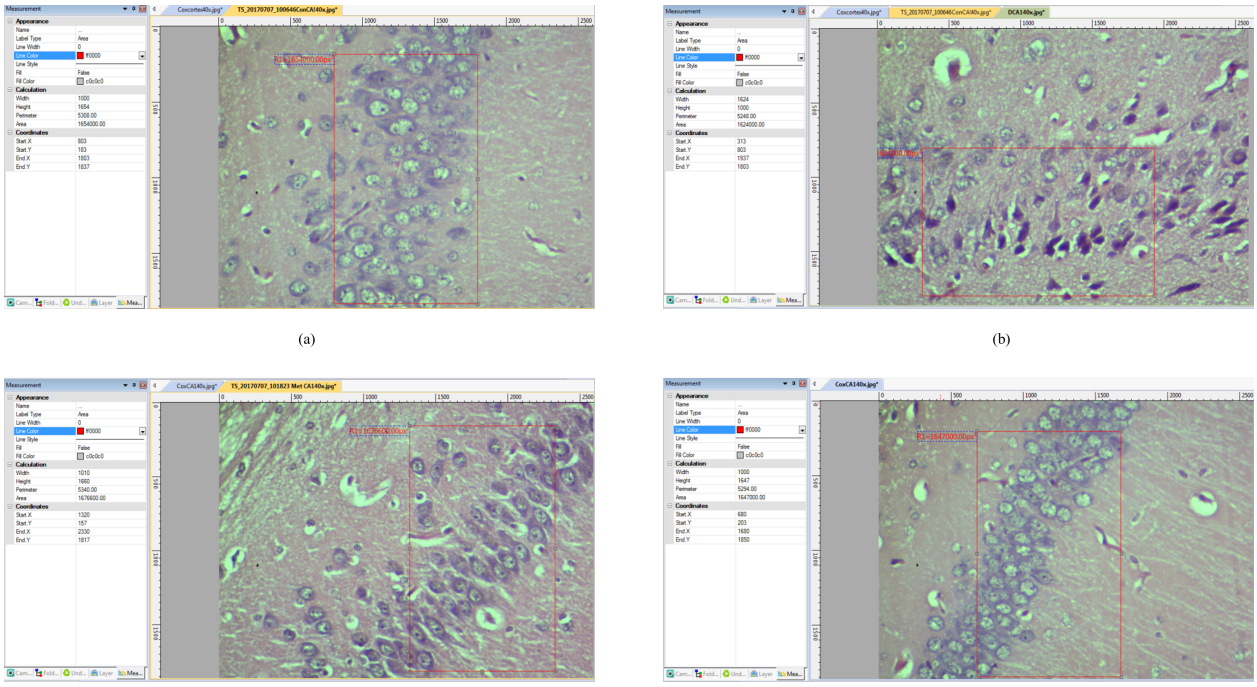
Prostaglandin Peroxidase (PG peroxidase) activity

Prostaglandin Peroxidase (PG peroxidase) activity was significantly (p<0.05) increased in the Brain on the 21st day by +143.63% in STZ induced diabetic rats when compared to controls (Figure 11). After treatment of diabetic with Metformin decrease of PG peroxidase activity in the Brain was +49.21%. However the PG peroxidase activity in the Brain recovered by +48.42%, when diabetic animals treated with Coccinia.

