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Neuroprotective Effects of Coriander and Garlic on Cerebellar Damage, Glial Activation and Synaptic Dysfunction in Diabetic Rats

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Abstract

THIS STUDY investigates neuroprotective effects of coriander seed extract (CSE) and garlic extract (GE) in alleviating these pathological changes in streptozotocin (STZ)-induced diabetic rat model. Adult male albino rats were given a single intraperitoneal injection of STZ (50 mg/kg) to induce diabetes. Diabetic rats were treated with CSE (250 mg/kg), GE (250 mg/kg), or glibenclamide (GLIB, 0.5 mg/kg) daily for 28 days. Cerebellar alterations, such as Purkinje cell count, glial fibrillary acidic protein (GFAP) expression, and synaptophysin expression, were evaluated by histopathological and immunohistochemical investigations. Additionally, the antioxidant ability (DPPH test) and total phenolic and flavonoid content of CSE and GE were assessed. STZ-induced diabetes resulted in a significant loss of Purkinje cells, increased GFAP expression indicative of reactive gliosis, and reduced synaptophysin expression, reflecting synaptic dysfunction. Treatment with CSE and GE significantly restored Purkinje cell numbers, reduced GFAP expression, and improved synaptophysin levels, with CSE demonstrating superior neuroprotective effects compared to GE and GLIB. The phytochemical analysis revealed that CSE contained higher phenolic content and comparable flavonoid content to GE, contributing to it powerful antioxidant and anti-inflammatory activities. CSE and GE exert neuroprotective effects by mitigating oxidative stress, reducing neuroinflammation, and preserving synaptic integrity in STZ-induced diabetic rats. These findings suggest their potential as natural therapeutic agents for managing diabetes-induced neurodegeneration.

Keywords: Diabetes, Coriander seed extract, GE; Histopathology, GFAP; SYP, cerebellum, Purkinje cells.

Introduction

Persistent hyperglycemia is a hallmark of diabetes mellitus, a complex metabolic disease that can cause injury to several organ systems, including the brain [1]. Neurodegeneration and cognitive impairment are hallmarks of diabetic encephalopathy, a dangerous side effect of diabetes. This disorder causes major alterations in brain through a variety of routes, such as oxidative stress, inflammation, and neuronal death [2].The cerebellum, an essential brain region for motor coordination and cognitive processes, is particularly vulnerable in diabetic conditions, showing evidence of neuronal loss, gliosis, and synaptic dysfunction [3]. Astrocytes, the primary glial cells involved in maintaining neuronal health, often respond to neuronal injury. In diabetic encephalopathy, GFAP levels reflects brain's attempt to counteract the harmful effects of prolonged hyperglycemia. In parallel, synaptic dysfunction, marked by synaptophysin expression—a key presynaptic vesicle protein—indicates the loss of synaptic integrity and neuronal communication [4,5].

Coriander and garlic have long been used in traditional medicine for their diverse medicinal properties[6].Coriander is known for its hypoglycemic, antioxidant, and anti-inflammatory effects, which have been attributed to bioactive components such as linalool, polyphenols, and flavonoids[7].Similarly, garlic contains sulfur-containing compounds like allicin and S-allyl cysteine, which are known to exert potent antioxidant and neuroprotective effects[8].These properties make

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both coriander and garlic promising candidates for mitigating diabetes-induced oxidative damage and neuronal dysfunction. However, their specific neuroprotective roles in preserving cerebellar architecture and synaptic integrity in diabetes remain not discovered.

This study aims to investigate effects of CSE and GE on cerebellar damage, astrocytic activation, and synaptic function in STZ-induced diabetic rat model. Unlike previous studies that primarily focused on systemic glucose control or antioxidant activity, this research delves into the neuroprotective mechanisms of CSE and GE at the cellular and molecular levels within the cerebellum. The results of this work offer novel highlight on their potential therapeutic roles in preventing diabetes-induced cerebellar neurodegeneration.

Material and Methods

Ethical considerations

The Scientific Research Ethics Committee of Benha University's Faculty of Veterinary Medicine gave its approval to all procedures of this study (Approval Ethical Number: BUFVTM 10-11-23). Animal welfare was prioritized throughout the study. The rats were handled with care to minimize stress, housed under hygienic and controlled environmental conditions, and monitored daily for signs of discomfort or distress. Euthanasia was performed humanely following the completion of the experimental procedures, in accordance with institutional guidelines.

Preparation of CSE and GE extracts

Ethanolic extracts of coriander seed (CSE) and garlic (GE) were prepared as described by [9].The prepared extracts were stored at -4 °C.

Total phenolic and flavonoid content

Gallic acid equivalents (mg GAE/g) were used to represent the extracts' total phenolic content (TPC), which was calculated using the Folin–Ciocalteu technique [10]. AlCl3 technique was carried out to estimate the total flavonoid content (TFC) [11] and expressed in rutin equivalents (mg RE/g). Standard solutions of gallic acid and rutin were used to validate the accuracy and reproducibility of the TPC and TFC measurements, respectively. All assays were performed in triplicate to ensure reliability.

DPPH Free radical scavenging assay

The DPPH free radical scavenging assay was performed**[12].**The % of inhibition was calculated using the following formula:

$$\text{Inhibition}(\%) = \frac{\text{Average absorbance of blank} - \text{average absorbance of the test}}{\text{Average absorbance of blank}} \text{X } 100$$

Inhibition % was plotted against the concentrations of the extracts to determine the IC_{50} (the concentration providing 50% inhibition). The assay was performed in triplicate, and the data were analyzed for statistical significance.

