Effects of Fat and Cinnamon Feeding on the Diabetogenic State after rat injection with Dexamethasone

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Abstract: Consumption of high levels of dietary fat is thought to be a major factor in the promotion of obesity and insulin resistance Several environmental factors, including high-fat diet, are reported to activate the functioning of the hypothalamus-pituitary-adrenal axis [HPA].Frequently evoked HPA-axis secretes excessive amount of cortisol and elevated cortisol level is implicated in the development of entire spectrum of the metabolic syndrome, including insulin resistance, visceral obesity and dyslipidemia as well as the kinds of [10]. Normal levels of glucocorticoids are important for glucose metabolism. In a fasting state, normal concentrations of cortisol stimulate several processes, which collectively serve to maintain normoglycemia, excessive levels of cortisol are characterized by the symptoms of abdominal obesity, hypertension, glucose intolerance or diabetes and dyslipidemia ,all of these features are shared by the condition of insulin resistance [5]. In vitro [3] and in vivo [1,9] studies have shown that cinnamon enhances glucose uptake by activating insulin receptor kinase activity, autophosphorylation of the insulin receptor, and glycogen synthase activity. The ability of cinnamon to reduce lipid levels in fructose-fed rats, potentially via inhibiting hepatic 3-hydroxy-3-methylglutaryl CoA reductase activity [2].
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Key words: fat feeding; cinnamon feeding ; diabetes; dexamethasone

1. Introduction

An excess of cortisol, as seen in Cushing's syndrome or with clinical administration of glucocorticoids that is used to treat acute and chronic inflammatory diseases, leads to symptoms of abdominal obesity, hypertension, glucose intolerance or diabetes and dyslipidemia, all of which are also features of insulin resistance [6,4].

In rats, cinnamon potentiates insulin-regulated glucose utilization[3].

In patients with diabetes, cinnamon extracts have beneficial effects in reducing fasting plasma glucose, cholesterol and triglycerides [1].

In overweight patients [2] and women with the polycystic ovary syndrome [5], nutritional intakes of cinnamon also improve insulin sensitivity and lead to beneficial antioxidant effects.

2. MATERIALS AND METHODS:

2.1 Animals:

Male Sprague-Dawley rats, weighing 250 ± 10 g. The animals were housed at 24±1 ºC, 45±5% humidity and 12 h light-12 h dark cycle. They were left to acclimatize for 1 week before the experiments. The experimental procedures were carried out in accordance with international guidelines for care and use of laboratory animals.

2.2 Drugs and chemicals:

Dexamethasone [DEX] sodium phosphate powder and cholesterol powder were obtained from Sigma-Aldrich Company, USA. Commercial cinnamon powder was prepared as a water extract at a concentration of 60 g/100 ml

distilled H2O2

2.3 Experimental protocol:

The rats were randomly divided into four equal groups [n = 8, each]. The first group [control group] was fed the standard laboratory chow and received daily intra-peritoneal injection[i.p] normal saline [vehicle of DEX] for 14 days. The second group animals were fed high-fat diet [4% cholesterol diet, w/w] for 14 days. The rats of the third and fourth groups were fed high-fat diet [4% cholesterol diet, w/w], and received a daily i.p. injection of dexamethasone for 14 days. The third and fourth group animals received a daily i.p. injection of normal saline [vehicle of cinnamon] or cinnamon water extract [1 g/kg], respectively, for 14 consecutive days.

2.4 Sample preparation and biochemical studies:

At the end of 2 weeks, the rats were sacrificed and blood samples were collected after 12 h-fasting. A drop of blood was used to measure fasting blood glucose by the blood glucose meter [Accu-Chek, Roche Diagnostics, Germany]. A portion of blood was kept in EDTA tubes and used for determination of glycohemoglobin [HbA1C] level using a colorimetric assay kit [Stanbio Laboratory, USA]. The other portion of the blood samples were centrifuged for 10 min at 5000 rpm to obtain clear sera. Subsequently, serum lipid profile [total cholesterol, HDL-C, and triglycerides] was assessed using colorimetric assay kits [Stanbio Laboratory, USA].

