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Satureja hortensis L. Alcoholic Extract Ameliorates Cadmium-Induced Pancreatic Damage in Rats

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Abstract: Cadmium is a toxic element with very long-term biological half-life. Cadmium is known to affect carbohydrate metabolism by injuring the Langerhans islet beta cells and reducing insulin secretion. This study was conducted to evaluate the ameliorating effect of *Satureja hortensis* (savory) extract on pancreatic damage in rats. Rats were divided into control, savory-treated control, cadmium-exposed and savory-treated cadmium exposed groups. Savory extract was administered at a dose of 100 mg/kg for two months. Finally, serum α-amylase, lipase and insulin were measured in addition to histological evaluation of the pancreas. It was found out that cadmium exposure significantly enhanced serum amylase ($p<0.001$) and lipase ($p<0.01$) versus control group with no significant effect on serum insulin and savory extract treatment of cadmium-exposed group did significantly improve serum amylase ($p<0.01$) and lipase ($p<0.05$). In addition, cadmium-exposed rats exhibited destruction of the exocrine pancreas with presence of inflammatory cells and degenerative and necrotic changes and savory extract-treated cadmium exposed group did not show such abnormal changes and had a normal architecture of the pancreatic tissue. It can be concluded that savory extract significantly restore serum amylase and lipase in cadmium-exposed rats and could protect pancreatic tissue in such rats.

Key words: *Satureja hortensis* · Cadmium · Pancreas · α-Amylase · Lipase · Insulin

INTRODUCTION

Cadmium (Cd) is a heavy metal that is toxic to both humans and animals which severely and adversely affects bodily tissues [1, 2]. Cd is an accumulative toxic element with a very long-term biological half-life [3]. Cd is not a biodegradable element and its level in the environment is increasing due to industrial activities and for this reason, human exposure to this element is inevitable [3]. Although Cd is not regarded as an essential element to humans, but they are get exposed to Cd one way or the other through environment and diet [4]. Cadmium is known to affect carbohydrate metabolism by injuring the Langerhans islet beta cells and reducing insulin secretion [5]. Cd also leads to necrosis, degeneration and degranulation of beta cells, causing an increase in the serum glucose level [6].

Using medicinal plant to treat diseases is becoming popular in human societies [7]. *Satureja hortensis* L. (summer savory, *S. hortensis*) is an aromatic and medicinal plant that is cultivated in the Middle East and with anti-nociceptive and anti-inflammatory activity [8]. Anti-genotoxic and cytoprotective effect of *Satureja hortensis* L. extract and its essential oil against oxidative stress in the rat lymphocytes exposed to hydrogen peroxide has been reported [9]. Until now, there has not been any investigation on the beneficial effect of this beneficial plant following Cd exposure. Therefore, we decided to evaluate whether *Satureja hortensis* alcoholic extract could ameliorate Cd-induced pancreatic damage in rats.

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MATERIALS AND METHODS

Animals: In this study, 32 male Wistar rats (Razi institute, Karaj, Iran), weighing 250-300 g, were used. The animals were housed in an air-conditioned colony room at 21±2°C and supplied with standard pellet diet and tap water ad libitum. Procedures involving animals and their care were conducted in conformity with NIH guidelines for the care and use of laboratory animals.

Extract Preparation: *S. hortensis* was purchased from the local herbal market in Tehran in June 2011. A specimen was deposited at Shahed University herbarium with a voucher number of 2012-173. The plant was washed out, dried under shade and powdered in a grinding mill. Then, powder was soaked in 80% ethanol for 24 hours. The solvent was decanted and residues macerated two more days with the same solvent. The obtained mixture was filtered and the filtrate was concentrated under reduced pressure. The extract was finally dissolved and diluted in normal saline.

Experimental Procedure: The rats were randomly divided into four 4 groups, each consisting of 8 animals, as follows:

Group I which subcutaneously received 2 ml/kg of normal saline, group II which was daily treated subcutaneously by Savory extract at a dose of 100 mg/kg, group III, that was daily and subcutaneously exposed to cadmium chloride at a dose of 3 mg/kg and group IV which daily received Savory extract at a dose of 100 mg/kg in addition to cadmium chloride.

After 2 months, the rats were killed by cervical dislocation and blood samples from their hearts were taken for biochemical analysis. For this purpose, non-heparinized blood sampling tubes were used. Finally, α-amylase and lipase were measured by colorimetric enzyme assay kits (BioAssay Systems, USA). In addition, ultra-sensitive rat-specific ELISA kit (Crystal Chem, USA) was used for insulin assay. Meanwhile, pancreatic tissue was removed, immersed in 10% formalin for 48 h, processed and paraffin-embedded blocks were prepared. After sectioning on a microtome (Leica, Germany), sections were stained with H&E. Light microscopy was used to evaluate the pancreatic tissue.

Statistical Analysis: The values are presented as means ±SEM. Statistical one-way ANOVA followed by Tukey post-hoc test was used for data analysis. A p value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Figure 1 shows amylase activity in different groups. In this respect, savory extract treatment of control group caused a non-significant mild increase of the amylase activity. In contrast, cadmium-exposed group showed a significant increase of amylase activity ($p<0.001$) and savory extract-treated cadmium-exposed group had a significantly lower level of amylase versus cadmium-exposed group ($p<0.005$).

Lipase activity in different groups has been shown in Fig. 2. In this respect, savory extract treatment of control group caused a non-significant and mild reduction of the lipase activity. In addition, cadmium-exposed group also showed a significantly increase of lipase activity ($p<0.01$) as compared to control group. Of interest, savory extract-treated cadmium-exposed group did show a significant reduction of lipase activity ($p<0.05$) in comparison with cadmium-exposed group.

