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Original Article

Potential Renal Protective effects of *Matricaria Chamomilla* Extract in Streptozotocin-Induced Diabetic Rats

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ABSTRACT

Background and aim: Diabetes mellitus is a chronic disease with significant burden on the patient, his/her family and overall healthcare system due to its complications. Herbs of medicinal use played an important role in many diseases and chamomile is one of these herbs. The current worm aimed to investigate potential ameliorative effects of chamomile against diabetic changes in rat model.

Methodology: Fourty rats were used in the current work and divided into four equal groups. The first (negative control) received nothing except water; the second received chamomile extract in a similar dose in the fourth group (300mg/kg/bodyweight/day). The third group included diabetic rats and the fourth one included diabetic rat who received chamomile extract after induction of diabetes. Rats completed the study duration (6 weeks). Then blood samples were collected for laboratory investigations and after sacrificing, the pancreatic and renal tissues were fixed and prepared for microscopical examination.

Results: The use of chamomile was associated with significant reduction of diabetic indices (serum glucose, insulin and glycated hemoglobin) and significant improvement in renal function markers (blood urea and creatinine). However, this did not reach the normal values. The diabetic groups showed histological alterations of renal and pancreatic tissues, mainly necrosis and lymphocytic infiltration. The changes which reduced with the use of chamomile.

Conclusion: Chamomile (300mg/kg/bodyweight daily) have ameliorating effects against diabetic changes in a rat model. This was evident on biochemical and histopathological levels.

Keywords: Chamomile; Nephropathy; Islet Cells of Langerhans; Diabetes mellitus.

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INTRODUCTION

Diabetes mellites (DM) is an endocrine disorder due to dysfunction of insulin secretion and/or action. The inadequate insulin leading to persistent elevation of blood glucose levels and intolerance [1]. It is a serious health problem with a rising tendency all over the world. This is attributed to rising rates of obesity (mainly central obesity), sedentary lifestyles, changing dietary habits and unregulated use of endocrine disrupting chemicals (e.g., pesticides). The disease burden increased by its complications (e.g., cardiovascular diseases, retinopathy, nephropathy, neuropathy and premature death) [2-7]. Globally, DM affects 382 million in 2013 and it is expected to affect 592 million by the year 2025 [8].

Besides insulin resistance, there is an increased production of free radicals with hyperglycemia imposing harmful cardiovascular effects [9,10].

Matricaria chamomilla (Matricaria recutita) usually referred as chamomile is a member of *Asteraceae* family. It is known for its medicinal use due to high concentrations of phenolic chemicals and terpenoids. The main pharmacological actions include anti-inflammatory, antioxidant, antibacterial, anti-cancer, anti-spasmodic, and sedation [11-13].

The current work designed to explore the protective renal and antidiabetic effects of chamomile leaves extract in streptozotocin-induced diabetic rats.

MATERIALS AND METHODS

This study was carried out at Al-Azhar Faculty of Medicine (Damietta). 40 male, adult, albino rats (120-150 g) were the study sample. Animals were obtained from and housed in the animal house (Faculty of Veterinary, Cairo University), in a room temperature, with a natural light and dark cycles. An adequate plastic cases were used for housing and each case used for 5 rats. Rats were fed a standard diet of store-bought rat food, with free access to tap water.

Chemicals: chamomile was obtained from the herbal marked and prepared by a pharmacist not included in the study. Streptozotocin provided by MP Biomedicals (France). Other kits were provided by Biotechnology Company (Egypt) (blood glucose, serum urea and glycated hemoglobin). Insulin provided by Immunospec Company (California, USA) and finally Biolabo Reagents (France) provided the kits of Sodium, potassium and creatinine.

The duration of the study was 6 weeks. At the end, the following parameters were evaluated: Serum glucose, insulin, creatinine, urea, Na^+, and K^+, and HbA1c, as described in the manufacture instructions of the kit.

