Original Research (XXXX) X(X); X - XX
https://doi.org/10.22103/VCBR.2026.26470.1111

Shahid Bahonar University of Kerman

Veterinary and Comparative Biomedical Research

ORIGINAL ARTICLE

Histological Effects of Cinnamon on Duodenal Tissue Architecture in Diabetic Rats

Rahmatallah Fatahian Dehkordi [1], Jahangir Kaboutari [1*], Hamidreza Fazel Chaharmahali [1]

[1] *Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran*

***Correspondence**

Author's Email:
Kaboutari-j@sku.ac.ir

Online ISSN: 3060-7663 **https://doi.org/10.22103/VCBR.2026.26470.1111**

Article History

Received: *13 December 2025*
Revised: *17 May 2026*
Accepted: *08 June 2026*
Published: *11 July 2026*

Keywords

Alloxan
Cinnamon
Diabetes
Duodenum
Histostereology

Abstract

Diabetes mellitus is a pervasive chronic metabolic disorder that induces significant structural changes in the gastrointestinal tract (GIT), notably in the duodenal mucosa, with consequent impairment of nutrient digestion and absorption. This study investigates whether a hydroalcoholic cinnamon extract can preserve or restore the histostereological architecture of the duodenum in an alloxan-induced diabetic rat model. Seventy-two adult male Wistar rats were randomly allocated into three groups: non-diabetic control; diabetic untreated and diabetic treated with cinnamon hydroalcoholic extract (60 mg/kg, orally) daily for four weeks. Diabetes was induced via a single intraperitoneal injection of alloxan (180 mg/kg). After the treatment period, duodenal samples were harvested, fixed, processed routinely, and stained with hematoxylin and eosin, and analyzed morphometrically and stereologically for villus height, crypt depth, goblet cell density, and mucosal vascularization ($P < 0.05$). Diabetes induced significant atrophy of the duodenal villi, reduced villus height to crypt depth ratio, increased crypt depth, and lower goblet cell density. Administration of cinnamon extract significantly mitigated these changes: villus height was restored toward normal levels, goblet cell numbers increased, crypt depth diminished, and mucosal vascularization improved ($P < 0.05$). These improvements indicate substantial preservative and restorative effects on duodenal structure. Hydroalcoholic extract of cinnamon exerts marked protective and restorative effects against diabetes-induced duodenal damage, likely mediated through antioxidant and anti-inflammatory mechanisms. These findings support its potential role as a complementary therapeutic agent for mitigating gastrointestinal complications associated with diabetes.

How to cite this article: Rahmatallah Fatahian Dehkordi, Jahangir Kaboutari, Hamidreza Fazel Chaharmahali. Histological Effects of Cinnamon on Duodenal Tissue Architecture in Diabetic Rats. *Veterinary and Comparative Biomedical Research*, XXXX X(X): X – XX. https://doi.org/10.22103/VCBR.2026.26470.1111

Introduction

Diabetes mellitus, a prevalent metabolic disorder characterized by persistent hyperglycemia, arises primarily from pancreatic β-cell dysfunction or destruction, leading to impaired insulin secretion (1). Its rapidly increasing global prevalence has made it a pressing public health concern (1, 2). In addition to metabolic dysfunction, diabetes induces multisystemic complications that extend to the gastrointestinal tract (GIT). Structural and functional abnormalities within the GIT, particularly in the duodenal mucosa, disrupt nutrient digestion and exacerbate metabolic instability (3).

The duodenum, as the proximal segment of the small intestine, plays a crucial role in the digestion and absorption of micronutrients. Any alteration in the integrity of villi, glands, or epithelial lining markedly impairs digestive efficiency. Histopathological studies have demonstrated that diabetes commonly triggers mucosal inflammation, villus atrophy, crypt hyperplasia, and goblet cell depletion; these changes compromise intestinal function and contribute to the persistence of metabolic imbalance and secondary diabetic complications (4-7).

Cinnamon, derived from the bark of *Cinnamomum* species, is an ancient medicinal spice with broad therapeutic potential. Experimental studies indicate that cinnamon extracts exert protective effects against diabetes-induced tissue injuries by enhancing antioxidant defense, reducing inflammation, and modulating glucose metabolism (7). Administration of cinnamon oil or hydroalcoholic extract has been reported to attenuate hepatic, renal, uterine, and intestinal degeneration in alloxan-induced diabetic rats, restoring histological integrity and improving biochemical profiles (8, 9). These effects are attributed to bioactive constituents such as cinnamic acid, tannins, and flavonoids, which enhance insulin receptor activity, facilitate glucose uptake, and inhibit carbohydrate-digestive enzymes (10). Nonetheless, some studies have documented limited or inconsistent outcomes, including only the partial reversal of hepatic lesions or reduced protection of somatostatin-producing gastric cells under diabetic conditions (8-10).