2.5 Histopathological examinations:

Parts of the isolated pancreatic tissues obtained from each animal were fixed in 10% formalin solution, dehydrated in ascending grades of alcohol and embedded in paraffin. Sections of 4-µm thickness were taken, stained with hematoxylin and eosin [H&E] and examined by light microscopy.

2.6 Statistical analysis:

Data are expressed as mean ± S.E.M. Statistical evaluation was performed by one-way analysis of variance [ANOVA] followed by Turkey test for multiple comparisons. All analyses were performed with SPSS software package [version 18]. $P < 0.05$ was selected as the criterion for statistical significance

3. Result Analysis

The results are shown in the following table and figures.

Table 1. Effects of cinnamon [CIN] treatment on fasting blood glucose, glycohemoglobin [HbA1C], and serum adiponectin and lipid profile in rats fed high-fat diet [HFD] and received dexamethasone [DEX] for 14 days:

Parameter Measured	Control	HFD	DEX + HFD	CIN + DEX + HFD
Blood glucose [mg/dl]	79.42 ± 5.85	105.41 ± 6.33	157.58 ± 10.91 **a, b**	97.65 ± 8.71 **c**
HbA1C [%]	5.62 ± 0.41	6.54 ± 0.44	7.92 ± 0.56 a, b	6.05 ± 0.43 c
Total Cholesterol [mg/dl]	78.23 ± 4.25	107.33 ± 6.54 a	139.63 ± 5.75 a, b	99.12 ± 5.22 c
HDL-C [mg/dl]	42.34 ± 3.25	27.56 ± 2.42 a	19.56 ± 3.42 a	34.27 ± 2.45c

All the values are expressed as mean ± S.E.M., n = 8 in each group.
aP < 0.05 vs. control group.
bP < 0.05 vs. HFD group.
cP < 0.05 vs. DEX + HFD group.

