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The Ameliorating Effect Of Co_Enzyme Q10 On Kidneys After Administration Of Ivermectin In Rabbits

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Abstract.*The goal of the current research is to ascertain whether Coenzyme Q10 can prevent or mitigate damage to the kidney tissues that are harmed when rabbits are given ivermectin. In this investigation, 48 healthy adult male albino rabbits, weighing between 1350 and 1800 grams, who were between 13 and 14 weeks of age, were used. Eight animals each were split up into six identical groups by the groups.Control group A. Groups B, C, and D of rabbits received 2 mg/kg of the drug every week. After stopping ivermectin for eight weeks,. B: Perform direct tissue slicing; C: Give Coenzym q 10 (10 mg/kg) once daily for 30 days; D: Use rabbits Give self-healing 30 days. F = just Coenzym q10 10mg/kg for 30 days; E = ivermectin 2 mg/kg every week For eight weeks and 10 mg/kg of Coenzyme Q10.. The outcomes revealed The renal polycysts, inflammatory cells infiltration and necrosis of the renal tubules' lining epithelial cells, and atrophy or vaculation of glomeruli were among the damage to the kidneys observed histopathologically in groups B and D. The current study recommends that while administering ivermectin, reasonable caution should be taken. Secondly Ivermectin toxicity-related kidney damage is ameliorated by Coenzyme Q10.*

Keywords: *Ivermectin, Co-enzyme Q10, Kidne*

Abstrak. Tujuan dari penelitian saat ini adalah untuk memastikan apakah Coenzyme Q10 dapat mencegah atau mengurangi kerusakan jaringan ginjal yang dirugikan ketika kelinci diberikan ivermectin. Dalam penyelidikan ini, digunakan 48 ekor kelinci albino jantan dewasa yang sehat dengan berat antara 1350 dan 1800 gram, berusia antara 13 dan 14 minggu. Delapan hewan masing-masing dibagi menjadi enam kelompok identik berdasarkan kelompok. Kelompok kontrol A. Kelinci kelompok B, C, dan D menerima 2 mg/kg obat setiap minggu. Setelah menghentikan ivermectin selama delapan minggu,. B: Lakukan pemotongan jaringan langsung; C: Berikan Coenzym q 10 (10 mg/kg) sekali sehari selama 30 hari; D: Gunakan kelinci Berikan penyembuhan diri 30 hari. F = hanya Koenzim q10 10mg/kg selama 30 hari; E = ivermectin 2 mg/kg setiap minggu Selama delapan minggu dan 10 mg/kg Koenzim Q10.. Hasil yang terungkap Polikista ginjal, infiltrasi sel inflamasi dan nekrosis sel epitel pelapis tubulus ginjal, dan atrofi atau vakulasi glomeruli adalah di antara kerusakan ginjal yang diamati secara histopatologis pada kelompok B dan D. Penelitian saat ini merekomendasikan bahwa saat memberikan ivermectin, kehati-hatian harus dilakukan. Kedua, kerusakan ginjal terkait toksisitas Ivermectin diperbaiki oleh Koenzim Q10.

Kata Kunci : Ivermectin, Ko-enzim Q10, Ginjal

1. INTRODUCTION

A broad-spectrum antihelminthic drug called ivermectin is used to treat ectoparasites and endoparasites in sheep and goats. (Gunn and Sadd, 1994) .As agents for protection of plants in agriculture (Zanoli et al., 2012). Ivermectin is used in humans to treat scabies, stronglyloidiasis, ascaraisis, trichuriasis, filariasis, and entrobiasis in addition to treating onchocerciasis, or river blindness.(Banerjee et al., 2009 and Del Giudice et al., 2003).