Experimental design and induction of diabetes

Thirty male adult albino rats (200 ± 20 g) were used. Rats were kept in clean, sanitary stainless-steel wire cages with a natural 12-h light/dark cycle, kept at 23 ± 3 °C, and given unrestricted access to clean water and a typical commercial ration.

The rats were haphazardly separated into 5 equal groups (N = 6 per group):

Control Group (Group 1): Rats were given citrate buffer orally (0.5 ml/kg) as a vehicle.

Diabetic (STZ) Group (Group 2): Rats were intraperitoneally (I.P.) injected with a single dose of STZ at 50 mg/kg body weight (Sigma, USA) dissolved in freshly prepared citrate buffer (0.1 M, pH 4.5).

(GLIB) Group (Group 3): Diabetic rats were received 0.5 mg/kg body weight of GLIB

GLIB (Daonil®, Sanofi Specialized Pharmaceuticals Company, Cairo, Egypt) [13].

(CSE) Group (Group 4): Diabetic rats were given 250 mg/kg body weight of CSE [14].

(GE) Group (Group 5): Diabetic rats were given 250 mg/kg body weight of GE [15].

Rats in Groups 2, 3, 4, and 5 were injected intraperitoneally with STZ. After 72 h post-injection, rats with fasting glucose levels above 250 mg/dl were considered diabetic [16].After induction of diabetes, diabetic rats in group 3, 4, 5 were administered CSE, GE, and GLIB orally, respectively by using a gavage needle daily for 28 consecutive days.

Histopathological studies

Brain specimens from each rat were preserved in 20% formalin, then serial sections were prepared and stained with H&E. These sections were examined under light microscope to assess the general histopathological alterations in the cerebellum [17].

Immunohistochemical analysis

Immunohistochemical staining was performed to evaluate glial activation and synaptic integrity in cerebellar sections using antibodies against GFAP and synaptophysin, respectively. Paraffin-embedded cerebellar sections were incubated with primary antibodies against GFAP, mouse monoclonal antibody at dilution 1:500 (SC58766, Santa Cruz Biotechnology) and synaptophysin mouse monoclonal antibody at dilution 1:500 overnight at 4

°C. After washing, sections were treated with biotinylated secondary antibodies, followed by streptavidin-peroxidase conjugate. The reaction was visualized using a DAB chromogen substrate, and sections were counterstained with hematoxylin.

Morphometric study

For these measures, 10 non-overlapping random fields per slide from every rat in every group under study were employed. ImageJ software (ImageJ 1.54 g, National Institutes of Health, USA) was used to evaluate the immunoexpressions. Immunohistochemical and histopathological slides were examined and photographed using a light microscope (Eclipse E800, Nikon) equipped with a digital camera.

Morphometric analysis was conducted to measure the following parameters:

1. Average number of Purkinje cells per ml of cerebellar lobules in sections stained with H&E at a ×200 magnification.
2. At a ×400 magnification, the % of necrotic Purkinje cells in the cerebellar lobules was measured in H&E-stained sections. Purkinje cells with shrunken, angular shapes, hypereosinophilic cytoplasm, and nuclear pyknosis were considered necrotic.
3. Average number of astrocytes/mm² in the cerebellar lobules' gray matter, as determined by GFAP expression in sections stained with DAB and magnified by 400 times.
4. Mean optical density and mean area % of GFAP expression in sections stained with DAB at a ×400 magnification.
5. Average optical density of synaptophysin expression at a ×400 magnification in sections stained with DAB.

Statistical analysis

GraphPad Prism software version 9 was used for statistical analyses. Tukey's multiple comparisons test was used after a one-way ANOVA. The M ± SD were used to express all data. Statistical significance was defined as a P value of < 0.05.

Results

Total phenolic and flavonoid contents of CSE and GE

Total phenolic content (TPC) of CSE and GE was measured and expressed in gallic acid equivalents (GAE). CSE showed a higher phenolic content (42.43 ± 2.13 mg GAE/g extract) compared to GE (30.55 ± 1.31 mg GAE/g extract). Total flavonoid content (TFC), expressed in rutin equivalents (RE), and was 8.92 ± 0.38 mg RE/g extract for CSE and 9.51 ± 0.24 mg RE/g extract for GE (Table 1).

DPPH radical scavenging assay

DPPH radical scavenging activity of CSE and GE was assessed and is presented in Table 1. CSE demonstrated higher scavenging activity, with an IC50 value of 63.72 ± 1.27 µg Trolox equivalent/ml, compared to GE (57.20 ± 1.52 µg Trolox equivalent/ml). Both extracts exhibited significant antioxidant activity, although slightly lower than the standard Trolox (7.32 ± 0.10 µg/ml).

Histopathological results

The cerebellum of control rats displayed a normal histological appearance of 3 layers of cerebellar cortex: molecular layer, granular cell layer, and Purkinje cell layer, which contains a single row of large, pear-shaped cells with vesicular nuclei and prominent nucleoli (Fig. 1A). In contrast, the diabetic group showed multifocal loss of Purkinje cells, leaving large, round, clear spaces (Fig. 1B). The remaining Purkinje cells exhibited significant necrosis (Fig. 1B Inset). Additionally, marked degeneration of Purkinje and basket cells was observed in the molecular layer (Fig. 1C). Multifocally, there was neuroglial cell infiltration, scattered areas of moderate spongiosis in the cerebellar medulla, and occasional mild thinning and hypocellularity of granular cell layer.