Given the paucity of evidence regarding duodenal morphology, examining the histostereological effects of cinnamon extract in diabetic models may offer novel insights into its gastrointestinal protective mechanisms. Hence, the present study was designed to evaluate the influence of hydroalcoholic cinnamon extract on duodenal microarchitecture in alloxan-induced diabetic rats.

Materials and Methods

Cinnamon Extraction

A hydroalcoholic extract of *Cinnamomum* bark was prepared by macerating 100 g of dried, powdered cinnamon in 1000 mL of 50% (v/v) ethanol (Merck, Germany) at room temperature with gentle, continuous stirring for 48 hours. This extraction process was repeated three times at 48-hour intervals between each cycle, to ensure the maximal recovery of bioactive compounds. Following each maceration, the mixture was filtered through Whatman No. 1 filter paper to remove solid residues (11).

Animals

This experimental study was conducted on seventy-two adult male Wistar rats, weighing 200–250 g. Animals were housed under standard laboratory conditions in accordance with international and institutional guidelines, maintaining a temperature of 22 ± 2°C, relative humidity of 55–60%, and a 12-hour light/dark cycle, with ad libitum access to standard chow and fresh water (Grant number 3GRN1M1903) (12).

After a one-week acclimatization period, the rats were randomly assigned to three groups: a non-diabetic control, a diabetic group, and a diabetic group treated orally with cinnamon hydroalcoholic extract (60 mg/kg). Each group consisted of three replicates (n = 8 per replicate), and the study was conducted over a period of 28 days. Diabetes was induced via a single intraperitoneal injection of alloxan (180 mg/kg). Animals with fasting blood glucose levels exceeding 200 mg/dL were considered diabetic (13).

At the end of the experimental period, the rats were euthanized via an intraperitoneal injection of sodium thiopental (150 mg/kg; Sigma-Aldrich). The duodenum was carefully excised and immediately fixed in 10% buffered formalin (Merck, Germany). Following fixation, tissues were processed according to standard paraffin embedding protocols. Serial sections of 5 µm thickness were prepared from each paraffin block. For stereological sampling, every 50th section was selected; two consecutive sections (a primary and a reference section) were mounted on slides and stained with hematoxylin and eosin. Two slides were prepared from each sampled level (primary and reference sections). Digital images were captured using a light microscope equipped with a CCD camera (DS-Fi3, Nikon, Japan). Morphometric and stereological analyses were performed under blinded conditions using ImageJ software to ensure an objective evaluation of the duodenal microarchitecture (Figure 1).

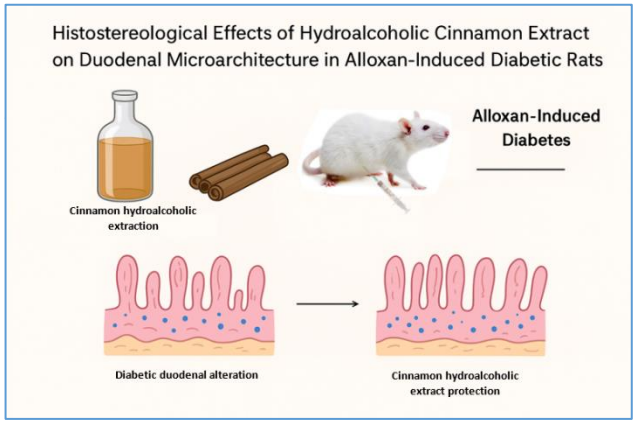

Figure 1: Cinnamon significantly restores the duodenal mucosal architecture damaged by diabetes in rats, as confirmed by morphometric and stereological analyses. It reverses villus atrophy, increases goblet cell density, and enhances vascularization through its antioxidant and anti-inflammatory effects.

Morphometry and Histo-stereology

The following parameters were assessed to evaluate duodenal microarchitecture. Villus height was defined as the distance from the tip of the villus to the crypt-villus junction and was measured in at least ten villi per section. Crypt depth was measured from the opening to the base of crypt; the villus height-to-crypt depth ratio was calculated as a recognized indicator of intestinal mucosal integrity. Mucosal thickness was quantified from the epithelial surface to the lamina propria, and goblet cells were manually counted within individual villi to determine the average number of mucus-secreting cells per villus.

Stereological techniques were applied to quantify the three-dimensional spatial and volumetric properties of the duodenal tissue, including the relative volumes of the mucosal and submucosal layers, the epithelial-to-lamina propria volume ratio, cell density, and the intercellular space ratio. Digital images of hematoxylin and eosin-stained sections were analyzed using point-counting methods under blinded conditions.

