# Study the Negative Effects of Pseudoephedrine on Brain Tissues in Adult Albino Male Rats

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## Abstract

In this study, (24) male animals were used, which were divided randomly into four groups. Each group included (6) animals, which are: the control group that was given drinking water and food daily, and the group of rats treated with pseudoephedrine at a dose of (40) mg / Kg of body weight for a period of (30) days, the group of rats treated with pseudoephedrine at a dose of (40) mg / kg of body weight for a period of (40) days, the group of rats treated with pseudoephedrine at a dose of (40) mg / kg of body weight for a period of (50) days, the animals dosed the drug by the oropharyngeal tube at a dose of (1) ml, and after the end of the experiment, the animals were scarified , brain samples were taken and preserved with formalin at a concentration of 10% until the tissue sections were made, when the meningeal membrane appeared the upper layers of the cerebral cortex in the group treated with pseudoephedrine for a period of 30 days were close to normal, while the group treated with pseudoephedrine for a period of (40) days showed shrinkage in the deep layers of the cerebral cortex and hemolysis in many blood vessels, and the meningeal membrane appeared.

***Key words:*** *nervous system, pseudoephedrine, brain tissue, male rats.*

## Introduction

The nervous system in the human body consists of the central nervous system and the peripheral nervous system, and the nervous system is responsible for controlling the functions of the human body, analyzing incoming stimuli and integrating internal and external responses, and the central nervous system (CNS) includes the brain and spinal cord, and the peripheral nervous system ( PNS) consists of sensory receptors that bring information to the central nervous system and motor nerves that transmit information away from the central nervous system to facilitate response to stimuli, and the autonomic nervous system uses components of the central nervous system and the peripheral nervous system to regulate automatic or involuntary responses to stimuli [(1)] People use many types of drugs in the treatment of various diseases, including pseudoephedrine, which is a drug that mimics the sympathetic nervous system of the chemical class of amphetamines, It is used as a sinus decongestant and as a tonic or vigilance enhancing agent that is found singly or in combination with antihistamines or with paracetamol [(2)].

The mechanism of action of pseudoephedrine depends directly on the adrenergic receptor system, as it is believed that the narrowing of the blood vessels produced by pseudoephedrine is primarily a response to the α-adrenergic receptors [(4)], alpha-adrenergic receptors are found on the muscles lining the walls of blood vessels, and when these receptors are activated, the muscles contract, which leads to constriction of the blood vessels that allow less fluid to enter the lining of the nose, throat and sinuses and thus Reduced inflammation of the nasal membranes as well as decreased production of mucus, relaxation of smooth muscles in the bronchi and expansion of the airways, which reduces congestion [(4.14)].

## Materials and Methods

### Experimental animals used in the study

In this study, adult white male rats, whose weight ranged between (230-270) gm, and their ages (2.5-3) months, were used in this study. They were prepared from the animal house of the College of Veterinary Medicine / University of Tikrit, and placed in cages for creditors with metal covers. With dimensions of (12 x 24 x 40) cm, water and food were given in sufficient quantities throughout the period of the experiment, which lasted 30 days, until the animals were dissected and brain samples were taken for the purpose of making the histological sections, examining and imaging them.

### The drug used in the study

Pseudoephedrine drug was used in the form of a powder, it was dissolved in distilled water and the animals were dosed at (1) ml at a concentration of (40) mg / kg of body weight [5], the solution was prepared daily.

### Experience design

In this study, (24) animals were used from the adult white male rats, which were randomly divided into four groups. Each group included (6) animals, which are as follows: -

**1- The first group (G1):** the control group. This group was given regular drinking water and food (standard diet) daily for (50) days.

**2- The second group:** the group of rats treated with pseudoephedrine at a concentration of (40) mg / kg of body weight, and the drug was dosed by the oropharyngeal tube at a dose of (1) ml and given water and normal food for a period of (30) days.

**3- The third group**: a group of rats treated with pseudoephedrine at a concentration of (40) mg / kg of body weight, and the drug was dosed by the oropharyngeal tube at a dose of (1) ml and given water and regular food for a period of (40) days.

4- **The fourth group:** the group of rats treated with pseudoephedrine at a concentration of (40) mg / kg of body weight, and the drug was dosed by the oropharyngeal tube at a dose of (1) ml and given water and normal food for a period of (50) days.

### Histological Study

Tissue sections were prepared and stained with hematoxylin and eosin stain according to the method by [6].