Regarding serum insulin activity in different groups (Fig. 3), savory extract treatment of control group did not cause a significant change of the insulin activity. In addition, cadmium-exposed group also did not show a significant increase of insulin activity and savory extract-treated group also did not show a significant change of insulin activity versus cadmium exposed group.

Histopathological Assessment of the Pancreas: Histopathological evaluation of the pancreas tissue (Fig. 4) showed that in the control group and savory extract-treated control groups, there was no trace of necrosis. In contrast, cadmium-exposed rats exhibited destruction of the exocrine pancreas with presence of inflammatory cells and degenerative and necrotic changes was also visible. In this group, intraluminal cell debris, karyorrhexis and glassy pink cytoplasm were also observed. However, savory extract-treated cadmium exposed group did not show such abnormal changes and had a normal architecture of the pancreatic tissue.

According to previous reports, acute pancreatitis due to cadmium is followed by increased level of plasma amylase and lipase [10]. In our study, level of amylase and lipase significantly increased following cadmium exposure, indicating that pancreatic damage has been to a great degree at its used dose and possibly for this reason, cadmium had exerted a toxic effect on pancreas tissue to lead to extrusion of pancreatic lipase and amylase into the plasma. In contrast, pancreas of rats

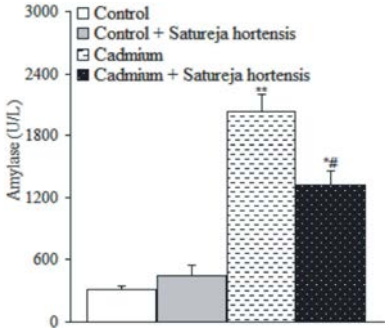

Fig. 1: Amylase activity in different groups
* p<0.005, ** p<0.001 (as compared to Control)
# p<0.01 (as compared to Cadmium)

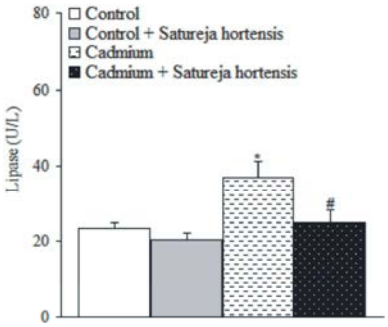

Fig. 2: Lipase activity in different groups
* p<0.01 (as compared to Control)
# p<0.05 (as compared to Cadmium)

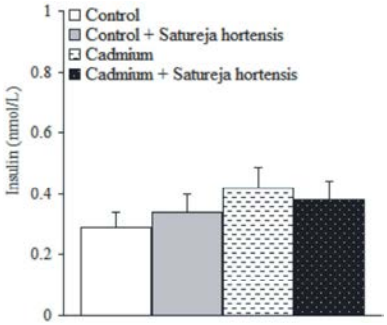

Fig. 3: Insulin activity in different groups

exposed to cadmium showed signs of inflammation and degenerative and necrotic changes. This finding is consistent with previous reports showing Cd exposure could induce necrosis, degeneration and degranulation in beta-cells of pancreatic islets [6].

In our study, savory extract treatment of cadmium exposed group for two months protect pancreatic tissue against abnormal changes. Since cadmium exposure is followed by tissue inflammation [11], part of beneficial effect of this extract could be attributed to its anti-inflammatory activity. In this respect, it has been

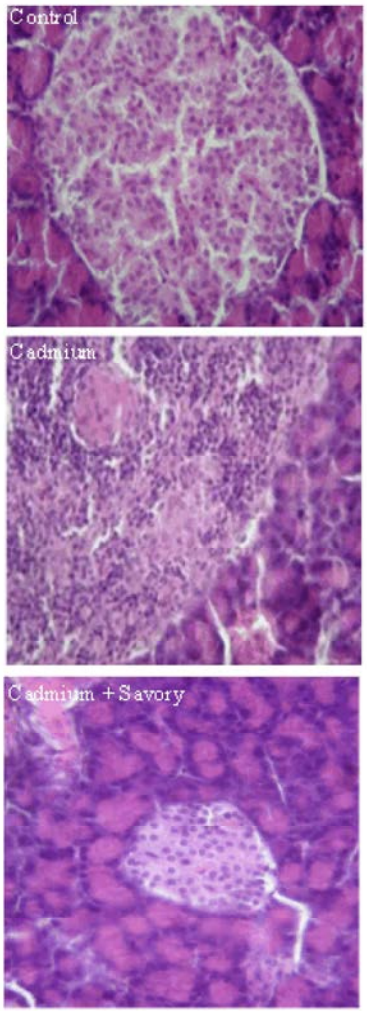

Fig. 4: Photomicrographs of exocrine and endocrine (Langerhans islets) portions of the pancreas in different groups. H&E staining

demonstrated that hydroalcoholic extract of *S. hortensis* seeds has potent anti-inflammatory activity following formalin application which is useful in painful and inflammatory ailments [12]. In addition, *Satureja hortensis* extract contains an anti-genotoxic effect in some cells like rat lymphocytes exposed to enhanced oxidative stress and this extract could attenuate oxidative damage of tissues [9]. This may have also occurred in our study. More studies are warranted to clarify the exact mechanisms responsible for protective effect of this extract in bodily tissues.

Taken together, it can be concluded that savory extract significantly restore serum amylase and lipase in cadmium-exposed rats and could protect pancreatic tissue in such rats.

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