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Original article

Histopathological Effects of Reserpine Treatment Using Fluoxetine and Hordeum vulgare Extract on Some Vital Organs in Rats Depression Model

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Abstract
The current study set out to examine the histopathological effects of reserpine (Res) with fluoxetine (Flux) and Hordeum vulgare aqueous extract (HVE) in a rat model with subchronic depression. The tissues of the liver, kidney, testes, and brain were examined histopathologically. Liver histological changes include inflammatory leucocyte infiltration and mild hydropic degradation of the hepatocytes. When compared with a liver section containing only Res, the liver section including Res, Flux, and HVE showed greater restoration and hepatocyte improvement. Degeneration of renal tubules and interstitial capillary congestion were observed in the kidney treated with Res. Where the kidney received Res., Flux., and HVE, normal interstitial tissue was also found, as were the Bowman capsules with the glomerulus and renal tubules. The testis that was generated with Res. showed an uneven layer of spermatogonia, necrosis of the lining germinal epithelium, and significant degeneration of seminiferous tubules. The testis, however, is almost under control with normal seminiferous tubules and the entire structure after receiving Res., Flux., and HVE. Rats exposed to Res. exhibited brain abnormalities, including the presence of dead neuronal and non-neuronal cells in the second and third layers of the cortex. Additionally, fluoxetine-exposed individuals exhibited pyramidal cell death and Purkinje cell loss, as well as atrophy, degeneration, necrosis, and inflammation. After receiving Res., Flux., and HVE, the brain displayed a high level of restoration and some indications of recovery, including a regression in the size of the degenerative vacuoles. In conclusion, light microscopic analyses revealed that Fluoxetine showed partial protective effects against reserpine-induced histopathological alterations. on the brain, testis, liver, and kidney. In these tissues, however, HVE and fluoxetine showed improvement.
Keywords. Hordeum Vulgare, Fluoxetine, Depression, Reserpine, Histopathology.

Introduction

The fundamental mechanism of depression has been studied using reserpine in animal models [1,2]. Depressive symptoms are widespread in patients with end-stage renal illness [3] and are linked to mortality [4,5]. Depression is a medical condition characterized by low mood, loss of interest, hopelessness, sadness, and a disinclination to engage in activities. There may be a genetic component to some forms of depression since they frequently run-in families. But depression can also strike those who have no family history of the condition [6]. One of the most prevalent brain illnesses, major depressive disorder (MDD), frequently co-occurs with other mental disorders [7]. Quality of life is significantly reduced by depressive disorder, which is defined by decreased activity, a considerable and persistently negative mood, and slower thinking and cognitive function [8,9]. Fluoxetine is frequently used to treat depression, which primarily affects unhealthy people. According to experimental research, fluoxetine raised oxidant levels by increasing superoxide anion levels, decreasing antioxidant levels, and causing oxidative stress, suggesting that fluoxetine may induce oxidative stress in certain tissues. However, other studies have demonstrated its neuroprotective and antidepressant effects in experimental depression models [10,11]. These effects could be the reason for brain neuronal damage. However, other research revealed that fluoxetine had neuroprotective properties [12,13]. Hordeum vulgare Linn. (Poaceae), often referred to as barley, is an erect annual herb that grows 50 to 100 cm tall and is grown in both the plains and the steep Himalayan region up to 4000 m [14]. The seeds of this plant, known locally as Jav, are utilized by traditional healers to treat a variety of illnesses, including liver disorders [15,16]. The annual grass Hordeum vulgare is the source of the cereal grain barley.

It is an ingredient in many nutritious dishes. The grain is used locally in bread, biscuits, and the traditional barley meal, and it is used in soups and stews [17]. In Arabian traditional medicine, barley has been used to treat a variety of disorders affecting the central nervous system (CNS), primarily depression. Antioxidative flavonoids found in green barley leaf may also have antidepressant properties [18]. The flavones C-glycoside, saponarin, and lutonarin are found in barley leaves, which are among the best sources of antioxidants [19,20]. The current study set out to examine the histopathological effects of reserpine (Res) with fluoxetine (Flux) and Hordeum vulgare aqueous extract (HVE) in a rat model with subchronic depression.

