Original Article

The Possible Protective Effect of Febuxostat on Venlafaxine Induced Structural Changes on the Parotid Gland of Adult Male Albino Rats: Histological and Immunohistochemical Study

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ABSTRACT

Background: Parotid gland is affected by structural and functional changes caused by diseases, medications, and oxidative stress. Venlafaxine, a common antidepressant, has been related to adverse effects, including structural changes in the parotid gland. Febuxostat, a xanthine oxidase inhibitor with antioxidant and anti-inflammatory properties.

Aim of the Work: This study aimed to evaluate the potential protective effects of febuxostat against venlafaxine-induced structural changes in the parotid gland of adult male albino rats using histological and immunohistochemical techniques.

Methods: Twenty-five adult male albino rats were divided into four groups: control, venlafaxine, carboxymethylcellulose+ven lafaxine, and febuxostat+venlafaxine. Treatments were administered orally for 30 days. The histological examination included staining with H&E, and Masson's Trichrome. Immunohistochemical markers (Ki67, α-SMA, HSP60) were assessed alongside morphometric analysis.

Results: Venlafaxine and carboxymethylcellulose+venlafaxine produced structural damage, including disorganized, widely separated acini with congested apparently dilated blood vessels. Serous acini revealed vacuolation of their lining cells with pyknotic nuclei besides separated cells. Also, some acini showed accumulated acidophilic material at their lumen while others were degenerated. The intercalated, striated and excretory ducts were apparently dilated with irregular lumen and pyknotic nuclei. Also inflammatory cellular infiltrations in-between the acini and congestion of blood vessels by H&E. besides, significant increase in amount and mean area percentage of collagen fibers. Also, significantly increased mean number of Ki67 positive cells, mean colour intensity of α-SMA, and HSP60. Febuxostat group showed nearly normal histological and immunohistochemical profiles.

Conclusion: Febuxostat effectively protected against venlafaxine-induced parotid gland damage. So, it is a promising therapy choice for salivary gland dysfunction.

Key Words: Febuxostat, histology, immunohistochemistry, parotid gland, venlafaxine, .

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INTRODUCTION

Parotid gland is one of the main salivary glands responsible for saliva production, which is required for appropriate oral hygiene and digestive support. Recent study has shed light on a variety of parotid gland illnesses, including infections, autoimmune diseases, and drug-related damage[1, 2].

Decreased salivary secretion, or hyposalivation, is a major clinical condition that can be caused by a range of factors including prescription side effects, systemic illnesses, and lifestyle choices[3]. Conditions such as Sjögren's syndrome, diabetes, and radiation therapy can all impair salivary gland function, resulting in reduced saliva production[3].

Medications, particularly antidepressants, are well known for causing hyposalivation by interfering with the autonomic nervous system regulation of salivary glands[4]. This decrease in saliva can result in dry mouth (xerostomia), difficulty swallowing, decreased taste perception, and increased susceptibility to dental caries and infections[5]. Saliva also promotes digestion, lubricates food, and contains antimicrobial properties, all of which benefit oral health[3].

Venlafaxine, a commonly prescribed antidepressant, is associated with several side effects in many organs[6],

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including structural changes in salivary glands, particularly parotid, which significantly reduces salivary flow[6]. The oxidative stress induced by venlafaxine plays a crucial role in damaging the salivary glands by affecting antioxidant defense systems and increasing the production of reactive oxygen species (ROS)[7]. This is accompanied by protein oxidation, membrane damage, and subsequent cellular and functional alterations in the gland[7].

Febuxostat, is a non-purine selective inhibitor of xanthine oxidase/xanthine dehydrogenase that converts hypoxanthine to xanthine and uric acid. Febuxostat decreases serum uric acid levels so, used for managing chronic gout[8]. It possesses potent antioxidant and anti-inflammatory properties, inhibiting the production of pro-inflammatory cytokines such as TNF-α and IL-6[9]. Its pleiotropic pharmacological effects include the modulation of oxidative stress and inflammation, positioning it as a potential therapeutic agent to mitigate venlafaxine-induced salivary gland damage[10, 11].

AIM OF THE STUDY

This study aimed to investigate the possible protective effect of febuxostat on venlafaxine- induced structural changes on rat parotid gland through using histological and immunohistochemical study.

MATERIAL AND METHODS

The present work included 25 adult male albino rats (180-250 gm) from the animal house, Tanta University, Egypt. Animals were kept in clean properly ventilated cages and were allowed a free access to diet and water.

ETHICAL APPROVAL

The present research was carried out in accordance with the guidelines for the care and use of the experimental animals in Tanta University, Faculty of Medicine, Egypt with approval code No. 36264PR922/10/24. The sacrificed animals were packed in a special package according to safety precautions and infection control measures of university.

The experimental groups:

- Group1 (Control): 10 rats that were further subdivided into: subgroup a: 5 rats with no treatments.

Subgroup b: 5 rats that received 0.1 ml saline orally via an intragastric tube for 30 consecutive days.

- Group 2 (VEN): 5 rats that received venlafaxine orally in a dose of 40 mg/kg/ day dissolved in 0.1% saline for 30 consecutive days.

- Group3 (CMC+VEN): 5 rats that received 0.5% carboxymethylcellulose by oral gavage and venlafaxine (40 mg/kg/ day) for 30 consecutive days.

- Group 4 (FEB+VEN): 5 rats that received febuxostat orally in a dose of 10 mg/kg/day dissolved in 0.5% carboxymethylcellulose 2hrs before an oral dose (40 mg/kg/ day) of venlafaxine for 30 consecutive days.

Venlafaxine dose was adjusted according to ***Mattioli et al. (2011) & Madrigal-Bujaidar et al. (2022)***[6, 12]. While, febuxostat (FEB) was given according to ***Abdelzaher et al.*** (2022)[10].

By the end of the experiment, rats were anesthetized by an intraperitoneal injection of 50 mg/kg pentobarbital[13] then, parotid glands were dissected out, washed with saline. Then, were undergo fixation in 10% formal saline for further processing.

Preparation of samples for paraffin sections[14]

After being fixed in 10% formol saline, parotid gland samples were undergoing processing to finally obtain thin slices (5 microns) for histological and immunohistochemical analysis.

Histological examination

Haematoxylin & eosin (H.& E.)

After deparaffinization, sections were immersed in xylene then rehydrated and stained, with hematoxylin and eosin (H&E), to reveal cellular and tissue features using a light microscope. The cytoplasm, connective and muscle fibers were stained pink while the nucleus was blue to purple.

Masson's trichrome[14]

Sections were undergoing deparaffinization then, immersion in xylene before passing them through graded alcohols. Then, Bouin's solution, Weigert's iron hematoxylin, Biebrich scarlet-acid fuchsin then, differentiated in phosphomolybdic-phosphotungstic acid. Followed by aniline blue staining. Finally, sections were dehydrated, cleaned, and mounted on a coverslip. Masson's trichrome stain produced black nuclei, red muscle and cytoplasm, and blue collagen.

