Original Article

The Possible Protective Role of Tannic Acid against Monosodium Glutamate-Induced Pancreatic and Liver Toxicity in Adult Male Albino Rats: Biochemical, Histological and Immunohistochemical Study

Sherine A. Mohammed[1], Palkis A. Mohamed[2], Soheir A. Mohamed[2], and Rania A. Radwan[2]

Departments of [1]Histology, [2]Forensic Medicine & Clinical Toxicology, Faculty of Medicine, Sohag University, Sohag, Egypt.

ABSTRACT

Background: Monosodium Glutamate (MSG) is a common flavor enhancer that has several toxic effects on different body organs. Tannic acid (TA) is a naturally occurring antioxidant component with several pharmacological properties.

Objectives: The present study was conducted to assess the possible protective role of TA on MSG-induced hepatic and pancreatic toxicity.

Materials and Methods: 40 adult male albino rats were divided into 4 equal groups. Group I was the control group, group II received TA, group III received MSG, and group IV received TA + MSG for 4 weeks. TA and MSG were received in a dose of 100mg/kg BW and 2g/kg BW respectively. At the end of the study, the evaluation was done by biochemical analysis and histopathology. Immunohistochemistry was used to measure BAX antibody and insulin expression.

Results: MSG increased the levels of pancreatic enzymes; amylase and lipase enzymes, as well as blood sugar levels. Liver enzymes were also increased. Histologically, degenerative changes were observed in the liver and pancreas with increased islets surface area. MSG increased the expression of the apoptotic marker BAX and decreased β-cells percentage. Co-administration of TA with MSG attenuated these degenerative effects.

Conclusion: MSG has toxic effects on the liver and pancreas leading to increased blood glucose levels. TA has an antioxidant role against MSG toxicity with a reduction of blood glucose levels.

Key Words: Insulin, liver toxicity, monosodium glutamate, pancreatic toxicity, tannic acid.

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Corresponding Author: Sherine Ahmed Mohammed, Department of Histology, Faculty of Medicine, Sohag University, Sohag, Egypt, **Tel.:** 01120301020, **E-mail:** sherinahmed@med.sohag.edu.eg

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INTRODUCTION

Monosodium glutamate (MSG) is a commonly used flavor enhancer. MSG is the sodium salt of glutamic acids and represents the principal component of most tissue proteins. The food and Drug Administration (FDA) stated MSG safety. However, the safety of MSG had become controversial in the last few years. Several studies on MSG toxicity caused a variety of health problems both in humans and experimental animals[1].

The liver and pancreas are considered important organs in the control of glucose levels. Toxicity of MSG was proved both in the liver and pancreas which was associated with hepatic histological degenerative changes and structural abnormalities both in the exocrine and endocrine pancreas in addition to disturbed blood glucose levels[2].

Tannic acid (TA) is a polyphenol that belongs to the family of hydrolyzable tannins. TA is most commonly present in many plants such as tea, coffee, and grapes. The antioxidant effects of TA are free radical scavenging and the prevention of DNA oxidative damage[3]. The present study was designed to study the possible protective role of TA on MSG-induced hepatic and pancreatic toxicity.

MATERIALS AND METHODS

I-Chemical compounds

Monosodium glutamate powder and tannic acid powder were purchased from Sigma Aldrich, German. Kits of enzymes (lipase and amylase), Insulin and glucose were purchased from Bio diagnostic company, Egypt.

Anti-Insulin Monoclonal was bought from Invitrogen (INS05 (2D11-H5)), Catalog # MA5-12037. Dilution: 1:100). Rabbit monoclonal Anti- Bcl-2-associated X protein (BAX) antibody [E63] bought from ABCAM (Catalog # ab32503, dilution: 1:100).

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II- The experimental animals

Forty healthy adult male albino rats of 2-3 months age with an average weight of (165-200 g) were used. Animals were purchased from the experimental animal house of the Faculty of Medicine, Sohag University. The animals were kept in the animal house with free access to water and diet, under an ambient temperature of 23 ± 2°C, and humidity 50:55%.

They were acclimatized to the laboratory condition for one week before starting the treatment protocol. Animals were fed with standard pellet food and water. The protocol was approved by the ethical committee of the Faculty of Medicine, Sohag University code: Sohag I ACUC 5-10-2022-2.

Experimental design:

Following their adaptation period, the rats were randomly assigned into four equal groups (10 rats each).

- **Group I (control group)**

The animals received water and diet for 4 weeks.

- **Group II (TA treated)**

The animals received oral TA daily100mg/kg BW[4] for 4 weeks.

- **Group III (MSG-treated group)**

The animals orally received MSG daily at 2g/kg BW[5] for 4 weeks.

- **Group IV (TA and MSG)**

The animals orally received both TA (100mg/kg BW)[4] and MSG (2g/kg BW) (5) for 4 weeks.

At the end of the experiment, the body weight of each animal was recorded. The animals were anesthetized by intraperitoneal injection of ketamine in a dose of 100 mg/kg BW[6].

The blood samples were obtained via cardiac puncture, collected into heparin-coated tubes, centrifuged at 4000 rpm for 15 min, and immediately stored at -20°C until their use for biochemical analysis. The liver and pancreas were dissected from each animal.

1. Body weight, Relative Liver Weight, and Relative pancreas Weight

The body weight of each animal was recorded before treatments and at the end of the experiment. The liver and pancreas of each rat were weighed after being washed with normal saline and dried using blotting paper, the Relative liver weight and relative pancreatic weight were calculated as follows:

Weight of the organ (g)/Body weight (g) ×100[7].

2. Biochemical measures:

A. The serum pancreatic enzymes (amylase and lipase) levels were estimated by using enzyme-linked immune sorbent assay kits[8] with UV2300 spectrophotometer (USA).

B. The liver enzymes: Serum alanine transaminase (ALT) and aspartate transaminase (AST) levels were estimated by using enzyme-linked immune sorbent assay[9] by spectrophotometry apparatus (Beckman Coulter AU480).

C. Detection of random blood glucose was determined by the automatic analyzer and blood glucose concentration was determined by enzymatic (glucose oxidase) colorimetric methods[10]

D. plasma insulin level was determined by radioimmunoassay kits (UV2300 spectrophotometer (USA) according to a method described by[11]

3. Histological examination of the liver and pancreas:

Specimens from the right lobe of the liver and pancreatic tail after dissection were rinsed in physiological saline and fixed in 10% formalin saline for 24 hours and processed for paraffin embedding. Paraffin wax blocks were sectioned at 5 um thickness using a microtome (Leica RM 2125). Pancreatic blocks were sectioned with at least 3 levels of serial sections 100 um apart for accurate islet measurements[12]. For light microscopic examination, sections were stained with:

- **Hematoxylin & Eosin (Hx&E):** stain used for general histological study. staining protocol according to[13].

• Immunohistochemical studies:

Anti-insulin antibody for detection of β cells in pancreatic islets, and *BAX antibody* for detection of apoptotic cells in the liver and pancreas. Deparaffinization of sections and rehydration in ascending grades of alcohol then antigen retrieval was carried out in 10 mmol/l citrate buffer (pH 6.2) in the microwave. Blocking of the endogenous peroxidase was done with 3% hydrogen peroxide for 10 min. Incubation of the sections overnight at 4 degrees temperature with the primary antibody after dilution to 1:100. Then they were subjected to biotinylated secondary antibody in a humid chamber. Enzyme conjugate streptavidin was applied.

Then they were subjected to biotinylated secondary antibody in a humid chamber. Conjugated streptavidin was applied.

The slides were stained by a substrate-chromogen mixture and then counterstained with Hematoxylin followed by dehydration in ascending grades of alcohol. Clearing in xylene and mounting with coverslip were done. Negative control was done with the omission of primary antibody. Positive cells showed brown cytoplasmic staining of β cells with insulin and brown cytoplasmic and sometimes nuclear staining of apoptotic cells with BAX[14].

4. Morphometric studies:

The light microscopy Leica ICC50 Wetzlar (Germany) was used at the Histology Department, Faculty of Medicine, Sohag University. Ten non-overlapping high power fields (x400) for each section in all groups were measured by Image J software. (Image J 1.47v national institute of health, USA) we measured:

1. β cell percentage (β cell surface area to islet surface area)[15]

2. BAX expression area percentage

3. The pancreatic islet of Langerhans surface area[16].

III-Statistical analysis

Statistical package SPSS for Windows, version 16.0 was used. Data were presented as means± standard deviation (SD) and the values were defined as statistical significance when the *P value* > *0.05*. Paired sample student t-test was used to compare the results between groups of the recordings reported by two observers.

RESULTS

• *Body weight gain*:

Mean weight gain significantly increased in group III compared to group I and group IV while there was a nonsignificant difference in group II and group IV as compared to group I (Table 1, Fig. 1).

• *Relative Liver weight and relative pancreatic weight:*

Both mean relative liver weight and mean relative pancreatic weight showed no statistically significant difference between group I and group II; but there was a significant increase in group III compared to group I. Group IV showed a significant decrease compared to group III but still significantly higher than the control (Table 2, Fig. 2).