Material and Methods

Using random assignment, thirty male rats were split into five equal groups: the first group was used as a control; the second group received 0.5 mg/kg of reserpine the model of depression (Res.) intraperitoneally (i.p.) for 20 alternate days; the third group received reserpine plus fluoxetine (Res. & Flux.) (10 mg/kg b.wt.); the fourth group received Res. plus HVE (1000 mg/kg b.wt.); and the fifth group was given Reserpine, Flux. & HVE.

studies involving histopathology. Following an instant saline wash, the tissues of the liver, kidney, testis, and brain were preserved in a 10% formalin solution. All these tissues were fixated, treated in a sequence of alcohols and xylenes, and finally embedded in paraffin wax. Haematoxylin and eosin were used to stain each of the serial sections, which were cut

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to a thickness of 5–6 µm. The slides were taken and examined under light microscopy (LM) for any structural alterations [21, 22].

Results

Histopathological examination

Liver

(Figure 1. A) depicts the typical anatomy of a healthy, controlled rat liver. Single-nucleated polyhedral hepatocytes are typical. From the lobule perimeter to its central vein, the hepatocytes are arranged radially, producing a layer that is one or two cells thick. Kupffer cells, which are phagocytic cells, are found in the liver sinusoids, which are extremely thin connections. Rats' livers in the Res-treated group had atypical hepatocytes, lymphatic infiltration in the portal region, and vacuolar degeneration (Figure 1.B). Res. & Flux were administered to the group. Infiltration and hemorrhage around hepatic cells, as well as an increase in Kupffer cells and vacuolation, were seen in (Figure 1.C). Res. & HVE were used to treat the group. In comparison to the Res alone, the liver portion had a higher level of repair (Figure 1.D), and hepatocytes also exhibited improvement. When Res., Flux., and HVE were administered to the group, the liver tissues showed a modest recovery (Figure 1.E). Although the size and activity of the Kupffer cells continued to expand, there was no discernible improvement.

Kidney

A photomicrograph of the T.S. kidney from an untreated control rat demonstrates typical Bowman's capsules with a glomerulus. Normal tubules in the kidneys. Interstitial is typical as well (Figure 2. A). Interstitial capillary congestion and renal tubule degradation were seen in the group receiving Res. kidney treatment (Figure 2. B). Mild renal tubule degradation and glomerular restoration were seen in the group treated with Res. & Flux (Figure 2.C). Normal Bowman capsules with glomerulus and normal renal tubules were seen in the group treated with Res. & HVE (Figure 2.D). Interstitial tissues are normal as well. When the kidney tissues were administered, Res., Flux., and HVE (Figure 2.E), the glomeruli and urinary tubules were shown to be normal.

Testis

The T.S. testis photomicrograph from the untreated control rat displays normal seminiferous tubules with normal primary and secondary spermatocytes, as well as spermatozoa-filled lumen. Normal interstitial tissues are shown in Figure 3. A. With necrosis of the lining germinal epithelium and an uneven layer of spermatogonia, the testis in the group treated with Res. showed extensive degeneration of seminiferous tubules (Figure 3. B). In the group, Res. & Flux were used. Some obvious indications of testis structures were shown in (Figure 3.C). The testicular anatomy of the group treated with Res. & HVE (Figure 3.D) was close to control, with normal seminiferous tubules and all structures. There are obvious indications of testis healing in the group administering Res., Flux. & HVE (Figure 3.E). Spermatozoa with normal interstitial tissue are seen in the lumen of seminiferous tubules and in the normal germinal epithelium.