Using ivermectin has a strong affinities for binding proteins, and isprimarily degraded via the oxidative pathway. It has also been found that ivermectin or any of its metabolites are nearly completely excreted Within the feces; however, this occurs only after 12 days and fewer

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than five percent of the dosages that were given are removed within the urine. (Klotz et al., 1990 and Plumb et al.,2008)

Furthermore,Trailovic and Varagic (2007) stated which the the majority well-known medical cases of IVM toxicity in both tamed and untamed animals were characterized by CNS depression, comas, and possibly even dying Ming et al. (2013) claimed wich following subchronic exposure to varying dosages of AVM at various times, ivermectin caused pathological alterations in pigeon brain tissues, including neuronal degeneration and necrosis. Also Al-Jassim et al. (2015) reported revealed hepatocyte vacuolation and fibrosis were among the pathological alterations brought on by repeated administration of various ivermectin dosages in the hepatic tissue of female rabbits. The amount Frederick was separate the 1,4-benzoquinone CoQ10, which has a 50-carbon isoprenoidside chain, from the mitochondria of cow hearts. in 1957..(FL et al.,1957). is an endogenous benzo-quinone molecule wich is lipid-soluble and functions as a respiration chain's diffusible electron carrier of the mitochondria. (Lenaz et al.,2007), Then, ATP production functions as an antioxidant and promotes the renewal of other antioxidants, influencing the stability and permeability of membranes and stimulating the proliferation of cells while inhibiting their dying (Crane ,2001 and Jones et al.,2002). Because it plays a part in the production of ATP, CoQ10 affects how all cells in the body function and is therefore essential to the wellbeing of every human organ and tissue. cells with the highest metabolic activity include those in the heart, immune system, gingiva, and stomach mucosa.(johnston,1998)

2. MATERIALS AND METHODS

Co_enzym q10 (PHARMACY, Poland) and 1% ivermectin. 48 healthy adult male albino rabbits, differing in age from 13 to 14 weeks and weighing between 1350 and 1800 g, for use in this research. meal and frish water given. Design Experiments Six identical groups of eight rabbits each were randomly assigned to the experimental rabbits after they had had a week to acclimate to their new diet, housing, and surroundings. Group A: receiving D.W. Sc. under control Ivermectin Sc was administered to 24 rabbits in order to damage their organs (Arise et al., 2012). For eight weeks, 2 mg/kg per week were increased.

(Al-Jassim et al.,2016) .and split up into groups B, C, and D. Eight rabbits in Group B Slice tissue directly after quitting ivermectin. Group C: For 30 days, the animals in this group are given oral Coenzyme Q10 (10 mg/kg b.w.).

(Abdel-Hady et al., 2011) following Ivermectin withdrawal. Eight rabbits make up Group D. Give yourself 30 days to recuperate when ivermectin was stopped. Group E: Weekly

ivermectin plus daily coenzyme Q10 for eight weeks Group F: For 30 days, take only Coenzyme Q10 (daily).

3. RESULTS

Macroscopic finding

The kidney was typical in terms of appearance and size, with a brownish reddish with normal texture within Group A, the control group, even though in group B the kidney has congestion and red_brown to dark in color .Groups C and E appear to be normal. The kidney's overall look in Group D was comparable to that of Group B's section.

Histological finding

The histological characteristics of the kidney in group A were completely typical, unchanged. They displayed two unique regions an external cortex and an internal medulla. Uriniferous tubules, which include nephrons and collecting ducts, make up the kidney parenchyma. The kidney corpuscle (detected in the cortex) and the the renal tubules are the two main components of the nephron (medullary and cortical tubules).The glomerular, It manifests as an intrusive globular capillary network within the glomerular or (Bowman's capsule), is a form of renal corpuscle made up of glomeruli. The capsule's epithelial cells are flat and plain, except near the system of tubules opening, where their cuboidal shape increases. In between cells of the epithelium covering the capsule's lining cells and the glomerulus, the urinary space may be seen. Furthermore, the glomerular capsule's basement membrane is normal and distinct. The convoluted tubules, both proximal and distal, additionally the loop of Henle and gathering tubules, make up the renal tubules. Cuboidal epithelium lines the collecting ducts at first, and columnar cells line them as they progress down to the medulla. Small 29 capillaries, some of which were filled with RBCs, were located in the interstitial of the renal cortical and medullar areas (Figure 1). Group B received ivermectin treatment (2 mg/kg), the kidney sections taken from this group showed glomeruli's atrophy with dilatation of Bowman’s capsule . formation of many cysts (renal polycysts), degeneration and necrotizing of the lining epithelial cells of renal tubules, as well as blood vessels congestion with infiltration of inflammatory cells.(Fig2,3). Following the cessation of Ivermectin administration, Group C, which was given Coenzyme Q10 (10 mg/kg B.w.) orally for a month, exhibits normal architecture, as indicated by Significant improvement of histopathological changes after giving coenzyme q10 and return to normal histological picture that represented by proximal renal tubules and mild changes representing by swelling of the renal tubule lining's epithelial cells and dilation of Bowman's

capsule. (Fig 4).(D group) After quitting ivermectin, these animals were maintained untreated for a month to allow for self-healing (recovery), and the results show pathological alterations in the kidney sections.

