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Original article

Black tea extract ameliorates pancreatic dysfunction in male Wistar rats exposed to cadmium chloride

Venkappa S Mantur[1], Manjunath S Somannavar [2], Satisha Hegde [3,4], Sunil Vernekar [5], Kusal K Das [6], Shivaprasad S Goudar [5]

[1] Department of Physiology, SSPM Medical College and Lifetime Hospital, Kasal, Sindhudurga, Maharashtra - 422004, India
[2] Department of Biochemistry, KAHER, J. N. Medical College, Belagavi, Karnataka - 590010, India
[3]Dr. Prabhakar Kore Basic Science Research Centre, KLE Academy of Higher Education and Research, Belagavi, Karnataka - 590010, India
[4] Department of Microbiology, Belagavi Institute of Medical Sciences, Belagavi, Karnataka - 590001, India
[5] Department of Physiology, KAHER, J. N. Medical College, Belagavi, Karnataka - 590010, India.
[6] Department of Physiology, BLDE University's Shri B. M. Patil Medical College, Vijayapura, Karnataka - 586103, India
Corresponding author: Dr. Venkappa S Mantur; E-Mail: venki.mantur@gmail.com

Abstract

Introduction: Cadmium is one of the most dangerous and toxic occupational heavy metal. Exposure of cadmium is one of the risk factor for diabetes. This study aimed to assess the simultaneous effects of Black Tea Extract (BTE) on cadmium chloride induced alterations in oral glucose tolerance.

Methods: In this study, BTE on cadmium chloride induced alterations in oral glucose tolerance test (OGTT) and pancreas histology were assessed. Adult rats were divided into four groups (n=6/group), group I (normal saline), group II ($CdCl_2$, 1.0 mg/kg body weight; intraperitoneal), group III (black tea extract, 2.5 gm tea leaf/dl of water that is 2.5% of aqueous BTE) and group IV (cadmium chloride + BTE).

Results: The study revealed cadmium chloride intoxicated rats showed significant impaired glucose tolerance and changes in normal architecture of pancreas compare to control group. Oral administration of black tea extracts with cadmium chloride significantly improved glucose tolerance and pancreas architecture as compared to the cadmium chloride group.

Conclusion: The results indicate that BTE is beneficial in preventing cadmium-induced impaired glucose tolerance with pancreatic cellular damage.

Keywords: Black Tea, Cadmium, Glucose tolerance, Pancreas, Toxicity

1. Introduction

Cadmium is one of the most toxic heavy metal in environment. [1-2] Cadmium is not biodegradable and has very long half-life. Cadmium can induce oxidative damage and apoptosis to pancreatic β cells that causes suppression of insulin secretions which leads to diabetes mellitus. [3] Further cadmium is a nephrotoxic pollutant that increases the risk of diabetic nephropathy. [4- 5] Several studies suggested that generation of Reactive Oxygen Species (ROS) and its interference with cellular antioxidant system is one of the major mechanisms by which toxic effect of cadmium is mediated. [6] Cadmium triggers oxidative stress by enhancing the production of free radicals, DNA damage, lipids and proteins. [7]

Cadmium induces the disturbance in the glucose homeostasis which is reflected in increased concentration of blood glucose, reduced liver glycogen and increased gluconeogenesis in hepatic tissue. [8] This may be due direct effect of cadmium chloride on pancreatic β cells. This is contributed by the abnormal secretory activity of beta cell in the pancreas. Autoxidation of glucose can generate OH-radicals. [9] Target tissues are liver, kidney, spleen, gastrointestinal tract, pancreas in the animal model. Our previous preliminary study showed that cadmium induced hepatic dysfunction and dyslipidemia in animal model. [10] Recent studies have proved that there is a positive association between environmental pollutant exposures (Cd) and incidence of diabetes mellitus.

Detoxification of organ from heavy metal and chelation therapies have not proved to be effective in case of cadmium toxicities. Tea (*Camellia sinuses*) is one of the popular beverage next to water and it is having medicinal value. Flavonoids are a group of polyphenols that occur in tea. Black tea is also good source of flavonoids. The presence of flavonoid compounds in tea and green tea is considered as an important therapeutic substance which make numerous reports on tea as an antioxidant. [11-12] Therefore, this investigation was performed to assess the ameliorating effect of black tea extract on cadmium chloride induced alteration of glucose tolerance and pancreas histopathology in rats.

