Science World Journal Vol. 21(No 2) 2026 https://dx.doi.org/10.4314/swj.v21i2.2
www.scienceworldjournal.org
ISSN: 1597-6343 (Online), ISSN: 2756-391X (Print)
Published by Faculty of Science, Kaduna State University

Full Length Research Article

QUERCETIN AND NARINGIN AMELIORATE DICHLORVOS-INDUCED SUBACUTE TOXICITY VIA MODULATION OF ANTIOXIDANT ENZYMES IN RATS

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ABSTRACT
Dichlorvos is an organophosphate insecticide widely used in domestic and agricultural settings, and exposure is associated with significant toxicological effects, largely mediated by oxidative stress. This study evaluated the protective effects of the flavonoids quercetin and naringin against dichlorvos-induced subacute toxicity in male Wistar rats. Eighty male albino rats were randomly allocated into eight groups (n = 10); negative control (water), positive (vehicle) control (Dimethyl sulfoxide (DMSO)), Dichlorvos (8mg/kg BW), Dichlorvos recovery, Dichlorvos + naringin, Dichlorvos + quercetin, quercetin only, naringin only, and orally treated for 28 days. At the end of the experimental period, plasma, red blood cells, liver, and brain samples were collected for biochemical analyses. Activities of superoxide dismutase (SOD), catalase (CAT), and glutathione S-transferase (GST) were determined spectrophotometrically. Subacute dichlorvos (28-day) exposure caused significant reductions in SOD, CAT, and GST activities across all examined tissues, reflecting impaired antioxidant defense and increased oxidative stress. Co-administration of quercetin or naringin significantly attenuated these alterations, with enzyme activities approaching control levels. Quercetin showed greater protective efficacy in liver and brain tissues, whereas naringin exerted comparatively stronger effects in plasma and red blood cells, indicating tissue-specific antioxidant responses. Overall, the findings demonstrate that quercetin and naringin effectively protect against dichlorvos-induced subacute toxicity by modulating endogenous antioxidant enzymes, supporting the potential use of dietary flavonoids as adjunct protective agents against organophosphate toxicity.

Keywords: Dichlorvos; Quercetin; Naringin; Oxidative stress; Organophosphate toxicity.

INTRODUCTION

Organophosphate compounds represent a major class of chemical substances widely used in both agricultural and domestic settings for the control of insects and other pests (Boots & Bast, 2008). Although their effectiveness has made them valuable tools in pest management, their widespread and often indiscriminate use has raised significant concerns. In particular, exposure to these compounds has been associated with adverse health effects, including acute toxicity and chronic neurotoxicity (Poonam, 2012). These risks are especially pronounced in developing countries, where cases of accidental and occupational poisoning are frequently reported (Olebunne, 2009; Karami-Mohajeri & Abdollahi, 2011).

Among the many organophosphate insecticides available, dichlorvos is one of the most widely used (Chtourou, 2014). However, its extensive application in pest control has been associated with numerous cases of acute and subacute poisoning, particularly in Nigeria, raising significant public health concerns (Olebunne, 2009)

The toxic effects of dichlorvos are multifaceted, with a primary mechanism involving the inhibition of acetylcholinesterase, a key enzyme in neurotransmission (Hou, 2014; Sharma, 2023). Inhibition of this enzyme leads to the accumulation of acetylcholine in the synaptic cleft, resulting in overstimulation of nerve endings (Hou, 2014). In addition to its cholinergic effects, dichlorvos toxicity promotes the generation of reactive oxygen species (ROS), contributing to oxidative stress and subsequent tissue injury. These biochemical disturbances can manifest clinically in a range of symptoms, from mild effects to severe complications, underscoring the need for effective preventive and therapeutic strategies (Ambali, 2011).