Grouping: Group I, received pure distilled water and work as a negative control (NC) group. Group II, received chamomile extract at a dose of 300mg/kg of body weight, starting from the first day of the experiment, and presenting the positive control (PC) group. Group III represented the study group, where diabetes mellitus was induced by a single dose of intraperitoneal streptozotocin (STZ; 60 mg/kg body weight) (MP Biomedicals, France) in a 0.1M sodium citrate buffer (pH 4.5) to overnight fasted rats. Then, rats were kept for the next 48 hours on an oral 10% glucose solution to prevent hypoglycemia because STZ. The diagnosis of diabetes was confirmed by the use of an Accu Check glucometer for blood samples drawn from the rat tail vein, three days after induction, and rats with blood glucose levels of 350 mg/dl or higher were included. The fourth group included diabetics rats that received a daily oral dose of 300mg/kg/bodyweight.

The Chamomile extract preparation was achieved through placing 10 g of Matricaria chamomilla L (chamomile) plant leaves in a glass jar. Then, 100 ml of boiling water were added. The jar was shaken and stirred. Then, left at room temperature for an overnight. After that, the extract was filtered by a filter paper. Finaly, a rotatory evaporator was used to concentrate the filtrate at 50°C with production of a greenish mass of leaf extract. Chamomile was fed for each rat by oral gavage at a fixed time daily.

Blood sampling for laboratory investigations: the retro-orbital venous plexus was the site for drawing morning blood samples, after a 12-hour overnight fasting. Samples were collected in a heparinized capillary tube and serum was separated by the centrifugation of the sample for 10 minutes at 5000 rpm. Serum was collected in Eppendorf tubes and kept at 20°C till the time of analysis.

Histopathological study: renal and pancreatic specimens were fixed in 10 neutral buffered formalin, embedded in paraffin, produced as 5-m-thick sections, and stained with hematoxylin and eosin (HE).

Statistical analysis: The software package (SPSS) version 13 (SPSS Inc., USA) was used to conduct the statistical analysis. The quantitative information was presented by their mean (for central tendency) ± standard deviation (SD, for dispersion). One-way analysis of variance (ANOVA) was used to measure variance between groups and post-Hoc least significant differences were calculated to determine the difference between two groups. P value < 0.05 was considered statistically significant.

RESULTS

In the current work, both negative and positive control groups showed non-significant differences from the statistical point of view. However, the diabetic groups (Group III) showed significant reduction of body weight, insulin, and sodium concentration when compared to control groups. Otherwise, there was significant increase of serum glucose levels, glycated hemoglobin, urea, creatinine and potassium in diabetic than control groups. The use of chamomile (300mg/kg daily) was associated with significant improvement of diabetic indices and renal changes. However, it did not reach the normal values, as there were still significant differences when compared to control groups and as the same time when compared to the diabetic group (Table 1).

Regarding histological examinations, there were no histological changes in the cells of the islets of Langerhans in the negative control group. In addition, all of the pancreatic cells were present in their normal proportions (Figure 1). In diabetic rats, there were atrophy and necrosis in the cells of the islets of Langerhans (Figure 2). In addition, using chamomile extract is associated with a small shrinkage and mild necrosis in the islet's cells. There was a minor lymphocytic infiltration in otherwise healthy islets of Langerhans (Figure 3). Additionally, the glomeruli and tubules were seen in a normal manner in the negative control group (Figure 4). Additionally, glomerulosclerosis, tubular deterioration, and infiltration of mononuclear cells were present (Figure 5). Additionally, the glomerular tufts were normal, and the tubal epithelium had mild lymphocytic infiltration. The glomerular basement membrane was also slightly thickened in normally healthy kidney tissue (Figure 6).