Table 1: The mean value of body weight (initial, final) and weight gain ratio in all the studied groups

Groups	Initial body weight (g) mean ± SD	Final body weight (g) mean ± SD	Weight gain (%)
I	192.40 ±9.80	214.00±13.49	10.80
II	215.00±12.19	238.00 ±13.16	9.46^{Ns}
III	203.00±5.36	270.50±20.33	32.82*
IV	209.70±11.02	231.00±23.89	10.53^{Ns+}

* : significant compared to group I, +: significant compared to group III, *P< 0.05* (significant), NS: Non-significant compared to group I
SD: Standard deviation, paired sample Student t-test

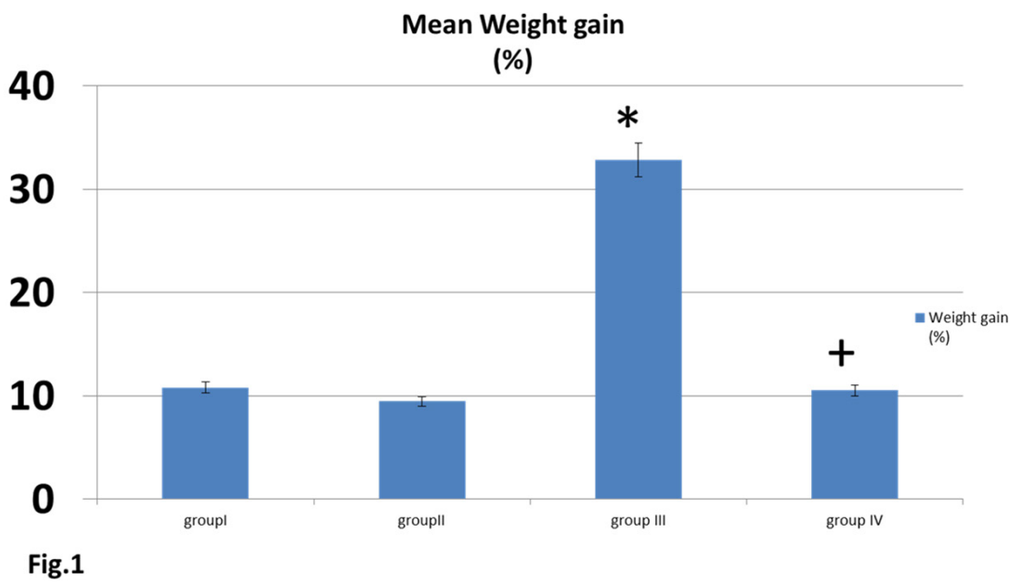

Fig.1: Histogram showing weight gain ratio in all the studied groups. * : significant compared to group I, +: significant compared to group III, *P< 0.05* (significant). Paired sample student t-test.

Table 2: The mean value of relative liver weight (g/100 g) and Relative Pancreatic weight (g/100 g) of rats in all the studied groups.

- Groups	Relative liver weight (g/100 g) mean ± SD	Relative Pancreatic weight (g/100 g) mean ± SD
I	2.46 ± 0.92	0.15 ± 0.01
II	2.61±•.32 NS	0.15 ± 0.08 NS
III	4.73±.022*	0.22 ± 0.05*
IV	3.00±•.74*+	0.16 ± 0.02*+

* : significant compared to group I *P< 0.05* (significant)
+: significant compared to group III
Non-significant compared to group I *p> 0.05*.(NS), SD: Standard deviation, Student t-test

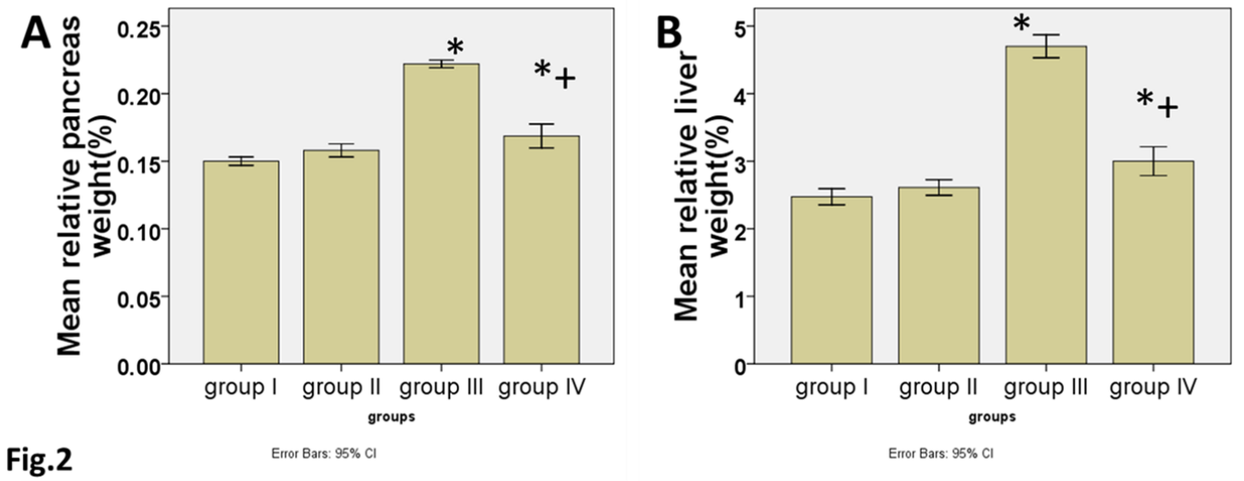

Fig.2

Fig. 2: Histogram showing the mean value of (A) relative liver weight. (g/100 g) and (B) Relative Pancreatic weight (g/100 g) in all the studied groups. * : significant compared to group I, +: significant compared to group III, *P< 0.05* (significant).Paired sample student t-test.

• *Biochemical results:*

1. Liver enzymes:

There was a non-significant difference in serum AST and ALT levels between group II and group I while there was a significant increase in group III and IV as compared to the control group. Group IV showed a significant decrease compared to group III (Table 3, Fig. 3).

2. Pancreatic enzymes:

There was a non-significant difference in the mean serum level of amylase between group II and group I. There was a significant increase in MSG treated group as compared to the control group. Also; there was a significant reduction in mean values of serum levels of amylase in group IV versus group III with a non-significant difference in group IV as compared to group I (Table 4, Fig. 4).

Regarding the serum level of lipase enzymes; there was a non- significant difference between group II and group I. there was a significant increase in mean values of serum levels of lipase enzymes in MSG treated group as compared to the control group. Similarly; group IV showed a significant increase in mean values of serum levels of lipase enzymes as compared to the control group While there was a non-significant difference in mean values of serum levels of lipase enzymes in group III as compared to group IV (Table 4, Fig. 4).

3. Blood glucose levels and serum insulin levels:

There was a significant increase in mean values in random blood sugar in MSG treated group as compared to the control group. Also, there was a significant reduction in the mean values of blood sugar levels in group IV as compared to group III. While there was non–significant difference in the mean values of random blood sugar in group II and group IV as compared to group I (Table 4, Fig. 4).

There was no significant difference in insulin levels between all the studied groups. MSG group was non-significantly decreased (Table 4, Fig.4).

Table 3: Comparison of the mean value (±SD) of liver function tests between the studied groups.

Liver enzymes / Groups	Serum ALT (U/L) mean ± SD	Serum AST (U/l) mean ± SD
I	39.27 ± 3.64	145.4 ± 24.4
II	38.03 ± 4.1	163.3 ± 26.4
III	62.1 ± 10.33*	254.7± 32.5*
IV	48.8 ± 5.77*+	213.7 ± 14.59*+

* : significant compared to group I $P< 0.05$ (significant)
+: significant compared to group III, analyzed by Student t-test

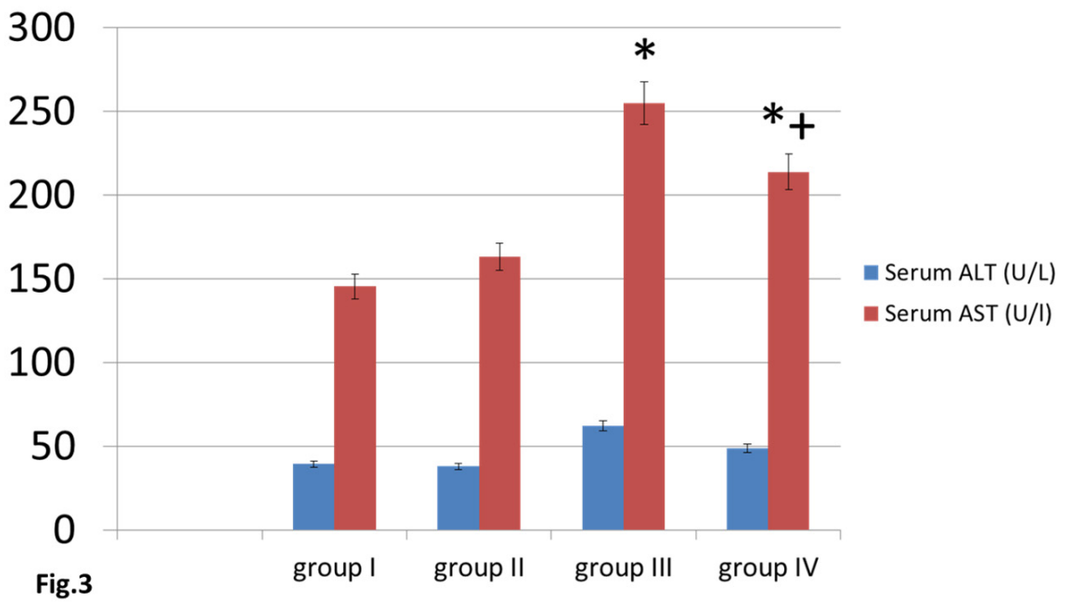

Fig. 3: Histogram showing the mean values of liver enzymes (serum AST&ALT) in all the studied groups. * : significant compared to group I, +: significant compared to group III, $P< 0.05$ (significant).Paired sample student t-test.