Flavonoids represent a diverse and important class of phytochemicals widely distributed in natural sources, particularly in fruits, vegetables, and plant-derived beverages (Babu, 2009). These compounds are characterized by a common flavan nucleus, which underlies many of their biological activities (Hou, 2014). Extensive research has highlighted the beneficial properties of flavonoids, including their potent antioxidant, anti-inflammatory, and cytoprotective effects (Boots & Bast, 2008).

Among the numerous flavonoids identified, naringin is a prominent member of this group. It is classified as a flavanone-7-O-glycoside and is primarily found in citrus fruits such as grapefruits and oranges (Kalender, 2012; Chtourou, 2014). Naringin has attracted considerable attention for its potent ability to scavenge reactive oxygen species, thereby reducing oxidative stress and preventing cellular damage (Zhang, 2013; Singh, 2024). This property makes it a promising compound in the prevention and management of oxidative stress–related diseases (Zhang, 2013; Singh, 2024).

Another important flavonoid is quercetin, a flavanol found in high concentrations in various fruits and vegetables, including apples, onions, and berries (Salem, 2016). This compound has been extensively studied for its protective effects against tissue damage arising from various drug-induced toxicities (Akande, 2017; Saka,

2025). The protective effects of quercetin are largely attributed to its antioxidant properties, which help mitigate oxidative stress and inflammation (Ozcan, 2015; David, 2016).

Given the growing interest in natural antioxidants as potential therapeutic agents, this study aims to evaluate the protective roles of quercetin and naringin against subacute dichlorvos-induced toxicity in healthy male albino rats. Superoxide dismutase (SOD), glutathione S-transferase (GST), and catalase (CAT) levels were assessed as biomarkers of oxidative stress and antioxidant response (Shadnia, 2007; Yan, 2014).

MATERIALS AND METHODS

Chemicals and Reagents

Dichlorvos (sniper) was obtained from Saro Agrosciences Limited, Nigeria (purity: 98%). All other chemicals used were of analytical grade, phosphate buffer, formalin, chloroform, coconut oil (Twin Faja Store, Lagos, Nigeria), distilled water, normal saline, heparin and ketamine injection (purchased from Newton Pharmacy, Lagos, Nigeria), naringin and quercetin (Sigma-Aldrich, St. Louis MO, USA), and dimethyl sulfoxide (DMSO) were used in this study. All kits used in this study were obtained from British Drug House (BDH) Chemicals Limited, Poole, England. Other chemicals were procured from Sigma-Aldrich Chemical Co. (Germany). All reagents were of analytical grade.

Experimental Design and Treatment Protocol

Eighty healthy male albino rats were obtained and housed under standard laboratory conditions with ad libitum access to food and water. The animals were allowed to acclimatize for one week prior to the commencement of the experiment. All procedures adhered to institutional ethical guidelines for the care and use of laboratory animals. Following acclimatization, rats were weighed and randomly assigned to eight experimental groups (n = 10 per group), and the subacute toxicity of dichlorvos was evaluated following repeated daily exposure for 28 days at a dose of 4 mg/kg body weight, as shown in Table 1.0. In this context, 'subacute' refers to the duration of exposure rather than the administered dose, consistent with standard toxicological classifications in which subacute studies involve repeated exposure over a period of up to 28 days (World Health Organization, 2009). The experimental design was structured to evaluate dichlorvos-induced toxicity, spontaneous recovery following exposure withdrawal, and the comparative protective effects of quercetin and naringin.

Table 1.0: Experimental Design

Group(n=10)	Treatment Description
Negative Control	Distilled Water
Vehicle Control	Dimethyl sulfoxide (0.05% DMSO)
Dichlorvos	Dichlorvos (4mg/kg BW)
Dichlorvos + Quercetin	Dichlorvos (4mg/kg BW) and quercetin (75mg/kg BW)
Dichlorvos + Naringin	Dichlorvos (4mg/kg BW) and naringin (100mg/kg BW)
Quercetin only	Quercetin (75mg/kg BW)
Naringin only	Naringin (100mg/kg BW)
Recovery	Dichlorvos (4mg/kg BW) + 14 day (no treatment) before sacrifice