The relative volume of the mucosal layer (Vv, %) was estimated by superimposing a random point grid on digital images and calculating the proportion of points intersecting the mucosa relative to the total number of points (Figure 1). Goblet cell numerical density (Nv, cells/mm³) was determined using the optical disector method, counting only cells whose uppermost portion came into focus within a defined counting frame while excluding those touching forbidden lines, and dividing by the disector volume. Blood vessel length density (Lv, mm/mm³) was quantified using a probe-counting approach, recording the number of intersections (I) between blood vessels and a test grid of known total line length (Ltotal) and calculating length density as:

The volume density of the mucosal layer (%) was assessed similarly using the point-counting technique, which is often reported interchangeably with relative volume in stereological analyses (14).

Statistical Analysis

Data are expressed as mean ± standard deviation (SD) and were analyzed using one-way analysis of variance (ANOVA), followed by Tukey's post-hoc multiple comparison test. Statistical analyses were performed using SPSS version 22, and statistical significance was defined as $P < 0.05$.

Results

Morphology

Histological examination revealed distinct differences among the experimental groups. In the control group, the duodenal architecture appeared normal and well-organized. Villi were tall and slender, lined with intact epithelial cells, and displayed an adequate density of goblet cells along their surfaces. Both the epithelial and submucosal layers were uniform in thickness and well-preserved, with no evidence of structural damage, degeneration, or inflammatory infiltration (Figure 2).

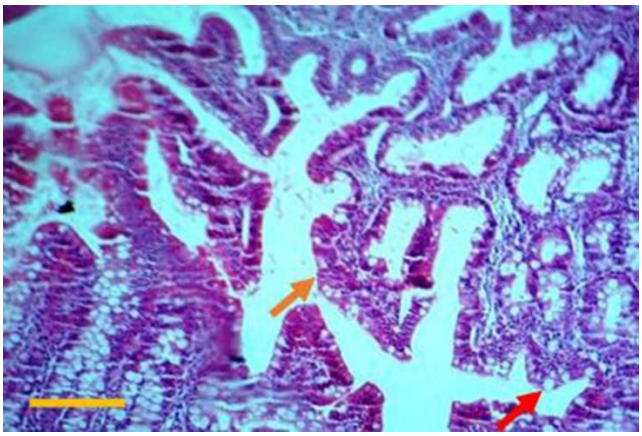

Figure 2: Photomicrograph of duodenal tissue from the control group, illustrating the normal and healthy tissue architecture. In this group, the villi are tall, narrow, and well-organized, with surfaces covered by healthy, intact epithelial cells (pink arrow). Goblet cells are present in typical numbers along the villi (red arrow). The epithelial layer remains intact, showing no signs of damage, inflammation, or degeneration (H&E staining, 200x magnification, scale bar = 200 µm).

In contrast, the diabetic group exhibited pronounced morphological alterations indicative of severe mucosal injury. Villi were shortened, blunted, and, in certain regions, completely absent. Goblet cell numbers were markedly reduced, compromising mucosal barrier integrity and mucus production. Crypt depth increased, and the villus height-to-crypt depth ratio was diminished. The epithelial layer showed abnormal thickening and structural disorganization, accompanied by significant inflammatory infiltration, reflecting extensive diabetes-induced duodenal damage (Figure 3).

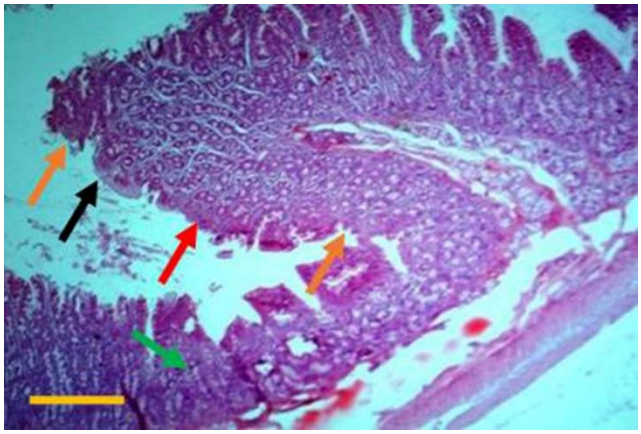

Figure 3: Photomicrograph of duodenal tissue from the experimental diabetic group, showing significant histological alterations indicative of severe damage. The duodenal villi are atrophic, shortened, and, in some areas, completely absent (pink arrow). There is also a marked reduction in the number of goblet cells (black arrow). The epithelial layer is abnormally thickened, with evident structural damage (red arrow). Cellular changes include a loss of epithelial integrity and clear signs of inflammation in various regions of the tissue (green arrow) (H&E staining, 200x magnification, scale bar = 200 µm).

