



Efficacy of *Urtica dioica* extract for amelioration of brain lesions induced by ethylene glycol in male rabbits

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Abstract

The nervous system is the most delicate organ to neurotoxic substances that affects the development of neurochemicals, including neurotransmitters, and organization of ion channels. *Urtica dioica* (Nettle) is one of the medicinal plants, which has been increasingly highlighted used for its anti-inflammatory and anti-oxidative components. This study aimed to evaluate the improvement effects of *Urtica dioica* extract on the histopathological lesions of nervous system in rabbit model. Fifteen male rabbits of 700-800 grams separated into three groups, the first group is the control, and the second group were treated with 0.75% ethylene glycol (EG) in water for 30 days, group three were combination treated group with both EG and *Urtica dioica* at 100 mg/kg for 10 days. Microscopic histological examination discovered generalized congestion of blood vessels at the cerebrum and cerebellum, degeneration and necrosis of the neuronal cells of the cerebral cortex which characterized by swelling of the degenerative cells, while necrotic cells characterized by shrunken and pyknosis of the cells in the cerebellum cortex presents of inflammatory cells in the meninges. In conclusion, the histopathological examination of brain sections of rabbits treated with ethylene glycol in addition to *Urtica dioica* extract showed slight improvement in the histological pictures of the cerebellum and cerebrum.

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Introduction

Recently, the interest of researchers and scientific studies has increased in the use of herbs and medicinal plants that contain effective compounds that give them medicinal and therapeutic properties (1). The cerebellum and cerebrum tissues are the most delicate organ to neurotoxic materials that affects the mechanisms of neurochemicals, like neurotransmitters, and organization of ion channels (2). *Urtica dioica* (Nettle) is a curative plant, which has been increasingly highlighted used for its anti-inflammatory and anti-oxidative components (3). Is a Persistent herbaceous green herbal in the family of Urticaceae; it includes several vitamins include A, C, D, thiamine and riboflavin as well as minerals Like cobalt, magnesium, calcium, phosphorus, copper, iron, potassium, sulfur and zinc. Theses numerous phytochemicals substance that important on

defeat free radical molecules have been seriously determined (4,5). Ethylene glycol (EG) is a well-known toxic compound, it is a colorless, odorless, sweet liquid, commonly found in antifreeze. the hypothesis of which can be deadly to animals in addition to man (6). EG intoxication can damage various organs and systems but predominantly encompasses the central nervous, cardiac, pulmonary and renal tissues. Limited information is available on the pathological features of EG poisoning specially on brain tissue. After absorption, EG is first break down in the liver to glycolaldehyde by dehydrogenase. Then glycolaldehyde is oxidized to glycolic acid, glyoxylic acid and transformed to oxalic acid, Whereas EG itself causes harmfulness, accumulation of poisonous metabolites is accountable for the lethal acidosis and kidney failure (7). Various organs hurt are for the most part because of the different poisonous metabolites which have various harmful impacts at the cell level including for the electron

transfer chain, oxidative phosphorylation, glucose digestion, and DNA replication (8). The goal of this research is to study of the effects EG on nervous parenchyma in rabbit animals, concentrates on microscopic lesions, and the viability of *Urtica dioica* extract for enhancement of cerebral tissue injuries.

Materials and methods

The present study was authenticated by scientific committee in the Pathology department, College of Veterinary Medicine, University of Mosul, Iraq. *Urtica dioica* (Nettle) was collected from Mosul area it was classified according to plant classification references related to medicinal plants. The extraction procedure started with drying the plant in room temperature at least 1-2 weeks. The dried out plant were smashed into powder. Two gram dissolved in 100 ml water, boiling at least for 1 hour and filtered before use (9).

Animal

The current research was authenticated by scientific committee in the Pathology and poultry diseases department, Veterinary Medicine College, Mosul University, Iraq. 15 Male locale rabbit's weightings between 700-800 gm were separated into 3 groups, 5 animals for each. The first group reflect control and treated on normal laboratory diet and water ad labium. The 2nd group treated with 0.75% EG in water for 30 days (10). The 3rd group were treated with both EG and *Urtica dioica* 100 mg/kg for 10 days. Finally, at the experiment end, animals euthanized and the brain tissue gathered, and saved in 10% neutral buffered formalin for the tissue slide sectioning (11). These slide sections examine for histopathological alterations.