Immunohistochemistry of Ki67 (Marker for Proliferation; Kiel 67), α-SMA (Alpha-Smooth Muscle Actin), HSP60 (Heat shock protein 60)[15-17].

Positive slides were used that undergo deparaffinization, and rehydration with graded alcohol. Next, sections were heated in a buffer for antigen retrieval. Followed by immersion in blocking solutions, such as bovine serum albumin. After blocking, sections were treated with anti-rabbit polyclonal primary antibodies of Ki67 (Abcam, United Kingdom; 1:200), α-SMA (Sigma-Aldrich, United States; 1:100), HSP60 (R&D Systems, United States;1:50) overnight at 4°C. After that, a horseradish peroxidase anti-rabbit polyclonal secondary antibody (R&D Systems, United States; 1:100) was added for 30 minutes at room temperature. Then, DAB (diaminobenzidine), is employed. Finally, sections were counterstained with hematoxylin and were examined by an Olympus light microscope. Through which Ki67 positive stained nuclei was seen, while α-SMA stained the myoepithelial cells while TNFα appeared as positive brownish cytoplasmic reaction. Negative control slides were obtained through replacing the primary antibody with PBS. On the other hand, breast carcinoma is a positive control for Ki67; aorta for α-SMA, and hepatocellular carcinoma for HSP60.

Morphometric evaluation

All morphometric evaluations were carried out at Histology Department, Faculty of /medicine, Tanta University. By which, a light microscopy (Olympus, Japan), coupled with a digital camera was used for doing image acquisition. Then, Image J (1.47 v) program (NIH, USA) with five separate images (x 400) from each experimental group was used. Finally, 5 non-overlapping fields from each image was used to evaluate the following morphometric measures:

1. The mean area percentage of collagen fibers in Masson's trichrome stained sections.
2. The mean number of Ki67 positive cells.
3. The mean color intensity of α-SMA.
4. The mean color intensity of HSP60.

Statistical analysis

Data were provided as mean ± SD. The data was then evaluated using Stat Software's Graph Pad (Inc., California, USA). It compared the experimental groups using one way ANOVA (One way Analysis of Variance). Results were considered statistically significant if the *P-value* was less than 0.05.

RESULTS

Results of H&E stain

Parotid gland sections of Group 1 (Control group) showed numerous serous acini surrounded by connective tissue stroma containing normally appeared blood vessels. The acini were lined with pyramidal-shaped serous cells with basally located, round nuclei. The intercalated ducts appeared with narrow lumen and were lined by low cuboidal cells with centrally located nuclei. The striated ducts appeared with wider lumen and were lined by simple columnar epithelium. The excretory ducts appeared lined with pseudostratified or stratified cuboidal epithelium (Figure 1 A&B).

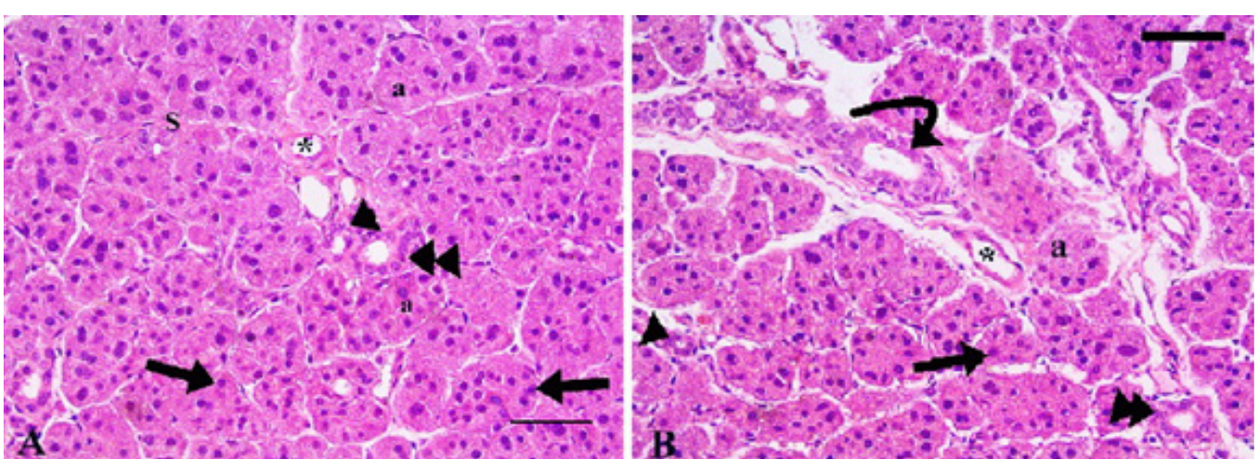


Fig. 1: Effect of febuxostat on venlafaxine induced structural changes on the parotid gland of rats at H&E stained sections of Group 1 (Control group). (H&E x 400); Scale bar= 50.
A&B) showing numerous serous acini (a) surrounded by connective tissue stroma (S) containing normally appeared blood vessels (*), the acini lined with pyramidal-shaped serous cells with basally located, round nuclei (→), intercalated ducts with narrow lumen lined by low cuboidal cells with centrally located nuclei (►), striated ducts with wider lumen lined by simple columnar epithelium (►►), and excretory ducts lined with pseudostratified or stratified cuboidal epithelium (curved arrow).

Group 2 (VEN) showed structural changes in the form of disorganized, widely separated acini with congested apparently dilated blood vessels. Furthermore, the serous acini revealed vacuolation of their lining cells with pyknotic nuclei besides separated cells. Also, some acini showed accumulated acidophilic material in their lumen while others were degenerated. As regards the intercalated, striated and excretory ducts; they were apparently dilated with irregular lumen and pyknotic nuclei. There were also inflammatory cellular infiltrations in-between the acini and congestion of blood vessels (Figure 2 A-D).