Effect of Coccinia on the number of degenerated neurons of the hippocampus

Light microscopic analysis at 40X magnification

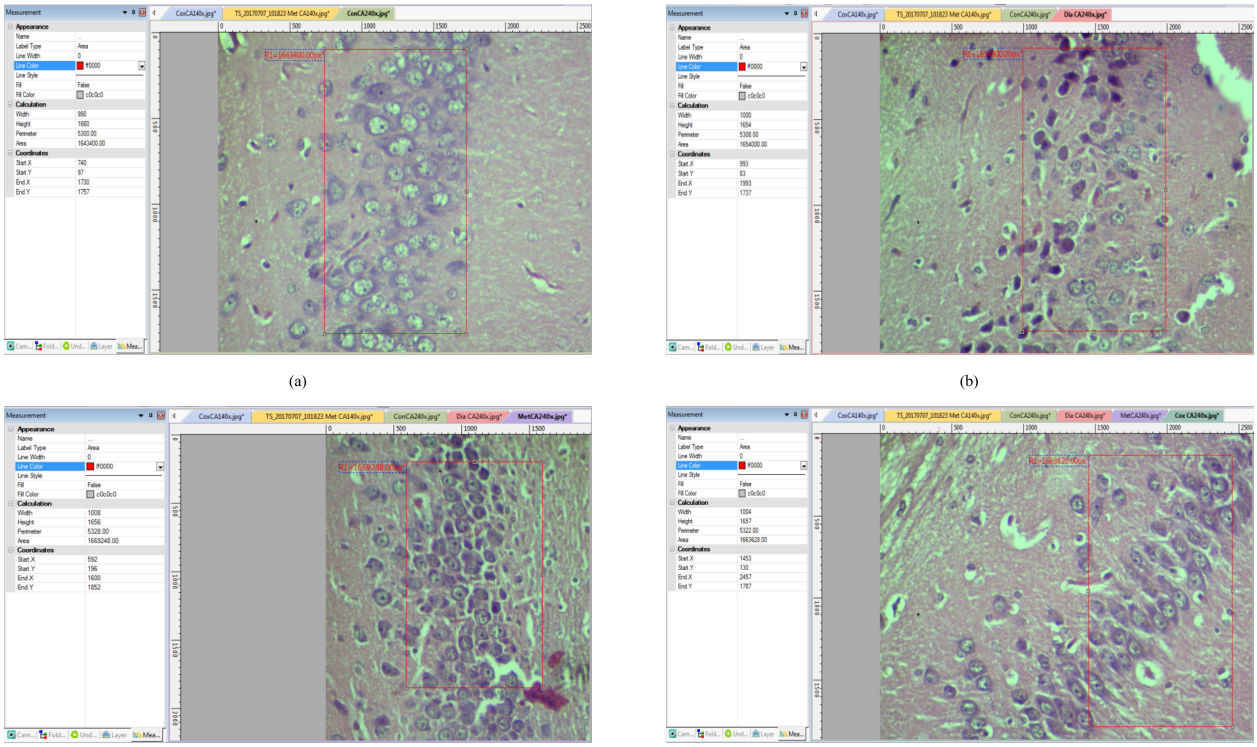
CA1 region of the hippocampus: There are significant changes on the microscopic examination of H&E stained sections other than the control group. The count of degenerated neurons is nominal in the control group but in a diabetic group the count of



(a) (b)

(c) (d)

Figure 12: H&E stained photomicrographs (a) Control, (b) diabetic, (c) metformin and (d) Coccinia treated of 21 days, STZ induced diabetic rat showing more number of degenerated neurons in CA1 region of hippocampus (40x)



(a) (b)

(c) (d)

Figure 13: H&E stained photomicrographs (a) Control, (b) diabetic, (c) metformin and (d) Coccinia treated of 21 days, STZ induced diabetic rat showing more number of degenerated neurons in CA2 region of hippocampus (40x)

degenerated neurons is high. But when we compared the Coccinia treated group the number of degenerated neurons is less. Metformin treated rats also showed a similar count as Coccinia group rats (Figure 12).

CA2 regions of the hippocampus: The CA2 regions of all groups except control observed a significant increase in degenerated neurons after 21 days in diabetic groups as compared to metformin treated and Coccinia treated rats (Figure 13).

The animals that were treated with Coccinia showed significant protection of neurons in comparison to metformin (Bancroft, 2007).

DISCUSSION

There is a constant search for natural products for treating diabetes since all available drugs in the market lead to many side effects. We have already reported in our previous studies that Coccinia *grandis* has a potent antidiabetic property in association with other reports of antibacterial activity, Anticancer, Antioxidant, Anti-inflammatory, Hypoglycemic property. The present study reports the potency of Coccinia in streptozotocin-induced diabetic brain damage using metformin as reference drug. Increased protein carbonyls were seen in diabetic rats indicating oxidative stress. Most workers reported increased protein carbonyls in both type I and II diabetes. These increased protein carbonyls were decreased by administration of Coccinia (250mg/kg body wt.) for 21 days. Increased protein carbonyls were reflected by decreased protein quantity, which was also recovered by Coccinia treatment.

Various researchers have reported oxidative stress is the main culprit for diabetic complications including diabetic neuropathy. Low *et al.* (1997) has proposed chronic oxidative stress due to the resulting hyperglycemia. The role of oxidative stress in brain damage has been shown by many researchers in diabetic patients and experimental diabetes. One of the pathways leading to oxidative stress is dysfunctioning of glucose metabolism. Hyperglycemia activates polyol pathway channeling glucose to divert from normal glycolysis. Decreased Hexokinase activity in diabetic rats is an indication of glucose diversion which results in diminished utilization of glucose for energy production. Diabetic rats treated with Coccinia and Metformin have predominantly reversed the Hexokinase activity that may lead to activation of glycolysis.

