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Quercetin and Naringin Mitigate Dichlorvos-Induced Multiorgan Histopathological Damage in Rats

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Abstract:

Introduction: The extensive use of dichlorvos, an organophosphate insecticide, in households and agricultural settings remains a public health concern due to its potential to induce multiorgan toxicity.

Aims: This study investigated the histoprotective effects of quercetin and naringin against dichlorvos-induced histopathological alterations in rats.

Materials and Methods: Eighty rats were randomly assigned to ten experimental groups (n=8). Following treatment, the brain, liver, kidney, and heart tissues were processed using standard histological techniques and examined under a light microscope after hematoxylin and eosin staining.

Results: Rats exposed to dichlorvos exhibited marked histopathological lesions, including neuronal degeneration, hepatocellular distortion, cardiomyocyte degeneration, architectural disorganisation, and glomerular and tubular damage in the kidneys. Quercetin administration markedly attenuated these histological alterations and improved tissue architecture across the examined organs. In contrast, naringin treatment produced only partial protection, with persistent degenerative changes, particularly in the brain, liver, and kidney.

Conclusion: These findings demonstrate the superior histoprotective efficacy of quercetin against dichlorvos-induced organ damage and suggest its potential therapeutic role in mitigating organophosphate-associated toxicity.

Keywords: Histology, Histopathology, Dichlorvos, Quercetin, Naringin, Organophosphate Toxicity

All co-authors agreed to have their names listed as authors.

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1. INTRODUCTION

Dichlorvos (2,2-dichlorovinyl O, O-dimethyl phosphate; DDVP) is an organophosphate insecticide widely used in households, agriculture, and vector control programs [1, 2]. Its widespread availability under various trade names has contributed to increased human and environmental exposure, particularly in developing countries [3]. Although dichlorvos is effective in pest control, its extensive use poses significant public health concerns due to its ability to induce multi-organ toxicity and tissue injury.

The primary toxic mechanism of dichlorvos involves irreversible inhibition of acetylcholinesterase, resulting in acetylcholine accumulation at synaptic junctions and subsequent cholinergic overstimulation [4, 5]. In addition to this classical mechanism, emerging evidence indicates that dichlorvos induces oxidative stress, mitochondrial dysfunction, and inflammatory responses, which collectively contribute to cellular and tissue damage [6-9]. These secondary mechanisms are particularly relevant in metabolically active organs such as the brain, liver, kidney, and heart [10].

The nervous system is especially susceptible to dichlorvos toxicity due to its high oxygen demand and dependence on tightly regulated neurotransmission. Previous studies have reported neuronal degeneration, synaptic disruption, and alterations in cortical architecture following dichlorvos exposure [11, 12]. The liver, as the primary site of xenobiotic metabolism, is also vulnerable, with dichlorvos-induced hepatocellular degeneration, sinusoidal congestion, and inflammatory infiltration commonly reported. Similarly, renal tissues involved in pesticide excretion frequently exhibit glomerular damage, tubular degeneration, and interstitial inflammation. Cardiac toxicity associated with dichlorvos exposure has been characterised by myocardial degeneration, impaired contractile integrity, and vascular disturbances [9, 13].

Histopathological evaluation remains one of the most reliable tools for assessing pesticide-induced toxicity, as it provides direct morphological evidence of tissue injury, severity, distribution, and potential reversibility [14, 15]. Such analyses are particularly valuable for detecting subchronic and low-dose toxic effects that may not be readily apparent through biochemical assays alone [14]. Such microscopic analyses are particularly valuable for understanding subchronic and low-dose toxic effects that may not be readily detected through biochemical assays alone.

In recent years, increasing attention has been directed toward naturally occurring antioxidants, particularly flavonoids, as protective agents against pesticide-induced toxicity [7, 16-18]. Flavonoids are polyphenolic compounds widely distributed in fruits and vegetables and are known for their antioxidant, anti-inflammatory, and cytoprotective properties. Among these, quercetin and naringin have attracted considerable interest due to their broad biological activities and favourable safety profiles [19-21]. Quercetin, a flavonol abundant in onions, apples, berries, and citrus fruits, exhibits strong free-radical scavenging activity, stabilises cellular membranes, modulates antioxidant enzyme systems, and inhibits lipid peroxidation. Experimental studies have demonstrated its protective effects on neural, hepatic, renal, and cardiac tissues against various xenobiotic-induced injuries. Naringin, a flavanone glycoside predominantly found in citrus fruits, also exhibits antioxidant, anti-inflammatory, and vasoprotective properties; however, its histoprotective efficacy appears to vary with dose, exposure duration, and tissue type [22-24].

Despite reports on the individual protective effects of quercetin and naringin against toxicant-induced oxidative damage, direct comparative studies evaluating their histopathological efficacy against dichlorvos-induced multiorgan injury remain limited. Moreover, information regarding the extent of tissue recovery following dichlorvos exposure and subsequent therapeutic intervention is insufficient [25, 26]. Therefore, this study aimed to investigate the histopathological effects of dichlorvos on the brain, liver, kidney, and heart of male Wistar rats and to comparatively evaluate the ameliorative and restorative potentials of quercetin and naringin using light microscopy.