Results

The microscopically slide inspection of brain specimens collected from rabbits treated with ethylene glycol at the dose 0.75% in water for 30 days, show degenerative and necrotic neuronal cells of the cerebral cortex which characterized by swelling of the degenerative cells, while necrotic cells characterized by shrunken and pyknosis of the cells in the cerebellum cortex and also generalized blood vessels congestion at the cerebrum and cerebellum. There is Hemorrhage and congestion of blood vessels with inflammatory cells infiltration in meninges (meningitis) also observed. Vasogenic edema with vasculitis, extracellular edema (vascularization) were remarkable in the cerebrum. Another sections revealed necrotic cells surrounded by macrophages (neurophagia). Focal infiltration of glial cells leads to development of glial nodules. Also there is thickening of blood vessels wall, infiltrated with inflammatory cells. The histopathological changes of cerebellum revealed severe congestion of blood vessels, Purkenji cells atrophy, which seem decrease in number, also

there were degenerative and necrosis of the granular cells of the cerebellum (Figure 1). As far the histopathological examination of brain sections of rabbits treated with ethylene glycol in addition to *Urtica dioica* extract showed slight improvement in the histological pictures of the cerebellum and cerebrum (Figure 2).

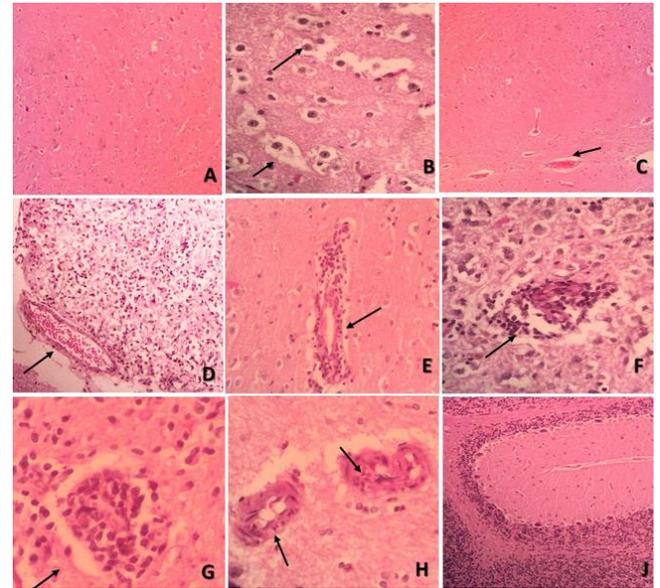


Figure 1: Brain of Rabbit of ethylene glycol group (A) control with normal architecture (H&E 10x). (B) Degenerative & necrotic neuronal cells in the cerebral cortex (arrow) (H&E 40x). (C) Vascular congestion at the cerebrum and cerebellum (arrow) (H&E 10x). (D) infiltration of inflammatory cells in the meninges (meningitis) with vascular congestion (arrow) (H&E 10x). (E) Vasogenic edema with vasculitis and extracellular edema (vascularization) (arrow) (H&E 40x). (F) neurophagia, which characterized by necrotic cells surrounded by macrophages (H&E 40x). (G) Focal infiltration of glial cells lead to development of glial nodules (Arrows) (H&E 40x). (H) thickening of blood vessels wall infiltrated with inflammatory cells. (H&E 40x). (J) degenerative and necrosis of the granular cells of the cerebellum (H&E 10x).

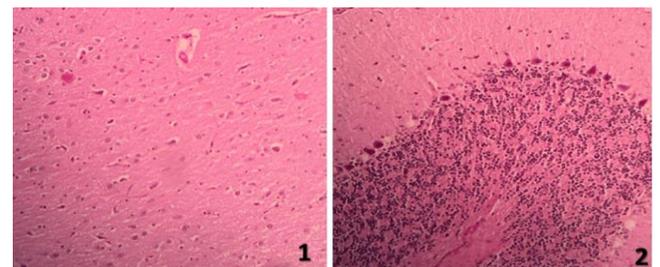


Figure 2: Brain of Rabbit of ethylene glycol and *Urtica dioica* group (1 & 2) slight improvement in the pathological lesions in cerebellum and cerebrum (H&E 10x).

Discussion

Urtica dioica is an herbaceous plant it is a flowering and perennial plant, it is from the family Urticaceae and the genus *Urtica*. It grows in Europe, Asia, North Africa and North America (12).