## Results and Discussion

### Control group

In the control group rats, the cerebral cortex appeared surrounded by the inner meningeal membrane (pia mater), below it the external molecular layer containing a few small neurons, and the number of neurons and glial cells increased at the external granular layer. Then, the cells increased more in the external pyramidal layer, while the inner granular and inner pyramid layer, most of the neurons were surrounded by a transparent band devoid of tissue features, as shown in Figure (1).

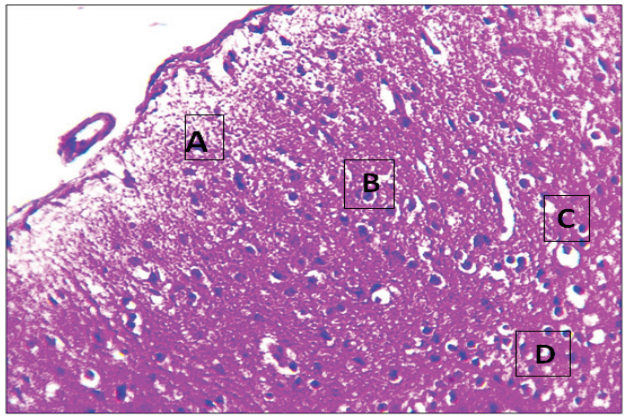


**Figure (1) cerebral cortex in the control group: shows the inner meningeal membrane (A), the molecular layer that contains neurons and glia (B) the outer granular layer (C) the inner pyramidal layer (D), magnification force X40, stained with H&E stain.**

**2. The group treated with pseudoephedrine for 30 days.**

The meningeal membrane and the upper layers of the cerebral cortex appeared in the group treated with pseudoephedrine drug for a period of 30 days, close to the normal state, as in figure (2), while the deep layers of the cerebral cortex showed thickening in the nuclei of nerve cells, breaking down and degenerating some other neurons and vacuolation around each other as in Figure (3).

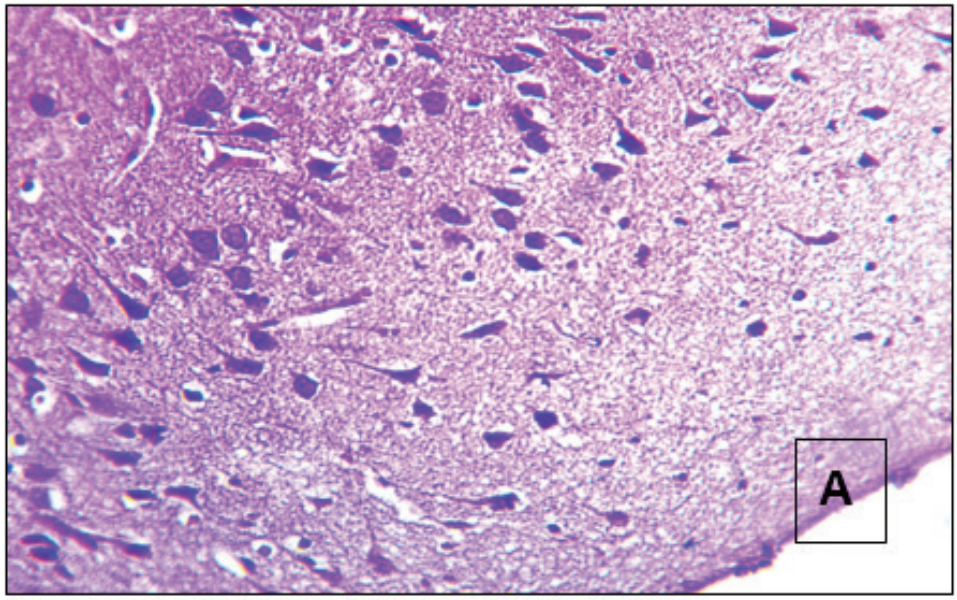


**Figure (2) the cerebral cortex in the treatment group for 30 days: the meningeal membrane appeared (A), the layers of the cerebral cortex close to normal, magnification force X40, stained with H&E stain.**