2. Material and methods

Adult male Wistar rats (160±10g) were divided into 4 groups i.e. group I, Control; group II, exposed with cadmium chloride (1mg/kg, i.p.)[13]; group III, treated with black tea (2.5g tea leaf/dl of water that is 2.5% of aqueous BTE) and group IV treated with cadmium chloride and BTE simultaneously for 21 days. Experiments were carried out after obtaining institutional animal ethical committee approval (1169/ac/08/CPCSEA). Animal breeding and maintenance were done in accordance with guidelines of Government of India for use of laboratory animals. [14]

2.1 *Preparation of black tea extract*

The black tea (*Camellia sinensis*) extract prepared from CTC (Cut, Tear and Crush) BOP (Broken Orange Pickoe) grade black clonal tea. A fresh 2.5% aqueous BTE prepared every day following the earlier method.[15] Twenty-five gram of black tea added to 500mL of boiling water and steeped for 15 minutes. The infusion cooled to room temperature and then filtered. The tea leaves extracted a second time with 500mL of boiling water and filtered, and the two filtrates combined to obtain a 2.5% aqueous black tea extract (2.5g of tea leaf/100mL water).

2.2 Oral glucose tolerance test (OGTT)

Animal was kept in an overnight fasting state. Oral 2 hours glucose tolerance test (OGTT) for rats were performed according to the standard method.[16] The

OGTT carried out after a corresponding dose in each group with acute exposure to each group of animals which were subjected for overnight fast. A blood sample was collected from the tail end and glucose estimation was done using a glucometer (Accu-chek active, Roche diagnostics, Germany).

A fasting blood samples were drawn and glucose tolerance test was done by feeding them orally with a glucose solution at a 0.35g/10g body weight.[17] Blood was collected at 0 min, 30min, 60min, 90min and 120min after glucose load.

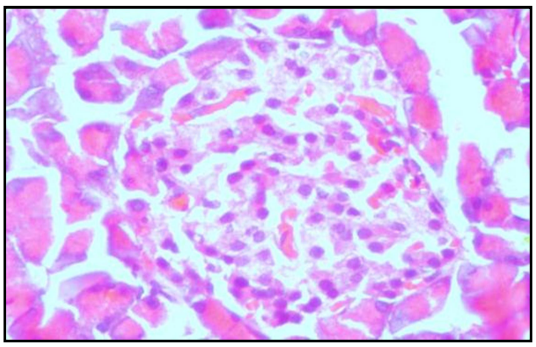
All the experimental procedures followed were performed in accordance with the approval of the Institutional Animal Ethics Committee (1169/ac/08/CPCSEA) under compliance of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines for the experimental studies.

2.3 *Histopathological studies*

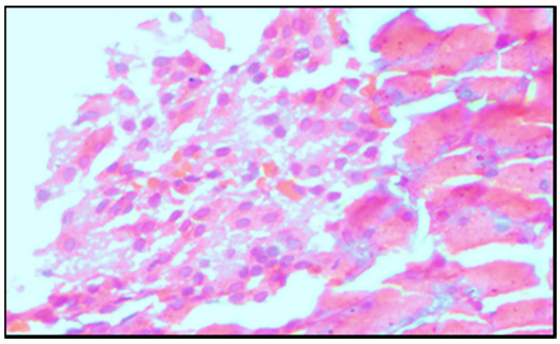
For the evaluation of histopathology, pancreas tissue from each rat was stored in 10% neutral buffered formalin solution. Pancreas was processed and sectioned. By following routine histological techniques, the samples were put into paraffin and serial sections of 5mm were taken from tissue blocks. Each slide was stained with haematoxylin and eosin. The preparations were evaluated under a photomicroscope and photo-graphed (Olympus BH-2 with Samsung Digital Color Camera, Medel No. SDC-242). The changes of the tissues of control and various treated groups were observed.

3. Statistical analysis

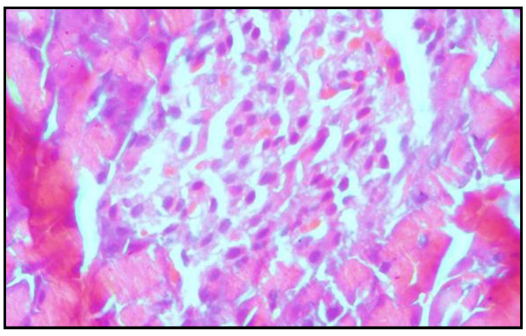
Data were expressed as mean ± standard deviation of mean (SD). Statistical comparisons were performed by one-way ANOVA followed by post-hoc t test and the values were considered statistically significant when $P<0.05$.