Brain:

Fluoride's effects on the brain revealed normal glial and pyramidal cell architecture as well as a normal grey matter architecture with several layers. A series of twisted folds make up the cortex. It is separated into three layers: the granular layer, Purkinje cell layer, and molecular layer (Figure 4. A). However, rats exposed to reserpine had abnormalities in their brains, including the presence of dead neuronal and non-neuronal cells in the second and third layers of the cerebral cortex. Atrophy, degeneration, necrosis, and inflammation are also present. (Figure 4. B).
Examining the rats' brains under a light microscope revealed that the granular layer, Purkinje cells, and molecular layer were all rather healthy in the group that received fluoxetine treatment. (Figure 4. C). The group received HVE and Res. In the brain portion, the degenerative vacuoles had receded in size, indicating some symptoms of recovery and an advanced degree of repair (Figure 4. D). The Purkinje cell layer clearly exhibited evidence of improvement, and the group administration of Res., Flux., and HVE. demonstrated better recovery. There were obvious signs of improvement in neuroglia cells (Figure 4. E).

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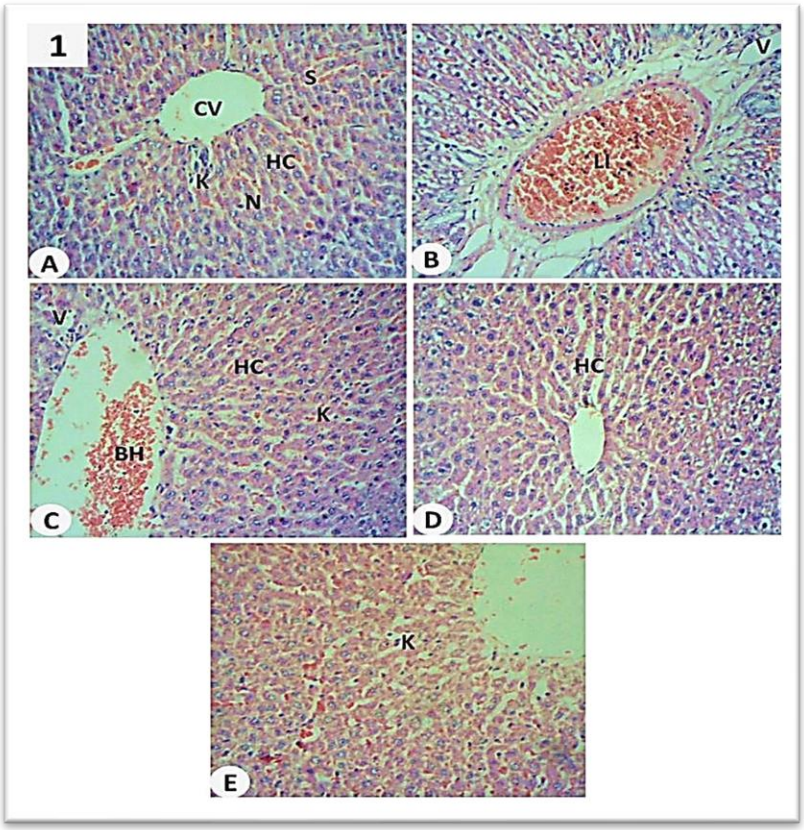

Figure 1. A. Photomicrograph of a section of liver control hepatocytes was normal polygonal with oval-shaped nuclei. (H.&E., 100X). B. Rat with Res. treated only. C. Res. treated animal with Flux. D. Res. treated model with HVE. E. Res treated model with Flux. and HVE.