2. MATERIALS AND METHODS

2.1 Experimental Animals

Eighty (80) adults male Wistar rats weighing 150-200 g were obtained from the animal house of the Faculty of Basic Medical Sciences. Animals were housed in well-ventilated cages under standard laboratory conditions (12 h light/12 h dark cycle, temperature 22-25 °C, relative humidity 50-60%) and fed standard commercial rat pellets with access to clean drinking water ad libitum. All animals were acclimatized for one week prior to experimentation. Experimental procedures were conducted in accordance with established guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Ethics Committee.

2.2 Chemicals and Reagents

Analytical grade dichlorvos (2,2-dichlorovinyl O,O-dimethyl phosphate; DDVP) was freshly prepared prior to administration. Quercetin and naringin were obtained as high purity compounds. Coconut oil and dimethyl sulfoxide (DMSO) were used as vehicle solvents for compound administration, as appropriate. All reagents used for tissue processing and histological staining were of standard laboratory grade.

2.3 Experimental Design

Following acclimatization, the rats were randomly assigned to ten (10) experimental groups (Table 1), each consisting of eight animals (n = 8). The grouping and treatment protocol were designed to assess the toxic effects of dichlorvos, the potential for spontaneous recovery following exposure withdrawal, and the comparative ameliorative effects of quercetin and naringin.

Table 1. Experimental groups and Treatment

Groups	Description
Group A (Control)	Distilled water
Group B (Baseline control)	Coconut oil.
Group E (Vehicle)	DMSO
Group C (Dichlorvos-treated)	Dichlorvos (4 mg/kg body weight).
Group D (Recovery group)	Dichlorvos (4 mg/kg) followed by a two-week recovery
Group F (Dichlorvos + Quercetin)	Dichlorvos (4 mg/kg) and Quercetin (75 mg/kg).
Group G (Dichlorvos + Naringin)	Dichlorvos (4 mg/kg) and Naringin (100 mg/kg).
Group H (Quercetin only)	Quercetin (75 mg/kg).
Group I (Naringin only)	Naringin (100 mg/kg)
Group J (Vehicle recovery)	Vehicle treatment comparable to the recovery group

All treatments were administered orally once daily for four weeks. The recovery group was observed for an additional two weeks following cessation of dichlorvos administration. Dosages were selected based on previous studies demonstrating toxicological relevance and safety.

2.4 Tissue Preparation:

At the end of the treatment period, rats were fasted overnight. They were anaesthetised, and the brain, liver, kidney, lungs, and heart were carefully excised, trimmed of connective tissues, rinsed in normal saline to remove blood contaminants, and immediately fixed in 10% neutral buffered formalin to preserve tissue architecture.

2.5 Histological Processing
Fixed tissues were processed using standard histological techniques. Tissues were dehydrated through graded ethanol concentrations, cleared in xylene, and embedded in paraffin wax. Sections of 5-6 µm thickness were cut using a rotary microtome, mounted on glass slides, deparaffinized, rehydrated, and stained with hematoxylin and eosin (H&E).

2.6 Histopathological Examination
Stained tissue sections were examined under a light microscope at magnifications of ×100 and ×400. Histopathological evaluation focused on the assessment of tissue architecture, cellular integrity, and the presence or absence of degenerative, inflammatory, or vascular alterations. Photomicrographs were captured using a digital microscope camera. Histological observations were recorded qualitatively, with emphasis on lesion severity and distribution across experimental groups.

2.7 Statistical Analysis
Histological observations were compared descriptively among experimental groups. Data were expressed as the mean ± standard error of the mean (SEM), where applicable. Statistical significance was set at $P = .05$.

3.0 RESULTS
Histopathological evaluation of hematoxylin and eosin (H&E) stained sections of the liver, brain, heart, and kidney revealed distinct structural alterations across experimental groups, reflecting dichlorvos-induced tissue injury and the modulatory effects of quercetin and naringin. Representative photomicrographs are presented in Figures 1-8.

3.1 Liver Histology
Liver sections from the control, baseline, vehicle, quercetin only, and naringin only groups (Groups A, B, E, H, and I) exhibited preserved hepatic architecture (Figures 1-2). Hepatic lobules were intact, with centrally located patent central veins. Hepatocytes were polygonal with well-defined cytoplasm and centrally positioned nuclei, while hepatic sinusoids appeared narrow and non-congested. No evidence of inflammatory infiltration, necrosis, or fibrotic changes was observed.

In contrast, liver sections from dichlorvos-treated rats and the recovery group (Groups C and D) showed marked histopathological alterations. These included severe central vein congestion, distortion of hepatic cords, sinusoidal dilatation, inflammatory cell infiltration, hepatocellular degeneration with pyknotic nuclei, and focal hemorrhagic areas. Early fibrotic changes were also evident in some sections, indicating significant hepatic injury induced by dichlorvos exposure (yellow arrows).

Sections from rats treated with dichlorvos and naringin (Group G) showed mild histological alterations. Although overall lobular architecture was largely preserved, mild sinusoidal congestion and focal inflammatory infiltration persisted, with occasional hepatocellular degenerative changes (black arrows).