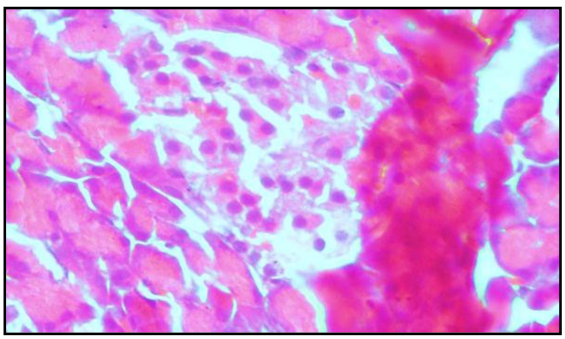
a) Pancreas section of normal control (I) (40x)



b) Pancreas section of $CdCl_2$ exposed (II) (40x)



c) Pancreas section of BTE treated (III) (40x)



d) Pancreas section $CdCl_2$ +BTE treated (IV) (40x)

Figure 1: Results of histopathology studies

Treatment Groups	0 h (FBS)	0.5 h	1.0 h	1.5 h	2.0 h
Control (I)	105.2±4.021	110.2±1.88	114.8±2.00	105.2±1.74	100 ±1.50
$CdCl_2$ (II)	134.5±3.391	144.3±1.97	143.7±1.56	140.3±0.33	141.3 ±1.05
BTE(III)	104±5.099	109.3±0.71	118.0± 0.85	112.3±0.91	105.5±1.3
$CdCl_2$+BTE (IV)	107.7±1.033	132.5±2.04	138±2.30	133.3±2.47	128.3±2.47

Table 1:Results of Oral Glucose Tolerance Test(OGTT)

4. Results and discussions

4.1 *Oral glucose tolerance test (OGTT)*

Before the commence of OGTT, the initial fasting blood sugar level was assessed in all groups. Normal control and BTE group were showing almost similar levels of fasting blood sugar (FBS) and also the glucose fluctuation of OGTT was almost matching with the same degree of glucose levels at 30, 60, 90 and 120 min on OGTT (Table 1). The $CdCl_2$ group II and $CdCl_2$+BTE group IV were showing discrimination in the fasting blood sugar level on performing OGTT. Preliminary studies have shown that cadmium exposed group increase in blood glucose levels prior to renal dysfunction. [18-19] Therefore, it reveals that BTE showed higher glucose tolerance compared to cadmium chloride group. Group IV ($CdCl_2$+BTE) has shown slightly higher glucose tolerance when compared with $CdCl_2$ group II (Table 1). This might because of oxygen radical scavenging properties of BTE which promotes prevention of oxidative stress. [20]

The histology sections from pancreas (haematoxlin and eosin stain) showed normal exocrine pancreatic acini amidst normal island of islet cells with group (I) (Fig.1). In group (II) (cadmium chloride) few islet cells with foamy pink cytoplasm with hydropic changes were seen. (Fig.2). Group III and group IV showed normal pancreatic islets (Fig. 3 & 4). There was significant improvement in the histology of pancreas in rats treated with cadmium chloride and BTE (Fig. 4). Several studies have suggested that generation of reactive oxygen species (ROS) and its interference with cellular antioxidant system is one of the major mechanisms by which toxic effects of cadmium is mediated.[21-22]

Black tea consists of epigallocathechin gallate, which reduces the hyperglycemia and prevent the oxidative damage.[23] In addition to the scavenging activity, theaflavin which is the one of the major content of BTE can activate the superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) and also causes reduction of lipid peroxidation.[24] Furthermore, simultaneous supplementation with BTE group showed better glucose tolerance which is further supported by histopathology of pancreas architecture.

5. Conclusions

The results revealed BTE is beneficial in preventing cadmium-induced impaired glucose tolerance with pancreatic cellular damage in male Wister rats.

6. Implications

This study emphasizes the influence of BTE on cadmium induced oral glucose intolerance and histopathology of pancreas. The study may be extrapolated to human for therapeutic use of modest plant extract like tea leaves in heavy metal toxicities exposed male industrial workers.

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