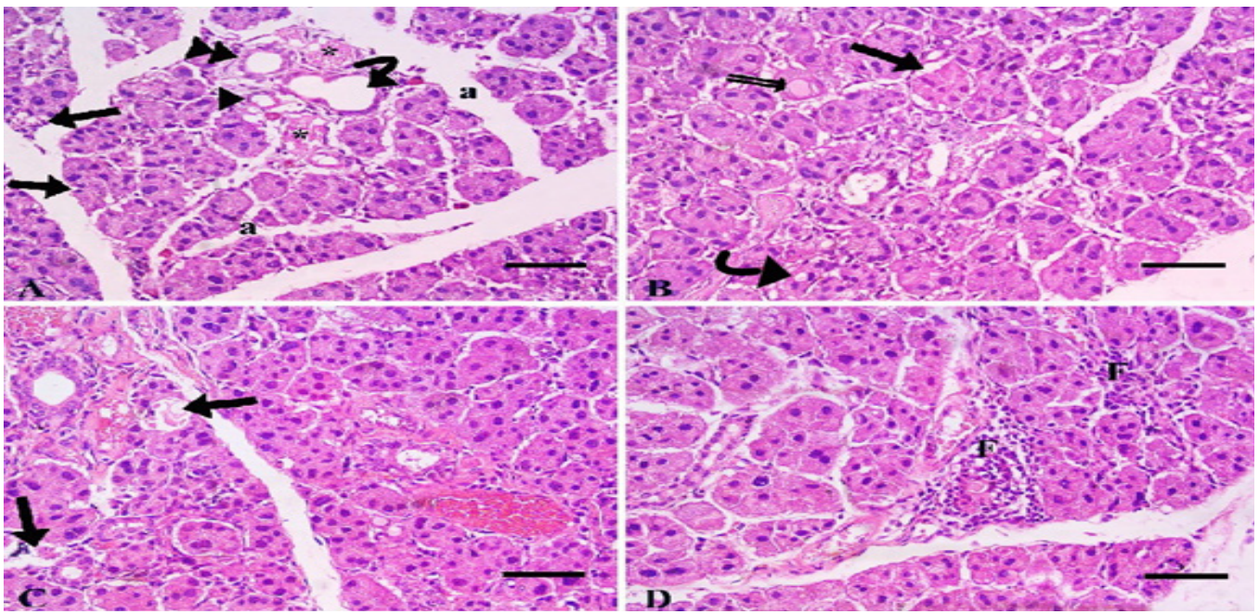


Fig. 2: Effect of febuxostat on venlafaxine induced structural changes on the parotid gland of rats at H&E stained sections of Group 2 (VEN). (H&E x 400); Scale bar= 50.
A) Showing disorganized, widely separated acini (a) with congested apparently dilated blood vessels (*), serous acini with pyknotic nuclei (→), intercalated (►), striated (►►) and excretory ducts (curved arrow) were apparently dilated with irregular lumen and pyknosis. B) Showing separated acinar cells from the acinar basement membrane (→), some acini showed vacuolations (curved arrow) and accumulated acidophilic material at their lumen (double arrow). C) Showing degenerated acini (→). D) Showing inflammatory cellular infiltrations in-between the acini and the congested blood vessels (F).

Group 3 (CMC+VEN) revealed a picture similar to VEN group with disorganized, degenerated and widely separated acini besides congested apparently dilated blood vessels. In addition to disorganized parotid gland ducts with irregular lumen and cell vacuolations (Figure 3A).

Group 4 (FEB +VEN) showed improvement with a nearly normal parotid gland histology. The acini were nearly normal with connective tissue containing nearly normal blood vessels. In addition to nearly normal parotid gland ducts (Figure 3B).

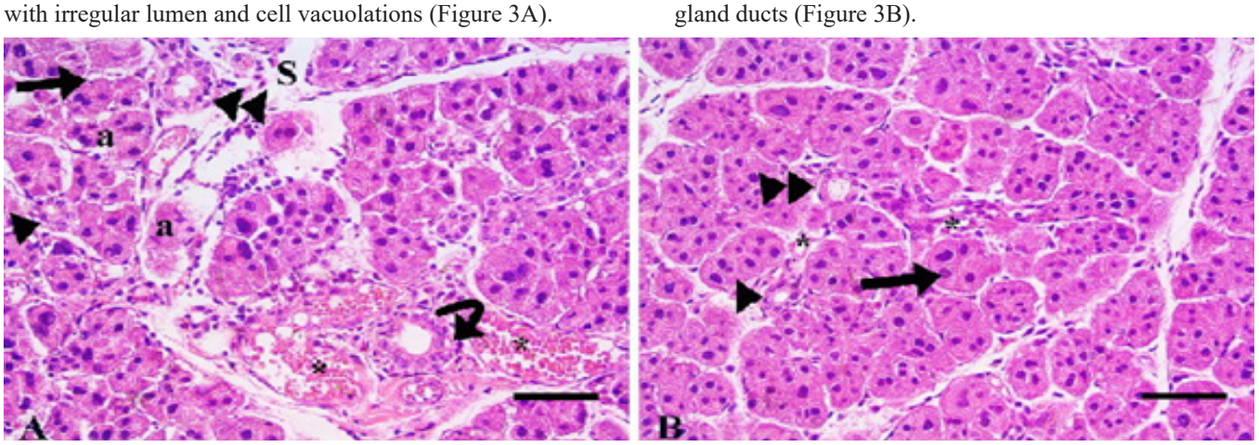


Fig. 3: Effect of febuxostat on venlafaxine induced structural changes on the parotid gland of rats at H&E stained sections. (H&E x 400); Scale bar= 50.
A) Group 3 (CMC+VEN) showing disorganized, degenerated (a) and widely separated acini (S), congested apparently dilated blood vessels (*), acinar cells with vacuolations and pyknosis (→), disorganized intercalated (►), striated (►►), and excretory (curved arrow) ducts with irregular lumen and cell vacuolations. B) Group 4 (FEB +VEN) showing acini lined with pyramidal-shaped serous cells with basally located, round nuclei (→), nearly normal blood vessels (*), intercalated ducts (►) and striated ducts (►►).

Masson's Trichrome results

It was noticed that, few collagen fibers were present in-between the parotid gland acini as well as its ducts in Group 1. Instead, markedly increased amounts of collagen fibers were found around the congested, apparently dilated blood vessels, acini and ducts in Groups 2& 3. Finally, Group 4 revealed improvement with few collagen fibers similar to Group 1 (Figure 4A-D).