Sample Collection and Preparation

At the end of the experimental period, animals were fasted overnight and anesthetized with a combination of 5% ketamine and 2% xylazine. Blood samples were obtained via cardiac puncture into a lithium-heparinized tube. The brain and liver were excised, trimmed of connective tissues, and rinsed in normal saline. Subsequently, 0.1 g of each tissue sample was homogenized in phosphate buffer. The homogenates were centrifuged at 4000 rpm for 5 minutes, after which the supernatants were collected into clean Eppendorf tubes and stored at -20°C for biochemical analysis.

Biochemical Assays

Determination of catalase activity

CAT activity in plasma, red blood cells, and liver and brain homogenates was determined spectrophotometrically and expressed as units/mL (U/mL) for plasma and red blood cells, and as units/g tissue for liver and brain samples, as described by Claiborne (1985). The reaction mixture (1 mL) contained 100 mM phosphate buffer (pH 7.4), 50 mM H_2O_2, and the appropriate sample (plasma, red blood cells, or tissue homogenate). The addition of H_2O_2 initiated the reaction, and its decomposition was monitored by measuring the decrease in absorbance at 240 nm for 1 minute.

Determination of superoxide dismutase activity

SOD activity in the tissues was determined using the modified method of Misra and Fridovich (1972). The reaction was initiated by adding 0.3 mL of 0.01% epinephrine to a mixture containing 2.5 mL of 0.05 M carbonate buffer and 0.2 mL of the sample. The change in absorbance was measured at 480 nm. Enzyme activity was expressed as units/mL for plasma and red blood cells, and as units/g tissue for liver and brain samples.

Determination of Glutathione Transferase Activity.

GST activity was determined by measuring the formation of 1-chloro-2,4-dinitrobenzene and the GSH conjugate at 340 nm, using a modified method described by Habig et al. (1974).

Statistical Analysis:

Statistical analysis was performed using GraphPad Prism version 10.0. Data were analyzed by one-way analysis of variance (ANOVA), followed by Tukey's post hoc test for multiple comparisons. Results are presented as mean ± SEM, and statistical significance was set at $p < 0.05$.

RESULTS

Effect of Quercetin and Naringin on Superoxide Dismutase Activity in Plasma and Red Blood Cells

Plasma SOD activity differed significantly among the treatment groups (Figure 1A). The negative control recorded a baseline value of 0.1985, while the vehicle control showed an increased activity of 0.3582, representing an 80.4% increase relative to the negative control. In contrast, dichlorvos-only exposure resulted in a marked reduction in plasma SOD activity (0.09197), corresponding to a 53.6% decrease compared with the negative control. Co-administration of flavonoids partially improved plasma SOD activity. The dichlorvos + naringin group recorded a value of 0.1254 (36.8% decrease relative to the negative control), while the

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dichlorvos + quercetin group showed 0.1005 (49.4% decrease). Neither treatment restored plasma SOD activity to control levels. Flavonoid-only treatment resulted in reduced plasma SOD activity compared with the negative control. The naringin-only group showed a 51.3% decrease, whereas the quercetin-only group exhibited a 69.6% decrease.

RBC SOD activity varied significantly across treatment groups (Figure 1B). The negative control exhibited a baseline activity of 0.3761. The vehicle control showed a marked elevation to 1.237, representing a 229% increase relative to the negative control. Dichlorvos exposure also increased RBC SOD activity to 0.625, corresponding to a 66.2% increase. Combined treatment with flavonoids further increased RBC SOD activity. The dichlorvos + naringin group recorded the highest activity (1.318), representing a 250.5% increase relative to the negative control, while the dichlorvos + quercetin group showed an activity of 1.069 (184% increase). Flavonoid-only groups also showed elevated RBC SOD activity. The naringin-only group exhibited a 246% increase, whereas the quercetin-only group showed a 24.2% increase relative to the negative control. The recovery group showed reduced RBC SOD activity (0.3043), representing a 19.1% decrease compared with the control groups.