Treatment of diabetic rats with hydroalcoholic cinnamon extract markedly ameliorated these pathological changes. Villi were partially restored, regaining a normal height and slender morphology, while epithelial integrity was substantially preserved. Goblet cell counts increased, supporting mucosal barrier function and mucus secretion. The epithelial and submucosal layers appeared more uniform, with minimal structural alterations. Notably, no signs of inflammation or abnormal cellular changes were observed, indicating that cinnamon exerted protective, anti-inflammatory, and reparative effects on the duodenal tissue damaged by diabetes (Figure 4).

Figures 5 and 6 illustrate point counting in stereology on histological tissue sections. In this method, a regular grid of points is superimposed on the microscopic image; the points falling on the structure of interest or other tissue components are then counted. The ratio of points hitting the target structure relative to the total number of grid points provides an estimate of its volume fraction within the tissue.

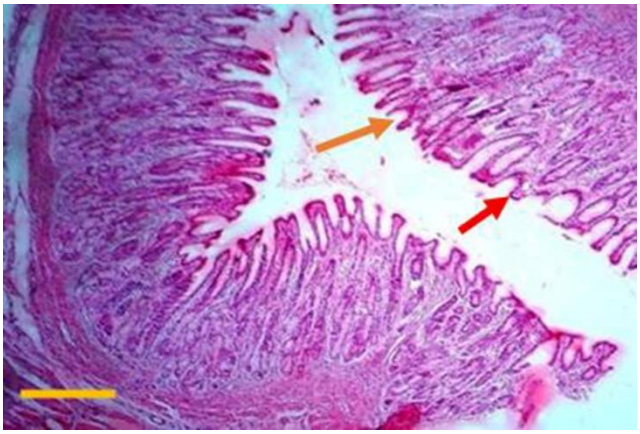

Figure 4: Photomicrograph of duodenal tissue from the experimental diabetic group treated with cinnamon hydroalcoholic extract, showing significant recovery of the tissue structure. The villi have regained normal length and density, and the number of goblet cells is significantly increased (red arrow). The epithelial layer (pink arrow) has returned to its typical structure, showing no signs of inflammation or abnormal cellular changes (200x magnification, H&E staining, scale bar = 200 µm).

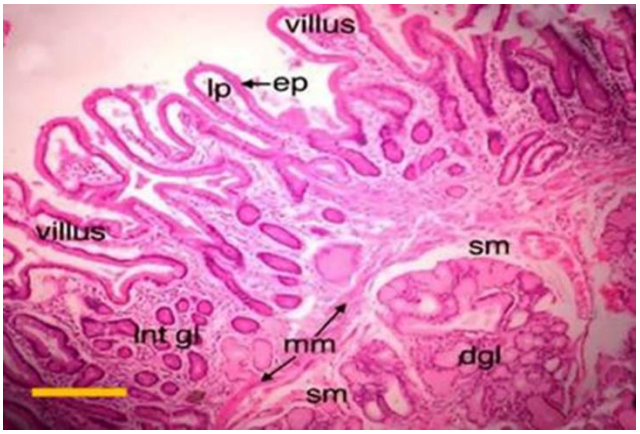

Figure 5: The abbreviations are defined as follows: dgl, deep glands (glandular structures located deeper within the mucosa or submucosa); sm, submucosa (connective and smooth muscle tissue beneath the intestinal mucosa); m, muscle (the muscle layer shown in this image as a line and probably related to the muscularis mucosae); and ep, epithelial tissue covering the mucosal surface (H&E staining, 200x magnification, scale bar = 200 µm).

Morphometric

The induction of diabetes resulted in a significant decrease in villus height, a pronounced increase in crypt depth, and a substantial reduction in the villus height-to-crypt depth ratio ($P < 0.05$). Additionally, goblet cell numbers were significantly reduced ($P < 0.05$), reflecting marked mucosal damage and atrophy.

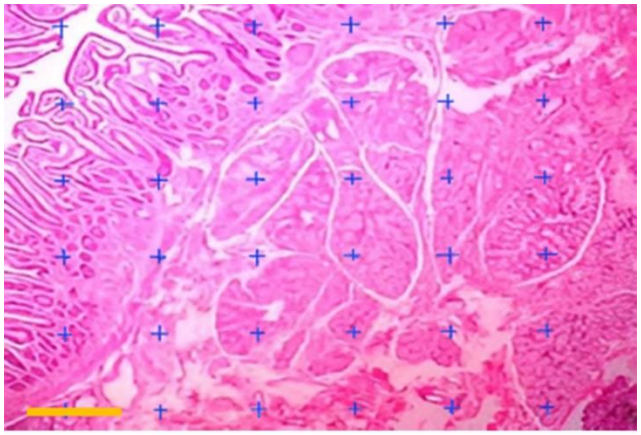

Figure 6: Microscopic image of the duodenum, showing the structure of the mucosa, submucosa, muscle layer, and Brunner's glands. This segment of the small intestine is characterized by mucosal folds and nutrient-absorbing villi. A point grid was utilized for the quantification and measurement of cellular structures (H&E staining, 200x magnification, scale bar = 200 µm).