Table (1): Comparison between groups study grading different variables at the end of the study

Variable	Group I (NC)	Group II (PC)	Group III	Group IV	ANOVA	*P*
Body weight (g)	211.00±7.41	209.70±5.68	165.20±7.38 *#	181.10±9.68 *#$	85.67	<0.001 S
Glucose (mg/dl)	109.90±2.92	106.80±4.98	404.10±9.39 *#	205.50±10.76 *#$	3276.7	<0.001 S
Insulin (µU/ml)	32.00±1.94	31.70±1.88	4.32±0.33 *#	17.42±1.02 *#$	825.4	<0.001 S
HbA1C%	6.22±0.15	6.09±0.32	13.36±0.96 *#	8.71±0.44 *#$	367.21	<0.001 S
Urea (mg/dl)	22.10 ±2.51	21.50±3.43	54.10±4.43 *#	36.10±2.7 *#$	206.72	<0.001 S
Creatinine (mg/dl)	0.57±0.082	0.55±0.084	1.34±0.10 *#	0.74±0.15 *#$	116.84	<0.001 S
Sodium (meq/L)	144.30±0.94	144.40±2.06	140.30±1.33 *#	143.0±2.05 #$	13.05	<0.001 S
Potassium (meq/L)	4.50±0.019	4.51±0.012	5.56±0.16 *#	4.62±0.13 *#$	244.26	<0.001 S

S Indicate significant variance between groups; * Indicate significant difference in groups III and IV than group I; # indicate significant difference in group III and IV than group II; $ indicate significant difference in group IV than group III.

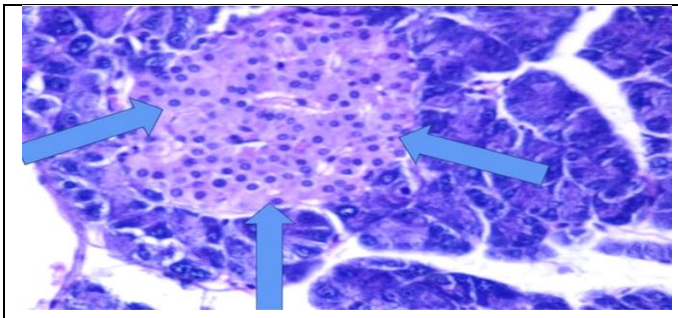

Figure (1): Photomicrograph of the negative control group showing normal architecture of the spleen and normal proportions of the cells.

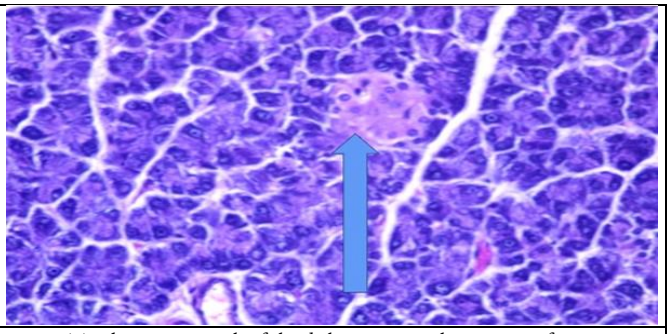

Figure (2): Photomicrograph of the diabetic group, showing significant necrosis of the islet cells

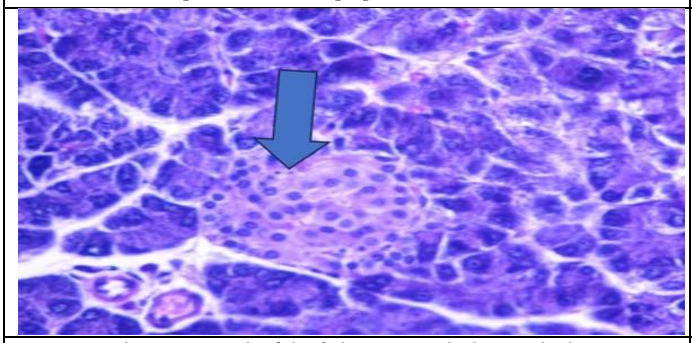

Figure (3): Photomicrograph of the diabetic rats with chamomile showing small shrinkage of the islet cells with lymphocytic infiltration.