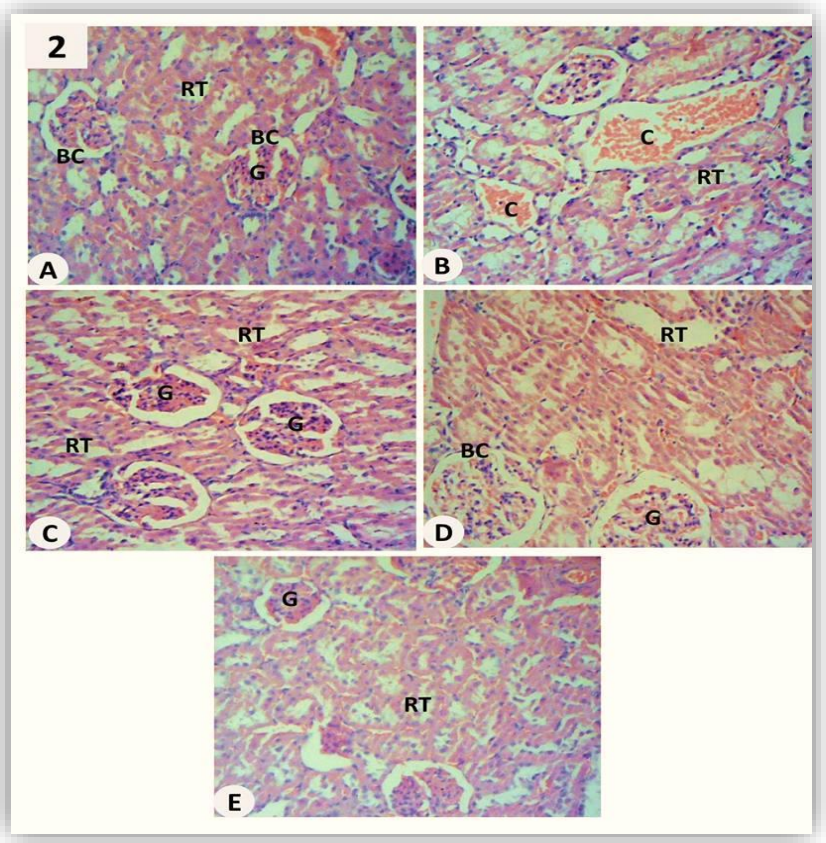

Figure 2. Transitional section of kidney tissue stained with H&E (magnification 100 X): A. Normal control rat was intact structure of kidney layers. B. Rat with Res. treated only. C. Res. treated animal with Flux. D. Res. treated model with HVE. E. Res treated model with Flux. and HVE.

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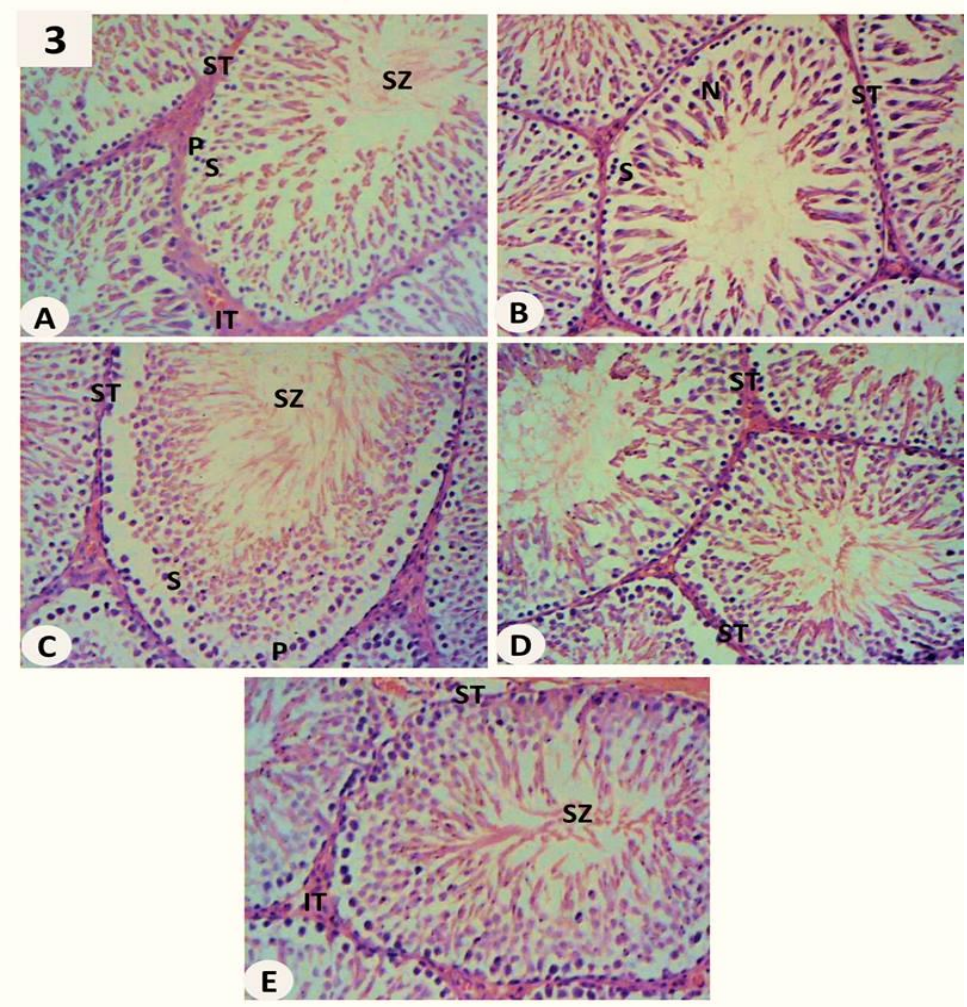