Treatment with hydroalcoholic cinnamon extract effectively ameliorated these diabetes-induced alterations. Villus height was significantly restored, crypt depth decreased, and the villus height-to-crypt depth ratio increased, indicating a partial normalization of the duodenal mucosal architecture ($P < 0.05$). Furthermore, goblet cell counts were significantly recovered ($P < 0.05$), suggesting a protective and regenerative effect of cinnamon on the intestinal mucosa (Table 1).

Stereology

The diabetic group exhibited a significant decline in all assessed stereological parameters ($P < 0.05$). Specifically, the volume density of the mucosal layer, the numerical density of goblet cells, and the length density of blood vessels were markedly reduced ($P < 0.05$), reflecting pronounced mucosal atrophy and compromised epithelial and vascular integrity.

In contrast, administration of hydroalcoholic cinnamon extract substantially ameliorated these diabetes-induced changes ($P < 0.05$). The restoration of mucosal volume density, goblet cell numerical density, and vascular length density indicates that cinnamon exerts pronounced protective and reparative effects on the three-dimensional structure of the duodenal mucosa under diabetic conditions (Table 2).

Table 1. Morphometric parameters of the duodenum in study groups (Mean ± SD)

	Parameters			
Groups	**Villus Height (µm)**	**Crypt Depth (µm)**	**Villus Height/Crypt Depth Ratio**	**Goblet Cell Count (per villus)**
Control	338.42±3.19	91.56±2.04	3.69±0.05	18.23±1.41
Diabetic Control	147.24±2.05 *	163.51±2.37 *	0.90±0.04 *	8.34±0.98 *
Diabetic + Cinnamon	285.31±2.87†	108.43±2.11†	2.63±0.03†	15.75±1.25†

* Significant difference compared to Normal Control ($P < 0.01$)
† Significant difference compared to Diabetic Control ($P < 0.05$)

Table 2. stereological parameters of the duodenum in study groups (Mean ± SD)

	Parameters			
Groups	**Mucosal Layer Volume Density (%)**	**Goblet Cell Numerical Density (cells/mm³)**	**Blood Vessel Length Density (mm/mm³)**	**Relative Volume of Mucosal Layer (%)**
Control	75.2±2.1	12500±350	5.4±0.3	75.2±2.1
Diabetic Control	51.8±3.2 *	6850±420 *	3.1±0.4 *	51.8±3.2 *
Diabetic + Cinnamon	69.5±2.8†	10900±380†	4.8±0.2†	69.5±2.8†

* Significant difference compared to Normal Control ($P < 0.01$)
† Significant difference compared to Diabetic Control ($P < 0.05$)

Discussion

The present study demonstrates that diabetes induces profound structural alterations in the duodenal mucosa, including villus atrophy, increased crypt depth, a reduced villus height-to-crypt depth ratio, and diminished mucosal volume, goblet cell density, and vascular length density. Collectively, these findings reflect severe mucosal atrophy and compromised intestinal architecture, aligning with previous reports that link diabetes to mucosal inflammation and villus degeneration in the small intestine (6).

In this experimental model, diabetes was primarily induced by alloxan, which targets pancreatic beta cells responsible for insulin synthesis (13). Alloxan is transported into these cells via GLUT2, where it generates reactive oxygen species (ROS), leading to severe oxidative stress and subsequent cellular injury (1). Furthermore, alloxan impairs beta-cell function by inhibiting glucokinase, elevating intracellular calcium levels, and promoting DNA fragmentation; these processes rapidly precipitate beta-cell loss and establish a sustained diabetic state (13).

Persistent hyperglycemia in diabetes drives pathological consequences through the excessive generation of ROS, continuous stimulation of inflammatory signaling pathways—notably the NF-κB cascade—and the accumulation of advanced glycation end products (AGEs) (4). These interrelated mechanisms contribute to cellular injury in neurons, epithelial cells, and the microvasculature (4). The interaction between AGEs and their receptors sustains intestinal inflammation, resulting in structural and functional disturbances such as villus shortening, crypt hyperplasia, enhanced epithelial apoptosis, and reduced proliferative activity, ultimately diminishing absorptive efficiency (15).

Compromised tight-junction integrity leads to increased intestinal permeability, facilitating the translocation of microbial components into the systemic circulation and perpetuating low-grade inflammation (15). Concurrently, the infiltration of immune cells into the lamina propria, elevated secretion of pro-inflammatory cytokines, and Peyer's patch dysfunction collectively reinforce chronic mucosal inflammation and architectural remodeling (16). Moreover, diabetic microangiopathy and diminished mucosal perfusion restrict nutrient and oxygen delivery, impairing tissue renewal and further predisposing the intestinal mucosa to injury (16, 17).