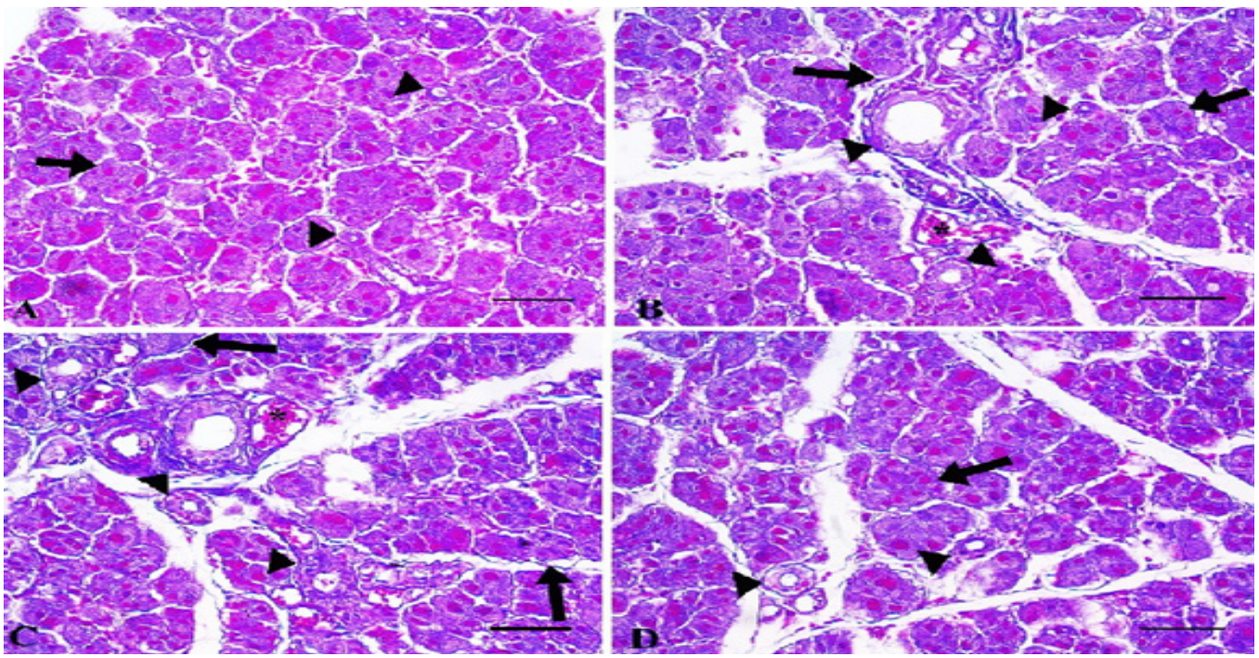
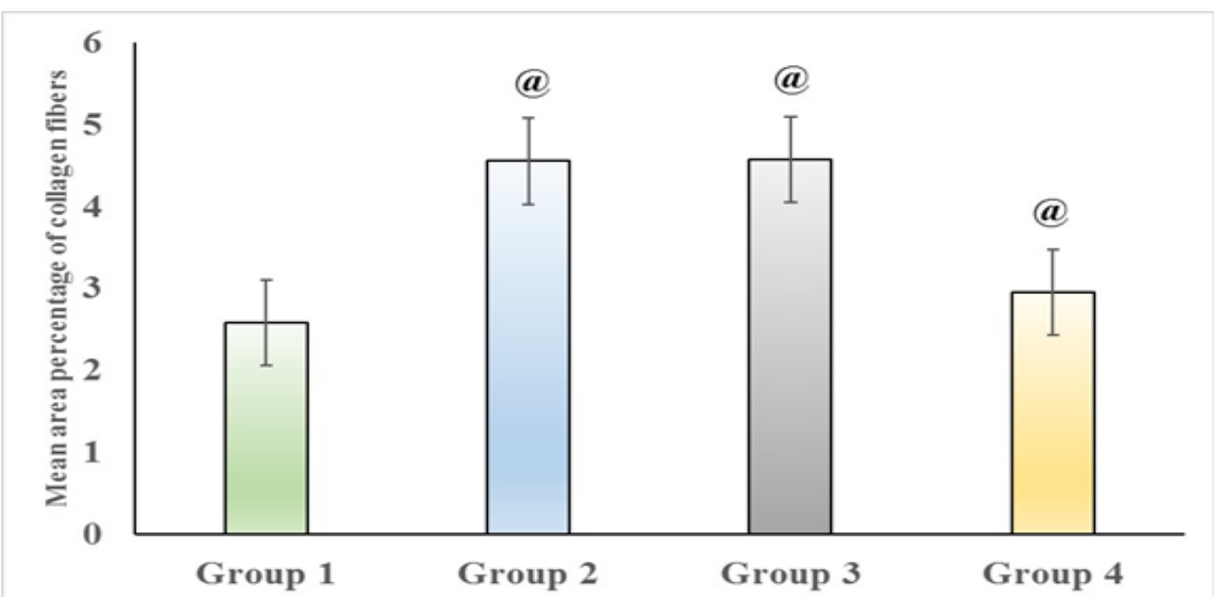


Fig. 4: Effect of febuxostat on venlafaxine induced structural changes on the parotid gland of rats at Masson's Trichrome stained sections. (Masson's Trichrome x 400); Scale bar= 50.
A) Group 1 showing few collagen fibers in-between the parotid gland acini (→) and ducts (►). B&C) Group 2& 3 showing markedly increased amounts of collagen fibers around the congested, apparently dilated blood vessels (*), acini (→) and ducts (►). D) Group 4 showing few collagen fibers in-between acini (→) and ducts (►).

As for the mean area percentage of collagen fibers; there was as a significant increase in Group 2 as well as Group 3; while decreased in Group 4 in comparison to Group 1 (Histogram 1).



Histogram 1: Effect of febuxostat on venlafaxine induced changes in the mean area percentage of collagen fibers expressed as mean ± SD. @ Group 2 (VEN); Group 3 (CMC+VEN), and Group 4 (FEB+VEN) significant compared to control group (Group 1).

Immunohistochemical results of Ki67

The negative control revealed no Ki67 immunohistochemical reaction. While, group 1 showed few acinar cells with positive nuclear reaction for Ki67. Considering group 2&3; same results were noticed with relatively increased number of cells positive for Ki67. For group 4; a nearly normal finding with few acinar cells showed positive Ki67 immunohistochemical reaction (Figure 5A-E).