Conversely, liver sections from rats treated with dichlorvos and quercetin (Group F) demonstrated marked attenuation of hepatic damage. Central veins, hepatic cords, and hepatocytes appeared largely preserved, with minimal sinusoidal congestion, closely resembling control liver architecture.

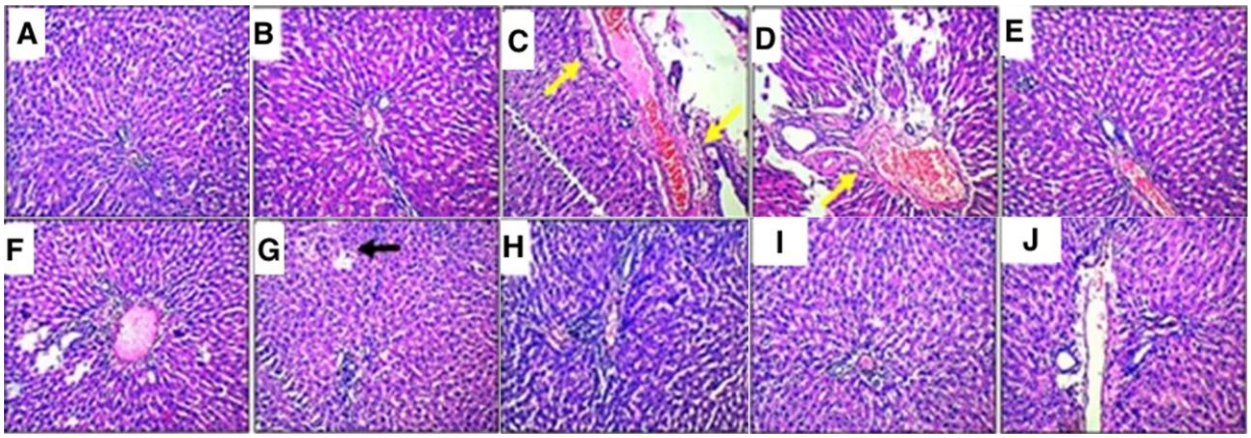

Figure 1: Representative photomicrographs showing panoramic views of liver histology across experimental groups. Hematoxylin and eosin (H&E) staining, ×100 magnification. Control and flavonoid-only groups show preserved hepatic architecture, while dichlorvos-treated groups exhibit central vein congestion, sinusoidal dilatation, and hepatocellular distortion (yellow arrows). Attenuation of hepatic lesions is evident in the quercetin-treated group, whereas mild residual changes persist in the naringin-treated group. 'Yellow arrows = severe lesions, while Black arrows = mild lesions'.

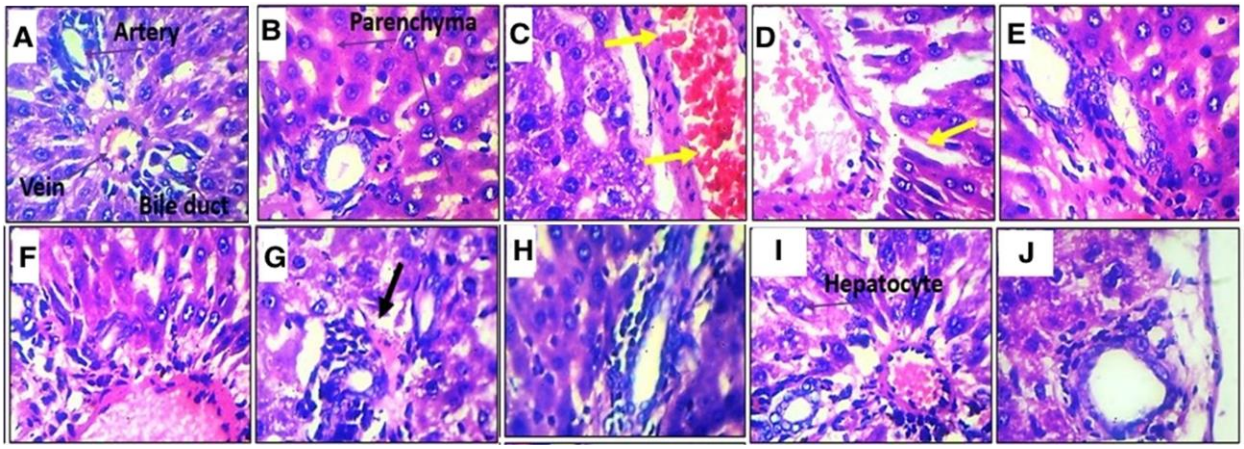

Figure 2: High-magnification photomicrographs of liver sections illustrating hepatocellular morphology. H&E staining, ×400 magnification. Dichlorvos exposure results in hepatocellular degeneration, pyknotic nuclei, inflammatory infiltration, and focal haemorrhage (yellow arrows). Quercetin treatment markedly preserves hepatocyte integrity, while naringin treatment shows partial protection with occasional degenerative changes (black arrows).

3.2 Brain Histology

Histological examination of the cerebral cortex from control, baseline, vehicle, quercetin-only, and naringin-only groups (Groups A, B, E, H, and I) revealed normal cortical organisation (Figures 3 and 4). Cortical layers were well defined, with intact neuronal populations. Pyramidal and granular neurons exhibited normal morphology, distinct nuclei, and minimal perineuronal spaces.