The observed reduction in villus height and increase in crypt depth indicate damage to the mucosal architecture, which may impair nutrient absorption and contribute to metabolic imbalances in diabetic patients. Furthermore, the decreased goblet cell count suggests a reduction in protective mucus production, which may weaken the intestinal mucosal barrier and increase susceptibility to inflammation and subsequent damage (4, 18, 19).

Cinnamon and its bioactive components exhibit the potential to counteract diabetes-induced structural alterations in the duodenum, including increased intestinal permeability, upregulated inflammatory signaling, and structural remodeling, via diverse molecular pathways. As a rich source of vitamins, minerals, and bioactive phytochemicals—including cinnamaldehyde and polyphenolic compounds such as quercetin, kaempferol, rutin, apigenin, *p*-cymene, and various essential oils—cinnamon exerts pronounced anti-inflammatory and antioxidant effects (20, 21).

Cinnamaldehyde, the principal active compound, exhibits strong antioxidant and anti-inflammatory properties (22). It reduces oxidative stress by lowering malondialdehyde levels and enhancing total antioxidant capacity, thereby supporting the preservation of intestinal integrity (7). Furthermore, cinnamaldehyde modulates inflammatory signaling by inhibiting the NF-κB pathway, which reduces the expression of pro-inflammatory cytokines and epithelial cell apoptosis, thus attenuating duodenal injury (8). It has also been shown to upregulate tight junction proteins, strengthening the intestinal barrier and decreasing mucosal permeability (23). Similarly, cinnamic acid scavenges free radicals and suppresses NF-κB activation, contributing to the reduction of intestinal inflammation and the preservation of mucosal architecture (22-25).

Cinnamon's polyphenolic compounds contribute to its anti-inflammatory effects by downregulating NF-κB signaling and suppressing inflammatory mediators (26). These compounds also enhance the expression of antioxidant genes, resulting in the upregulation of Nrf2 and increased levels of downstream proteins, including NADPH quinone dehydrogenase 1, heme oxygenase 1, glutathione peroxidase 1, and catalase (7). Additionally, trans-cinnamaldehyde and *p*-cymene reduce IL-8 secretion and inhibit Akt and IκBα phosphorylation, while essential oils such as 1,8-cineole and spathulenol inhibit pro-inflammatory cytokines (IL-1 and IL-6) in macrophages (25, 26). These effects, mediated through pathways such as NF-κB inhibition and peroxisome proliferator-activated receptor activation, collectively reduce inflammatory mediators and preserve intestinal integrity (25-27).

In this study, cinnamon administration induced significant morphometric improvements; villus height was markedly restored, crypt depth was reduced, and the villus height-to-crypt depth ratio returned to near-normal values. These findings indicate a protective effect on duodenal

tissue architecture, likely due to the potent anti-inflammatory and antioxidant properties of its bioactive compounds, which mitigate the damage induced by oxidative stress and inflammation in diabetes. The concurrent increase in goblet cell count suggests a strengthened mucosal barrier, which may protect the duodenum from further damage (21, 28).

This study also demonstrated that diabetes significantly reduced the volume density of the mucosal layer, goblet cell numerical density, and blood vessel length density in the duodenum. These results are consistent with reports of tissue atrophy and diminished cellular and vascular components in the diabetic small intestine. The reduction in mucosal volume and goblet cell density reflects extensive structural damage and a compromised mucosal barrier, while decreased blood vessel density suggests impaired tissue vascularization, which hinders regeneration and exacerbates complications (4, 6, 28).

Cinnamon significantly improved all diabetes-induced modifications in the stereological parameters of the duodenum; the volume density of the mucosal layer, goblet cell numerical density, and blood vessel length density were all markedly restored. These findings highlight the protective and regenerative effects of cinnamon on the three-dimensional architecture of the duodenum. Cinnamon's potent antioxidant and anti-inflammatory properties likely mitigate diabetes-induced oxidative stress and inflammation, supporting cellular and vascular recovery, tissue repair, and the enhancement of the mucosal barrier (29, 30). The observed morphometric and stereological improvements are largely attributable to cinnamon's ability to counteract oxidative stress and inflammation, which are key drivers of tissue damage and impaired regeneration in diabetes (16).

Conclusion

Diabetes markedly impairs the duodenal mucosa, leading to villus atrophy and barrier dysfunction driven by oxidative stress and inflammation. Treatment with hydroalcoholic cinnamon extract effectively reverses these morphometric and stereological alterations, restoring the mucosal architecture to a near-normal state. These protective effects are likely mediated by the extract's antioxidant and anti-inflammatory constituents, including cinnamaldehyde, cinnamic acid, and cinnamtannin B1, supporting its potential as a complementary therapy for diabetes-related gastrointestinal complications.