Figure 3. Transitional section of testis stained with H&E (magnification 100 X): A. Normal control rat was intact structure of the testis layers. B. Rat with Res. treated only. C. Res. treated animal with Flux. D. Res. treated model with HVE. E. Res treated model with Flux. and HVE.

Discussion

The detrimental effects of fluoxetine exposure on the liver in both human and animal models have been the subject of several studies. In clinical studies, fluoxetine treatment has been linked to acute hepatitis, hepatic alterations, and elevated aminotransferase levels in both humans and animals [23, 24]. When compared to liver sections of fluoxetine that were not administered, these histological alterations included the existence of hydropic degeneration of hepatocytes, which was consistent with the findings of [25], and inflammatory leucocyte infiltration, which was also shown in the results of [26]. These liver histological alterations might be brought on by fluoxetine's harmful effects [27]. Fatty hepatocytes, hepatic sinusoidal congestion, damaged cells, hepatic strand disruption, vacuolated cytoplasm, and necrosis were all observed in the liver. Concurrent HVE supplementation has improved liver tissues and almost brought them back to normal [28, 29]. The experimental groups' brain slices showed Purkinje cell degeneration and edema. Neuronal damage is suggested by these findings [30, 31].

According to research by [32], fluoxetine can cure the behavioral abnormalities shown in mice that received a combination of stress and fluoxetine (10 mg/kg) for five weeks, plus a week of pre-treatment. Studies by Yau JL et al., also revealed similar results, showing that treating stressed rats with antidepressants corrected their behavioral abnormalities [33].

Like the findings of [34,35] revealed that fluoxetine produced injury to the male genital organs, which resulted in a substantial decrease in sperm concentration and reduced sperm motility (reversible). However, our histopathological results support the previous finding of Elbakry et al., on a physiological and behavioral study on a depressed rat model treated with Hordeum vulgare extract [36], Although some studies have suggested that fluoxetine may induce oxidative stress and tissue damage under certain conditions, the present study showed that fluoxetine treatment partially improved the histopathological alterations induced by reserpine. This suggests that fluoxetine may exert protective effects in the context of reserpine-induced depression.