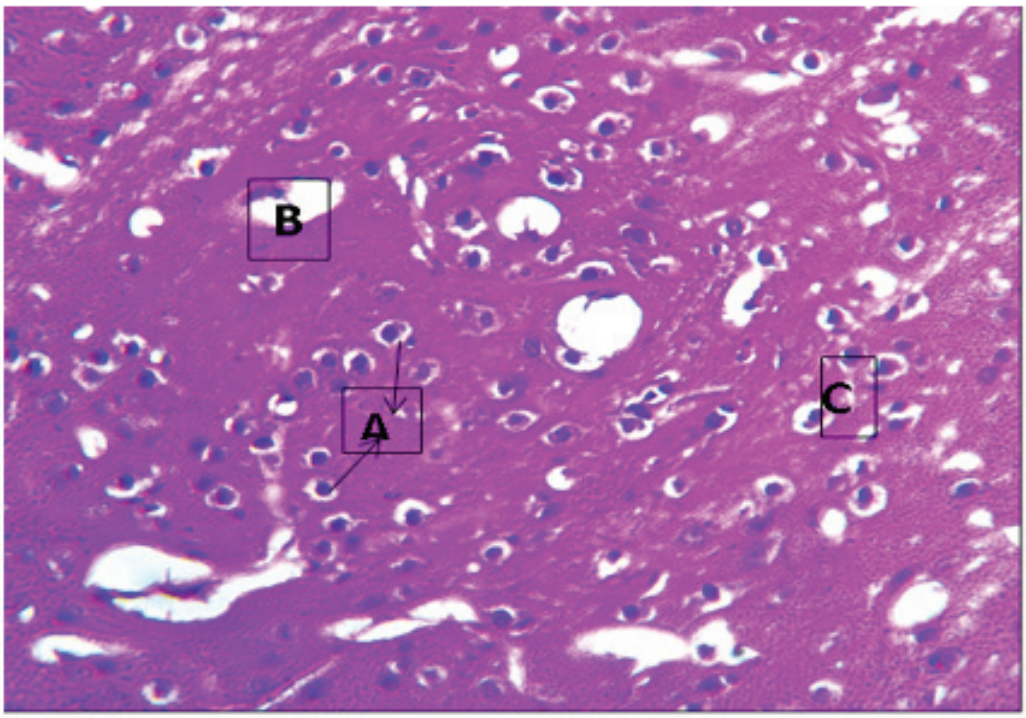


**Figure (3) the cerebral cortex in the pseudoephedrine group for 30 days: the nuclei of the neurons thicken (A), the nerve cells are broken and ruptured (B), the cells around the nerve cells are shattered (C), Magnification force X40, stained with H&E .**

**3. The group treated with the Pseudoephedrine drug for (40) days.**

The meningeal membrane of the cerebral cortex appeared in the group treated with pseudoephedrine for a period of (40) thickened days, and many vacuole were found around many pyramidal cells as in figure (4), while the deep layers of the cerebral cortex showed shrinkage of neurons and hemolysis in the blood vessels as in the figure (5).

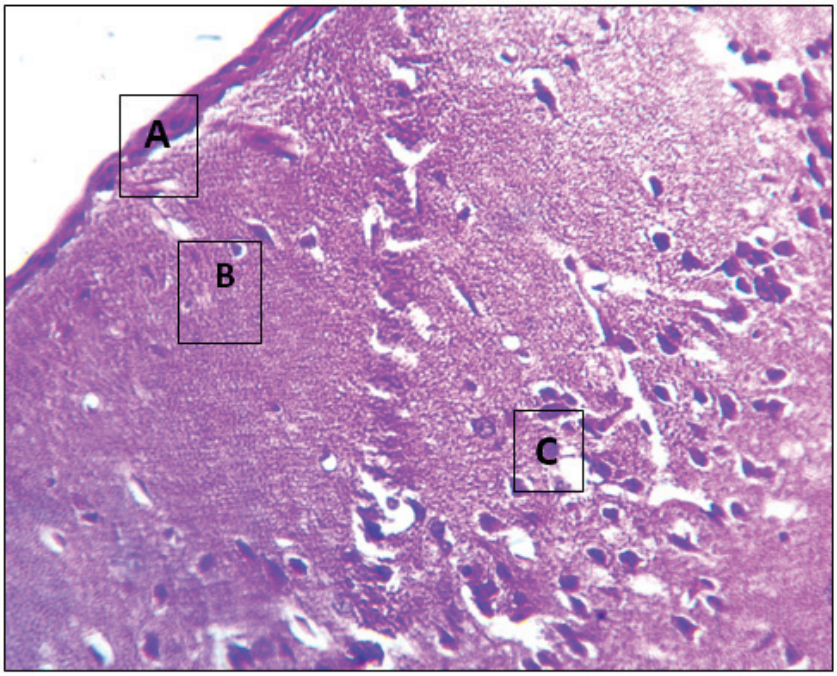


**Figure (4) Cerebral cortex in the pseudoephedrine group for 40 days: the meningeal membrane of the cerebral cortex thickens (A), the molecular layer with specific neurons (B) vacuolation around the outer pyramidal cells (C), magnification force X40, stained with H&E stain.**