Acknowledgements

The authors express their gratitude and appreciation to Shahrekord University.

Authors' Contributions

Rahmatallah Fatahian Dehkordi: Conceived and designed the study. **Jahangir Kaboutari:** Performed the experiments and collected the data. **Hamidreza Fazel Chaharmahali:** Analyzed the data and drafted the manuscript. All authors reviewed and approved the final version of the manuscript.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

This research was done according to the international and institutional standards to obtaining animal welfare and rights, approved by Shahrekord University (Grant No.: 7825381).

Conflict of Interest

The authors declare that they have no conflict of interest

Consent for Publication

Not applicable.

Funding

The authors declare that they have not received any financial support.

References

1. Amiri A, Dehkordi RAF, Heidarnejad MS, Dehkordi MJ. Effect of the zinc oxide nanoparticles and thiamine for the management of diabetes in alloxan-induced mice: a stereological and biochemical study. *Biol. Trace Elem. Res*. 2018;181(2):258-264. https://doi.org/10.1007/s12011-017-1035-x

2. Cordero-Pérez P, Hernández-Cruz FE, Garza-Guzmán D, Moreno-Peña DP, Sánchez-Martínez C, Torres-González L, et al. Antidiabetic and anti-inflammatory effect of Cinnamomum cassia oil in alloxan-induced diabetic rats. *Pharmaceuticals (Basel).* 2024;17(9):1135. https://doi.org/10.3390/ph17091135
3. El Maksoud AIA, Al-Karmalawy AA, ElEbeedy D, Ghanem A, Rasheed Y, Ibrahim IA, et al. Symbiotic antidiabetic effect of Lactobacillus casei and the bioactive extract of Cleome droserifolia (Forssk.) Del. on mice with type 2 diabetes induced by alloxan. *Chem. Biodiversity*. 2024;21(1):e202301397. https://doi.org/10.1002/cbdv.202301397
4. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. *Int. J. Mol. Sci*. 2020;21. https://doi.org/10.3390/ijms21176275
5. Lerkdumnernkit N, Sricharoenvej S, Lanlua P, Niyomchan A, Baimai S, Chookliang A, et al. The effects of early diabetes on duodenal alterations in the rats. *Int J Morphol*. 2022;40(2):389-395. https://doi.org/10.4067/S0717-95022022000200389
6. Qureshi AS, Ghaffor J, Usman M, Ehsan N, Umar Z, Sarfraz A. Effect of ethanolic preparations of cinnamon (*Cinnamomum zeylanicum*) extract on hematologic and histometric parameters of selected organs in alloxan-induced diabetic female albino rats. *J Diabetes Metab Disord*. 2019;18(1):505-512. https://doi.org/10.1007/s40200-019-00402-x
7. Yildiz SE, Bakir B, Aras Y, Da S, Sari EK. Immunohistochemical distribution of somatostatin in stomach tissue of diabetic rats treated with cinnamon extract. *Kafkas Univ Vet Fak Derg*. 2019;25(3):427-433. https://doi.org/10.9775/kvfd.2018.21175
8. Mohsin SN, Saleem F, Humayun A, Tanweer A, Muddassir A. Prospective nutraceutical effects of cinnamon derivatives against insulin resistance in type II diabetes mellitus: evidence from the literature. *Dose Response*. 2023;21(3):15593258231200527. https://doi/org/10.1177/15593258231200527
9. Marathe CS, Rayner CK, Wu T, Jones KL, Horowitz M. Gastrointestinal disorders in diabetes. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al., editors. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2024.
10. Kowalska J, Tyburski J, Matysiak K, Jakubowska M, Łukaszyk J, Krzymińska J. Cinnamon as a useful preventive substance for the care of human and plant health. *Molecules*. 2021;26(17):5299. https://doi.org/10.3390/molecules26175299
11. Shokri G, Fathi H, Jafari Sabet M, Nasri Nasrabadi N, Ataee R. Evaluation of anti-diabetic effects of hydroalcoholic extract of green tea and cinnamon on streptozotocin-induced diabetic rats. *Pharm. Biomed. Res.* 2015;1(2):20-29. https://doi.org/10.18869/acadpub.pbr.1.2.20
12. Zimmerman JL. Taxes and firm size. *J. Account. Econ*. 1983;5:119-149. https://doi.org/10.1016/0165-4101(83)90008-3
13. Kim J-M. Induction of diabetes mellitus using alloxan in Sprague Dawley rats. *Cureus*. 2024;16(6):e63359. https://doi.org/10.7759/cureus.63359
14. Warille AA, Kocaman A, Elamin AA, Mohamed H, Elhaj AE, Altunkaynak BZ. Applications of various stereological tools for estimation of biological tissues. *Anat. Histol. Embryol*. 2023;52(2):127-134. https://doi.org/10.1111/ahe.12896
15. Nie H-Y, Ge J, Huang G-X, Liu K-G, Yue Y, Li H. New insights into the intestinal barrier through "gut-organ" axes and a glimpse of the microgravity's effects on intestinal barrier. *Front. physiol*. 2024;15:1465649. https://doi.org/10.3389/fphys.2024.1465649
16. Nakhal MM, Yassin LK, Alyaqoubi R, Saeed S, Alderei A, Alhammadi A, et al. The microbiota–gut–brain axis and neurological disorders: A comprehensive review. *Life*. 2024;14(10):1234. https://doi.org/10.3390/life14101234
17. Ullah H, Arbab S, Tian Y, Liu C-q, Chen Y, Qijie L, et al. The gut microbiota–brain axis in neurological disorder. *Front. Neurosci*. 2023; 17:1225875. https://doi.org/10.3389/fnins.2023.1225875
18. Marathe CS, Rayner CK, Wu T, Jones KL, Horowitz M. Gastrointestinal disorders in diabetes. Endotext. 2024.
19. Rubino F, Forgione A, Cummings DE, Vix M, Gnuli D, Mingrone G, et al. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes. *Ann. Surg*. 2006; 244(5): 741-749. https://doi.org/10.1097/01.sla.0000234806.01121.18
20. Ojo O, Otunola GA, Oshungade OR, Joshua B. Cinnamon improves glycated haemoglobin and body mass index, but not inflammatory parameters in patients with type 2 diabetes: evidence from a systematic review and meta-analysis of randomised controlled trials. *Endocrines*. 2025;6(1):3. https://doi.org/10.3390/endocrines6010003
21. Jalil Faddladdeen KA. The possible protective and therapeutic effects of ginger and cinnamon on the