show histopathological changes representing by fibrosis (proliferation of fibroblasts) between renal tubules and swelling of the renal tubule lining's epithelial cells and pathological changes representing by cystic formation, vacuolation of glomeruli and infiltration of inflammatory cells and pathological changes representing by severe cell swelling and hydropic renal tubule epithelial cells' deterioration and necrosis, as well as the invasion of inflammatory cells.(Fig 5,6,7) .(Group E) receives Coenzyme Q10 (every day) and Ivermectin (weekly) simultaneously for eight weeks, demonstrating the kidney section.

showed almost renal tissue's typical structure were distinguished by cloudy degeneration lining the renal tubules with epithelial cells and dilation of Bowman's space in the glomeruli (Fig8,9). (F group) receives Coenzyme Q10 for a maximum of 30 days; this indicates typical renal tissue architecture was distinguished by the presence of glomeruli, distal and proximal renal tubules. (Fig10,11).

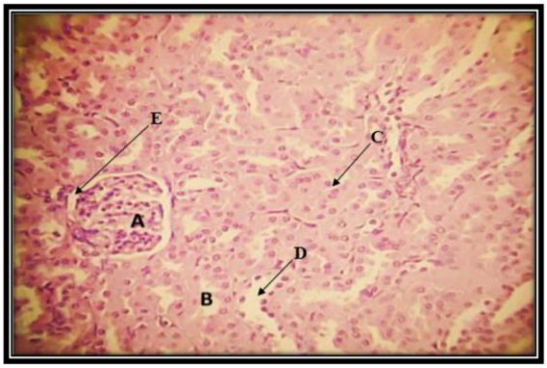

Fig. 1: Photomicrograph of kidney (A group) exhibiting a standard appearance of glomeruli (A) , renal tubules , (B) proximal tubule(C),distal tubule(D) Bowman's space(E). H&E stain. 200X.

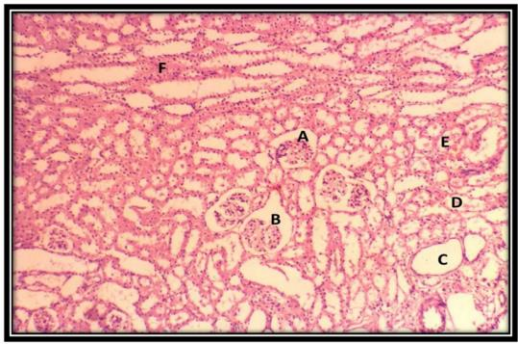

Fig 2: Photomicrograph of kidney at (B Group) Atrophy of the glomeruli (A) with dilatation of Bowman's capsule(B) formation of many cysts (renal polycysts)(C) ,degeneration

and necrosis of epithelial cells lining renal tubules (D) , and blood vessel congestion (E) inflammatory cells infiltration (F). H&E stain 100x

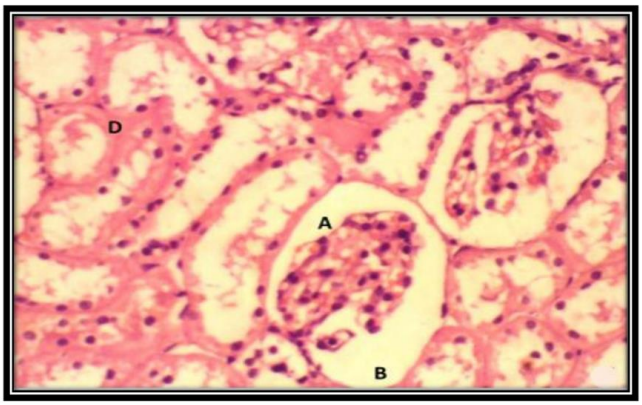

Fig 3: Photomicrograph of kidney (B Group) Atrophy of the glomeruli (A) with Bowman's capsule dilating (B), renal tubule lining epithelium cells' deterioration and necrosis (D). H&E stain 400x.