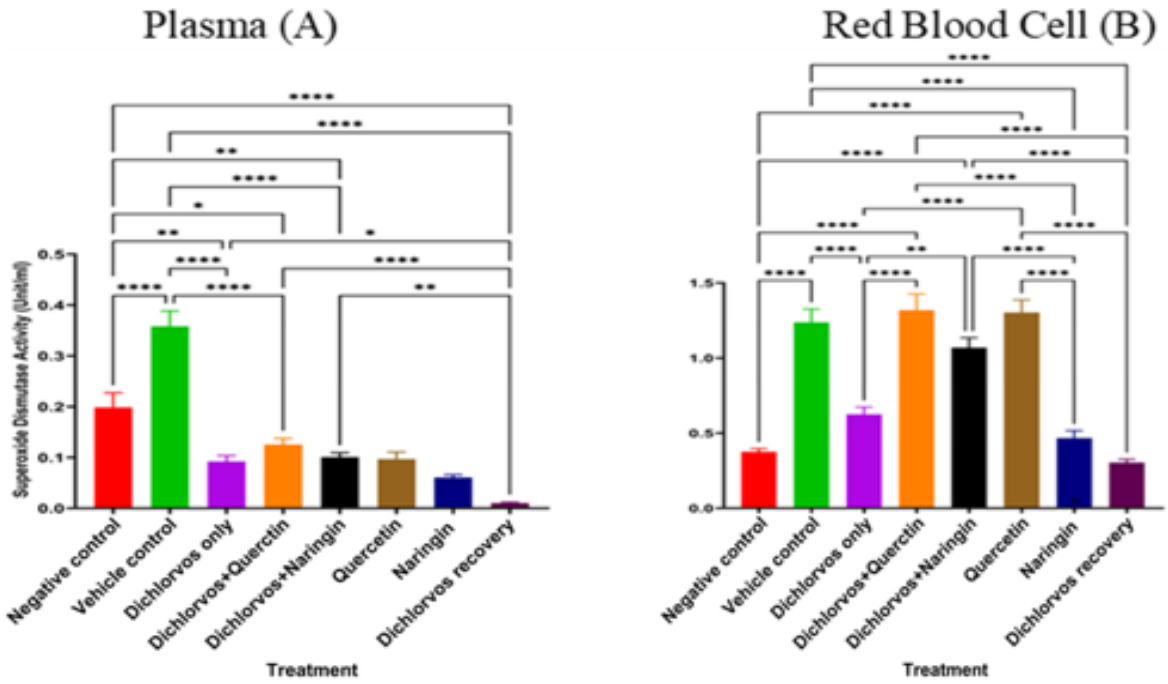

Figure 1: Effect of Quercetin and Naringin on Superoxide Dismutase Activity in Plasma (A) and Red Blood Cell (B). Each bar represents the means±S.E.M. of 10 rats. Bars with *p<0.05, **p<0.01, ****p <0.0001 are significantly different from the controls.

Effect of Quercetin and Naringin on Superoxide Dismutase Activity in Brain and Liver

Brain SOD activity differed across the experimental groups (Figure 2A). The negative control group recorded a baseline activity of 4.395 U/ml. The vehicle control group showed a 53.9% increase compared with the negative control. Exposure to dichlorvos alone resulted in a moderate increase in brain SOD activity (16.3%) compared with the negative control. A similar increase was observed in the dichlorvos plus naringin group (17.0%). In contrast, the dichlorvos plus quercetin group demonstrated a more pronounced elevation in brain SOD activity (54.3%), comparable to that observed in the vehicle control group. Administration of flavonoids alone produced substantial increases in brain SOD activity. Naringin-only treatment resulted in a 169.4% increase, while quercetin-only treatment produced a 148.7% increase relative to the negative control. These values exceeded those observed in both the negative and vehicle control groups. Conversely, the recovery group showed a reduction in brain SOD activity, corresponding to a 24.9% decrease relative to the negative control.