In contrast, cortical sections from dichlorvos-treated and recovery groups (Groups C and D) displayed pronounced neurodegenerative changes. These included neuronal shrinkage, nuclear pyknosis, cytoplasmic fragmentation, widened perineuronal spaces, reduced neuronal density, and disruption of cortical layering, indicative of severe dichlorvos-induced neurotoxicity (yellow arrows).

Brain sections from the dichlorvos plus naringin group (Group G) showed partial neuroprotection. While many neurons appeared intact, scattered pyknotic neurons and mild cortical disorganisation were observed (black arrows).

Notably, cortical sections from the dichlorvos plus quercetin group (Group F) exhibited well-preserved neuronal morphology and cortical architecture, with minimal evidence of degenerative changes, closely comparable to control groups.

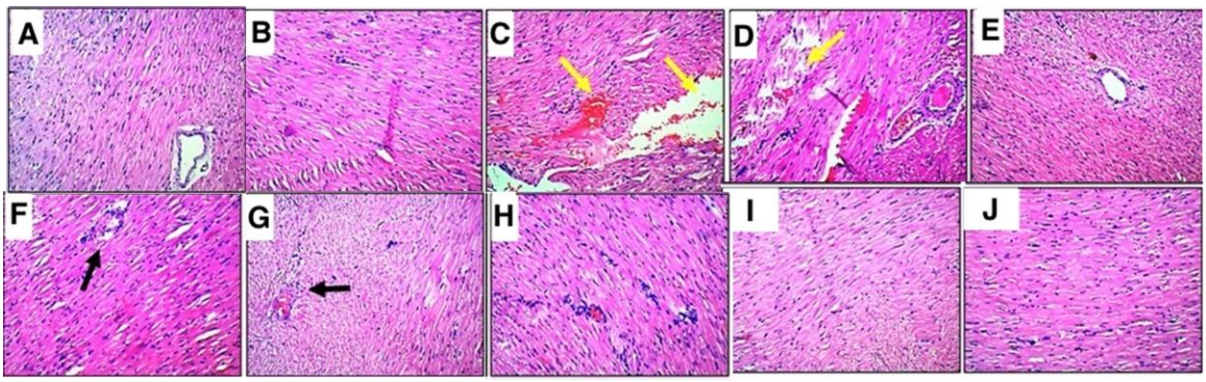

Figure 3: Panoramic photomicrographs of cerebral cortex histology across experimental groups. H&E staining, ×100 magnification. Normal cortical layering (Layers I-VI) is observed in control and flavonoid-only groups. Dichlorvos-treated and recovery groups show cortical disorganisation, neuronal loss, and widened perineuronal spaces (yellow arrows). Improved cortical organisation is evident following quercetin treatment.

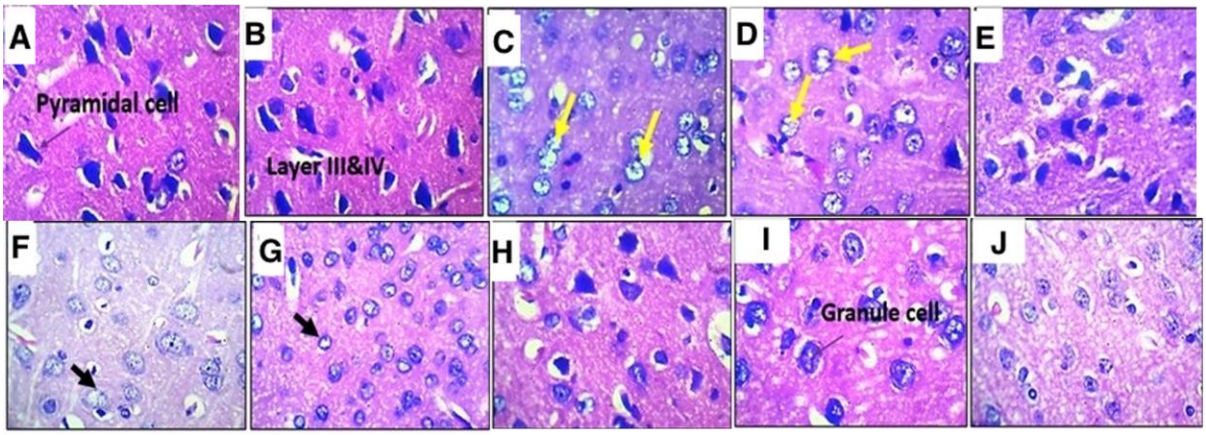

Figure 4: High-magnification photomicrographs of the cerebral cortex showing neuronal morphology. H&E staining, ×400 magnification. Dichlorvos exposure induces neuronal shrinkage, nuclear pyknosis, and cytoplasmic fragmentation (yellow arrows). Partial neuroprotection is observed in the naringin-treated group (black arrows), while quercetin treatment preserves neuronal structure comparable to controls.