testis and coda epididymis of streptozotocin-induced-diabetic rats: histological and biochemical studies. *Saudi J. Biol. Sci*. 2022;29(12):103452. https://doi.org/10.1016/j.sjbs.2022.103452

22. Kumar CU, Reddy SS, Suryanarayana P, Patil MA, Chary PM, Kumar PU, et al. Protective effect of cinnamon on diabetic cardiomyopathy in nicotinamide-streptozotocin induced diabetic rat model. *J. Diabetes Metab. Disord*. 2022;21(1):141-150. https://doi.org/10.1007/s40200-021-00948-3
23. Lu Y, Han X. Therapeutic implications of phenolic acids for ameliorating inflammatory bowel disease. *Nutrients*. 2024;16(9):1347. https://doi.org/10.3390/nu16091347
24. Qi L, Mao H, Lu X, Shi T, Wang J. Cinnamaldehyde promotes the intestinal barrier functions and reshapes gut microbiome in early weaned rats. *Front. nutr*. 2021;8:748503. https://doi.org/10.3389/fnut.2021.748503
25. Chao LK, Hua K-F, Hsu H-Y, Cheng S-S, Liu J-Y, Chang S-T. Study on the antiinflammatory activity of essential oil from leaves of Cinnamomum osmophloeum. *J. Agric. Food Chem.* 2005;53(18): 7274-7278. https://doi.org/10.1021/jf051151u
26. Schink A, Naumoska K, Kitanovski Z, Kampf CJ, Fröhlich-Nowoisky J, Thines E, et al. Anti-inflammatory effects of cinnamon extract and identification of active compounds influencing the TLR2 and TLR4 signaling pathways. *Food Funct.* 2018;9(11):5950-5964. https://doi.org/10.1039/c8fo01203e
27. Yulug B, Kilic E, Altunay S, Ersavas C, Orhan C, Dalay A, et al. Cinnamon polyphenol extract exerts neuroprotective activity in traumatic brain injury in male mice. *CNS Neurol Disord Drug Targets*. 2018;17(6):439-447. https://doi.org/10.2174/1871527317666180501110918
28. Al-Qulaly M, Okasha MA, Hassan MG. Effect of ginger and cinnamon on induced diabetes mellitus in adult male albino rats. *bull. egypt. soc. physiol. sci*. 2021;41(3):373-388. https://doi.org/10.21608/besps.2020.45577.1078
29. Khedkar S, Ahmad Khan M. Aqueous extract of cinnamon (Cinnamomum spp.): Role in cancer and inflammation. *Evid Based Complement Alternat Med*. 2023;2023:5467342. https://doi.org/10.1155/2023/5467342
30. Kowalska J, Tyburski J, Matysiak K, Jakubowska M, Łukaszyk J, Krzymińska J. Cinnamon as a useful preventive substance for the care of human and plant health. *Molecules*. 2021;26(17):5299. https://doi.org/10.3390/molecules26175299