The cerebellum of the GLIB-treated group revealed a generally preserved normal architecture with only a few necrotic Purkinje cells and mild spongiosis in cerebellar medulla (Fig. 1D). Similarly, the CSE-treated group showed a mostly normal cerebellar architecture, with only occasional degeneration and necrosis of a few Purkinje cells (Fig. 1E). Multifocally, loss of Purkinje cells was rarely observed, and scattered areas of mild spongiosis were present in the cerebellar medulla. The cerebellum of the GE-treated group exhibited an almost normal histological architecture, with only a few multifocal losses of Purkinje cells and mild spongiosis in the cerebellar medulla (Fig. 1F).

Immunohistochemical results

Bergmann glial fibers of molecular layer, the astrocytes of granular cell layer and white matter exhibit GFAP positivity. The cerebellar sections of control rats reveal mild GFAP expression. Bergmann glial fibers exhibit an intact, thin, straight, and parallel network with erect morphology, while astrocytes show thin processes (Fig. 2A). In contrast, the diabetic group exhibits strong GFAP immunoreactivity, with markedly increased expression in all cerebellar layers. Bergmann glial fibers are increased in number, intensely stained, hypertrophied and disorganized (Fig. 2B). Astrocytes in this group appear larger, with darkly stained cell bodies and thick, dense, distorted processes (Fig. 2C). The GLIB-treated group shows moderate GFAP expression. Bergmann glial fibers are increased in

number, mildly disorganized, and moderately stained. Astrocytes in the granular cell layer and white matter display thick distorted processes and moderately stained cell bodies (Fig. 2D). In the CSE-treated group, GFAP expression is mild. Bergmann glial fibers appear normal—thin, straight, parallel and intact, while mild astrogliosis is observed with astrocytes showing thin processes (Fig. 2E). Similarly, the GE-treated group demonstrates almost mild GFAP expression. Bergmann glial fibers are thin, slightly increased in number, and mildly disorganized. Mild astrogliosis is present, with astrocytes exhibiting thin processes (Fig. 2F).

Immunoreactivity for Synaptophysin is broadly expressed in the cerebellar layers. Cerebellar sections from control rats show intense brown labeling, with marked expression of Synaptophysin in all cortical layers (Fig. 3A). In contrast, the diabetic group exhibits weak immunoreactivity, with mild Synaptophysin expression in both molecular and granular layers (Fig. 3B), while Purkinje layer shows very mild expression or appears almost negative (Fig. 3C). The GLIB-treated group displays moderate Synaptophysin expression (Fig. 3D). Similarly, the CSE-treated group (Fig. 3E) and the GE-treated group (Fig. 3F) show moderate expression of Synaptophysin in all cortical layers.

Morphometric analysis

The morphometric analysis revealed significant alterations in the cerebellar histological parameters among the experimental groups. The Purkinje cells number per mm (Fig. 4A) showed a significant decrease in the STZ (23.15 ± 2.58) group compared to the control (40.16 ± 2.94, $P < 0.0001$) group. Treatment with GLIB, CSE, and GE significantly restored Purkinje cells number compared to the STZ group, with the CSE group showing the most pronounced recovery (38.63 ± 2.85, $P < 0.0001$). Similarly, the % of necrotic Purkinje cells (Fig. 4B) was elevated in the STZ (29.2%) group compared to controls (5%), reflecting glial activation. All treatments reduced Purkinje cells necrosis with CSE showing the most pronounced recovery. Additionally, the number of astrocytes (Fig. 4C) in the cerebellar gray matter per mm² was significantly elevated in STZ group (1008 ± 90.9) compared to controls (392.5 ± 153.8, $p < 0.0001$), reflecting glial activation. Treatment with CSE (598.6 ± 111.8 $P < 0.001$), and GE 664.5 ± 63.95 $P < 0.01$) were significantly reduced astrocyte numbers, with CSE showing the strongest effect.

The GFAP area % of molecular (Fig. 4D) and granular layers (Fig. 4E) and optical density (Fig. 4F), a marker of astrocytic activation, the STZ group exhibited a significant increase compared to controls. All treatments reduced GFAP area % and density, with CSE and GE groups showing comparable reductions. In contrast, non-significant differences were recorded between GLIB, CSE, and GE groups compared to controls. For synaptophysin optical density (Fig. 4G), a marker of synaptic integrity, was significantly treatment reduced in STZ group compared to control. CSE, GE, and GLIB significantly increased synaptophysin density, with CSE showing the highest recovery effect.

Discussion

Nervous system comprises neurons and glial cells, each playing essential roles in its functionality. In diabetes, hyperglycemia has been shown to induce progressive neuronal network decline, cognitive impairment, and neurodegeneration [5]. Both human and animal studies [18,19] highlight diabetes as a contributing factor to neurological disorders, including cerebellar dysfunction. The cerebellum, known for its motor coordination and balance functions [20].The cerebellar cortex is particularly susceptible to injury from hyperglycemia, as evidenced by the high expression of insulin receptors in this region.