3.3 Heart Histology

Cardiac sections from control, baseline, vehicle, quercetin-only, and naringin-only groups (Groups A, B, E, H, and I) demonstrated normal cardiac histology (Figures 5 and 6). The epicardium, myocardium, and endocardium were intact, with well-aligned cardiomyocytes, preserved cross-striations, intact intercalated discs, and normal vascular structures.

In contrast, heart sections from dichlorvos-treated and recovery groups (Groups C and D) exhibited severe pathological alterations, including cardiomyocyte degeneration, loss of striation patterns, widened intercellular spaces, focal fibrosis, large fenestrations, and occasional intravascular clot formation, indicating significant cardiotoxicity (yellow arrows).

Sections from the dichlorvos plus naringin group (Group G) showed mild myocardial alterations, with slight disruptions in cardiomyocyte alignment and focal degenerative changes (black arrows).

Heart tissues from the dichlorvos plus quercetin group (Group F) demonstrated substantial preservation of myocardial architecture, with intact cardiomyocytes, preserved striations, and minimal histological abnormalities

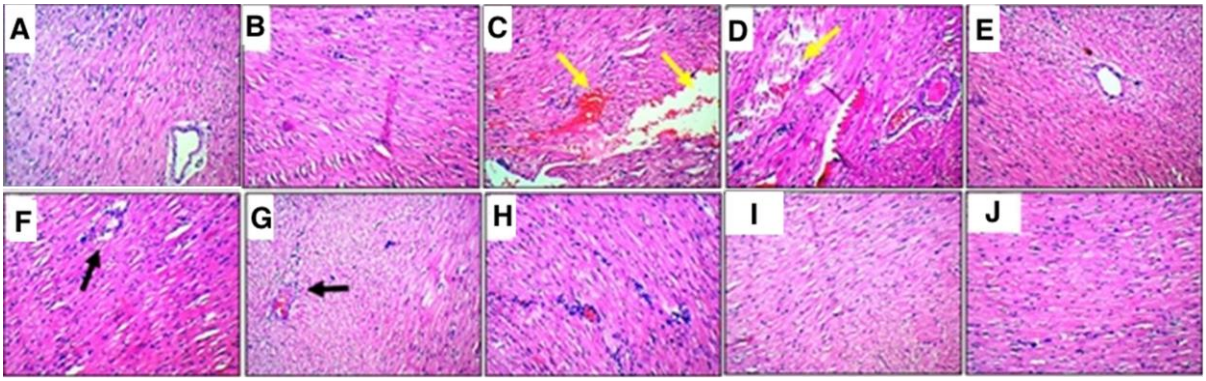

Figure 5: Representative panoramic photomicrographs of heart histology across experimental groups. H&E staining, ×100 magnification. Normal myocardial architecture with intact cardiomyocytes and vascular structures is evident in control groups. Dichlorvos-treated groups show myocardial degeneration, widened intercellular spaces, and vascular abnormalities (yellow arrows). Improved myocardial integrity is observed in the quercetin-treated group

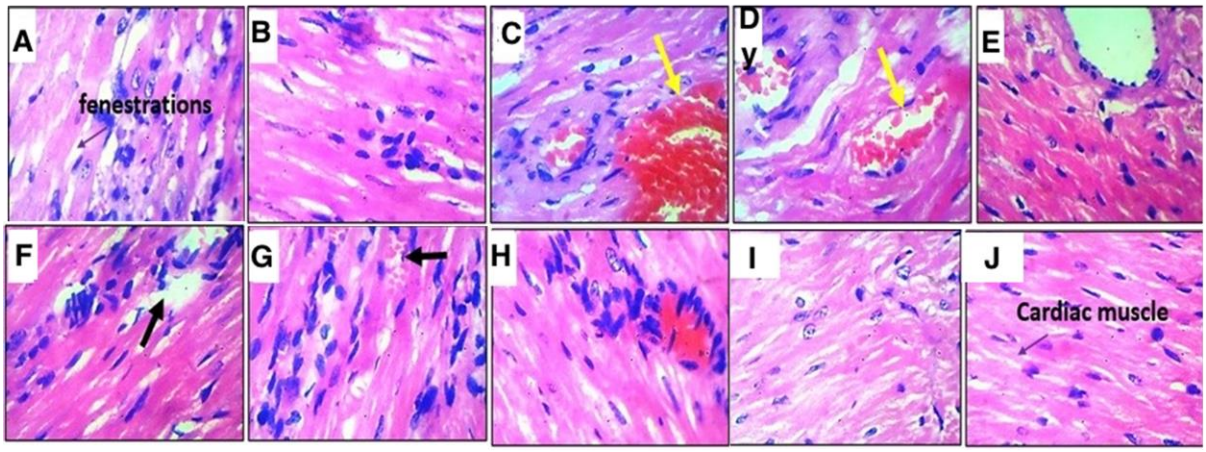

Figure 6: High-magnification photomicrographs of cardiac tissue illustrating cardiomyocyte morphology. H&E staining, ×400 magnification. Dichlorvos exposure results in loss of striations, cardiomyocyte degeneration, and focal fibrosis (yellow arrows). Naringin treatment shows mild residual alterations (black arrows), whereas quercetin treatment markedly preserves myocardial structure

3.4 Histology of the Kidney

Renal sections from control, baseline, vehicle, quercetin-only, and naringin-only groups (Groups A, B, E, H, and I) exhibited normal renal architecture (Figures 7 and 8). Glomeruli were intact with normal Bowman's spaces, mesangial cells appeared unremarkable, and renal tubules were well defined without evidence of degeneration.