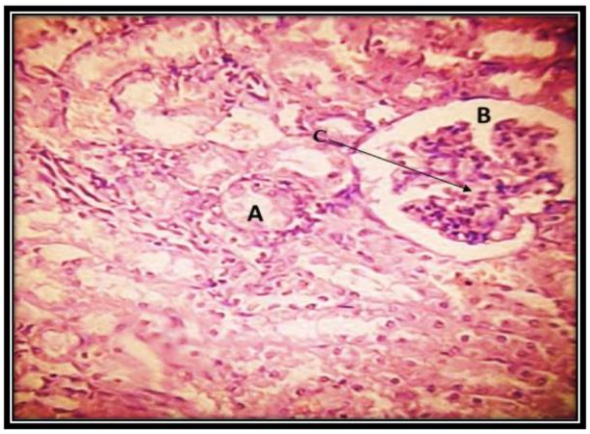

Fig.4: Photomicrograph of kidney of (C group) exhibiting mild changes representing by epithelial cells lining the renal tubules exposed to cell swelling (A) and dilation of Bowman's capsule (B) and Segnentation of Glomeruli (C). H&E stain. 200X.

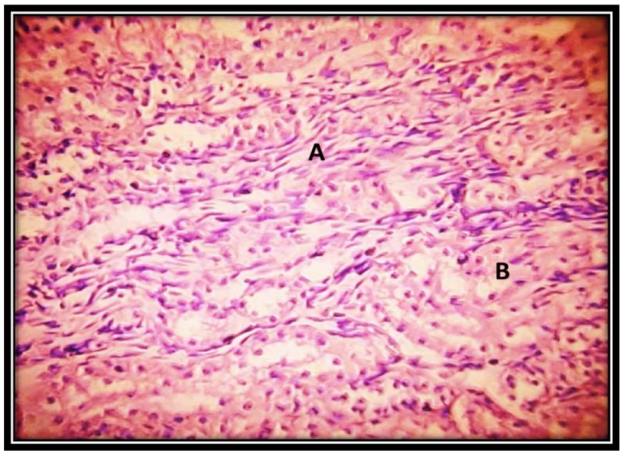

Fig.5: Photomicrograph of kidney of (D group) exhibits pathological alterations, such as fibrosis. (proliferation of fibroblasts) between renal tubules (A) and cell swelling of epithelial cells lining renal tubules (B). H&E stain. 200X.

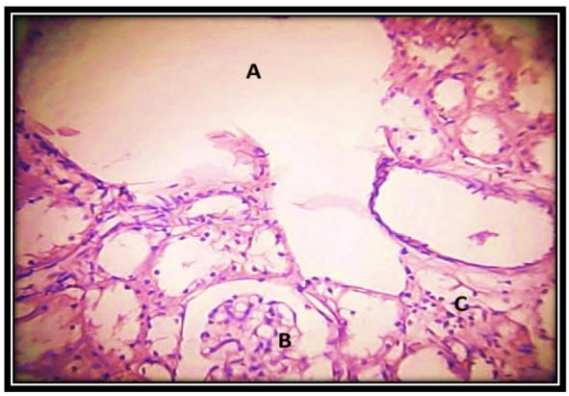

Fig.6: Photomicrograph of kidney of (D group) exhibits pathological alterations such as cystic formation (A), vacuolation of glomeruli (B) and inflammatory cells infiltration (C). H&E stain. 200X.

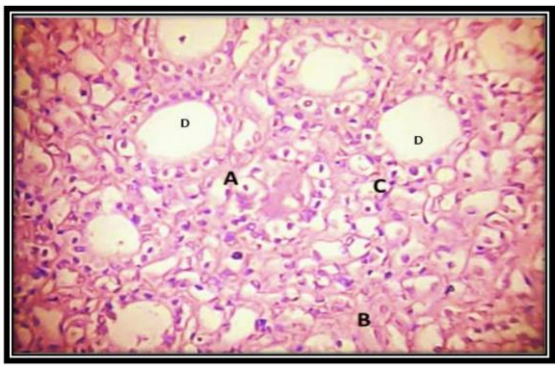

Fig. 7: Photomicrograph of kidney of (D group) exhibits pathological changes representing by severe cell swelling and vacuolar degeneration (A) and epithelial cells lining the renal tubules exposed necrosis (B) and inflammatory cells infiltration (C),Collecting duct(D). H&E stain. 200X