Our histopathological findings revealed significant cerebellar architectural disruptions in diabetic rats, including Purkinje cell loss and necrosis, spongiosis, and neuroglial infiltration in the cerebellar medulla. Purkinje cells, pivotal for cerebellar functionality, are highly sensitive to oxidative stress, inflammation, and excitotoxicity caused by hyperglycemia. Reactive oxygen species (ROS) generation, combined with reduced antioxidant defenses, disrupt neuronal membranes, calcium homeostasis, and neurotrophic signaling, leading to apoptosis and degeneration [21]. Neuroinflammation, driven by pro-inflammatory cytokine production and glial activation, further contributes to these alterations [22].These pathological processes were evident in the diabetic group, with pronounced necrotic changes and disorganization in cerebellar layers.

Treatment with CSE and GE demonstrated significant neuroprotective effects. Both extracts effectively restored Purkinje cell numbers, reduced the activation of astrocytic evidenced by glial fibrillary acidic protein (GFAP) expression, and improved synaptic integrity marked by synaptophysin expression. Antioxidant and antiinflammatory properties of CSE and GE, attributed to their bioactive compounds e.g. linalool in coriander [23] and allicin in garlic [8], likely mitigate hyperglycemia-induced oxidative stress and neuroinflammation. These compounds scavenge free radicals, inhibit pro-inflammatory pathways, and enhance neuronal survival. The phytochemical analysis revealed that CSE's higher phenolic content may account for its superior neuroprotective effects compared to GE and GLIB. CSE also likely provides neurotrophic support and stabilizes neuronal membranes, as evidenced by the significant reduction

in Purkinje cell necrosis and the preservation of cerebellar architecture in CSE-treated rats.

GLIB treatment showed moderate neuroprotective effects, primarily through glycemic control, which reduces oxidative stress indirectly [24].However, the persistent gliosis and less pronounced recovery in synaptic integrity observed in the GLIB group highlight the limitations of conventional diabetes treatments in addressing neuroinflammatory and oxidative damage. In contrast, the direct actions of CSE and GE on oxidative and inflammatory pathways offer a broader therapeutic advantage.

Astrocytic activation, a hallmark of reactive gliosis, was evident in the diabetic group, as shown by increased GFAP expression and astrocyte hypertrophy. Reactive gliosis can exacerbate neuronal dysfunction by disrupting extracellular homeostasis and impairing synaptic plasticity [25, 26]. Both CSE and GE significantly reduced astrocyte numbers and GFAP optical density, indicating their potential to counteract glial activation and preserve Bergmann glial fibers. Notably, CSE treatment restored the thin, parallel, and intact morphology of Bergmann glial fibers, underscoring its superior anti-inflammatory and antioxidative properties.

The reduced synaptophysin immunoreactivity and optical density observed in diabetic rats highlight significant synaptic dysfunction in the cerebellum, driven by oxidative stress, neuroinflammation, and excitotoxicity [27]. Synaptophysin is critical for synaptic vesicle trafficking and neurotransmitter release, and its loss reflects impaired synaptic integrity. Both CSE and GE treatments significantly improved synaptophysin levels, reflecting restored synaptic function. The observed recovery suggests their ability to protect presynaptic vesicles, maintain synaptic architecture, and enhance synaptic plasticity. CSE's superior recovery effect may be attributed to its bioactive compounds, including linalool and geranyl acetate, which modulate longevity pathways like SIRT1 and reduce oxidative stress [28].

These results align with other works [4, 29] demonstrating cerebellar damage in diabetes and the neuroprotective effects of antioxidant therapies. However, our study provides novel insights by emphasizing the role of CSE and GE in preserving cerebellar integrity at cellular and molecular levels, making them promising candidates for managing diabetes-induced neurodegeneration.

Conclusion

This investigation demonstrates neuroprotective potential of CSE and GE in mitigating diabetes-induced cerebellar damage. Diabetes resulted in significant structural and functional impairments in the cerebellum, including Purkinje cell loss, astrocytic activation, synaptic dysfunction, and alterations in cerebellar architecture. Treatment with CSE and GE effectively alleviated these changes, as evidenced by the restoration of Purkinje cell numbers, reduction in reactive gliosis (GFAP expression), and improvement in synaptic integrity (synaptophysin expression). CSE, in particular, demonstrated superior neuroprotective effects, likely due to its higher phenolic content and stronger antioxidant and anti-inflammatory properties.

Also, highlight importance of addressing oxidative stress and neuroinflammation in managing diabetes-induced neurodegenerative changes. CSE and GE offer promising natural therapeutic options for preserving cerebellar function and preventing diabetes-associated neurological complications.

Limitations and future directions

The sample size of 6 rats per group, though standard for initial experimental studies, may not capture the full variability of responses. Future studies should include larger cohorts and explore molecular pathways underlying the observed histological and immunohistochemical changes. Additionally, long-term studies are essential to evaluate whether protective effects of coriander and garlic are sustained over time. Investigating the combined effects of these natural extracts with conventional treatments could also provide insights into synergistic therapeutic approaches.

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Declaration of Conflict of Interest

The authors state that there is no conflict of interests.