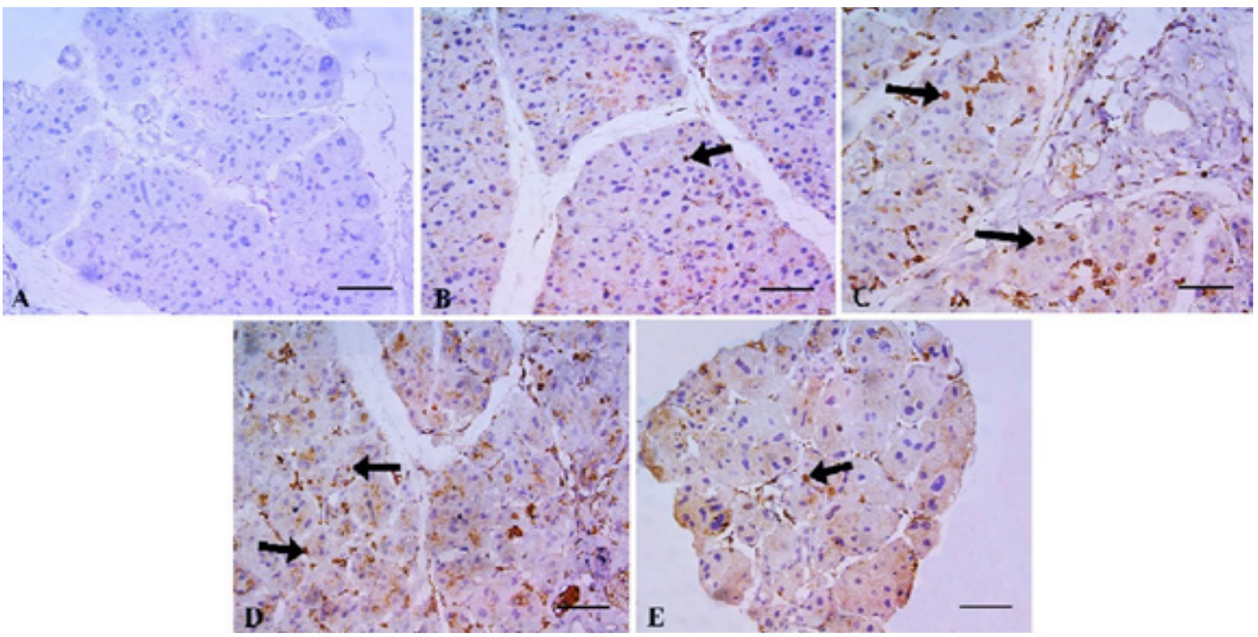
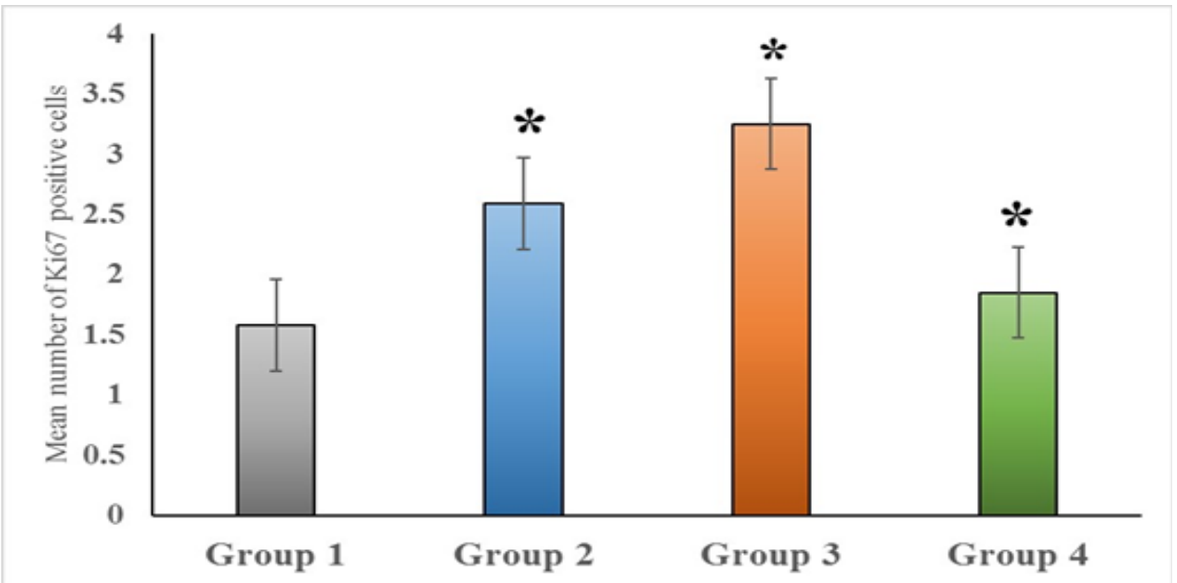


Fig. 5: Effect of febuxostat on venlafaxine induced Ki67 immunohistochemical changes on the parotid gland of rats. (Ki67 x 400); Scale bar= 50.
A) Negative control showing no Ki67 immunohistochemical reactions. B) Group 1 showing few acinar cells with positive nuclear reaction for Ki67 (→). C&D) Group 2&3 showing relatively increased number of cells positive for Ki67 (→). E) Group 4 showing few acinar cells showed positive Ki67 immunohistochemical reaction (→).

As regards the mean number of Ki 67 positive cells. There was a significant increase in Group 2&3 while significantly decreased in Group 4 when compared to the control group (Group 1) (Histogram 2).



Histogram 2: Effect of febuxostat on venlafaxine induced changes in the mean number of Ki 67 positive cells. The present data were expressed as mean ± SD. Through which, * Group 2 (VEN); Group 3 (CMC+VEN), and Group 4 (FEB+VEN) significant compared to control group (Group 1).

Immunohistochemical results of α-SMA

As regards the negative control for α-SMA; no obvious immunohistochemical reactions. Group 1 showed myoepithelial cells of surrounding both secretory acini and intercalated ducts with positive cytoplasmic immunohistochemical reaction for α-SMA. In contrast, Group 2& 3 revealed intense α-SMA immunohistochemical expression. While the treated group with FEB (Group 4) showed a nearly normal expression of α-SMA (Figure 6A-E).