Table 4: Comparison of the mean value (±SD) of pancreatic function tests insulin level and blood glucose between the studied groups.

Pancreatic Function tests / Groups	Serum Insulin (microunit/ml) mean ± SD	Blood glucose (mg/dl) mean ± SD	Serum amylase (U/l) mean ± SD	Serum lipase (U/l) mean ± SD
I	3.07 ±1.4	112.7 ± 8.6	2474 ± 694.8	11.91 ± 3.1
II	3.0 ±1.38	113.6 ±10.3	2336.1 ±370.6	12.23 ±2.64
III	3.75 ± 1.66	158 ±25.17*	3208.9 ± 421*	37.9 ± 8.9*
IV	3.18 ±1.7	119.4 ±8.39+	2452.3 ±417.3+	34.37 ±5.9*

* : significant compared to group I
+: significant compared to group III, analyzed by Student t-test, $P< 0.05$ (significant)

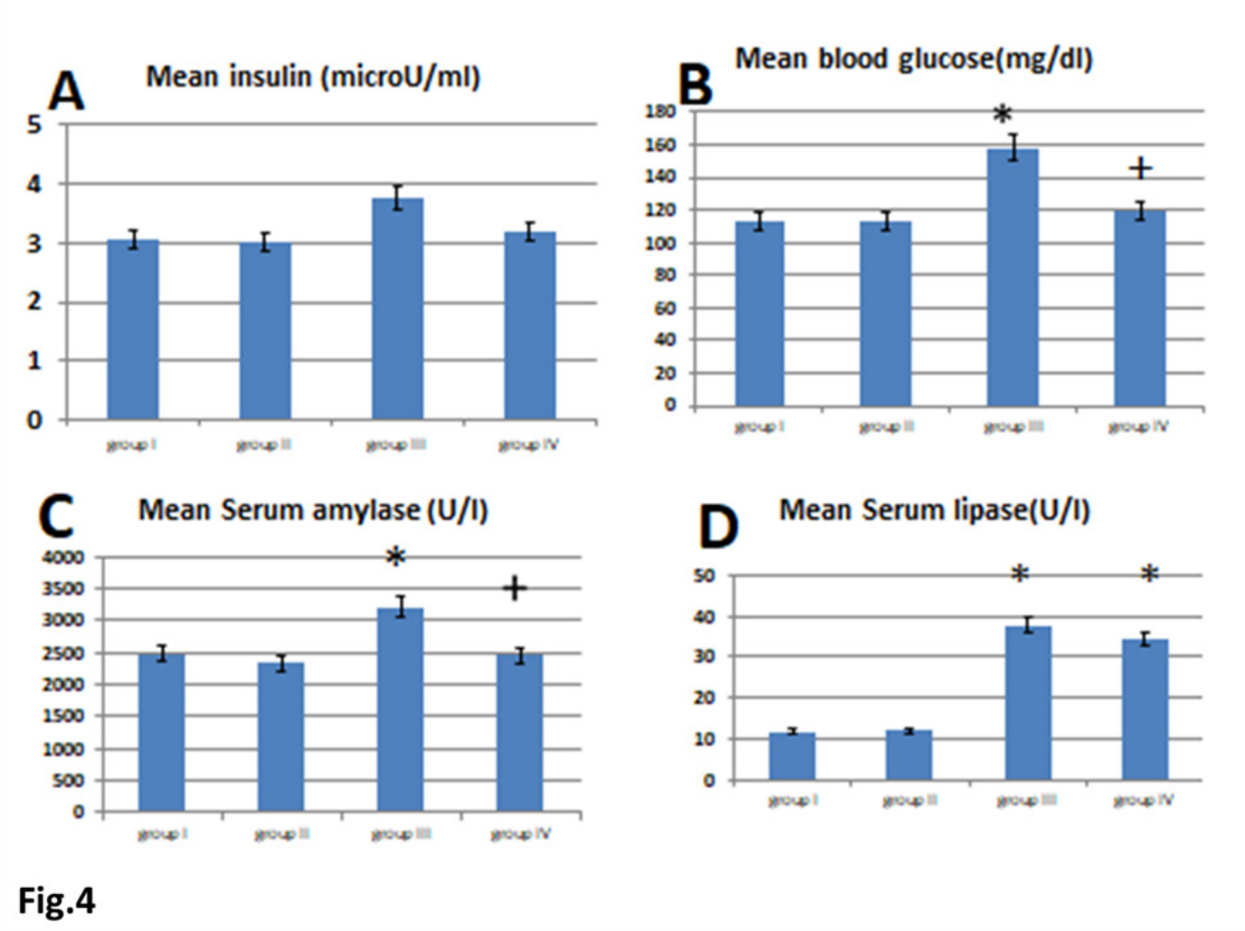

Fig.4: Histogram showing the mean values of A: insulin levels, B: blood glucose levels, C: serum amylase, and D: serum lipase levels between all the studied groups. *: significant compared to group I, +: significant compared to group III, *P< 0.05*: significant. Paired sample student t-test.

• *Histological studies:*

1) Hx&E:

Liver

H&E examination of liver sections of control group I and group II showed normal liver architecture; cords of hepatocytes radiating from the central vein without any histopathological changes; hepatocytes appeared as polyhedral cells with central rounded vesicular nuclei and slightly vacuolated acidophilic cytoplasm, as in (Fig. 5A). In group III, there were different degenerative cellular changes; some hepatocytes were necrotic with acidophilic vacuolated cytoplasm, others were apoptotic with highly acidophilic cytoplasm and pyknotic nuclei. Inflammatory infiltration was seen. Kupffer cells were more prominent compared to the control, as in (Fig. 5B). Meanwhile, administration of TA to MSG in group IV rats showed that most hepatocytes were more or less normal with vesicular nuclei and acidophilic cytoplasm. Few apoptotic hepatocytes and less prominent Kupffer cells were seen as in (Fig. 5C).

Pancreas

Histological sections of the pancreas of control group I and group II rats showed the architecture of the pancreas formed of lobules separated by loose connective tissue septa. The exocrine part was formed of serous acini. The islets of Langerhans were seen as scattered pale areas between the serous acini and were formed of irregularly arranged cords of cells separated by blood vessels. The pancreatic acini were lined by pyramidal cells having peripheral basophilic and apical acidophilic cytoplasm with normal rounded vesicular nuclei as in (Fig. 6A). Pancreas sections of group III showed hypertrophy of islets of Langerhans with increased vascularity. Also, the Islet cells showed vacuolated cytoplasm and some cells appeared with pyknotic nuclei. Some acinar cells had highly acidophilic cytoplasm and pyknotic nuclei as seen in (Fig. 6B).On the other hand, group IV rats showed more or less normal pancreatic architecture with smaller islets than in groupIII and normal appearance of most cells of islets with normal vascularity. Few cells had slightly vacuolated cytoplasm. Normal acinar cells were observed as seen in (Fig. 6C).

2) Morphometric studies

• Pancreatic islet of Langerhans surface area

There was no significant difference in the mean pancreatic islet area in group II compared to group I. a significant increase in the mean value of pancreatic islet area was observed in group III compared to group I. Also, there was a significant statistical reduction in group IV compared to group III, but still group IV was significantly increased compared to group I (Table 5, Fig. 6D).

3) Immunohistochemistry:

Liver Expression of BAX antibody area percentage

Positivity was expressed as brown cytoplasmic staining and sometimes nuclear in apoptotic hepatocytes. Few positive hepatocytes with cytoplasmic staining were seen in the control liver. There was no significant statistical difference in the mean of BAX expression area percentage in group II and group I. Many positive hepatocytes with cytoplasmic staining and nuclear staining were seen in group III. A significant increase in the expression percentage area of BAX in the liver of group III compared to group I. TA administration significantly decreased the expression of BAX in the liver compared to group III, but still, group IV was significantly increased compared to group I (Table 5, Figs. 7 A, B, C, D).

Pancreas:

Insulin antibody (β-cells area percentage):

β-cells appeared positive for anti-insulin antibody in the form of brownish cytoplasmic staining in islet cells. β-cell percentage area was not significantly different in group II compared to group I. There was a significant decrease in β cell area percentage in group III compared to the control group. TA administration significantly inhibited the decrease in the β cell Mass and significantly increased insulin expression in group IV versus group III, but still, group IV was significantly less than group I (Table 5, Figs. 8 A, B, C, D).