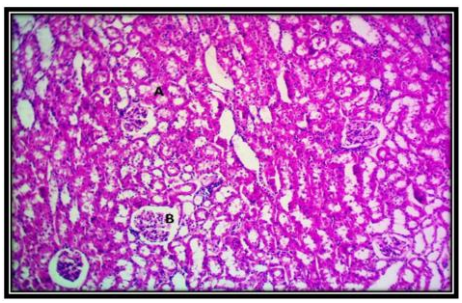

Fig.8: Photomicrograph of kidney of (E group) exhibits cloudy degeneration of epithelial cells lining renal tubules (A) and dilation of Bowman's space in the glomeruli(B). H&E stain, 100X.

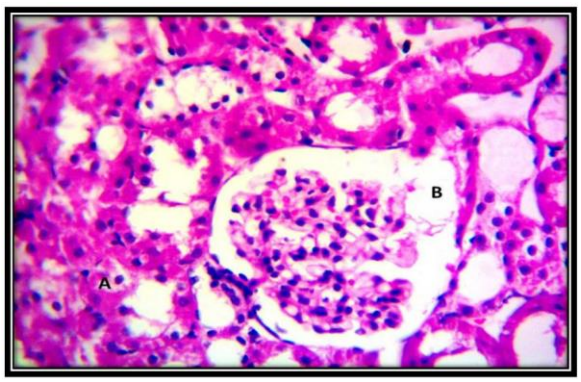

Fig.9: Photomicrograph of kidney of (E group) exhibits cloudy degeneration of epithelial cells lining renal tubules (A) and dilation of Bowman's space in the glomeruli (B). H&E stain, 400X.

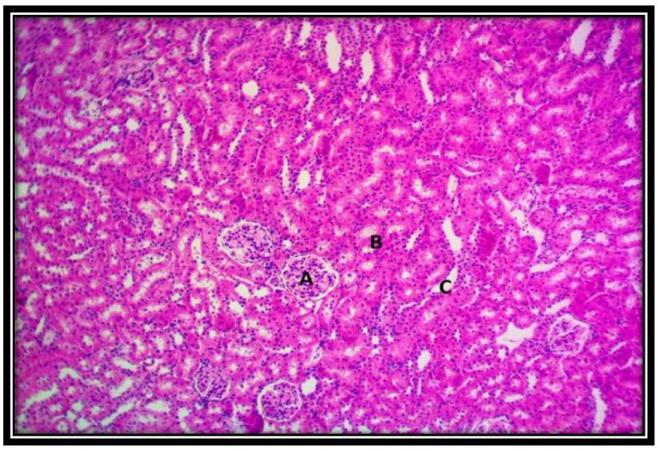

Fig.10: Photomicrograph of kidney of (F group) exhibiting a standard appearance of renal tissue characterized by glomeruli (A), proximal renal tubules (B) and distal renal tubules (C). H&E stain, 100X.

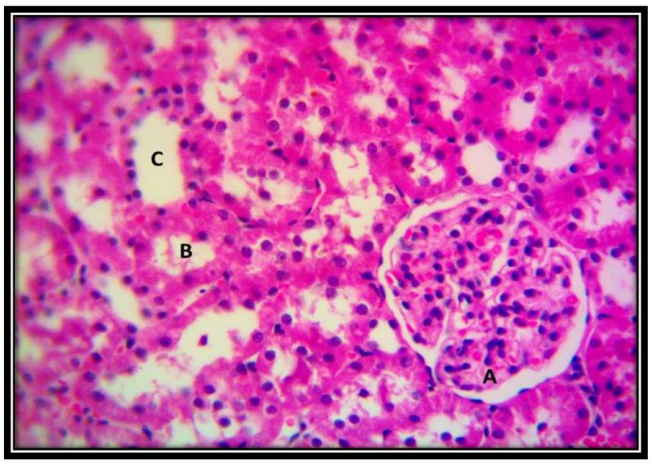

Fig.11: Photomicrograph of kidney of (F group) exhibiting a standard appearance of renal tissue characterized by glomeruli (A), proximal renal tubules (B) and distal renal tubules (C). H&E stain, 400X.