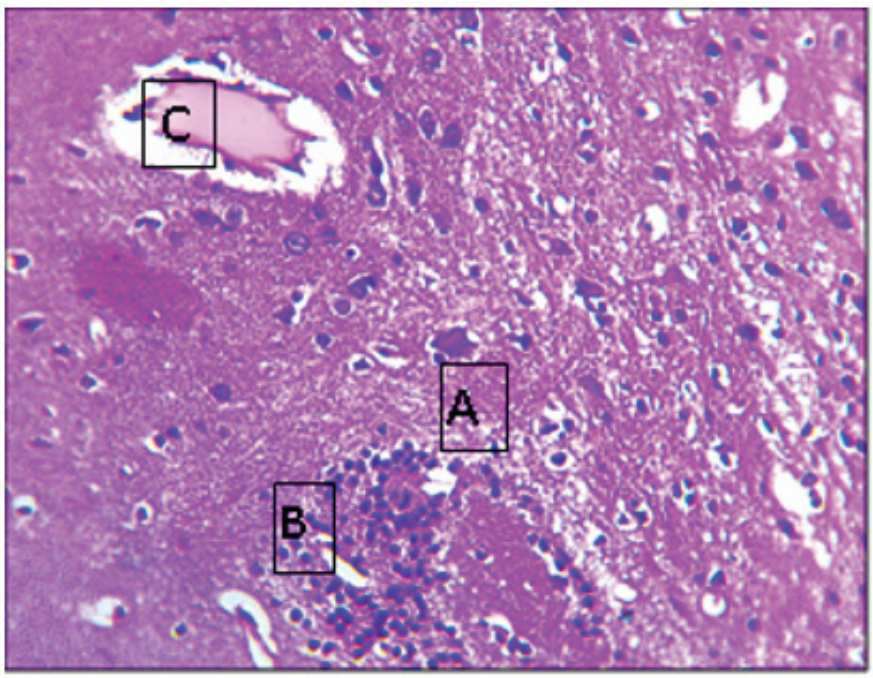


**Fig. (5) The cerebral cortex in the pseudoephedrine group for 40 days: Neuronal shrinkage (A) vacuolation (B) hemolysis in a blood vessel (C),.magnification force X40, stained with H&E stain.**

**4. The group treated with pseudoephedrine for (50) days**.

The meningeal membrane (arachnoid pain) appeared in the group treated with the drug ephedrine for a period of (50 days) thickened, highly tortuous and semi-separated from (pia mater). The meningeal artery was subarachnoid with large blood congestion, and a pool of blood appeared under the pia mater and surrounded by numbers of Glial cells, as the molecular layer appeared in the form of multiple foamy vacuoles and similar to a sponge pattern as in Figure (6).