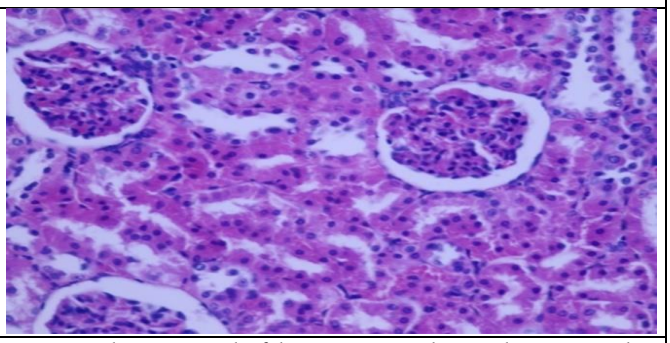

Figure (4): Photomicrograph of the negative control group showing normal renal structure.

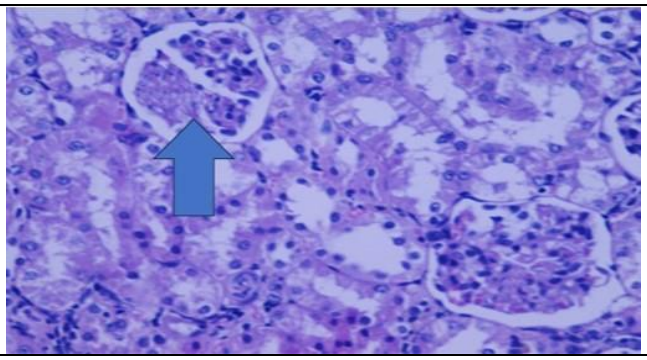

Figure (5): Photomicrograph of the diabetic group glomerulosclerosis (Arrow), tubular deterioration, and infiltration of mononuclear cells.

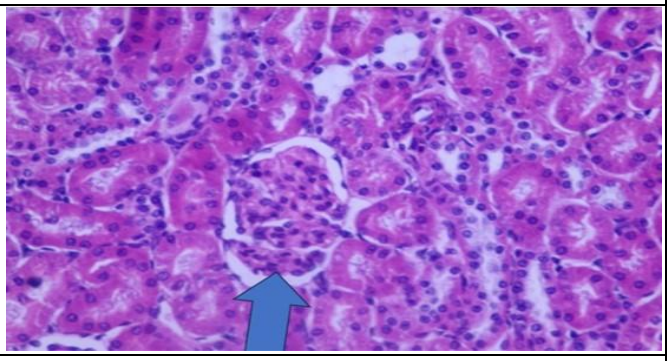

Figure (6): Photomicrograph of the diabetic group with chamomile showing normal glomerular tufts and mild lymphocytic infiltration of the tubal epithelium (arrow).

DISCUSSION

The current work was designed to investigate the value of the chamomile in potential protection against harmful effects of diabetes on the kidney and pancreases. These effects were evident in the STZ-induced diabetic rats by biochemical and histological changes (e.g., there was significant increase of glucose and glycated hemoglobin, associated with significant reduction of insulin). In addition, there was significant increase of urea and creatinine. A marked changes were hyperkalemia and hyponatremia. These changes reflected the necrotic and other histological changes in pancreatic and renal tissues. The use of chamomile

(300mg/kg/day) was associated with amelioration of these pathological changes either laboratory or even histologically. The use of chamomile was also associated with significant increase of body weight when compared to diabetic group, but it still lower than the control group. This increase in weight beside other ameliorating effects could be explained by the antioxidant effects of chamomile, which prevent protein-catabolic changes. In addition, the use of chamomile was found to increase the glycogen content of the liver as reported by Cemek *et al.* [15] and Kato *et al.* [16].