4. DISCUSSION

Although some medicines are beneficial to certain organs, they may be harmful to other tissues in the body. The amount of dose given and the type of medicine used are usually related to this effect (Dzoboet al., 2018).

Ivermectin is Veterinary medicine's broad-spectrum antiparasitic drug. treatment that was first used in humans in 1987.It is the recommended medication for infections caused by strongyloidiasis and onchocerciasis., and it is still a viable alternative for mass treatment of lymphatic filariasis,

Additionally, during the process of water reabsorption, medications are usually concentrated in the renal tubules, exposing the tubules to the drug's concentrated action. (Liu et al.,2019).

In the chronic phases of exposure to toxins, pharmaceuticals have been identified to produce toxins that contribute to both programmed cell death and cellular damage and necrosis. Additionally, drug metabolites interact similarly with target molecules, changing these molecules.

(Perazella, 2019) . Reactions that are not comparable include the superoxidation of fats, the production of dangerous Free radicals of oxygen, the exhaustion of glutathione, and the alteration of the sulfhydryl group in enzymes. Comparable responses cause direct toxicity towards the compounds that are the target. (Chorna et al., 2019).

Our results show that in (B) Ivermectin only in dose of 2mg/kg weekly subcutaneous injection for 8 weeks resulted in the appearance of clinical neurological symptoms, such as the severity of the animal's excitement and depression. This outcome was consistent with other studies that found neurological symptoms in rabbits treated with ivermectin. Treatment with high dosages of ivermectin resulted in symptoms and indicators of toxicity of the central nervous system in laboratory animals, owing to the fact that ivermectin crosses the blood-brain barrier and causes oxidation and damage to membrane glycoproteins, resulting in oxidative stress in the brain(Liu et al.,2019).

After 8 weeks of treatment with ivermectin alone, this study found similar alterations in the kidney tissue. Glomerular atrophy, with the extension of Bowman's capsule and the formation of numerous cysts, epithelial cell degeneration and necrosis lining the renal tubules, and blood vessel congestion with inflammatory cell infiltration were among the abnormalities. These results are consistent with previously research, which found that injecting ivermectin into rats caused significant histopathological changes in the kidneys, including

hyperglomerulosclerosis, pink deposits in Bowman's capsule, and hydrodegeneration of the convoluted tubules' epithelium (Rabab et al., 2015).

Ivermectin treatment induced disruption in the cells of the subcortical tubules (proximal convoluted tubules) and glomeruli atrophy (Al-Jassimet al., 2016). According to another study they discovered that the proportion of urea and creatinine was extremely high, indicating a decrease in glomerular filtration in the kidneys, which was reflected in renal tubule failure(Elsawy et al., 2016).

The current study's findings indicate that ivermectin caused oxidative stress in kidney cells, which resulted in a significant reduction in the histopathological changes in the kidneys and a return to normal activity in the animals when administered 10 mg/kg of body weight of coenzyme Q10 and ivermectin orally for Thirty days following the cessation of treatment (Group E)

In basis of our conclusions, we hypothesize that the occurrence of these pathological changes is related to the oxidative stress caused by ivermectin administration. This is because The formation of free oxygen radicals or active metabolites can cause the super-oxidation of unsaturated fats, and Lipid peroxidase is capable of generating lipid peroxy radical, which stimulates the production of more free oxygen radicals . Because it affects the integrity of the cell membrane, This process, which includes membrane proteins interacting with products of lipid oxidation, changes lipids in membranes and causes cell disintegration and death. (Flores-Romero et al., 2020).

Because glutathione depletion produces oxidative stress is a condition that can happen either organically as a result of metabolite buildup or by interactions with hazardous drugs and pharmaceuticals, it may be involved in this. (García-Caparróset al.,2020).

Oxidative toxins build up when levels of glutathione drop less than 20–30% of typical. This causes a range of degenerative changes, including necrosis and death of cells. (Azouz&Korany, 2020).

Active oxygen strains may also modify the sulfhydryl group (SH) and thus affect glutathione in reverse, as these free groups play a vital part in the catabolic activity of enzymes, as any change in them causes the enzyme's activity to be removed and they are an important element within some enzymes, including glutathione reductase, calcium transport enzymes in the plasma membrane, and endoplasmic reticulum Furthermore(Ahmedet al., 2020),any inactivation of these enzymes raises the level of calcium inside the cells or increases calcium efflux through the cell membrane, which is fatal to the cell and a predisposing cause for the

enzymatic activation of each protease, phospholipase, endonuclease, and protein kinase, resulting in the destruction of mitochondria and cell death and necrosis(Rossi et al., 2019).