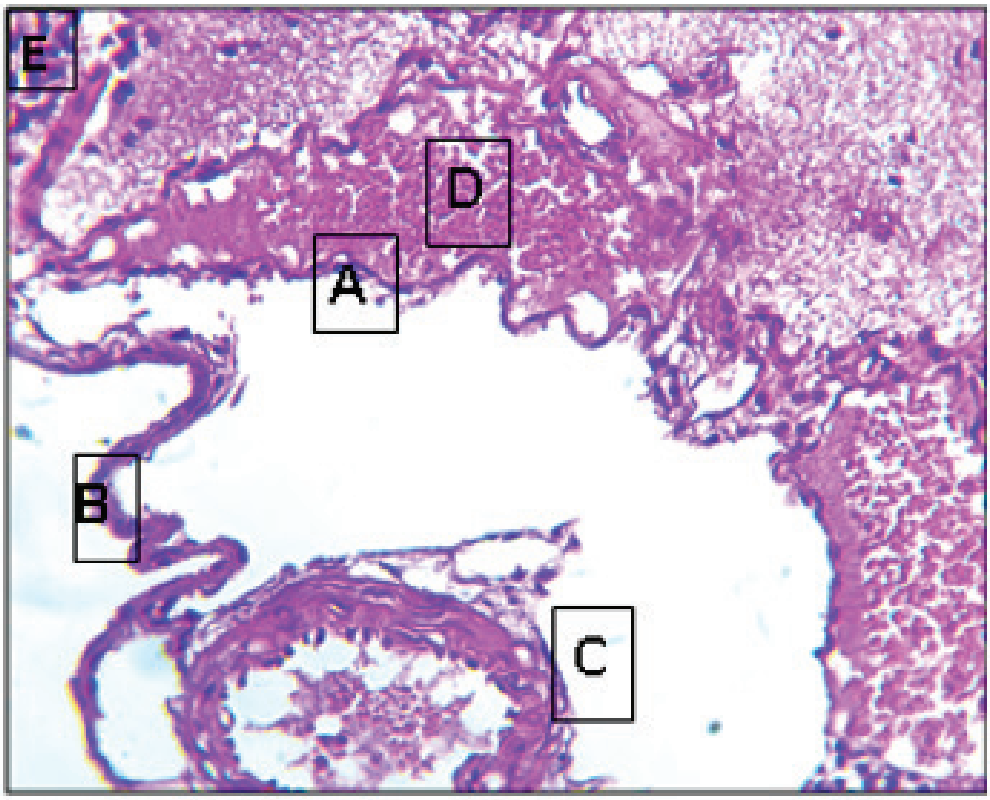


**Fig (6) cerebral cortex in the pseudoephedrine group for 50 days: the inner meningeal membrane of the cerebral cortex (A), arachnoid membrane (B), almost complete detachment, congestion (C), pool of blood under the inner meningeal (D), glial cells (E) ,agnification force X40, stained with H&E stain.**

The results of the histological examination of the brains of rats treated with the drug Pseudoephedrine for (30) days showed that the nuclei of some nerve cells thicken, degenerated in other nerve cells and vaculation around many cells of the cortex and medulla, as well as the degeneration of Purkinje cells. These effects may be due to the occurrence of neuritis resulting from take pseudoephedrine drug, which leads to the overproduction of dopamine and thus worsens the neurodegeneration, and thus this study agrees with a study [7,8] which showed the occurrence of neurodegeneration by increasing the intake of the drug Pseudoephedrine.

The tissue injury appeared more severe in the brains of rats treated with the drug pseudoephedrine for a period of (40) days, as the meningeal membrane was thicker than in the previous group and degeneration and shrinkage occurred in many nerve cells, and in many layers of the brain, as well as hemolysis and glial cell enlargement, which it may indicate that pseudoephedrine has triggered an immune response in the brain and activated a special type of immune cells called c-fos immunohistochemistry that is an indicator of neuronal damage [9], which is expressed under the influence of some addictions inducing drugs such as opiates, amphetamines and ephedrine [10,11] the effect of pseudoephedrine reached

its maximum in the brains of the group treated with this drug for a period of (50) days, as the arachnoid membrane appeared almost separate from the pia mater. Arterial congestion and widespread vacuolization and thickening of the nuclei of nerve cells and the gathering and infiltration of a number of glial cells, which in most cases leads to the occurrence of gliosis which is a non-specific, reactive change of glial cells that occurs in response to the central nervous system(CNS) injury and in which the enlargement of different types of glial cells such as astrocytes, microglia and oligodendrocytes, leads in chronic cases to the formation of glial scars[12], or perhaps chronic use of pseudoephedrine leads to the activation of a special type of neuron that is considered a protein called Regenerating islet-derived protein 3 alpha that is encoded by the REG3A genes and these cells have an effect on the functions of the meninges and thus increase the degeneration of neurons, especially in the cerebral cortex. Thus, this study is in agreement with the study [13.15], which showed the occurrence of degeneration in nerve cells after chronic use of the pseudoephedrine drug.

## Conclusion

The results of the histological examination of the brains of rats treated with the drug Pseudoephedrine for 30 days showed that the nuclei of some nerve cells thicken, degenerated in other nerve cells and vaculation around many cells of the cortex and medulla, as well as the degeneration of Purkinje cells. These effects may be due to the occurrence of neuritis resulting from take pseudoephedrine drug, which leads to the overproduction of dopamine and thus worsens the neurodegeneration, and thus this study agrees with a study, which showed the occurrence of neurodegeneration by increasing the intake of the drug Pseudoephedrine.

**Ethical Considerations:** All Research participants haven't been subjected to any kind of harm in any way.

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**Conflict of Interest:** The author declare no conflict of interest regarding this research.

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