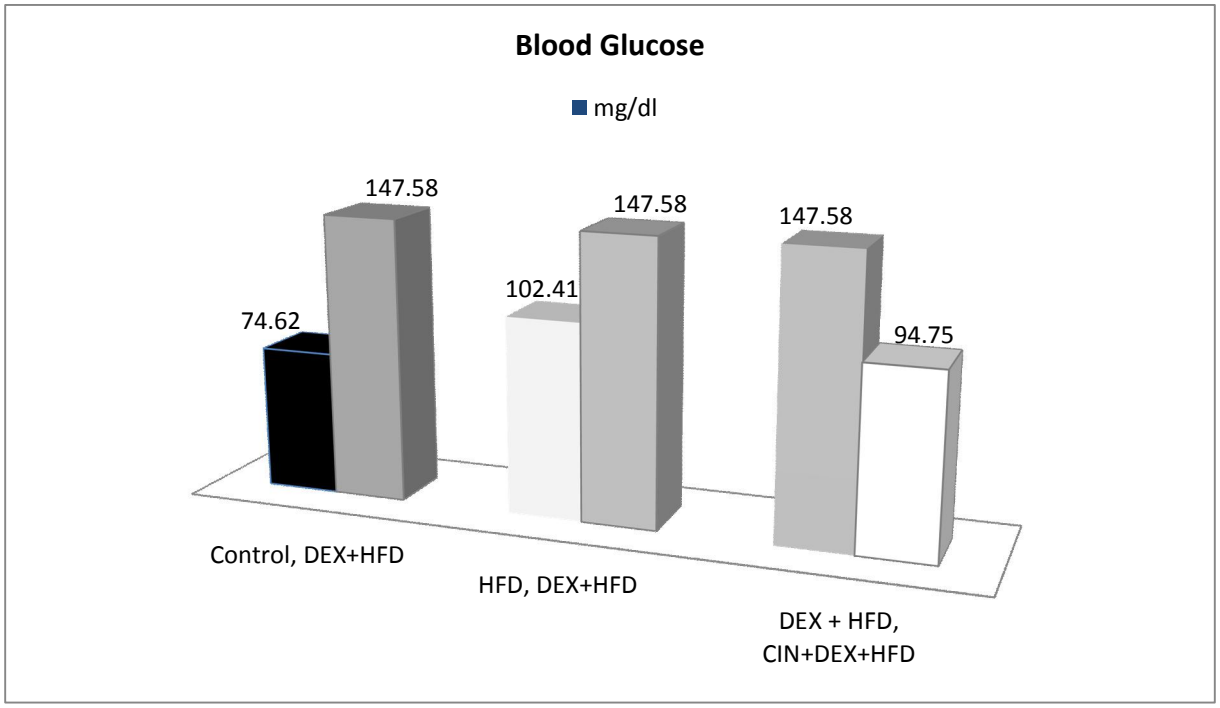

Figure 1. Blood Glucose

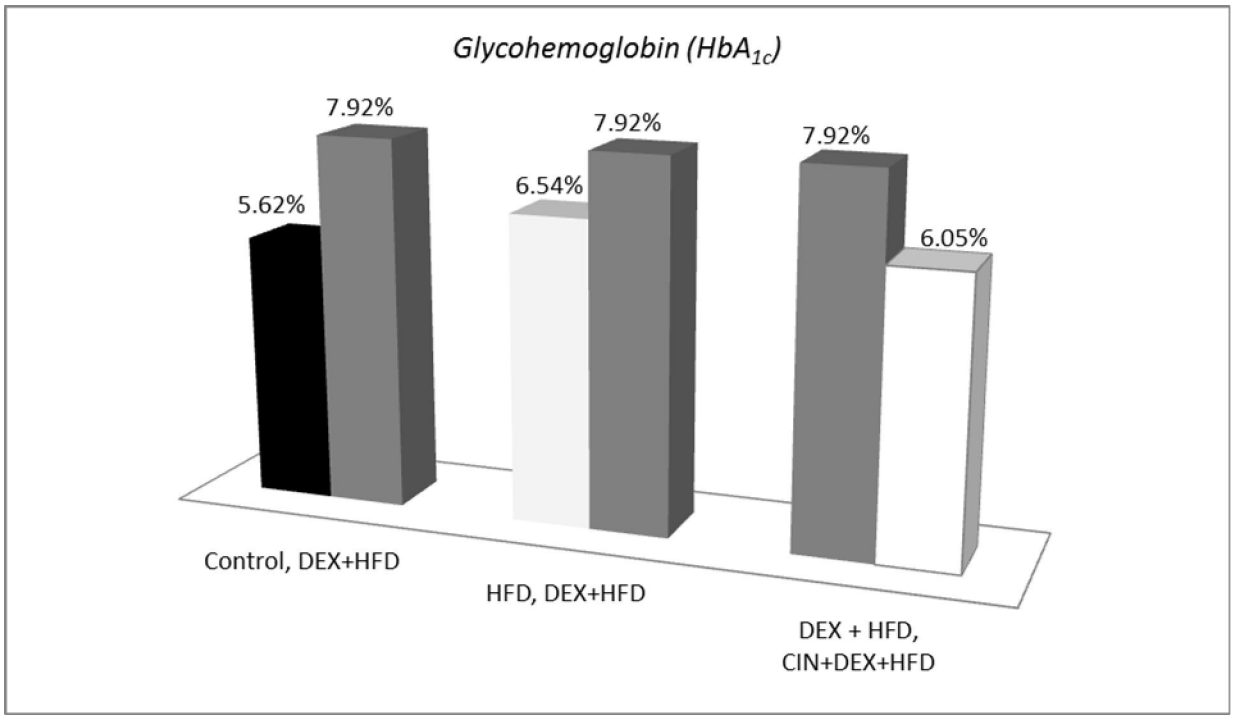

Figure 2. Glycohemoglobin (HbA1c)