Pancreatic Expression of BAX antibody area percentage:

Immunoexpression of BAX appeared as brown cytoplasmic staining and sometimes nuclear in both islet cells and serous acini in the pancreas. Few positive cells in the islets and serous acini were seen in the control pancreas. There was no significant difference in the mean of BAX expression area percentage between group II compared and group I. Many positive cells in the islets and serous acini were seen in group III. There was a significant increase in the expression percentage area of BAX in the pancreas of the MSG group. TA administration significantly decreased the expression percentage area of BAX in the pancreas compared to the MSG group, but still, group IV was significantly increased compared to group I (Table 5, Figs. 8E, F, G, H).

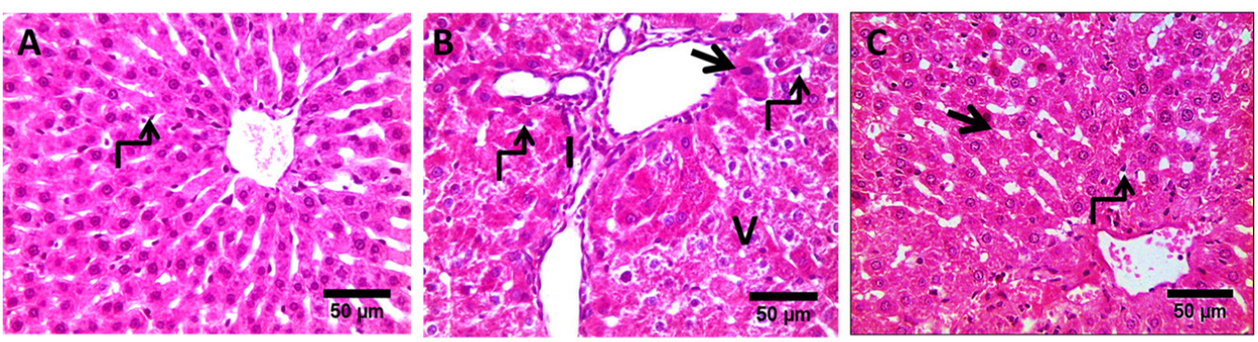

Fig.5

Fig. 5: Photomicrographs of liver sections of animals from A: control (group I and group II) showing a normal architecture of classic hepatic lobule; cords of hepatocytes radiating from the central vein; hepatocytes have central rounded vesicular nuclei and acidophilic cytoplasm, hepatic sinusoids between these cords with Kupffer cells (stepwise arrow) bulging into the lumen B: Group III showing some hepatocytes have vacuolated cytoplasm (V), others are apoptotic (arrow). Inflammatory cell infiltrations were seen (I). Kupffer cells (stepwise arrow) were more prominent compared to the control. C: Group IV showing the less disturbed liver architecture. Most hepatocytes are more or less normal with vesicular nuclei and acidophilic cytoplasm. Few apoptotic cells (arrow) and less prominent Kupffer cells (stepwise arrow) were seen (Hx, E X400; scale bar=50um).

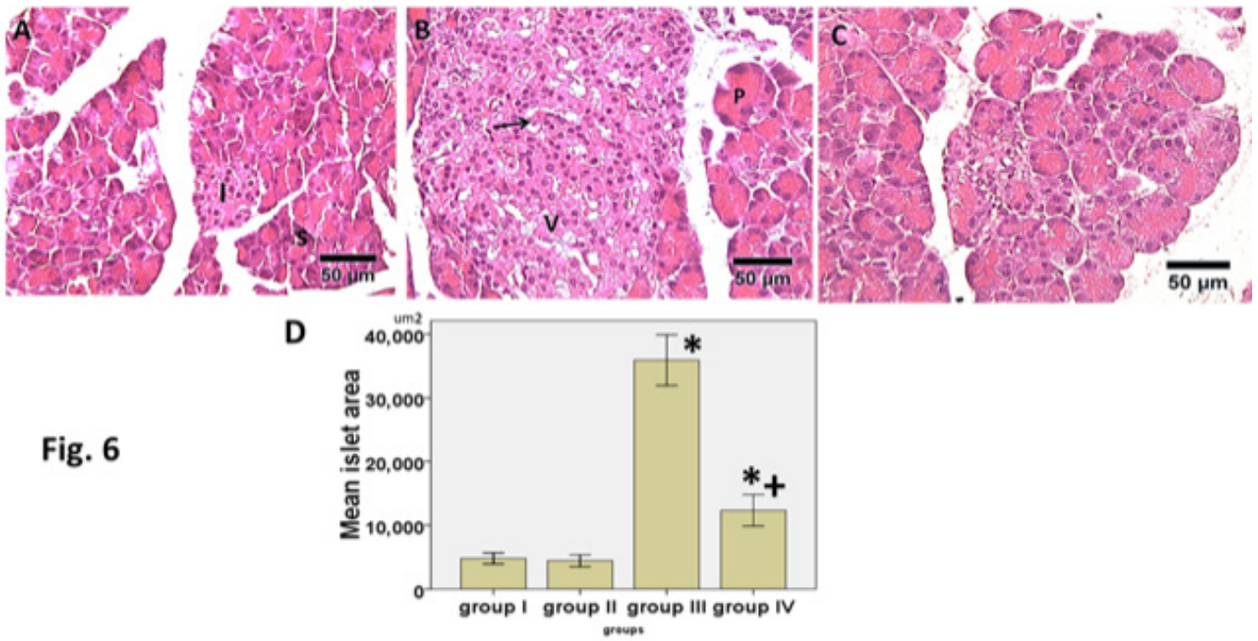

Fig. 6

Fig. 6: Photomicrographs of pancreas sections of A: Control (group I and group II) showing pancreatic lobules separated by loose connective tissue septa. The islet cells (I) are seen interspersed between the serous acinar cells (s). The islets are lightly stained and formed of irregularly arranged cords of cells separated by blood vessels. The pancreatic acini are lined by pyramidal cells having peripheral basophilic and apical acidophilic cytoplasm with normal vesicular nuclei B: Group III showing hypertrophy of islets of Langerhans. Islet cells are showing vacuolations (V) and some apoptotic cells (arrow). Some acinar cells have pyknotic nuclei (P). C: Group IV rats showing more or less normal pancreatic architecture and serous acini. The normal appearance of islets of Langerhans with Slightly vacuolated cells and normal vascularity is seen (Hx, E X400; scale bar=50um). D: Histogram showing the mean values of islet surface area in all studied groups, *: significant compared to group I, +: significant compared to group III, *P< 0.05*: significant. Paired sample student t-test.

Table 5: comparison of the mean value (±SD) of islets surface area, β-cell percentage and BAX expression between the studied groups

Groups	Mean islet area(um^2) (mean ± SD)	β-cell percentage (mean ± SD)	BAX expression percentage area in the pancreas (mean% ± SD)	BAX expression percentage area in the liver (mean% ± SD)
I	4788±235	67.34±4	8.74±0.8	8.68±0.7
II	4437±283	65.74±5	8.61±0.9	8.31±1.1
III	35930± 1091 *	37.78±4 *	49.00±10*	51.33±9.2*
IV	4019 ± 671 *+	56.63± 9 *+	27.91±4*+	29.84±0.8*+

* : significant compared to group I
+: significant compared to group III, *P< 0.05* (significant). paired sample Student t-test