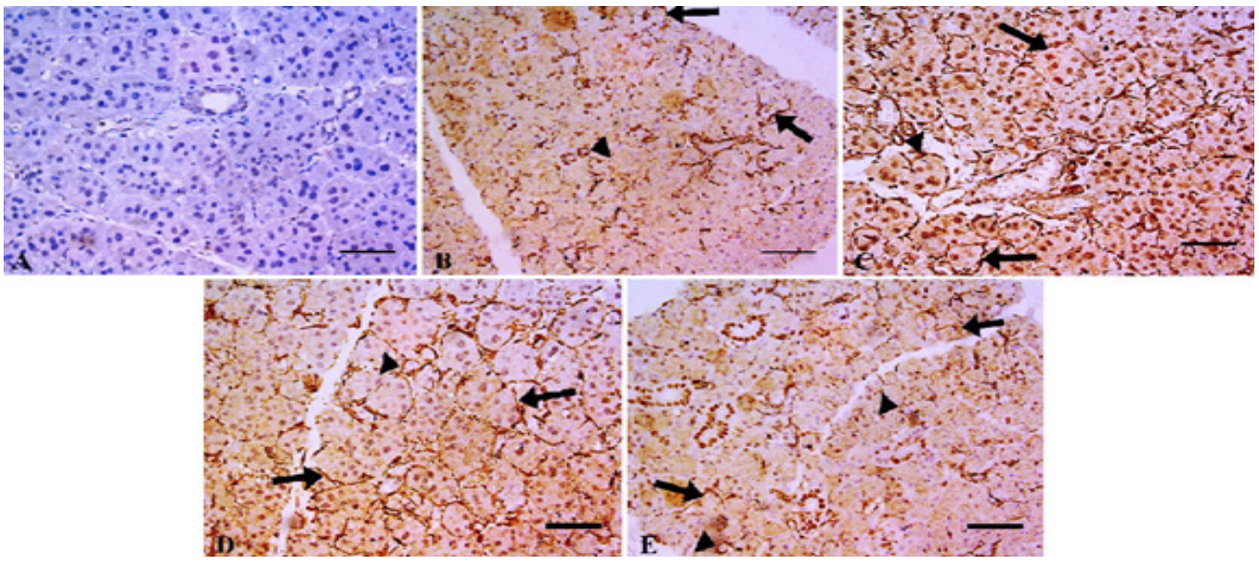
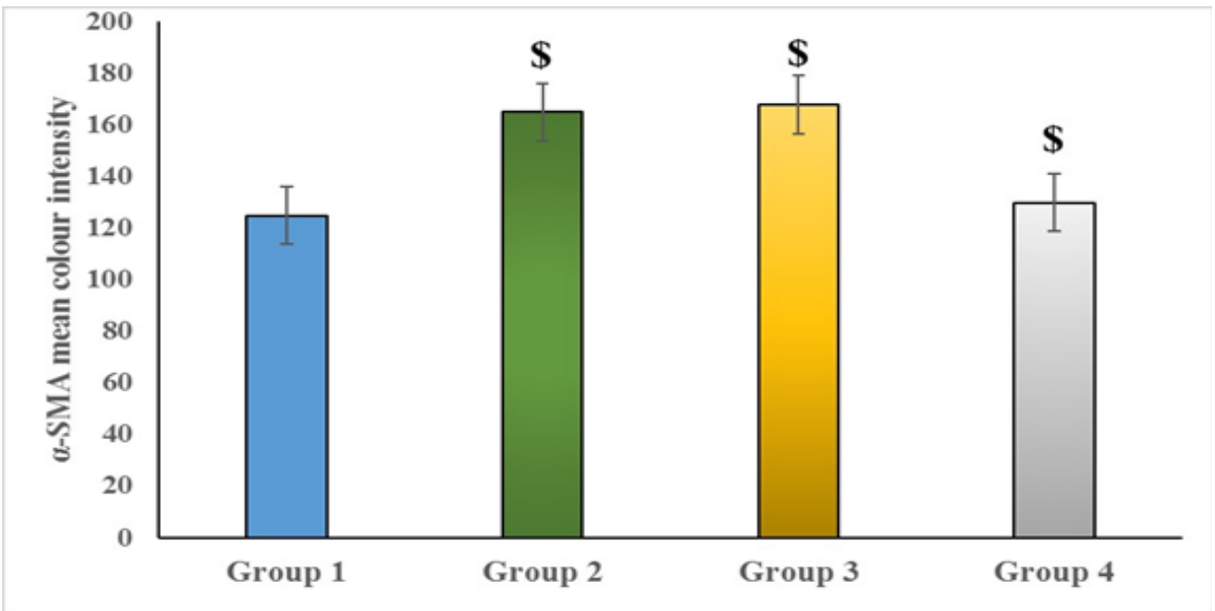


Fig. 6: Effect of febuxostat on venlafaxine induced α-SMA immunohistochemical changes on the parotid gland of rats. (α-SMA x 400); Scale bar= 50.
A) Negative control for α-SMA showing no obvious immunohistochemical reactions. B) Group 1 showing myoepithelial cells surrounding both secretory acini (→) and intercalated ducts (►) with positive cytoplasmic immunohistochemical reaction for α-SMA. C&D) Group 2& 3 showing the myoepithelial cells around acini (→) and intercalated ducts (►) with intense α-SMA immunohistochemical expression. E) Group 4 showing positive cytoplasmic immunohistochemical reaction for α-SMA of myoepithelial cells around the acini (→), and intercalated ducts (►).

The mean colour intensity of α-SMA revealed a significant increase in Groups 2&3, while a significant decrease in Group 4 if compared to Group 1 (Histogram 3).



Histogram 3: Effect of febuxostat on venlafaxine induced changes in the mean colour intensity of α-SMA expressed as mean ± SD. $ Group 2 (VEN); Group 3 (CMC+VEN), and Group 4 (FEB+VEN) significant compared to control group (Group 1).

Immunohistochemical results of HSP60

The immunohistochemical expression of HSP60 of negative as well as control groups showed no reaction. While, Group 2& 3 showed positive cytoplasmic reaction for HSP60 of the secretory acini and gland ducts. Contrarily, Group 4 showed an immunohistochemical reaction nearly similar to control (Figure 7A-E).