Consistent with the preceding discussion, this study reports that fibrosis was detected in the group D of rabbits that were abandoned for a month following the cessation of ivermectin medication.

(fibroblast proliferation) between the renal tubules, swelling of cells in the epithelial cells lining the renal tubules, cyst formation, and infiltration of inflammatory cells severe swelling of cells, hydropic degeneration, and necrosis of epithelial cells lining the renal tubules are all illustrations of pathogenic alterations.

The existence of liver fibrosis and kidney tissues, along with inflammation and necrosis that persisted for a month after the ivermectin medication was stopped, suggests that ivermectin affects the liver's histopathology and kidneys that over time are not pathologically reversible

This might be clarified by the Animal bodies' exhaustion of antioxidant defenses against oxidative damage caused by ivermectin. The bodies of both humans and animals contain mechanisms of defense that can prevent this damage, including coenzyme Q10, glutathione peroxidase, and vitamin E. Therefore, when oxidants and antioxidants are not present, cell death results. (Farouk et al., 2021).

An increase in the enzyme Plasma aspartate transaminase can sometimes induce liver damage, which starts with hepatitis in acute instances and develops to cirrhosis in chronic cases, Hepatotoxicity can also occur when the liver is harmed by the active compounds or metabolites of medications as a result of the cytochrome P 450 enzyme's 55 metabolism, which causes liver damage(Guengerich, 2020 ;Teschke&Uetrecht, 2021). Nephrotoxicity is usually connected with liver injury, in which the kidneys are exposed to high quantities of medicines or their metabolites, which then concentrate in the urine and induce tubular necrosis(Cohen et al., 2021).

The aforementioned mechanisms elucidate the histological alterations that the rabbits experienced post-ivermectin treatment, as well as the clear favorable modifications in kidney tissues that were observed upon coenzyme Q10 10 mg/kg therapy (Group E). Because CoQ10 is involved in the electron and proton transport chain in mitochondrial membranes during aerobic cellular respiration, adequate amounts of CoQ10 are required for cellular respiration and the synthesis of ATP, as well as its participation in electron transport outside of mitochondria (plasma membranes, lysosomes).

(Rodick et al., 2018). The impact of one of the organelles, the mitochondria whose influence results in an interruption in energy generation that impacts the activity of the cell and

its capacity to carry out its intended work,(Filadi et al., 2018). Necrosis results from a failure of mitochondrial cellular metabolism because they are more susceptible to outside influences. Because of internal sodium and the osmotic influence within the damaged cell, vacuoles form in the cytoplasm. Cytoplasmic vacuoles are a common morphological phenomena and are thought to be a protective, adaptive, and reactive physiological state, according to numerous research. This research also took into account the fact that exposure to certain medications, harmful substances, and even bacteria and viruses that cause cytoplasmic vacuolation is commonly regarded as an early stage of degeneration. Furthermore, cytoplasmic vacuoles have been shown in multiple investigations to be a common morphological feature (56), and they are believed to represent a protective physiological adaptation condition (Kim et al., 2020).

Clinical research (Farsiet al., 2019) shows that CoQ10 reduces levels of the inflammatory mediators necrosis factor-alpha (TNF-), interleukin-6 (IL-6), and C-reactive protein (CRP) by a complementary effect on nuclear transcription factor NF kappa beta. Through these mechanisms, CoQ10 prevents the onset of degenerative diseases. It also has a role in DNA repair and replication (by serving as a crucial cofactor in the production of pyrimidines), controls the physical-chemical characteristics of The membranes of cells, and modifies gene expression. (Abiri&Vafa, 2021).

Coenzyme Q10 has now been discovered in other cellular membranes and blood plasma, and its significance as an antioxidant has been intensively researched (Pastor Maldonado et al., 2020)..

Coenzyme Q10 is an essential chemical found in practically every cell in the human and animal body, and its structure is known as ubiquinone because of its existence(Maitra& Dutta, 2021). Because endogenous levels are restricted by physiological variables associated to oxidation, CoQ10 supplementation is often required for animal cell synthesis. Degenerative illness in humans with a well-documented pathology(Navas et al., 2021).