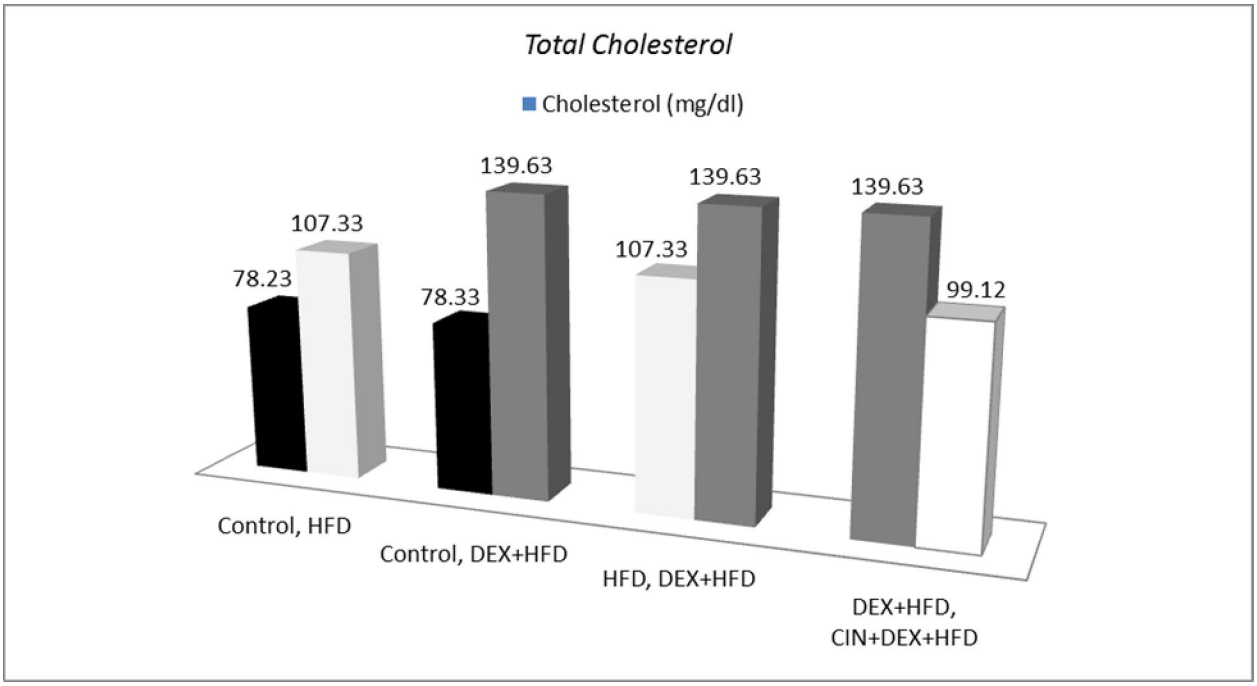

Figure 3. Total Cholesterol

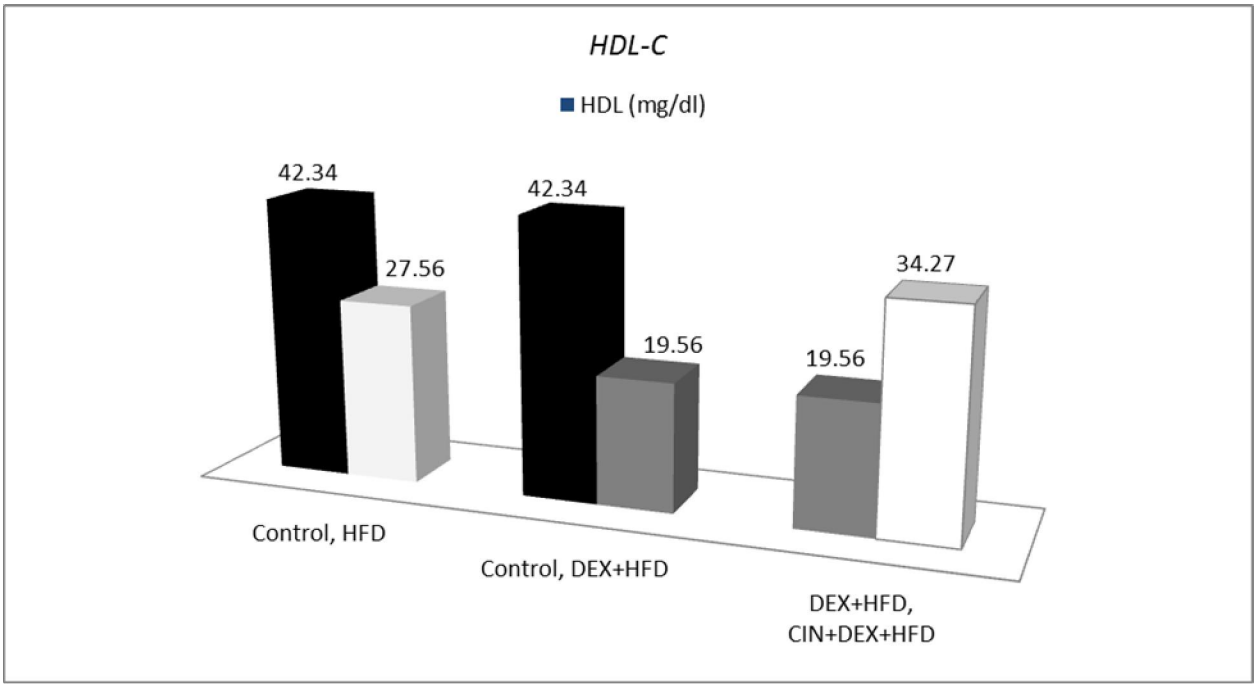

Figure 4. HDL-C

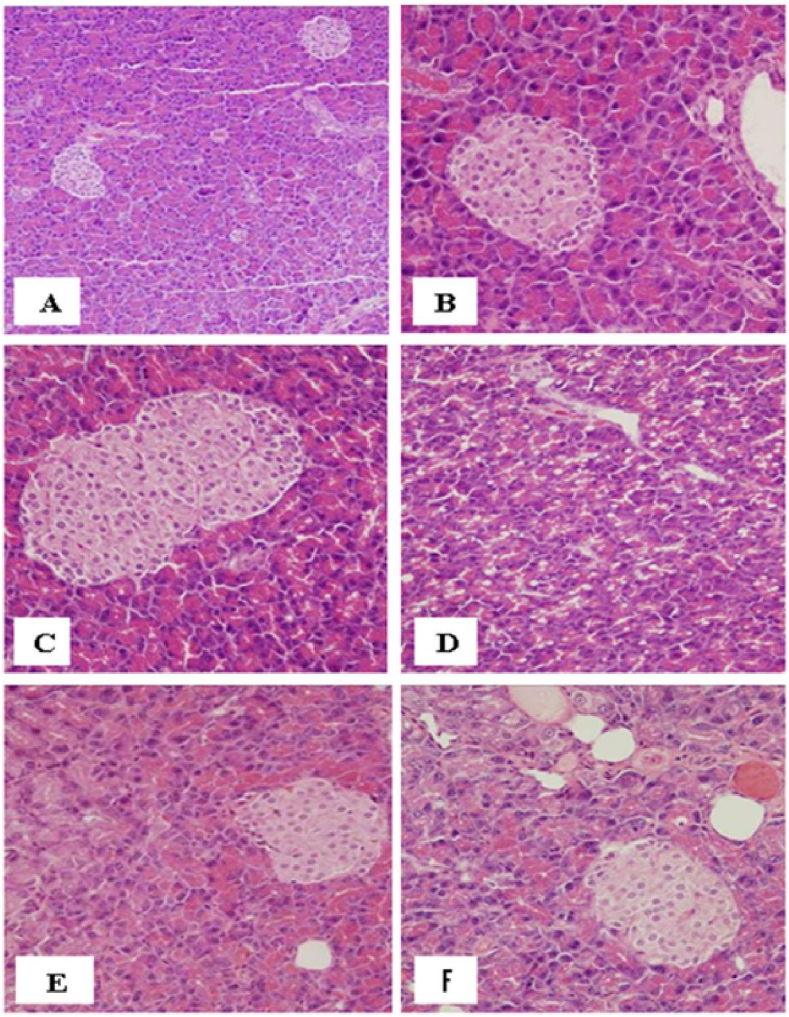

Fig.5.1

Fig. 5.1 Light photomicrographs of rat pancreas:
- [A and B] control group showing normal pancreatic structure
[A:H&E;200X] ,[B:H&E;400X]
- [C and D] rats received dexamethasone showing increased size of islets Langerhans and diffuse vacuolization of the pancreatic cells;
[C and D:H&E ;400X]
- [E and F] rats received dexamethasone and cinnamon showing decreased size of Langerhans islets and decrease of vacuolization in the acinar cells.
[E and F:H&E ;400X]

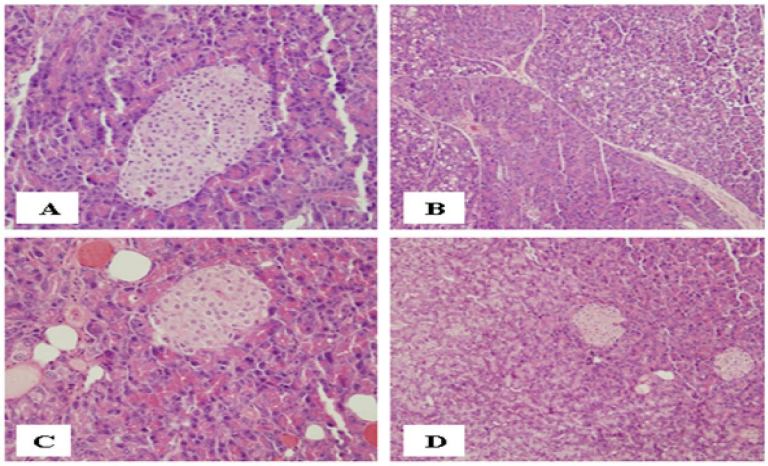

Fig.5.2

Fig. 5.2 Light Photomicrographs of rat pancreas:
- A and B Rats received dexamethasone and high-fat diet showing diffuse vacuolization of the pancreatic cells [A and B, H&E 400×]
- [C and D] rats received dexamethasone and fat and cinnamon showing decrease size of Langerhans islets with significant decrease of vacuolization in acinar cells.