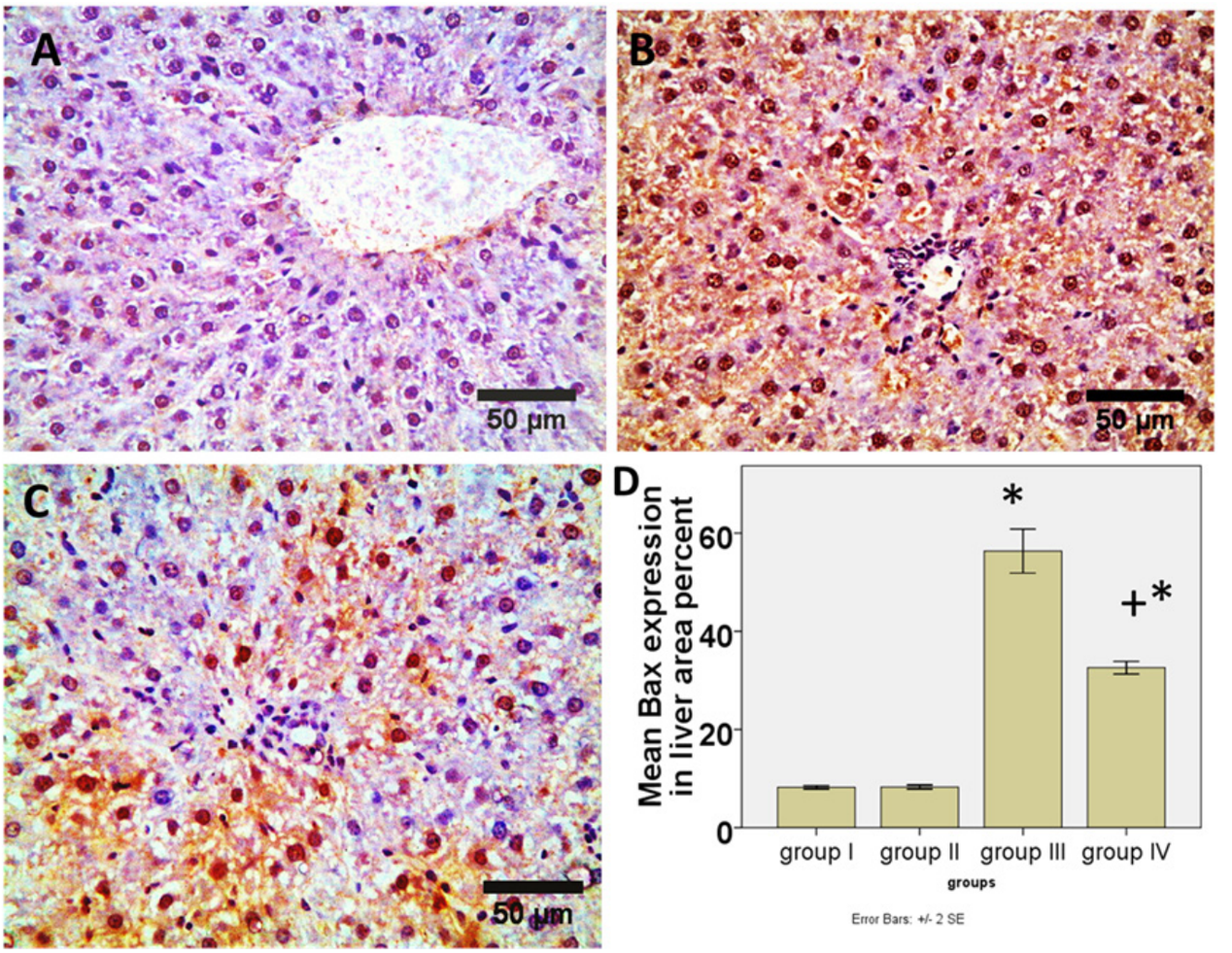

Fig.7

Fig. 7: Photomicrographs of liver sections immunostained with BAX antibody. A: Control (group I and group II) showing BAX immunoexpression appeared as brown cytoplasmic staining hepatocytes. B: Group II showing many positive hepatocytes expressing BAX as brown cytoplasmic staining and sometimes nuclear in hepatocytes. C: Group IV showing decreased expression of BAX (BAX antibody x400, scale bar= 50). D: Histogram showing mean values of liver BAX antibody expression in all studied groups, *: significant compared to group I, +: significant compared to group III. *P< 0.05*: significant. Paired sample Student t-test.

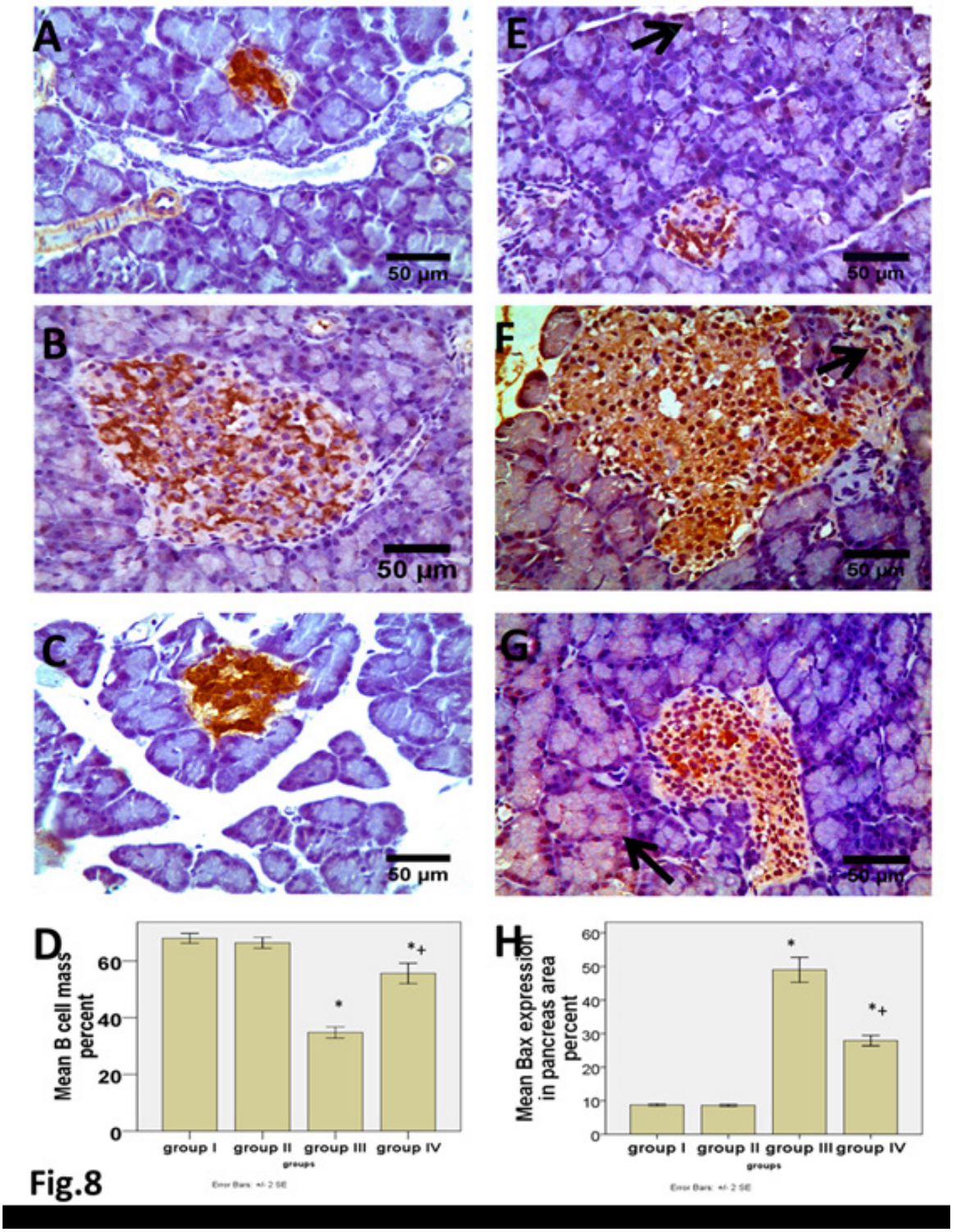

Fig.8

Fig. 8: Photomicrographs of pancreas sections immunostained with insulin antibody (A, B, C, D), BAX antibody (E, F, G, H). A: Control (group I and group II). B: Group III showing decreased insulin expression in islets of Langerhans. C: Group IV showing many insulin positive cells. (anti-insulin antibody x400, scale bar= 50). D: Histogram showing the mean values of insulin antibody expression percentage in all studied groups. * : significant compared to group I, +: significant compared to group III, $P< 0.05$: significant. Paired sample Student t-test. E: Control (group I and group II) showing BAX immunoexpression appeared as brown cytoplasmic staining in islet cells and serous acinar cells (arrow). F: Group III showing many positive cells expressing BAX, immunoexpression appeared as brown cytoplasmic and nuclear staining in islet cells and serous acinar cells (arrow). G: Group IV showing decreased expression of BAX in islet cells and serous acinar cells (arrow). (BAX antibody x400, scale bar= 50). H: Histogram showing the mean values of Pancreas BAX antibody expression in all studied groups. * : significant compared to group I, +: significant compared to group III, $P< 0.05$: significant. Paired sample Student t-test.

DISCUSSION

MSG is an important dietary component that is widely utilized to impart a savory flavor to foods all over the world[1]. The toxicity of MSG was proved in both the liver and pancreas which was associated with disturbed blood glucose level[2]. Tannic acid (TA) is a polyphenol that belongs to the family of hydrolysable tannins TA with antioxidant effects[3].

The present study was designed to study the possible protective role of TA on MSG-induced hepatic and pancreatic toxicity.

The current results revealed that weight gain was significant in MSG treated group compared with thst in the control group.

The mechanism of MSG-induced obesity is not quite clear. it might act as a neurotoxin that causes neuronal necrosis in the hypothalamic arcuate nucleus[17]. Another explanation is the neurotransmission signaling of glutamate and its relation with energy balance which interrupts the signaling of leptin in the hypothalamus and increased leptin activity in visceral adipogenesis[18].

The current results were in agreement with *Akataobi*[18] who observed a dose-dependent increase in body weight in MSG treated versus control.

In the present study, in the MSG group, the relative liver weight and relative pancreas weight significantly increased compared to the control group.

This could be attributed to inflammatory changes in the liver and pancreas. In addition to the compensatory islets hypertrophy observed in our histopathological results. The current results were in agreement with *Liu et al*.[19] who reported decreased relative weights of both liver and pancreas in MSG-treated rats. In contrast, *Ibegbulem et al*.[20] observed that alterations in liver indices were not significantly different. This could be due to a lower dose or shorter duration than that used in our study. This difference could be attributed to the longer duration of their study which reached 24 weeks of MSG injection for induction of obese diabetic models.