TABLE 1. Total phenolics، flavonoids، and free radical scavenging activity of CSE and GE

Sample	TPC (mg GAE/g)	TFC (mg RE/g)	DPPH (µg TE/ml)
CSE	42.43 ± 2.13	8.92 ± 0.38	63.72 ± 1.27
GE	30.55 ± 1.31	9.51 ± 0.24	57.20 ± 1.52
Trolox	-	-	7.32 ± 0.10

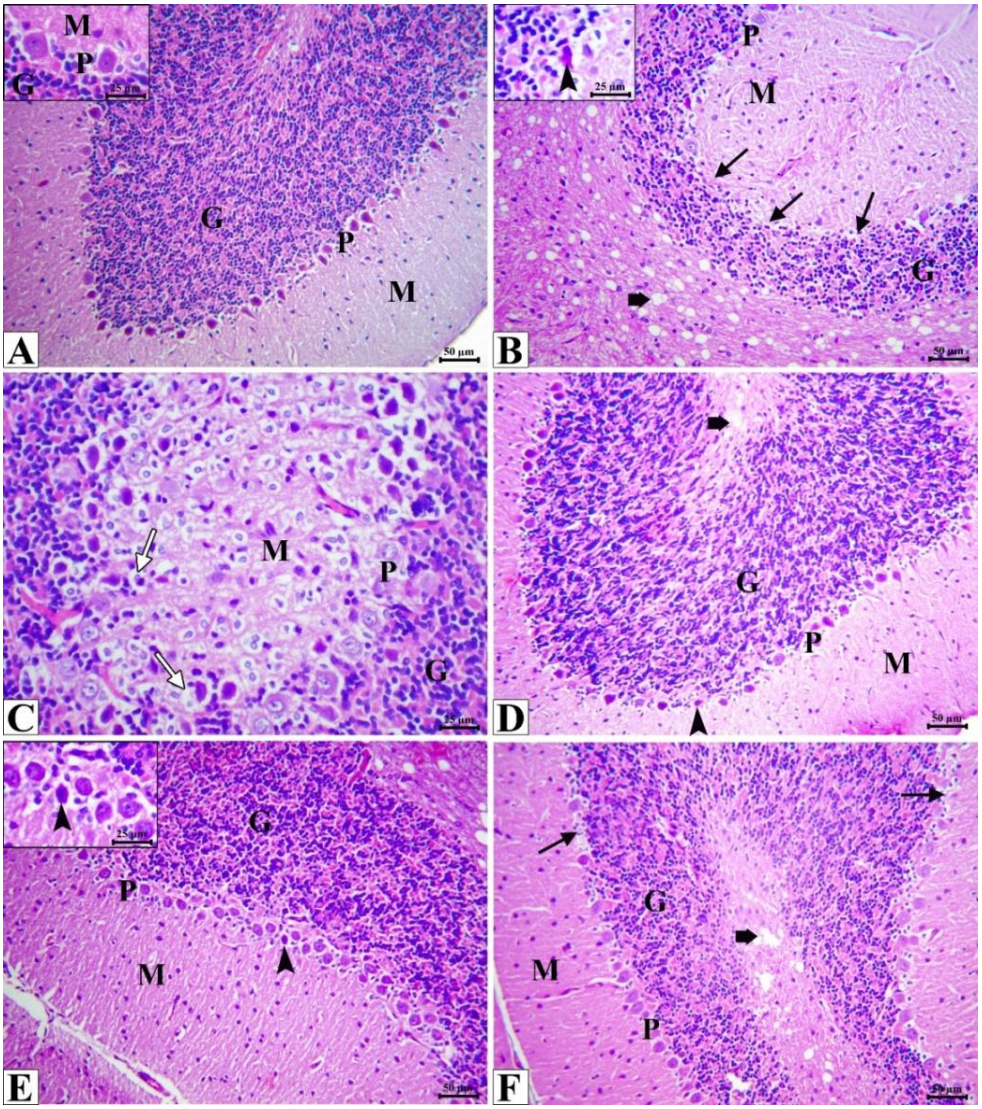

Fig. 1. H&E-stained cerebellar sections. (A) Control group, typical histoarchitecture of three layers of the cortex. Inset: higher magnification. (B) Diabetic group, multifocal loss of Purkinje cells. Inset: Purkinje cell necrosis, with hypereosinophilic cytoplasm and nuclear pyknosis. (C) Diabetic group, marked degeneration of Purkinje and basket cells within the molecular layer. (D) GLIB-treated group, normal cerebellar architecture with few necrotic Purkinje cells and mild spongiosis in the medulla. (E) CSE-treated group, histoarchitecture in the cortex, with necrosis of a few Purkinje cells (Inset). (F) GE-treated group, an almost normal histological architecture of the cortex, with a few multifocal losses of Purkinje cells and mild spongiosis in medulla. M: Molecular layer, G: Granular layer, P: Purkinje cells layer, arrow head: necrosis of Purkinje cells, black arrow: loss of Purkinje cells, white arrow: degeneration of Purkinje cells or basket cells, thick arrow: spongiosis of cerebellar medulla.