[C and D ,H&E 400×]

Figure 5. Histology

Discussion:

In the present study total cholesterol was higher, while HDL was lower in HFD -fed rats, as compared to control animals. However, 'glycosylated hemoglobin, HbA1C [%] and triglycerides were not statistically different

When cortisone was administered with HFD further increase in total cholesterol and decrease in HDL was observed .Moreover the levels of glucose and HbA1C [%] increased significantly as compared to the control

When cinnamon was administered for 14 days to rats receiving HFD and dexamethosone , the changed parameters went back toward normal though still higher than the control .

Furthermore in rats receiving dexamethasone and HFD, the administration of cinnamon caused decrease in size of Langerhans islets with significant decrease of vacuolization in acinar cells of the pancreas in addition to decreased glycogen storage in hepatocytes of the liver.

Meanwhile, cinnamon- in rats- potentiates insulin-regulated glucose utilization [3]. cinnamon extract also significantly increases insulin sensitivity, reduces serum, and hepatic lipids, and improves hyperglycemia and hyperlipidemia possibly by regulating the PPAR-medicated glucose and lipid metabolism.

In patients with diabetes, cinnamon extracts have beneficial effects in reducing fasting plasma glucose, cholesterol and triglycerides [1]. In overweight patients [2] and women with the polycystic ovary syndrome , nutritional intakes of cinnamon also improve insulin sensitivity and lead to beneficial antioxidant effects.

Conclusion:

Therefore the beneficial effect of cinnamon on blood glucose and HbA1C [%] observed in the present study could be due to decrease of insulin resistance

The improvement in the histopathological changes of the pancreas after cinnamon in rats fed on high fat diet and injected with dexamethasone is confirmatory to the beneficial effect of the cinnamon which needs further investigations

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