The present study showed that MSG caused a significant elevation in the serum levels of AST and ALT enzymes. This could be attributed to MSG-induced hepatotoxicity and released cytoplasmic enzymes (AST and ALT) into circulation due to cell death and membrane damage to the hepatocytes. Previous results were in accordance with our results[21]. The deleterious effect of MSG on the liver could be explained by that the excess concentrations of glutamate led to ammonium overload-induced hepatotoxicity[22] and on the other hand, MSG caused depletion of cellular GSH and increased reactive oxygen species. Consequently, this disturbs polyunsaturated fatty acids in the cell membrane causing enzymatic leakage and mitochondrial function impairment[21].

In previous studies, MSG administered to rats at a dose of 0.6 mg/g BW caused elevation in the levels of AST and ALT enzymes[23]. ALT is specific to the liver and localized to the cytosol of hepatocytes alone and is a strong positive indicator of hepatotoxicity[23].

In the present study, MSG treated group showed a significant increase in random blood glucose levels compared to the control group.

The hyperglycemia caused by MSG may be explained by that the GLUT 2 glucose transporters diminished; in addition to insulin resistance due to decreased insulin receptors sensitivity[24].

The current results go in harmony with[19, 25].

Contrary to the present study,[26] found that there was no significant difference in glucose levels between the control and group receiving MSG at 9 months of study due to exhaustion of the compensatory mechanisms that were inducing hyperglycemia at chronic long duration.

Takahashi et al.[27] explained that the pharmacological concentrations of glutamate potentiate insulin secretion from pancreatic islets while when excessively high concentrations of extracellular glutamate, the endogenous glutamate suppresses insulin secretion.

The current study showed a non-significant difference in insulin levels between all experimental groups. The present results were in line with the results done by *Boonnate et al*.[26] and they explained that this might be due to oxidative stress-induced β-cell apoptosis.

In contrast, hyperinsulinemia was reported by *Helal et al*.[28] due to insulin resistance.

The current results showed destruction of the normal hepatic architecture and degenerative changes of most hepatocytes in the form of vacuolated cytoplasm or apoptotic cells with highly acidophilic cytoplasm and pyknotic nuclei in the MSG-treated group. Inflammatory cell infiltrations were seen as prominent Kupffer cells. The cytoplasm is highly acidophilic with apoptosis due to condensation and denaturation of cytoplasmic proteins which increased its affinity for eosin stain[29]. These results were in agreement with *Elshafey et al*.[30] who explained that hepatocyte degeneration was due to oxidative stress and increased lipid peroxidation. *Eweka et al*.[31] noted hemorrhagic necrosis of hepatocytes in doses of (0.04mg/kg and 0.08mg/kg) daily for 42 days in adult Wister rats.

Inflammatory cell infiltrations and the prominent Kupffer cells observed in our study could be due to that MSG triggers inflammatory mediators; interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). Kupffer cells play an important role in cellular inflammation as they release pro-inflammatory and act as a defense against injury of the hepatic tissue intoxication[32].

In our study, the immunohistochemical results confirmed the apoptosis observed by Hx and E. we observed a significant increase in the apoptotic marker BAX both in the liver and pancreas of the MSC group. In line with our results, *Kassab et al*.[33] reported a significant increase in the immunoexpression of BAX was observed in hepatic and renal tissue in MSG administration.

Similarly, *Koohpeyma et al*.[34] reported that MSG significantly decreased renal expression of BCl2 and increased Caspase-9 compared to the control group.

That could be attributed to that MSG triggers the intracellular Ca2+ signaling pathway. Increased calcium in the organelles activates the calcium-dependent enzymes as caspases which propagate the apoptotic cascade for apoptosis[35].

The present study displayed histopathological changes in both the exocrine and endocrine pancreas. Some islet cells showed pyknotic nuclei and others showed vacuolation in addition to congestion and dilation in the blood vessels. Also; the pancreatic islet surface area in the MSG-treated group was significantly higher than that of the control group in the MSG-treated group. Similar results were reported in previous studies[26]. we observed degenerative changes in the acinar cells of the exocrine pancreas. This was in accordance with *Al-hayyali et al*.[36].

These histological changes may be due to either the direct effect of the glutamate on islet cells or due to oxidative stress[26].

Our results revealed decreased pancreatic β-cell area percentage compared to the control. similar results were reported by the previous study in the same dose both in long and short duration[26]. This could be attributed to oxidative stress-induced degeneration and cell death which caused this reduction in β cells[26].

Severe hypertrophy of pancreatic islets was observed in neonatal MSG-treated mice[37]. Hypertrophy of pancreatic islets with MSG treatment was reported in a previous study both in low and high doses[38].

The observed islet hypertrophy in the MSG in our study might be explained as a reactive response to injury because this has been also reported in partial pancreatectomy[39] which confirms that islet injury via different mechanisms induces islet cells regeneration which may cause islet hypertrophy.

In contrast, *Liu et al*.[19] observe the decreased surface area of islets with MSG administration. which could be explained by oxidative stress-induced degeneration of islet cells.

We observe in our study a significant decrease in insulin expression and beta cell mass by immunohistochemistry. Similar results were reported by *Boonnate et al*.[26]. Despite that, there were non-significant changes in insulin levels in the MSG group compared to the control in our study. moreover, glucose levels were increased.

The presence of glutamate transporters in pancreatic β-cells which regulate insulin secretion[27] compensated for the decreased β cell mass so that the insulin level was not decreased in our study. Despite that, the observed hyperglycemia emphasizes the presence of insulin resistance in our study.

In our study, Apoptosis of β cells was confirmed by a significant increase in BAX expression. In addition to oxidative stress-induced cell death, glutamate directly damages β cells[40]. A high level of extracellular glutamate impaired cysteine antiporter in pancreatic β-cells, leading to decreased glutathione and subsequent oxidative stress and cell death[41].

In normal conditions, BAX is located in the cytoplasm and translocation to the mitochondria. In apoptotic condition, BAX translocates and oligomerizes to the mitochondrial outer membrane and release cytochrome C then reach the nucleus[42].

The present results revealed TA administration decreased body weight gain (10.52%) in group IV compared to group III, but this decrease was a non-significant difference However, relative weights of both liver and pancreas were decreased significantly in group IV compared to groupIII but still significantly higher than control.

Similarly, TA reduced the body weight of rats in a previous study on animals receiving a diet of 18% of crude protein and supplemented with TA[43]. They explained that this was due to the antioxidant as well as the anti-inflammatory roles of TA.

The current study revealed that co-administration of TA with MSG was effective in improving MSG-induced liver damage through a decrease in relative liver weight and a significant reduction in the levels of ALT and AST enzymes compared to the MAG group.

This was because TA decreased lipid peroxidation, and improved antioxidant status through the elevation of the reduced glutathione (GHS) levels[44].

Similarly, *Babby and Elanchezhiyan*[45] also revealed that TA reversed the increased level of ALT and AST and attenuated hepatocellular degeneration in diabetic rats, which also explains the decrease in relative liver weight with TA.

In the present study, TA attenuated the histopathological degenerative changes induced by MSG. There was a significant decrease in apoptosis in group IV as indicated by HX&E and confirmed by decreased BAX expression compared to the MSG group.

The present study was in agreement with *Zhang et al*.[46] who found that TA suppressed the inflammatory reactions and attenuated hepatic degenerative changes and hepatocyte apoptosis in acetaminophen-induced hepatoxicity and acetylene toxicity[47]. Similarly, the antiapoptotic activity of TA was observed against toluene-induced hepatocyte apoptosis in rats in a previous study[48].

In contrast to our results, TA Induces the Mitochondrial Pathway of Apoptosis in cancer cells[42].

Regarding pancreatic function, TA in the present study showed a significant decrease in the plasma level of amylase and Lipase enzymes mean value compared to MSG which reflects the antioxidant role of TA in preventing MSG's toxic effects on the pancreatic parameters.

Supporting our results, *Lou et al*.[49] reported that TA had antioxidant as well as α -amylase inhibitory activities

Administration of TA in group IV in the present study significantly decreased the mean value of the plasma level of blood glucose compared to MSG treated group. In accordance with our results, *Calis et al*.[5] found that TA pretreatment decreased blood glucose levels and oxidative stress in adult rats received MSG (2 g/kg BW for 7 days) treated groups. That could be attributed to the TA-induced insulin receptor phosphorylation as well as cellular translocation of the glucose transporter GLUT4[50].

In our study, tannic acid decreased pancreatic Islet area compared to MSG with less vacuolation and vascularity of islet cells. In addition, TA attenuated apoptosis both in the exocrine and endocrine pancreas. Beta cell area percentage consequently increased compared to that MSG-treated group due reduction in β cell apoptosis as indicated by decreased BAX expression.

TA has an antioxidant mechanism increasing the reduced glutathione (GHS); a potent free radical scavenger within the islets of β-cell of pancreatic tissue. Similar to our results, TA decreased β-cell apoptosis during diabetic conditions as reported previously[51].

CONCLUSION

TA could ameliorate MSG-induced pancreatic and liver toxicity via an anti-oxidant effect. TA attenuated MSG-induced hyperglycemia and insulin resistance. In the future, further research on the protective effect of TA on MSG is needed to examine its safety profile.