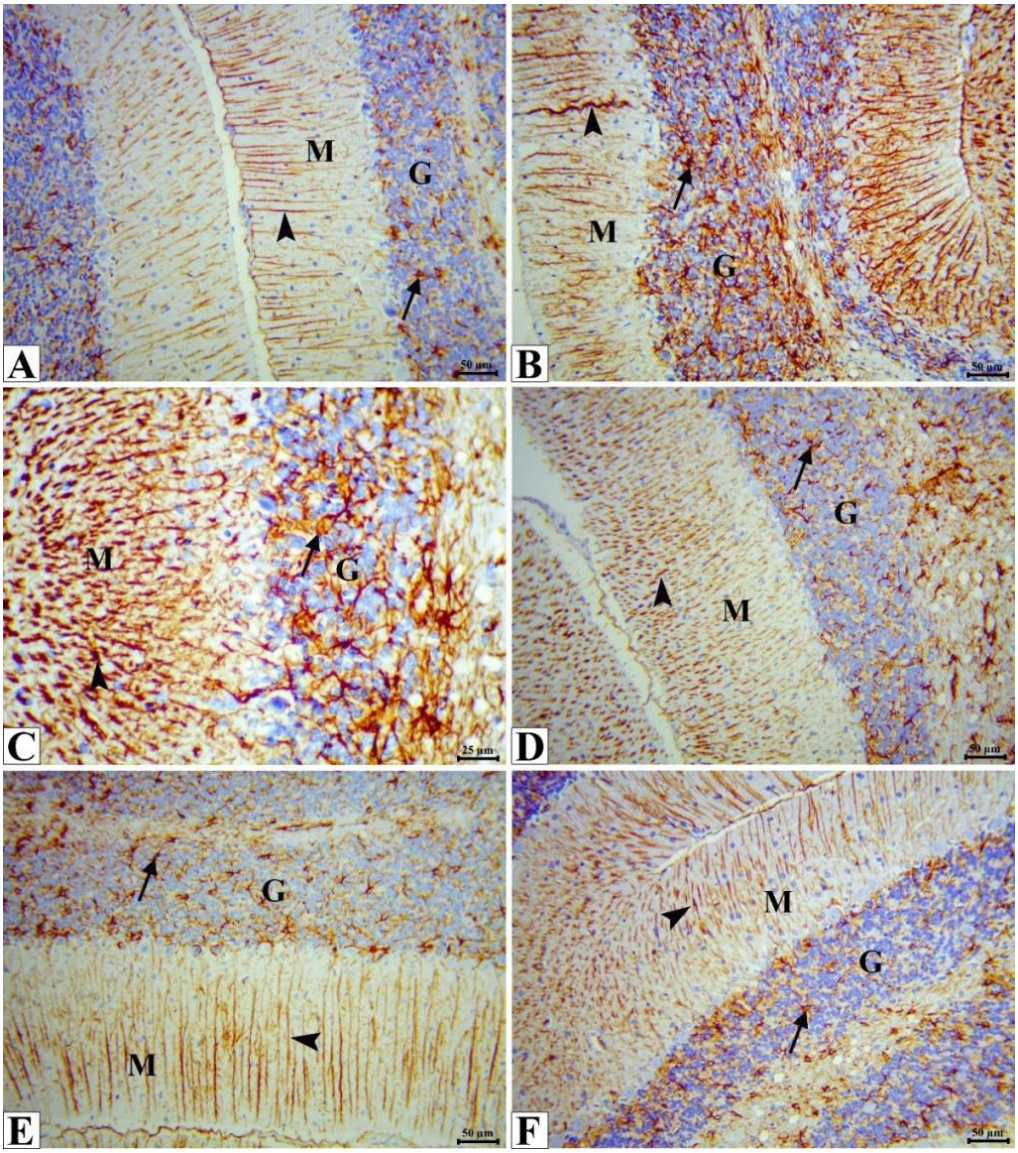

Fig. 2. GFAP-immunostained cerebellar sections. (A) Control shows mild expression; Bergmann glial fibers are intact, thin, straight and parallel, and astrocytes have thin processes. (B) Diabetic group exhibits marked expression; Bergmann glial fibers and astrocytes are increased in number, hypertrophied and disorganized. (C) Diabetic group, higher magnification; large astrocytes with darkly stained cell bodies and thick, dense processes. (D) GLIB-treated group shows moderate expression; Bergmann glial fibers are increased in number and astrocytes display thick distorted processes. (E) CSE-treated group reveals mild expression; Bergmann glial fibers appear thin, straight, parallel and intact, while astrocytes display thin processes and mild astrogliosis. (F) GE-treated group demonstrates mild expression; Bergmann glial fibers and astrocytes are slightly increased in number and mildly disorganized. M: Molecular layer, G: Granular layer, arrow head: Bergmann glial fibers, arrow: Astrocyte GFAP positive astrocyte.