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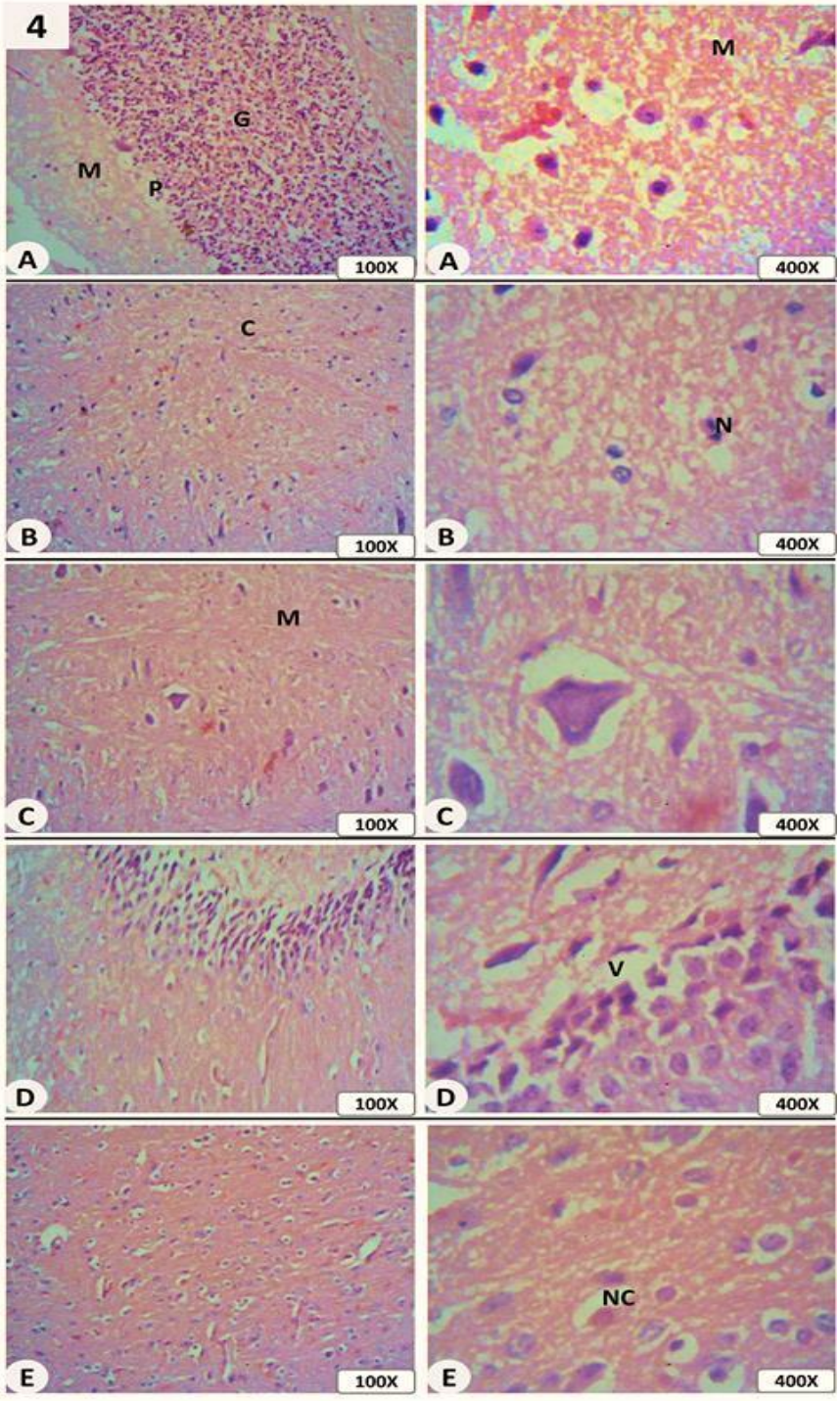

Figure 4. Transitional section of cerebellum tissue stained with H&E (magnification 100 X & 400 X): A. Normal control rat was intact structure of cerebellar cortex layers. B. Rat with Res. treated only. C. Res. treated animal with Flux. D. Res. treated model with HVE. E. Res treated model with Flux. and HVE.

Conclusions

Based on the histological examination of liver, kidney, testis, and brain tissues, the results suggest that both HVE (Herbal Extract/Experimental Variable) and fluoxetine possess notable antidepressant-like activity. These effects were reflected not only in the behavioral outcomes but also in the preserved or improved structural integrity of key organs involved in systemic and neurological function. The findings point toward the potential therapeutic value of HVE as a natural antidepressant alternative, either alone or in combination with conventional drugs like fluoxetine. However, to fully validate these observations, further detailed scientific and clinical studies are essential. These should aim to clarify the precise mechanisms of action, determine optimal dosages, evaluate potential side effects, and establish the specificity of HVE's effects in comparison to standard antidepressants. Moreover, investigating pharmacokinetics, long-term safety, and efficacy in human subjects will be crucial before clinical application can be recommended.

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