ABBREVIATION

Monosodium Glutamate; MSG
Tannic acid; TA
Bcl-2-associated X protein; BAX.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Moldovan, O.-L., Rusu, A., Tanase, C., and Vari, C.-E. Glutamate - A multifaceted molecule: Endogenous neurotransmitter, controversial food additive, design compound for anti-cancer drugs. A critical appraisal. Food and Chemical Toxicology. 2021; 153: p. 112290.

2. Moen, S., Elhalwagy, M., and Ayaz, N. Alteration in pancreas of rats treated with individual and combined food additives. J med sci. 2020; 24(103): p. 1544-1552.

3. Ajebli, M. and Eddouks, M. The promising role of plant tannins as bioactive antidiabetic agents. Current medicinal chemistry. 2019; 26(25): p. 4852-4884.

4. Winiarska-Mieczan, A., Kwiecień, M., Bąkowski, M., Krusiński, R., Jachimowicz-Rogowska, K., Demkowska-Kutrzepa, M., Kiczorowska, B., and Krupa, W. Tannic Acid and Tea Prevents the Accumulation of Lead and Cadmium in the Lungs, Heart and Brain of Adolescent Male Wistar Rats—Possible Therapeutic Option. Animals. 2022; 12(20): p. 2838.

5. Calis, I.U., Cosan, D.T., Saydam, F., Kolac, U.K., Soyocak, A., Kurt, H., Gunes, H.V., Sahinturk, V., Mutlu, F.S., and Koroglu, Z.O. The effects of monosodium glutamate and tannic acid on adult rats. Iranian Red Crescent Medical Journal. 2016; 18(10).

6. Linsenmeier, R.A., Beckmann, L., and Dmitriev, A.V. Intravenous ketamine for long term anesthesia in rats. Heliyon. 2020; 6(12): p. e05686.

7. Ashafa, A.O., Orekoya, L.O., and Yakubu, M.T. Toxicity profile of ethanolic extract of Azadirachta indica stem bark in male Wistar rats. Asian Pacific journal of tropical biomedicine. 2012; 2(10): p. 811-7.

8. de los Angeles Camacho-Ruiz, M., Mateos-Díaz, J.C., Carrière, F., and Rodriguez, J.A. A broad pH range indicator-based spectrophotometric assay for true lipases using tributyrin and tricaprylin. Journal of lipid research. 2015; 56(5): p. 1057-1067.

9. Huang, X.J., Choi, Y.K., Im, H.S., Yarimaga, O., Yoon, E., and Kim, H.S. Aspartate Aminotransferase (AST/GOT) and Alanine Aminotransferase (ALT/GPT) Detection Techniques. Vol. 2006 Jul 31;6(7):756-82. eCollection 2006 Jul.: Sensors (Basel). .

10. Kunst, A., Draeger, B., Ziegenhorn, J., Ziwegenhorn, J., and Ziegernhorn, J. Colorimetric methods with glucose oxidase and peroxidase. 1988.

11. Flatt, P.R. and Bailey, C.J. Abnormal plasma glucose and insulin responses in heterozygous lean (ob/+) mice. Diabetologia. 1981; 20(5): p. 573-7.

12. Fernández-Díaz, C.M., Merino, B., López-Acosta, J.F., Cidad, P., Fuente, M.A.d.l., Lobatón, C.D., Moreno, A., Leissring, M.A., Perdomo, G., and Cózar-Castellano, I. Pancreatic β-cell-specific deletion of insulin-degrading enzyme leads to dysregulated insulin secretion and β-cell functional immaturity. American Journal of Physiology-Endocrinology and Metabolism. 2019; 317(5): p. E805-E819.

13. Suvarna, K.S., Layton, C., and Bancroft, J.D. Bancroft's theory and practice of histological techniques E-Book. 2018: Elsevier health sciences.

14. Schacht, V. and Kern, J.S. Basics of immunohistochemistry. The Journal of investigative dermatology. 2015; 135(3): p. e30.

15. Laker, R., Gallo, L., Wlodek, M., Siebel, A., Wadley, G., and McConell, G. Short-term exercise training early in life restores deficits in pancreatic B-cell mass associated with growth restriction in adult male rats. American journal of physiology. Endocrinology and metabolism. 2011; 301: p. E931-40.

16. Faizah, Z., Amanda, B., Ashari, F., Triastuti, E., Oxtoby, R., Rahaju, A., Aziz, M., Lusida, M., and Oceandy, D. Treatment with Mammalian Ste-20-like Kinase 1/2 (MST1/2) Inhibitor XMU-MP-1 Improves Glucose Tolerance in Streptozotocin-Induced Diabetes Mice. Molecules (Basel, Switzerland). 2020; 25.

17. Hernández Bautista, R.J., Mahmoud, A.M., Königsberg, M., and López Díaz Guerrero, N.E. Obesity: Pathophysiology, monosodium glutamate-induced model and anti-obesity medicinal plants. Biomedicine & Pharmacotherapy. 2019; 111: p. 503-516.

18. Akataobi, U. Effect of monosodium glutamate (MSG) on behavior, body and brain weights of exposed rats. Environmental Disease. 2020; 5(1): p. 3-8.

19. Liu, C., Yuan, Y., Zhou, J., Hu, R., Ji, L., and Jiang, G. Piperine ameliorates insulin resistance via inhibiting metabolic inflammation in monosodium glutamate-treated obese mice. BMC Endocrine Disorders. 2020; 20(1): p. 152.

20. Ibegbulem, C.O., Chikezie, P.C., Ukoha, A.I., and Opara, C.N. Effects of diet containing monosodium glutamate on organ weights, acute blood steroidal sex hormone levels, lipid profile and erythrocyte antioxidant enzymes activities of rats. Journal of Acute Disease. 2016; 5(5): p. 402-407.

21. Ahmed, R.R., Abdul-Hamid, M., Galaly, S.R., and Hamdalla, H.M. Monosodium glutamate-induced liver microscopic and biochemical changes in male rats, and the possible amendment of quercetin. Egyptian Journal of Zoology. 2019; 71(71): p. 44-55.

22. Krynytska, I., Marushchak, M., Naumova, L., and Mazur, L. The toxic impact of monosodium glutamate in rats. J Med J. 2019; 53(2): p. 91-101.

23. Manal Said, T. and Nawal, A.-B. Adverse effects of monosodium glutamate on liver and kidney functions in adult rats and potential protective effect of vitamins C and E. Food and Nutrition Sciences. 2012; 3: p. 651-659

24. Quines, C.B., Jardim, N.S., Araujo, P.C.O., Cechella, J.L., Prado, V.C., and Nogueira, C.W.

Resistance training restores metabolic alterations induced by monosodium glutamate in a sex dependent manner in male and female rats. Journal of cellular biochemistry. 2019; 120(8): p. 13426-13440.

25. Banerjee, A., Mukherjee, S., and Maji, B.K. Worldwide flavor enhancer monosodium glutamate combined with high lipid diet provokes metabolic alterations and systemic anomalies: An overview. Toxicology reports. 2021; 8: p. 938-961.

26. Boonnate, P., Waraasawapati, S., Hipkaeo, W., Pethlert, S., Sharma, A., Selmi, C., Prasongwattana, V., and Cha'on, U. Monosodium glutamate dietary consumption decreases pancreatic β-cell mass in adult Wistar rats. PloS one. 2015; 10(6): p. e0131595.

27. Takahashi, H., Yokoi, N., and Seino, S. Glutamate as intracellular and extracellular signals in pancreatic islet functions. Proceedings of the Japan Academy. Series B, Physical and biological sciences. 2019; 95(6): p. 246-260.

28. Helal, E.G., Barayan, A.W., Abdelaziz, M.A., and El-Shenawe, N.S. Adverse effects of mono sodium glutamate, sodium benzoate and chlorophyllins on some physiological parameters in male albino rats. The Egyptian Journal of Hospital Medicine. 2019; 74(8): p. 1857-1864.

29. Kari, S., Subramanian, K., Altomonte, I.A., Murugesan, A., Yli-Harja, O., and Kandhavelu, M. Programmed cell death detection methods: a systematic review and a categorical comparison. Apoptosis : an international journal on programmed cell death. 2022; 27(7-8): p. 482-508.

30. Elshafey, M., Eladl, M.A., El-Sherbiny, M., Atef, H., and El Morsi, D.A. Hepatotoxicity of monoglutamate sodium: Oxidative stress and histopathlogical study. The FASEB Journal. 2017; 31: p. lb31-lb31.

31. Eweka, A., Igbigbi, P., and Ucheya, R. Histochemical studies of the effects of monosodium glutamate on the liver of adult wistar rats. Ann Med Health Sci Res. 2011; 1(1): p. 21-9.

32. Wijayasekara, K.N. and Wansapala, J. Comparison of a flavor enhancer made with locally available ingredients against commercially available Mono Sodium Glutamate. International Journal of Gastronomy and Food Science. 2021; 23: p. 100286.

33. Kassab, R.B., Theyab, A., Al-Ghamdy, A.O., Algahtani, M., Mufti, A.H., Alsharif, K.F., Abdella, E.M., Habotta, O.A., Omran, M.M., Lokman, M.S., Bauomy, A.A., Albrakati, A., Baty, R.S., Hassan, K.E., Alshiekheid, M.A., Abdel Moneim, A.E., and Elmasry, H.A. Protocatechuic acid abrogates oxidative insults, inflammation, and apoptosis in liver and kidney associated with monosodium glutamate intoxication in rats. Environmental science and pollution research international. 2022; 29(8): p. 12208-12221.