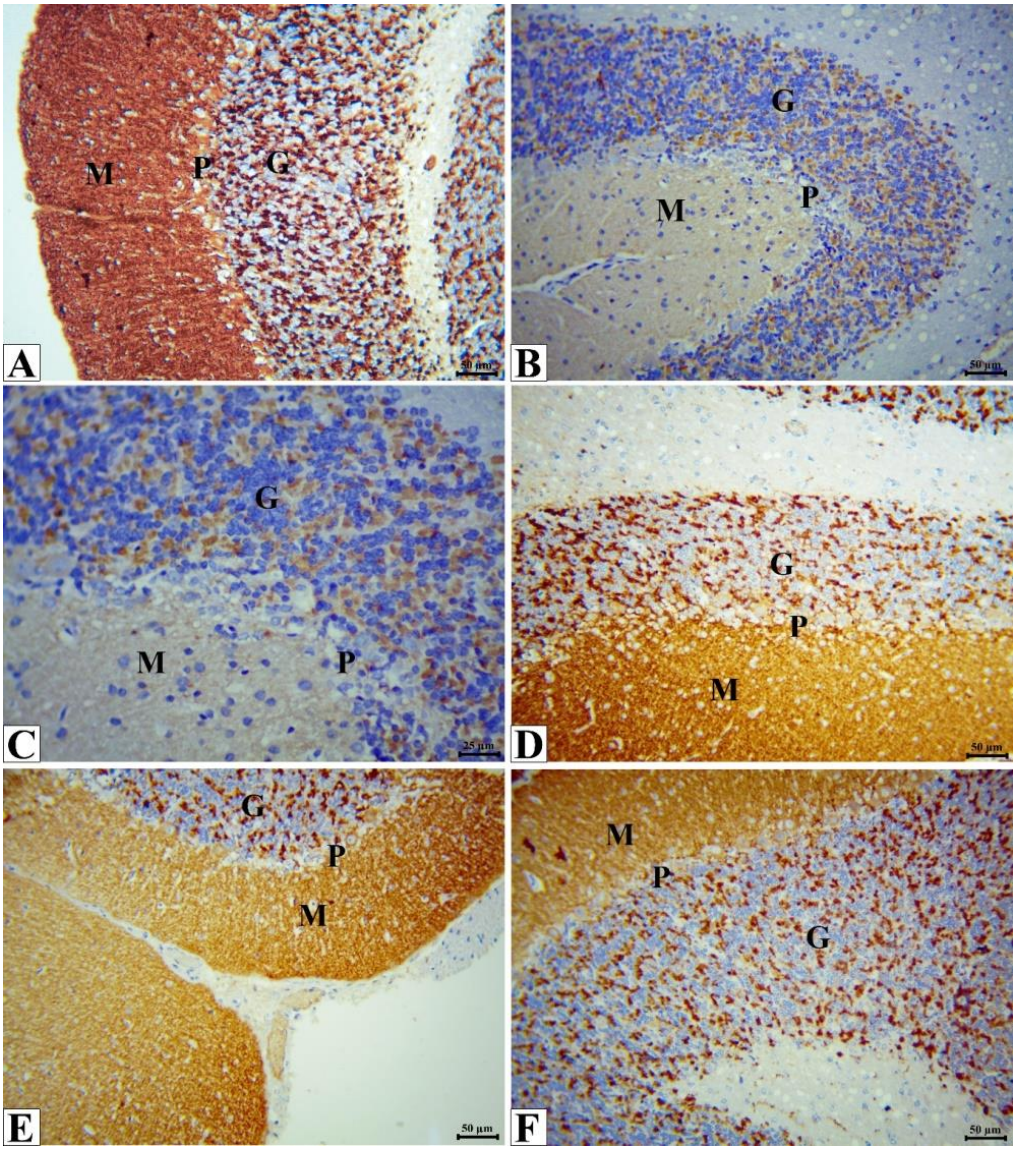

Fig. 3. Synaptophysin-immunostained cerebellar sections. (A) Control shows marked expression in all cortical layers. (B) Diabetic group exhibits mild Synaptophysin expression in both molecular and granular layers. (C) Diabetic group, higher magnification; Purkinje layer shows very mild expression. (D) GLIB-treated group displa0ys moderate Synaptophysin expression. (E) CSE-treated group reveals moderate expression of Synaptophysin in all cortical layers. (F) GE-treated group demonstrates moderate Synaptophysin expression in all cortical layers.