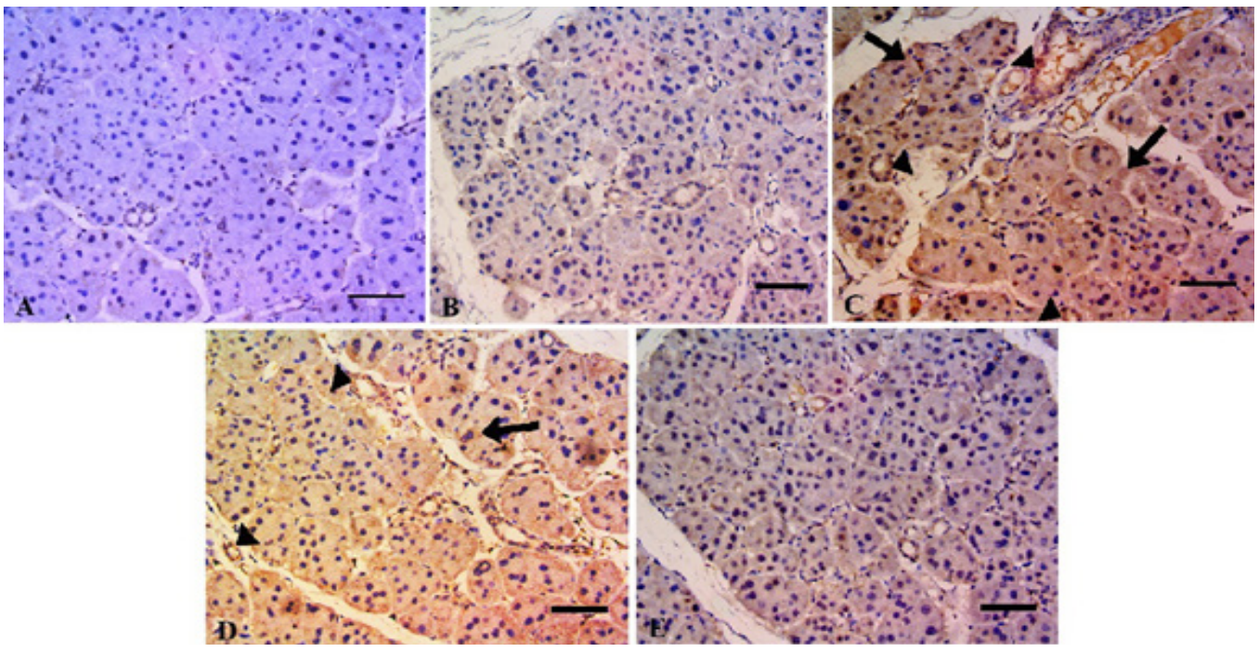
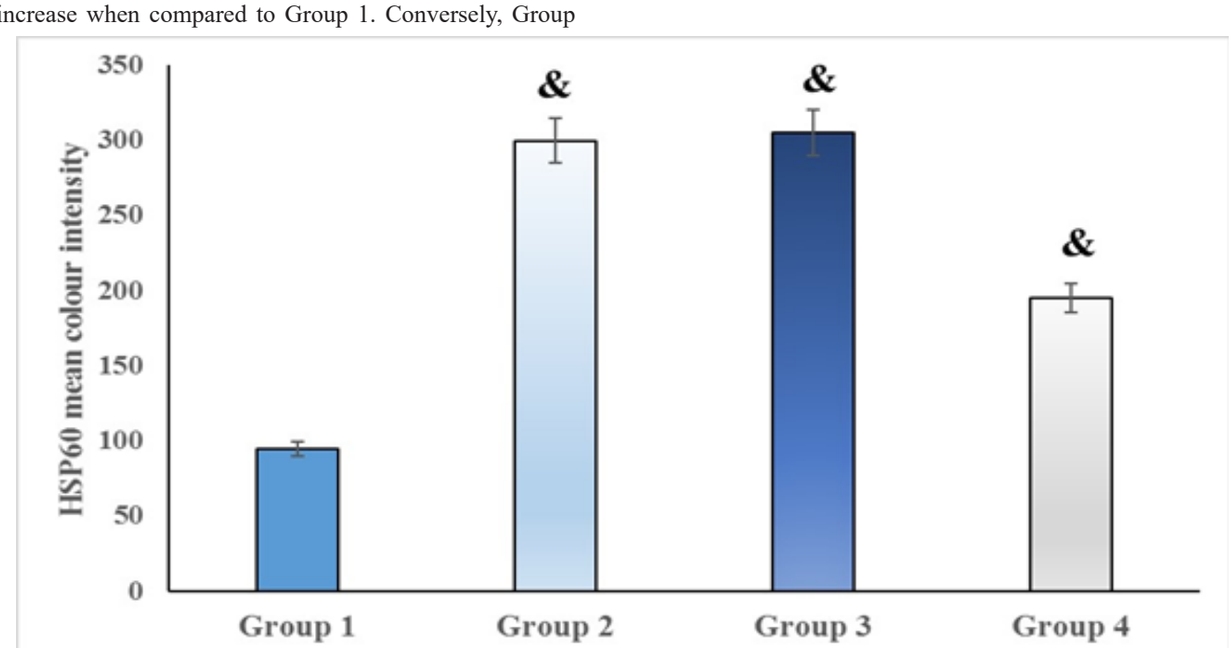


Fig. 7: Effect of febuxostat on venlafaxine induced HSP60 immunohistochemical changes on the parotid gland of rats. (HSP60 x 400); Scale bar= 50.
A&B) Negative & control groups showed no immunohistochemical expression of HSP60. C&D) Group 2& 3 showed positive cytoplasmic reaction for HSP60 of the secretory acini (→) and gland ducts (►). E) Group 4 showed no immunohistochemical expression of HSP60.

By recording the mean colour intensity of HSP60; it was observed that Groups 2&3 expressed a significant increase when compared to Group 1. Conversely, Group 4 expressed a significant decrease when compared to Group 1 (Histogram 4).



Histogram 4: Effect of febuxostat on venlafaxine induced changes in the mean colour intensity of HSP60 expressed as mean ± SD. & Group 2 (VEN); Group 3 (CMC+VEN), and Group 4 (FEB+VEN) significant compared to control group (Group 1).

DISCUSSION

One of the antidepressant drugs is VEN. It is undergoing liver metabolism into O-desmethylvenlafaxine. It is used for the treatment of different psychiatric disorders like depression, anxiety, panic attacks as well as social phobia. But unfortunately it is associated with different organ side effects[13].

The decreased salivary production as well as secretion are considered to be major side effects from VEN intake. Its mechanism is still not clear and needs more investigations with histological and histomorphometric evaluation to be clarified[18].

In the present work, Group 2 (VEN) revealed disorganized, widely separated acini, congested apparently dilated blood vessels, vacuolated serous acinar cells with pyknotic nuclei, besides separated cells. Also, some acini showed accumulated acidophilic material at their lumen while others were degenerated. Besides, the intercalated, striated and excretory ducts were apparently dilated with irregular lumen and pyknosis. In addition to inflammatory cellular infiltration. Also, significant increase of amount and mean area percentage of collagen fibers when compared to Group 1.

The previously mentioned structural changes may be related to VEN's pharmacological activity as a reuptake inhibitor of serotonin, noradrenaline, and dopamine. This could lead to either a decrease in saliva flow or changes in salivary content. Furthermore, VEN blocks the binding of acetylcholine to M3 (muscarinic) receptors, causing saliva to be produced but not ejected[19, 20]. As a result, salivary secretions pooled inside the acini and gland ducts, causing disorder, irregularity, and the accumulation of acidophilic material at their lumen. In addition, acinar and duct cells exhibit degenerative alterations such as vacuolations and pyknosis[12].

The congested, presumably dilated blood vessels seen in this study could be attributable to serotonin's indirect impact on 5-hydroxytryptamine receptors in peripheral circulation. Which causes uneven blood flow in the salivary glands[20, 21]. Furthermore, VEN-induced cytotoxicity in the glandular structure was due to oxidative stress damage and the release of reactive oxygen species (ROS)[22]. ROS causes damage to cell proteins, membrane lipids, and DNA mutation with DNA methylation. Consequently, conformational changes of cell nuclei with pyknosis in addition to cell separation[23]. Furthermore, changes in the composition of cell membranes due to oxidative stress could lead to changes in the membrane permeability. The latter results in initiation of inflammatory cell response with the passage of different inflammatory cells with increased cell infiltrations. Moreover, inflammatory cell responses could upregulates the release of different fibrotic agents like TGF-B1 leading to fibrosis with increased deposition of collagen fibers as well as their mean area percentage[24].

Group 2 had considerably higher levels of Ki67 positive cells, α-SMA, and HSP60. As previously established, VEN causes oxidative stress by releasing ROS, which puts the cell under constant stress, resulting in increased expression of heat shock proteins (HSP60) (stress proteins). Thus, proliferation occurs to compensate for the injured cells. Furthermore, increased mean color intensity of α-SMA is attributable to increased number of myoepithelial cells, which is might be due to the compensatory activity of the gland with increased number of myoepithelial cells. This causes a contractile action, therefore helping in the release of the trapped secretions. Furthermore, myoepithelial cells with their processes enhance salivary emptying flow velocity and facilitate drainage of any nearby extracellular fluid, in addition to compressing the acinar and ductal cells[12].