34. Koohpeyma, F., Siri, M., Allahyari, S., Mahmoodi, M., Saki, F., and Dastghaib, S. The effects of L-carnitine on renal function and gene expression of caspase-9 and Bcl-2 in monosodium glutamate-induced rats. BMC nephrology. 2021; 22(1): p. 162.

35. Rahimi Anbarkeh, F., Baradaran, R., Ghandy, N., Jalali, M., Reza Nikravesh, M., and Soukhtanloo, M. Effects of monosodium glutamate on apoptosis of germ cells in testicular tissue of adult rat: An experimental study. International journal of reproductive biomedicine. 2019; 17(4): p. 261-70.

36. Al-hayyali, F.Q.M., Ali, K.A., and Kareem, Z.S. Oral glycine and l-arginine administration attenuates monosodium glutamate complications on pancreas structure in albino rats. Systematic Reviews in Pharmacy. 2020; 11(4): p. 491-7.

37. Bahadoran, Z., Mirmiran, P., and Ghasemi, A. Monosodium Glutamate (MSG)-Induced Animal Model of Type 2 Diabetes. Methods in molecular biology (Clifton, N.J.). 2019; 1916: p. 49-65.

38. Sasaki, Y., Suzuki, W., Shimada, T., Iizuka, S., Nakamura, S., Nagata, M., Fujimoto, M., Tsuneyama, K., Hokao, R., and Miyamoto, K.-i. Dose dependent development of diabetes mellitus and non-alcoholic steatohepatitis in monosodium glutamate-induced obese mice. Life sciences. 2009; 85(13-14): p. 490-498.

39. Laybutt, D.R., Glandt, M., Xu, G., Ahn, Y.B., Trivedi, N., Bonner-Weir, S., and Weir, G.C. Critical reduction in β-cell mass results in two distinct outcomes over time: adaptation with impaired glucose tolerance or decompensated diabetes. Journal of Biological Chemistry. 2003; 278(5): p. 2997-3005.

40. Di Cairano, E.S., Davalli, A.M., Perego, L., Sala, S., Sacchi, V.F., La Rosa, S., Finzi, G., Placidi, C., Capella, C., Conti, P., Centonze, V.E., Casiraghi, F., Bertuzzi, F., Folli, F., and Perego, C. The glial

glutamate transporter 1 (GLT1) is expressed by pancreatic beta-cells and prevents glutamate-induced beta-cell death. The Journal of biological chemistry. 2011; 286(16): p. 14007-18.

41. Perego, C., Di Cairano, E.S., Galli, A., Moretti, S., Bazzigaluppi, E., Centonze, V.F., Gastaldelli, A., Assi, E., Fiorina, P., Federici, M., Porzio, O., Bertuzzi, F., Davalli, A.M., and Folli, F. Autoantibodies against the glial glutamate transporter GLT1/EAAT2 in Type 1 diabetes mellitus-Clues to novel immunological and non-immunological therapies. Pharmacological research. 2022; 177: p. 106130.

42. Wang, J., Xiao, H., Zhu, Y., Liu, S., Yuan, Z., Wu, J., and Wen, L. Tannic Acid Induces the Mitochondrial Pathway of Apoptosis and S Phase Arrest in Porcine Intestinal IPEC-J2 Cells. Toxins. 2019; 11(7): p. 397.

43. Barszcz, M., Taciak, M., Tuśnio, A., and Skomiał, J. Effects of dietary level of tannic acid and protein on internal organ weights and biochemical blood parameters of rats. PloS one. 2018; 13(1): p. e0190769.

44. Jing, W., Xiaolan, C., Yu, C., Feng, Q., and Haifeng, Y. Pharmacological effects and mechanisms of tannic acid. Biomedicine & Pharmacotherapy. 2022; 154: p. 113561.

45. Babby, A. and Elanchezhiyan, C. Tannic acid administration ameliorates the levels of Hepatic markers, Carbohydrate metabolizing enzymes and Inflammatory markers in the liver of Streptozotocin-induced diabetic Albino Wistar rats. Research Journal of Pharmacy and Technology. 2020; 13(12): p. 6156-6162.

46. Zhang, J., Song, Q., Han, X., Zhang, Y., Zhang, Y., Zhang, X., Chu, X., Zhang, F., and Chu, L. Multi-targeted protection of acetaminophen-induced hepatotoxicity in mice by tannic acid. International Immunopharmacology. 2017; 47: p. 95-105.

47. Aladesanmi, O.O., Akinmoladun, A.C., Josiah, S.S., Olaleye, M.T., and Akindahunsi, A.A. Modulatory activities of polyphenols on crude acetylene-induced cardiac and hepatic dysfunctions in a rat model. Drug and Chemical Toxicology. 2022; 45(4): p. 1670-1678.

48. Arkoub, F.Z., Hamdi, L., Kahalerras, L., Hamoudi, M., and Khelili, K. Evaluation of the in vitro and in vivo antioxidant potential of Punica granatum L. against toluene-induced liver injuries in rats. Veterinary World. 2022; 15(2): p. 374-382.

49. Lou, W., Chen, Y., Ma, H., Liang, G., and Liu, B. Antioxidant and α-amylase inhibitory activities of tannic acid. Journal of food science and technology. 2018; 55(9): p. 3640-3646.

50. Brus, M., Frangež, R., Gorenjak, M., Kotnik, P., Knez, Ž., and Škorjanc, D. Effect of Hydrolyzable Tannins on Glucose-Transporter Expression and Their Bioavailability in Pig Small-Intestinal 3D Cell Model. Molecules. 2021; 26(2).

51. Babby, A., Elanchezhiyan, C., Hassan, T., and Naseer, I. Effect of tannic acid on lipid peroxidation and antioxidants status in streptozotocin induced diabetic rats. International Journal of Recent Scientific Research. 2019; 10(05): p. p32591-32594.

الملخص العربى

الدور الوقائى المحتمل لحمض التانيك ضد السمية المحدثة بمادة الجلوتاميت احادي الصوديوم فى بنكرياس وكبد ذكور الجرذان البيضاء البالغة. دراسة بيوكيميائية ,نسيجية و نسيجية كيميائية مناعية.

شيرين احمد محمد[1] ,سهير علي محمد[2] , بلقيس احمد محمد[2], رانيا احمد راضوان[2]

[1]قسم الهستولوجى , كلية الطب , جامعة سوهاج

[2]قسم الطب الشرعي و السموم الاكلينيكية, كلية الطب , جامعة سوهاج

المقدمة: يعد الجلوتاميت أحادي الصوديوم من المواد التي تستخدم على نطاق واسع لتعزيز النكهة والتي لها العديد من الآثار الضارة على أعضاء الجسم المختلفة . ويعتبرحمض التانيك هو مكون طبيعي مضاد للأكسدة وله العديد من الخصائص الدوائية.

الهدف من الدراسة: دراسة التاثير الوقائى المحتمل لحمض التانيك ضد التأثير السام لمادة الجلوتاميت احادي الصوديوم علي البنكرياس والكبد.

مواد و طرق البحث: تم تقسيم 40 ذكر جرذ ابيض بالغ إلى 4 مجموعات متساوية. المجموعة الأولى كانت المجموعة الضابطة، المجموعة الثانية تلقت حمض التانيك ، المجموعة الثالثة تجرعت الجلوتاميت أحادي الصوديوم، والمجموعة الرابعة تلقت حمض التانيك مع الجلوتاميت أحادي الصوديوم لمدة 4 أسابيع. وكانت جرعة حمض التانيك و الجلوتاميت أحادي الصوديوم 100 مجم / كجم من وزن الجسم و 2 جم / كجم من وزن الجسم على التوالي. في نهاية الدراسة ، تم التقييم عن طريق التحليل البيوكيميائي والنسيجى وتم استخدام الكيمياءالنسيجية المناعية لقياس الجسم المضاد لـ BAX وتعبير الأنسولين.

النتائج: زاد الجلوتاميت أحادي الصوديوم من مستويات إنزيمات البنكرياس. إنزيمات الأميليز والليباز ، وكذلك مستويات السكر في الدم. كما أحدث زيادة في إنزيمات الكبد. من الناحية النسيجية ، لوحظت تغيرات تنكسية في الكبد والبنكرياس مع زيادة مساحة سطح جزر لانجرهانز. زاد الجلوتاميت أحادي الصوديوم من الموت الخلوى المبرمج مما زاد من التعبيرالكيمياء نسيج مناعى BAX وخفض نسبة الخلايا بيتا البنكرياسية. تجرع حمض التانيك مع الجلوتاميت أحادي الصوديوم قلل من حدوث هذه الآثار التنكسية.

الخلاصة: الجلوتاميت أحادي الصوديوم لها تأثيرات سامة على الكبد والبنكرياس مما يؤدي إلى زيادة مستويات السكر في الدم. حمض التانيك يعمل كمضاد الأكسدة ضد سمية الجلوتاميت أحادي الصوديوم مع خفض مستويات السكر في الدم.