In contrast, kidney sections from dichlorvos-treated and recovery groups (Groups C and D) showed marked pathological alterations, including glomerular fluid accumulation, distorted glomerular architecture, tubular lumen occlusion with casts, interstitial inflammatory infiltration, and early glomerulosclerotic changes, consistent with severe nephrotoxicity.

The dichlorvos plus naringin group (Group G) exhibited moderate renal alterations, characterised by occasional sclerotic glomeruli and mild vascular congestion (black arrows).

Conversely, renal sections from the dichlorvos plus quercetin group (Group F) showed marked attenuation of renal damage, with preservation of glomerular and tubular structures and minimal histopathological alterations.

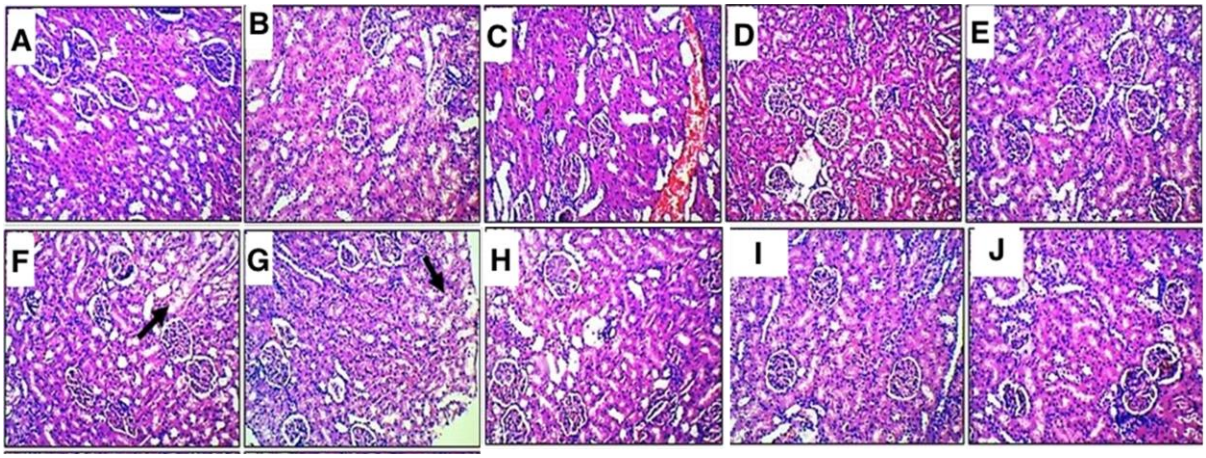

Figure 7: Panoramic photomicrographs of kidney histology across experimental groups. H&E staining, ×100 magnification. Control groups show intact renal architecture with well-defined glomeruli and tubules. Dichlorvos-treated and recovery groups exhibit glomerular distortion, tubular degeneration, and interstitial inflammation (yellow arrows). Attenuation of renal damage is evident following quercetin treatment.

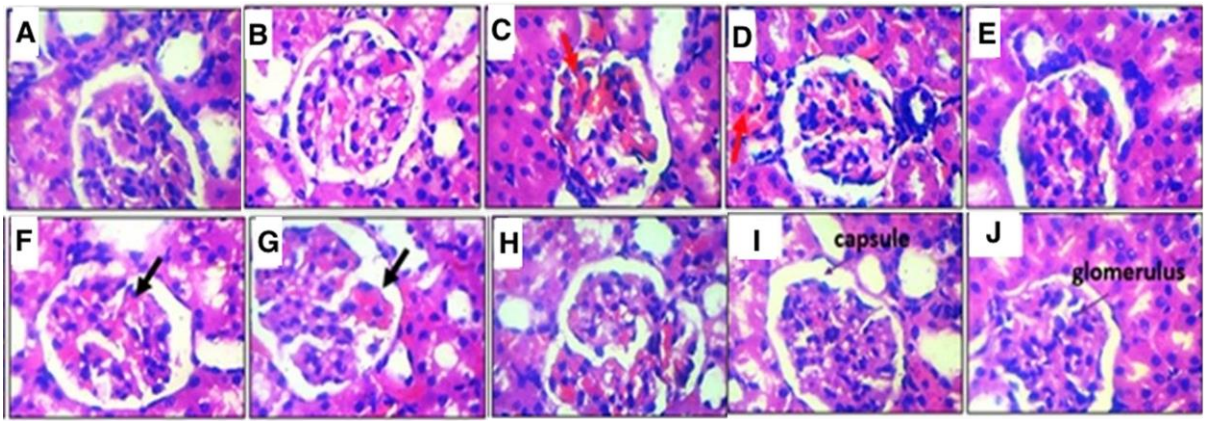

Figure 8: High-magnification photomicrographs of kidney sections illustrating glomerular and tubular morphology. H&E staining, ×400 magnification. Dichlorvos exposure induces glomerular sclerosis, tubular lumen occlusion, and inflammatory infiltration (yellow arrows). Partial protection is observed in the naringin-treated group (black arrows), while quercetin treatment preserves near-normal renal histoarchitecture.