Studies have shown if the glucose concentration is well maintained in PNS, there won't be abnormal transport of glucose to the brain (Mcewen and Reagan, 2004). Activation of the polyol pathway will be indicated by the presence of increased activity of Aldose reductase (AR) and Sorbitol dehydrogenase in diabetic rats. Most of the drugs available are AR inhibitors and other natural products are tested for inhibition of Aldose reductase. That is because of the AR activity is inhibited means glucose is not diverted from normal glycolysis. Diabetic rats treated with Coccinia and Metformin have shown reduced activity of AR, indicating increased utilization, especially through glycolysis. This mechanism can also be confirmed by the higher activity of the Hexokinase enzyme. The results showing a decreased amount of tissue glucose, sorbitol also confirms it.

The diabetic rats showed decreased acitivity of Na^+ K^+ATPase, which was significantly reversed with Coccinia treatment. This property of Coccinia reveals the potentiality in elevating the excitability of neuronal tissue. Coccinia *grandis* leaf extract has a high potency of lipid peroxidation (Umaheshwari and Chatterjee, 2008) and anti-lipidperoxidative property, which might have activated sodium-potassium ATPase activity. That is because the activation of Phospholemma (PLM) is required for Na^+ K^+ATPase activity which can be done by a substance with anti-lipidperoxidative and lipid peroxidation property (Feschenko *et al.*, 2003).

Uncontrolled hyperglycemia leads to inflammation which is a characteristic feature of diabetes. Inflammation mediators are both COX-1 and COX-2, which sensitizes nociceptors neurons in the CNS. This study reports a decreased quantity of both COX and Prostaglandins. Tan *et al.* (2011) have shown that the anti-inflammatory property of any substances appears to be mediated through inhibition of induction of COX-2, and suppresses the synthesis of prostaglandins. The role of Coccinia in bringing down the inflammation was seen in this work which further endorses its anti-inflammatory property.

The direct consequence of chronic hyperglycemia destroys the brain histology especially the hippocampus. Various studies on animals have revealed a distinguished effect of chronic glucose on the hippocampus in the form of neuronal death at the certain regions and also disruption of a normal neuronal layer. Damage to neurons was indicative by the clumping of neuronal processes. Neuronal excitotoxicity is induced by hyperglycemia, where glucose enters into neurons through NMDA receptor-mediated calcium, which ends with the release of ROS (Jayanarayanan *et al.*, 2013). Hence if any product which could block the NMDA receptor,

thereby maintains optimum glucose and insulin levels. Maybe the ameliorative effect of Coccinia is through this mechanism.

Previous studies have reported that in experimental diabetes the damage is induced in hippocampus neurons after 30 days (Pamidi and Nayak, 2012). But our study reports noticeable changes in the histology of the hippocampus of diabetic rats within 21^{st} day when compared to control rats. Most studies have revealed that histological changes in the brain of diabetic rats are due to disturbances in the metabolism of glucose, i.e. polyol pathway activation, which further leads to a cascade of events including glucose auto-oxidation, AGEs products formation (Pamidi and Nayak, 2012), and finally diminishing the antioxidant defense system. These all events will lead to inflammation in neuronal tissues causing histological changes in the brain of diabetic rats.

Our previous study on Coccinia had reported behavioral and nociceptive abnormalities of diabetic rats and also glucose metabolism (Monnier, 2003); Cox metabolism (Nagilla and Reddy, 2014a) on the sciatic nerve, which is consistent with different studies that have reported to be a potent hypoglycemic agent (Nagilla and Reddy, 2014b). Those results along with the current study we can conclude that Coccinia is a more potent agent when compared to most of the naturals products that are reported to be hypoglycemic agents.

Many studies had proposed that oxidative stress induced by diabetes is the main reason for changed neuronal pathology. But we propose that chronic hyperglycemia which activates the polyol pathway further induce oxidative stress leading to inflammation may be directly related to morphological alterations in regions of diabetic rats the brain. After 21 days of treatment with Coccinia *grandis* leaf extract diabetic rats showed decreased activities of all the polyol pathway enzymes and also the decreased quantity of its metabolites when compared with the reference drug. Amelioration of inflammation was evident by the values of Cycloxygenase and prostaglandins.

CONCLUSION

In conclusion, our study shows STZ diabetes induces brain damage both morphologically and biochemically, which was potentially attenuated by Coccinia administration than the reference drug. And inhibition AR, leads to inhibition of the conversion of glucose to Sorbitol, which is a crucial pathway for activating the polyol pathway. Coccinia has shown neuroprotection by directly improving the effect of hyperglycemia as well as its antioxidant and radical scavenging properties. Moreover, by attenuating active polyol pathway and COX pathway and histological damage, shown in diabetic rat brain, the study shows the neuroprotective efficiency of Coccinia.

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Conflict of Interests

All authors have none to declare.

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