Currently, the treated groups with FEB revealed marked improvement of VEN- induced structural changes of rat's parotid gland. Through which a nearly normal parotid gland histology was seen in H&E stained sections. Besides, significant decrease of the mean area percentage of collagen fibers, mean number of Ki 67 positive cells, mean colour intensity of both α-SMA and HSP60.

The previously mentioned findings show that FEB effectively reduces oxidative stress, inflammatory responses, and cellular proliferation, leading to considerable histological improvements. Through which FEB maintains the parotid gland's structural integrity and function by reducing ROS production and collagen deposition while normalizing cellular stress markers. These findings are in consistent with ***Nessa et al.*** (2021)[25].

The pharmacological actions of FEB include antioxidation, anti-inflammation, and anti-fibrosis that was also proved by ***Abdel-Aziz et al.*** (2020)[10]. In addition, different clinical researches proved that FEB possess a downregulating effect on the inflammatory as well as oxidative cell responses[9]. Febuxostat (FEB) is a non-purine-selective xanthine oxidase (XO) inhibitor used to treat chronic gout[26]. As a result, XO-induced oxidative stress and inflammatory reactions are decreased. FEB lowers inflammation by blocking TNF-α and IL-6 production[25]. Additionally, it was proved that FEB induced its anti-inflammatory effect through downregulating NF-κB signaling[27]. Moreover, it has the ability to downregulate the release of TGF-β1 so, inhibit the process of fibrosis[28].

Furthermore, FEB's antioxidant action is reported to be attributable to its downregulation of lipid peroxides and superoxide dismutase[10]. This is supported by other studies showing FEB antioxidant activity against a number of illnesses, including reduced hypertension and kidney damage. Furthermore, by reducing oxidative cell stress,

the regeneration of cell proteins, membranes, and DNA occurs. That is proven by the considerable improvement of cell proliferation status and restoration to normality, with Ki67 markedly reduced to normal levels[29]. Besides, the markedly decreased mean colour intensity of α-SMA be FEB is attributed to the improvement of cell state due to relieve of acinar and duct cell compression by the accumulated secretions caused by VEN[2]. In addition, it was previously proved that FEB could alleviates stress of the endoplasmic reticulum[30], an organelle concerned for protein synthesis so, alleviating cell stress-induced HSP60 immunohistochemical expression[31].

CONCLUSION

The previously described findings indicate that FEB could be a suitable therapy option for salivary gland dysfunction caused by antidepressants such as VEN. However, turning these insights into therapeutic applications would necessitate additional study, notably human trials, to demonstrate febuxostat's efficacy and safety in patients. To completely comprehend FEB's therapeutic potential, further study must investigate dose-response interactions, long-term effects, and functional outcomes.

AUTHOR CONTRIBUTION

Dr. Samah Kandeel: Research idea, collecting samples, slides examination, imaging, results interpretation, and scientific publication.; Dr. Remon Estfanous: Writing and results discussion, reference managing, collection of the scientific materials, writing revision.

CONFLICT OF INTERESTS

There is no conflicts of interest.

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التأثير الوقائى المحتمل لفيبوكسوستات على التغيرات التركيبية المستحدثة بالفينلافاكسين في الغدة النكفية فى ذكورالجرذان البيضاء البالغة: دراسة نسيجية و هستوكيميائية مناعية

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المقدمة: تتأثر الغدة النكفية بشكل متكرر بالتغيرات التركيبية والوظيفية الناجمة عن الأمراض والأدوية والإجهاد التأكسدي. وقد إرتبط فينلافاكسين، وهو مضاد إكتئاب شائع، بتأثيرات سلبية، بما في ذلك التغيرات التركيبية في الغدة النكفية. فيبوكسوستات، وهو مثبط أوكسيديز الزانثين ذو خصائص مضادة للأكسدة ومضادة للإلتهابات.

الهدف: هدفت هذه الدراسة إلى تقييم التأثيرات الوقائية المحتملة للفيبوكسوستات ضد التغيرات التركيبية الناجمة عن الفينلافاكسين في الغدة النكفية لدى ذكورالجرذان البيضاء البالغة بإستخدام التقنيات النسيجية والهستوكيميائية المناعية.

المواد والطرق: تم تقسيم خمسة وعشرين جرذ من ذكورالجرذان البيضاء البالغة إلى أربع مجموعات: المجموعة الضابطة، والفينلافاكسين، والكاربوكسي ميثيل سلولوز + فينلافاكسين، والفيبوكسوستات + فينلافاكسين. تم إعطاء العلاجات عن طريق الفم لمدة ٣٠ يومًا. وشمل الفحص النسيجي بإستخدام صبغة الهيماتوكسيلين والإيوسين وماسون ثلاثى الألوان هذا إلى جانب جانب التحليل المورفومتري. SMA، وHSP60وKi67

النتائج: أحدثت مجموعات فينلافاكسين وكاربوكسي ميثيل سلولوز + فينلافاكسين أضرارًا تركيبية واسعة النطاق، يوجد حويصلات غير منظمة ومنفصلة على نطاق واسع مع أوعية دموية متضخمة. وعلاوة على ذلك، أظهرت الحويصلات المصلية فجوات في خلايا بطانة الخلايا مع أنوبة متضخمة إلى جانب الخلايا المنفصلة. كما أظهرت بعض الحويصلات تراكم مادة محبة للحمض في تجويفها بينما كانت حويصلات أخرى متحللة. وفيما يتعلق بالقنوات المتداخلة والمخططة والإفرازية؛ فقد كانت متوسعة مع تجويف غير منتظم ونوى متضخمة. كما كانت هناك ارتشاح خلوي التهابي بين الحويصلات والأوعية الدموية المتضخمة..,زيادة ذو دلالة اجصائية فى النسبة المؤية المتوسطة لمساحة ألياف الكولاجين.

كما أن هناك زيادة ذو دلالة إحصائية لمتوسط عدد الخلايا الإيجابية لـ Ki67، ومتوسط شدة لون α-SMA، و HSP60 ونجحت مجموعة فيبوكسوستات في إحداث تحسن نسيجي هستوكيميائى مناعي مثل الطبيعى تقريبًا.

الإستنتاج: لقد نجح عقار فيبوكسوستات في حماية الغدة النكفية من التلف الذي يسببه عقار فينلافاكسين. كما أن خصائصه المضادة للأكسدة والإلتهابات تجعله خيارًا علاجيًا واعدًا لخلل وظائف الغدة اللعابية.