EG is considered one of the oxidizing compounds that have high toxicity in the nervous system. The present study demonstrated that rabbits treated with EG for a period of 30 days showed thickening of the blood vessel wall of the central nervous system, additionally to the degeneration and necrosis of nerve cells. as well as the occurrence of vasogenic edema that reported and agreed with other researcher Pomierny *et al.* (13) where they concluded that the harmfulness of EG agents leads to the incidence of cerebral edema and brain injuries.

The rapidly absorbed characteristic of ethylene glycol the digestive tract, and the metabolized by the action of the alcohol dehydrogenase enzyme present in the liver, this leads to fast turns into four secondary molecules, which are (glycolaldehyde, glycolic acid, glyoxylic acid and oxalic acid), which are considered high toxic to cells and cause deposition of Ca⁺ oxalate crystals in the wall of blood capillaries with cerebral edema, petechial hemorrhage and perivascular infiltration (14).

The direct toxicity of the metabolites of the ethylene glycol leads to the occurrence of hypoxic ischemic encephalopathy, which causes degeneration and necrosis of nerve cells due to the lack of blood supply (15).

Also the histopathological lesions in the brain parenchyma may be correlated to the free radicals that causing oxidative damage, and the uncontrolled among ROS formation and the ability of anti-oxidant substances to scavenge them. These reactive oxygen species causing cell membrane and organelles damage and formation of another lethal molecule.

Free radicals can trigger of NF-κB, a redox-sensitive transcription factor that activated the inflammatory genes and leads to releasing of mediators of inflammation (2).

The nettle plant has a protective effect by containing phenolic compounds that have the ability to scavenge the free radicals resulting from the oxidation process by the action of the agent compound glycol (16).

The outcomes of this research showed that the dealing of rabbits with the *Urtica dioica* for 15 days after being treated with the ethyl glycol showed an enhancement in the histological lesions of the central nervous tissue, this might be due to the anti-inflammatory characteristics of herbal substances (17), also other studies demonstration that animals treated with *Urtica dioica* showed decline in free radicals and oxidative stress in central nervous tissue as well as increase in the binding of DNA with activator protein -1 (AP-1), hence *Urtica dioica* consider as an active antioxidant and anti-apoptotic herbs additions which can enhancement and promoting cell survival in brain tissues (18).

Conclusions

This research discussed the threats of central nervous tissue damage because of exposure to ethylene glycol and *Urtica dioica* extract showed slight enhancement in the histologic pictures of the cerebellum and cerebrum.

Acknowledgment

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Conflict of interest

The researcher announce that no conflict of interest exists.

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قابلية مستخلص القريص على الحد من آفات الدماغ المستحدثة بالإيثيلين كلايكول في ذكور الأرانب

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الخلاصة

الجهاز العصبي هو الجهاز الأكثر حساسية للمواد السامة العصبية التي تؤثر على تطور المواد الكيميائية العصبية، بما في ذلك الناقلات العصبية وتنظيم القنوات الأيونية. نبات القراص هو أحد النباتات الطبية والتي تم تسليط الضوء بشكل متزايد على استخدامها لمكوناتها المضادة للالتهابات والمضادة للأكسدة. هدفت هذه الدراسة إلى تقييم التأثيرات التحسينية لمستخلص نبات القراص على الآفات النسيجية المرضية للجهاز العصبي في نموذج الأرانب. خمسة عشر أرنباً من الذكور تراوحت أوزانها بين ٧٠٠-٨٠٠ غم قسمت عشوائياً إلى ثلاث مجموعات، المجموعة الأولى هي مجموعة السيطرة والمجموعة الثانية عوملت بتركيز ٠,٧٥٪ من الإيثيلين كلايكول في الماء لمدة ٣٠ يوماً، المجموعة الثالثة عوملت بالإيثيلين كلايكول ونبات القراص ١٠٠ ملغم/كجم لمدة ١٠ أيام. أظهر الفحص النسيجي احتقان في الأوعية الدموية في كل من المخ والمخيخ، مع ملاحظة تنكس وتخر في الخلايا العصبية للقشرة الدماغية وفي المخ فضلاً عن ارتشاح الخلايا الالتهابية في السحايا. وفي الاستنتاج، أظهر الفحص النسيجي المرضي لأجزاء المخ للأرانب المعالجة بالإيثيلين كلايكول بالإضافة إلى مستخلص نبات القراص تحسناً طفيفاً في الصورة النسيجية للمخيخ والمخ.