As in the current work, chamomile extracts are effectively reducing the serum glucose levels. However, it did not reach the normal values. These findings confirm that reported in the previous literature [15,17]. These glucose lowering effects were attributed to the total flavonoids in the chamomile, as they have a hypoglycemic effect by reducing the fibrinogen, glycated hemoglobin and glycated serum proteins, with improvement of glucose intolerance and increasing insulin secretion [18,19].

In alloxan-induced diabetes mellitus, Prasanna *et al.* [20] showed that, using chamomile extract is associated with significant improvement of glycemic control due to significant increase of insulin secretion. This is in line with the current work. The same authors confirmed the protective effects of chamomile extracts against renal changes in diabetic rat's model. They attributed these effects to anti-oxidant properties of chamomile.

Our results are agreeing with Rafraf *et al.* [21] who reported that using chamomile extract is associated with significant reduction of glycated hemoglobin in diabetic rats.

Interestingly, Cemek *et al.* [15] reported that, the chamomile extract antidiabetic effects were dose-dependent. They examined two doses (150 and 300 mg/kg/day). However, we used only the higher dose in order to gain the maximum benefits. However, values over 300mg/kg/day are required to validate the notion of Cemek *et al.*

The histological changes and protective effects of chamomile on the histological levels of renal tissues are in line with El-shaer and Nofal [22]. They demonstrated an enhanced ameliorative impact of chamomile on the histological changes of liver, kidney and spleen.

In conclusion, chamomile (300mg/kg/bodyweight daily) have ameliorating effects against diabetic changes in a rat model. This was evident on biochemical and histopathological levels.