It has been demonstrated that dietary supplements that alter the body's levels of CoQ10 have cytoprotective effects. This effect can be attributed to the fact that CoQ10 significantly influences the expression of multiple genes whose main function is cell signaling, serving as mediators in the regulation of transcription, inflammation, metabolism, and transport. Therefore, CoQ10 is likely a potent genetic regulator. (Guescini et al., 2017).

The current study concludes that kidney tissues experienced histological effects after receiving ivermectin injections with a single dosage of 2 mg/kg subcutaneously over a period of 8 weeks. However, the histological effects were counteracted by giving out CoQ10 orally 10 milligrams per kilogram. These degenerative consequences are brought on by oxidative

stress, and the antioxidant capacity of CoQ10 directly contributes to the partial healing of kidney tissues.

5. CONCLUSION

1. When administered weekly in a dosage of 2 milligrams per kilogram, ivermectin has toxic effects on the kidney that are typified by Atrophy of the glomeruli with dilatation of Bowman's capsule , renal polycysts, degenaration and necrosis of epithelial cells lining renal tubules and congestion of blood vessels.
2. When Coenzyme Q10 is administered in a dosage of 10 milligrams per kilogram for 30 days following the cessation of Ivermectin, the kidneys recover, with the majority of the lesions disappearing and the histology clearly improving.
3. No notable histological alterations were observed after 8 weeks of ivermectin (2 mg/kg weekly) + Coenzyme Q10 (10 mg/kg daily); as a result, coenzyme Q10 has a preventive effect on the kidneys against abnormal alteration.
4. Renal portions of rabbits given a month to recover naturally without ivermectin did not exhibit a discernible improvement. This demonstrates the restorative and protecting properties of coenzym Q10.
5. The Coenzyme Q10 was given daily for 30 days in a dosage of 10 milligrams per kilogram, did not result in any abnormal clinical signs or histological alterations.

تأثير الانزيم المساعد Q10 على تحسين التغيرات النسيجية في كلى الارانب المعالجة بالايفرمكتين

صهيب اسماعيل محمد طيب طاهر

كلية طب الموصل

جامعة الموصل

الخلاصة

صَممت الدراسة الحالية لدراسة التأثير العلاجي والوقائي المحتمل لمركب الإنزيم Q10 ضد أنسجة الكلى المتأثرة بإعطاء عقار الإيفرمكتين للأرانب. تم استخدام ثمانية وأربعين من الذكور البالغين الأصحاء من الأرانب البيضاء التي تتراوح أعمارهم بين 13 و 14 أسبوعًا ، وتتراوح أوزانهم بين 1350 و 1800 جرامًا في هذه الدراسة. تم تقسيم المجموعات إلى ست مجموعات متطابقة من 8 حيوانات. المجموعات B و C و D جميع الأرانب حقنت بمادة الإيفرمكتين 2 مجم / كجم تحت الجلد أسبوعياً لمدة 8 أسابيع ، ثم بعد إيقاف الايفرمكتين ، B = تقطيع مباشر للأنسجة ، C = إعطاء جرعة يومية من الإنزيم Q10 (0 1 مجم / كجم) لمدة 30 يومًا ، D = تركت الارانب 30 يومًا للشفاء الذاتي. A = السيطرة ، E = ايفرمكتين 2 مجم / كجم أسبوعيًا +الانزيم Q10 (0 1 مجم / كجم) يوميًا لمدة 8 أسابيع ، F = فقط الانزيم Q10 (0 1 مجم / كجم) لمدة 30 يومًا. أظهرت النتائج أن أنسجة الكلى طبيعية في المجموعات A و C و E و F. أظهرت الملاحظات النسيجية للمجموعة B و D تلفًا في الكلى و ضمور الكبيبات ، والتكيسات الكلوية ونخر الخلايا الظهارية المبطنة للأنابيب الكلوية

وارتشاح الخلايا الالتهابية. تقترح الدراسة الحالية ضرورة : اولا توخي الحذر عند تناول عقار الإيفرمكتين. ثانيًا ، يعمل الإنزيم Q10 على تحسين تلف الكلى الناتج عن تسمم الإيفرمكتين.

مفاتيح الاستدلال: الايفرمكتين, الانزيم المساعد q10,الكلى

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