4.0 DISCUSSION

The present study demonstrated that dichlorvos exposure induces marked histopathological alterations in multiple organs, including the liver, brain, heart, and kidney. Furthermore, this study comparatively evaluated the histoprotective effects of quercetin and naringin against dichlorvos-induced tissue injury. The observed organ-specific lesions are consistent with the known toxicological profile of organophosphate pesticides and support the role of oxidative stress and inflammation as central mechanisms underlying dichlorvos-induced toxicity [27, 28].

The liver, as the primary organ responsible for xenobiotic metabolism, is particularly susceptible to dichlorvos-induced oxidative injury. In this study, dichlorvos exposure resulted in central venous congestion, hepatocellular degeneration, sinusoidal dilatation, inflammatory infiltration, and early fibrotic changes. These findings are in agreement with previous reports describing organophosphate-induced hepatotoxicity mediated through lipid peroxidation, mitochondrial dysfunction, and disruption of hepatocellular membrane integrity [29, 30].

Neurohistological examination revealed pronounced cortical degeneration in dichlorvos-treated rats, characterized by neuronal pyknosis, cytoplasmic fragmentation, and disruption of cortical organization. These observations further corroborate the established neurotoxicity of dichlorvos, which has been attributed to acetylcholinesterase inhibition as well as oxidative stress–mediated neuronal injury. Similarly, cardiac tissues exhibited cardiomyocyte degeneration, loss of striations, focal fibrosis, and vascular abnormalities, indicative of cardiotoxic effects. These alterations are consistent with previous studies linking organophosphate exposure to oxidative injury of cardiac myofibrils, impaired

calcium homeostasis, and inflammatory responses within myocardial tissue [28, 31]. The fibrotic changes observed may represent a reparative response to sustained cellular injury.

Renal histopathological findings further demonstrated the nephrotoxic potential of dichlorvos, as evidenced by glomerular distortion, tubular degeneration, interstitial inflammation, and early sclerotic changes. Given that dichlorvos and its metabolites are primarily eliminated via the kidneys, renal tissues are exposed to high concentrations of reactive intermediates, rendering them particularly vulnerable to oxidative and inflammatory damage [3, 32].

Notably, cessation of dichlorvos exposure alone, as observed in the recovery group, was insufficient to reverse the histopathological alterations across the examined organs. The persistence of tissue damage following exposure withdrawal suggests that dichlorvos-induced injury may be sustained beyond the period of active exposure, particularly in metabolically active and highly differentiated tissues such as the brain and heart [33].
In contrast, administration of flavonoid supplements demonstrated varying degrees of histological protection. Quercetin treatment markedly attenuated dichlorvos-induced tissue injury across all examined organs, with preservation of cellular architecture and reduced severity of histopathological lesions. The pronounced protective effect of quercetin may be attributed to its strong antioxidant capacity, ability to scavenge reactive oxygen species, modulation of endogenous antioxidant enzyme systems, and inhibition of pro-inflammatory signaling pathways [5]. These properties likely contribute to its superior histoprotective efficacy.

Naringin administration, although beneficial, provided only partial protection, as mild residual lesions persisted in the liver, brain, heart, and kidney. While naringin possesses antioxidant and anti-inflammatory properties, its comparatively reduced efficacy may be related to differences in bioavailability, cellular uptake, or metabolic conversion to its active aglycone, naringenin [25, 34]. The persistence of mild vascular congestion and focal sclerosis in naringin-treated tissues suggests that its protective capacity may be limited under conditions of sustained toxic insult.
Collectively, these findings support the central role of oxidative stress in dichlorvos-induced multi-organ toxicity and highlight the therapeutic potential of antioxidant flavonoids in mitigating such damage. The differential protective outcomes observed between quercetin and naringin further emphasize the importance of molecular structure and pharmacokinetic properties in determining histoprotective efficacy. Although this study relied on histopathological evaluation, the findings provide compelling morphological evidence of dichlorvos-induced organ injury and flavonoid-mediated protection. Future studies incorporating biochemical and molecular markers would further strengthen the mechanistic understanding of these protective effects.