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REFERENCES

1. Guthrie RA, Guthrie DW. Pathophysiology of diabetes mellitus. Crit Care Nurs Q. 2004 Apr-Jun;27(2):113-25. doi: 10.1097/00002727-200404000-00003.
2. Fletcher B, Gulanick M, Lamendola C. Risk factors for type 2 diabetes mellitus. J Cardiovasc Nurs. 2002 Jan;16(2):17-23. doi: 10.1097/00005082-200201000-00003.
3. Volaco A, Cavalcanti AM, Filho RP, Précoma DB. Socioeconomic Status: The Missing Link Between Obesity and Diabetes Mellitus? Curr Diabetes Rev. 2018;14(4):321-326. doi: 10.2174/1573399813666170621123227.
4. Malone JI, Hansen BC. Does obesity cause type 2 diabetes mellitus (T2DM)? Or is it the opposite? Pediatr Diabetes. 2019 Feb;20(1):5-9. doi: 10.1111/pedi.12787.
5. Carpenter DO. Environmental contaminants as risk factors for developing diabetes. Rev Environ Health. 2008 Jan-Mar;23(1):59-74. doi: 10.1515/REVEH.2008.23.1.59.
6. Leso V, Capitanelli I, Lops EA, Ricciardi W, Iavicoli I. Occupational chemical exposure and diabetes mellitus risk. Toxicol Ind Health. 2017 Mar;33(3):222-249. doi: 10.1177/0748233715624594.
7. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018 Feb;14(2):88-98. doi: 10.1038/nrendo.2017.151.
8. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract. 2014 Feb;103(2):137-49. doi: 10.1016/j.diabres.2013.11.002.
9. Fiorentino TV, Prioletta A, Zuo P, Folli F. Hyperglycemia-induced oxidative stress and its role in diabetes mellitus related cardiovascular diseases. Curr Pharm Des. 2013;19(32):5695-703. doi: 10.2174/1381612811319320005.
10. Babizhayev MA, Strokov IA, Nosikov VV, Savel'yeva EL, Sitnikov VF, Yegorov YE, Lankin VZ. The Role of Oxidative Stress in Diabetic Neuropathy: Generation of Free Radical Species in the Glycation Reaction and Gene Polymorphisms Encoding Antioxidant Enzymes to Genetic Susceptibility to Diabetic Neuropathy in Population of Type I Diabetic Patients. Cell Biochem Biophys. 2015 Apr;71(3):1425-43. doi: 10.1007/s12013-014-0365-y.
11. McKay DL, Blumberg JB. A review of the bioactivity and potential health benefits of chamomile tea (Matricaria recutita L.). Phytother Res. 2006 Jul;20(7):519-30. doi: 10.1002/ptr.1900.
12. Sharifi-Rad M, Nazaruk J, Polito L, Morais-Braga MFB, Rocha JE, Coutinho HDM, Salehi B, et al. Matricaria genus as a source of antimicrobial agents: From farm to pharmacy and food applications. Microbiol Res. 2018 Oct; 215:76-88. doi: 10.1016/j.micres.2018.06.010.
13. Shinomiya K, Inoue T, Utsu Y, Tokunaga S, Masuoka T, Ohmori A, Kamei C. Hypnotic activities of chamomile and passiflora extracts in sleep-disturbed rats. Biol Pharm Bull. 2005 May;28(5):808-10. doi: 10.1248/bpb.28.808. PMID: 15863883.
14. Mehmood MH, Munir S, Khalid UA, Asrar M, Gilani AH. Antidiarrhoeal, antisecretory and antispasmodic activities of Matricaria chamomilla are mediated predominantly through K(+)-channels activation. BMC Complement Altern Med. 2015 Mar 24; 15:75. doi: 10.1186/s12906-015-0595-6.
15. Cemek M, Kağa S, Simşek N, Büyükokuroğlu ME, Konuk M. Antihyperglycemic and antioxidative potential of Matricaria chamomilla L. in streptozotocin-induced diabetic rats. J Nat Med. 2008 Jul;62(3):284-93. doi: 10.1007/s11418-008-0228-1.
16. Kato A, Minoshima Y, Yamamoto J, Adachi I, Watson AA, Nash RJ. Protective effects of dietary chamomile tea on diabetic complications. J Agric Food Chem. 2008 Sep 10;56(17):8206-11. doi: 10.1021/jf8014365.
17. Zemestani M, Rafraf M, Asghari-Jafarabadi M. Chamomile tea improves glycemic indices and antioxidants status in patients with type 2 diabetes mellitus. Nutrition. 2016 Jan;32(1):66-72. doi: 10.1016/j.nut.2015.07.011.
18. Miraj S, Alesaeidi S. A systematic review study of therapeutic effects of Matricaria recuitta chamomile (chamomile). Electron Physician. 2016 Sep 20;8(9):3024-3031. doi: 10.19082/3024.
19. Khan SS, Najam R, Anser H, Riaz B, Alam N. Chamomile tea: herbal hypoglycemic alternative for conventional medicine. Pak J Pharm Sci. 2014 Sep;27(5 Spec no):1509-14. PMID: 25176245.
20. Prasanna R, Ashraf EA, Essam MA. Chamomile and oregano extracts synergistically exhibit antihyperglycemic, antihyperlipidemic, and renal protective effects in alloxan-induced diabetic rats. Can J Physiol Pharmacol. 2017 Jan;95(1):84-92. doi: 10.1139/cjpp-2016-0189.
21. Rafraf M, Zemestani M, Asghari-Jafarabadi M. Effectiveness of chamomile tea on glycemic control and serum lipid profile in patients with type 2 diabetes. J Endocrinol Invest. 2015 Feb;38(2):163-70. doi: 10.1007/s40618-014-0170-x.
22. El-shaer NH, Nofal AE. The Enhancing Effect of Chamomile on Histological and Immunohistochemical Alterations in Diabetic Rats. Egyptian Academic Journal of Biological Sciences, D. Histology & Histochemistry. 2019 Jun 1;11(1):15-32. DOI:10.21608/eajbsd.2019.29932

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