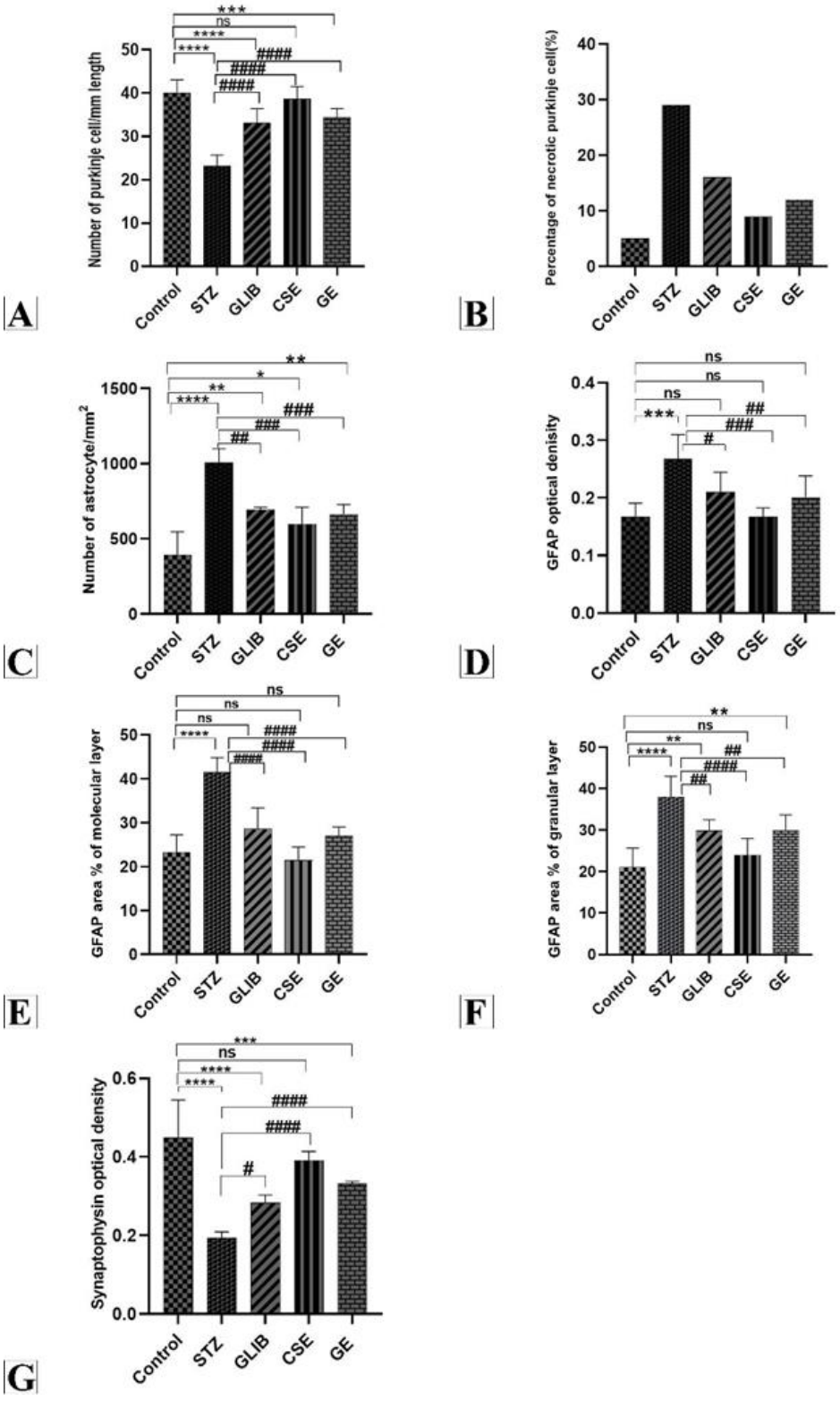

Fig. 4. Statistical analysis of mean Purkinje cells number (A), % of necrotic Purkinje cells (B) and mean number of astrocytes (C) in the cerebellar lobules, (C), GFAP optical density (D), GFAP area percent in molecular layer (E), GFAP area percent in granular layer (F) and synaptophysin optical density (G). *******P* < 0.0001, ******P* < 0.001, *****P* < 0.01, and ****P* < 0.05 compared to control. $^{\#\#\#\#}P$ < 0.0001, $^{\#\#\#}P$ < 0.001, $^{\#\#}P$ < 0.01, and $^{\#}P$ < 0.05 compared to STZ group. ns indicates non-significant differences.

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التأثيرات العصبية الوقائية للكزبرة والثوم على تلف المخيخ وتنشيط الخلايا الدبقية والخلل المشبكي في الفئران المصابة بمرض السكري

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الملخص

هذه الدراسه تدرس التأثيرات العصبية الوقائية لمستخلص بذور الكزبرة (CSE) ومستخلص الثوم (GE) في تقليل التغيرات المرضية في الفئران المصابة بمرض السكري الناجم عن الستربتوزوتوسين (STZ). تم إعطاء ذكور فئران ألبينو البالغة حقنة واحدة داخل الصفاق من (50) STZ مجم / كجم) لتحفيز الإصابة بمرض السكري. تم علاج الفئران المصابة بمرض السكري باستخدام (250 مجم / كجم) من مستخلص الكزبره ، و(250 مجم / كجم) من مستخلص الثوم، و (0.5 مجم / كجم) من عقار الجليبنكلاميد يوميًا لمدة 28 يومًا. تم تقييم التغيرات المخيخية، مثل عدد خلايا بوركنجي، وتعبير البروتين الحمضي الليفي الدبقي (GFAP)، وتعبير السينابتوفيزين، من خلال التحقيقات النسيجية المرضية والمناعية الكيميائية. بالإضافة إلى ذلك، تم تقييم القدرة المضادة للأكسدة (اختبار DPPH) ومحتوى الفينول والفلافونويد الكلي لـمستخلصي الكزبره والثوم. أدى مرض السكري الناجم عن STZ إلى فقدان كبير لخلايا بوركنجي، وزيادة التعبير عن GFAP الذي يشير إلى تضخم الخلايا الدبقية التفاعلي، وانخفاض التعبير عن السيناتوفزين، مما يعكس خللًا في التشابك العصبي. أدى العلاج باستخدام مستخلصي الكزبره والثوم إلى استعادة أعداد خلايا بوركينجي بشكل ملحوظ، وتقليل التعبير عن GFAP، وتحسين مستويات السينابتوفيزين، حيث أظهر مستخلص الكزبره تأثيرات عصبية وقائية متفوقة مقارنةً بمستخلص الثوم وعقار الجليبنكلاميد. كشف التحليل الكيميائي النباتي أنمستخلص الكزبره يحتوي على محتوى فينولي أعلى ومحتوى فلافونويد مماثل لـ مستخلص الثوم، مما يساهم في أنشطته المضادة للأكسدة والالتهابات القوية. تمارس CSE وGE تأثيرات عصبية وقائية من خلال تخفيف الإجهاد التأكسدي وتقليل الالتهاب العصبي والحفاظ على سلامة المشابك في الفئران المصابة بمرض السكري الناجم عن STZ. تشير هذه النتائج إلى إمكاناتها كعوامل علاجية طبيعية لإدارة التنكس العصبي الناجم عن مرض السكري.

الكلمات الداله: مرض السكري، مستخلص بذور الكزبره، مستخلص الثوم، الفحص النسيجي، GFAP، السينابتوفيزين، المخيخ، خلايا بوركنجي.