This study demonstrated the dichlorvos-induced histopathological effects on multiple organs, especially on the liver, brain, heart, and kidney. Comparative analysis of the potentials of quercetin and naringin against these effects was also evaluated [27, 28]. The liver, being the primary site of xenobiotic metabolism, is particularly vulnerable to dichlorvos-induced free radical generation, leading to lipid peroxidation and structural damage to hepatocytes [30]. Dichlorvos-induced hepatotoxicity, as observed in this study, is characterized by central venous congestion, hepatocellular degeneration, sinusoidal dilation, inflammatory infiltration, and early fibrotic changes [29, 30]. These alterations are consistent with previous studies where organophosphate pesticides cause hepatic injury through oxidative stress, mitochondrial dysfunction, and disruption of cellular membrane integrity.
Neurodegenerative changes, including neuronal pyknosis, cytoplasmic fragmentation, and cortical disorganization, were also observed in the cerebral cortex of dichlorvos-treated rats, further corroborating the established neurotoxicity of organophosphates. Cardiac tissue from the rats exposed to dichlorvos showed degeneration of cardiomyocytes, loss of striation, fenestrations, fibrosis, and vascular abnormalities, indicating cardiotoxicity. These findings align with previous reports where organophosphate toxicity is linked to oxidative injury to cardiac myofibrils, impaired calcium homeostasis, and inflammatory responses within myocardial tissue. The observed fibrosis may reflect a reparative response to sustained cellular injury [28, 31]. Renal histopathology further revealed glomerular and tubular damage following dichlorvos exposure, including glomerular fluid accumulation, tubular casts, and interstitial infiltration. Such alterations are indicative of compromised renal filtration and tubular function. Given that dichlorvos metabolites are eliminated primarily via the kidneys, renal tissues are exposed to high concentrations of reactive intermediates, rendering them susceptible to oxidative and inflammatory injury [3, 32].

Findings from this study revealed that post-exposure withdrawal of dichlorvos (as demonstrated in the recovery group) alone was not sufficient to restore to normalcy the altered structure and architecture of the liver, brain, heart, and kidney [33]. The persistence of these alterations in the recovery group suggests that cessation of exposure alone may not be sufficient to reverse dichlorvos-induced neuronal damage [5]. In rats administered with flavonoid supplements (quercetin and naringin), a significant preservation and restoration of histological integrity was observed across the examined organs, consistent with previous studies where flavonoid supplements were shown to protect against the dichlorvos-induced effects [4, 26, 34].

Administration of quercetin significantly mitigated dichlorvos-induced histological damage across all examined organs. Quercetin-treated rats displayed near-normal tissue architecture, suggesting robust cytoprotective effects. The protective efficacy of quercetin may be attributed to its potent antioxidant capacity, membrane permeability, and ability to scavenge reactive oxygen species at both aqueous and lipid interfaces. Additionally, quercetin has been shown to modulate endogenous antioxidant enzyme systems and inhibit inflammatory signaling pathways, thereby preserving cellular and tissue integrity [5]. Naringin administration, on the other hand, showed a partial histological protection, as indicated by the mild residual lesions remaining in the liver, brain, heart, and kidney of dichlorvos-exposed rats administered with naringin [29]. Although naringin has been demonstrated to possess several biological and pharmacological properties, including antioxidant, anti-inflammatory, and anti-atherogenic, its limitation in efficacy when compared to quercetin may be due to differences in bioavailability, cellular uptake, or metabolic conversion to its active aglycone, naringenin [10, 25, 29, 34]. Also, the persistence of mild vascular congestion and focal sclerosis in naringin-treated tissues may suggest that naringin's protective effects may be less pronounced under conditions of sustained toxic injury [5].

Findings from this study collectively support the hypothesis that oxidative stress plays a central role in dichlorvos-induced organ damage and that antioxidant flavonoids can effectively attenuate these effects. These findings particularly highlight the significant health risks associated with dichlorvos exposure, with emphasis on the importance of early therapeutic intervention with protective agents [30]. The differential protective outcomes observed between quercetin and naringin further emphasize the importance of molecular structure and pharmacokinetic properties in determining therapeutic efficacy against dichlorvos-induced damages [28].

5.0 CONCLUSION

The findings of this study demonstrate that dichlorvos exposure induces significant histopathological alterations in multiple organs, including the liver, brain, heart, and kidney. The observed lesions such as hepatocellular degeneration, neuronal damage, myocardial distortion, and glomerular injury highlight the systemic toxic potential of dichlorvos and reinforce concerns regarding its extensive use and associated public health risks. The persistence of histological alterations in the recovery group indicates that withdrawal of dichlorvos exposure alone may be insufficient to fully ameliorate tissue damage, particularly in highly metabolically active organs.

Administration of quercetin and naringin conferred varying degrees of protection against dichlorvos-induced tissue injury. Quercetin treatment markedly attenuated histopathological damage across all examined organs, with preservation of tissue architecture and reduced severity of lesions. In contrast, naringin treatment provided partial protection, as residual degenerative changes remained evident in several organs. The differential protective efficacy observed between these flavonoids may be attributed to differences in their antioxidant capacity, bioavailability, cellular uptake, and molecular structure.

Overall, this study underscores the therapeutic relevance of dietary flavonoids as protective agents against organophosphate-induced histological toxicity. Quercetin, in particular, emerges as a promising candidate for mitigating dichlorvos-associated organ injury. Future studies incorporating biochemical assays, molecular analyses, and quantitative histological scoring are warranted to further elucidate the mechanisms underlying flavonoid-mediated protection and to strengthen the translational relevance of these findings.

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COMPETING INTERESTS
The authors declare there is no conflict of interest regarding this study.

AUTHORS' CONTRIBUTIONS
ADW designed the study, wrote the protocol, and finalised the first draft, JSO and OIO collected, processed, and analyzed samples, AOK conducted the statistical analysis of the data, JOI and AOA wrote the first draft of the manuscript, OAA and AEO assisted with sample collection and protocol, ATO assisted with study design and sample analyses, and the final copy was proofread by all authors.

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