Liver SOD activity also varied significantly among the treatment groups (Figure 2B). The negative control group recorded a baseline activity of 4.395 U/ml, while the vehicle control group showed a 53.9% increase relative to this value. Dichlorvos only exposure increased hepatic SOD activity to 5.109 U/ml, representing a 16.3% increase compared with the negative control. Co-administration with naringin resulted in a similar increase of 17.0%. In contrast, co-treatment with quercetin produced a greater elevation in liver SOD activity (6.781 U/ml), corresponding to a 54.3% increase, comparable to the vehicle control group.

Flavonoid-only treatments produced the highest hepatic SOD activities. Naringin-only administration increased SOD activity to 11.84 U/ml (169.4% increase), while quercetin-only administration increased activity to 10.93 U/ml (148.7% increase) relative to the negative control. These increases exceeded those observed in both the negative and vehicle control.

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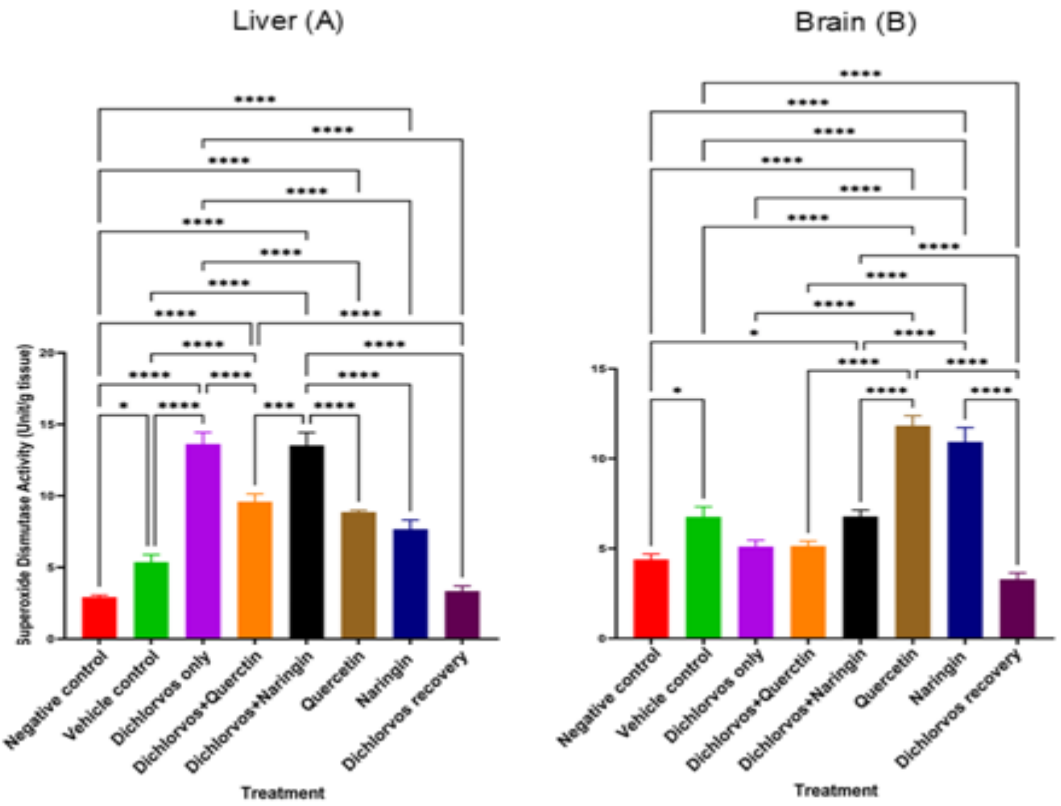

Figure 2: Effect of Quercetin and Naringin on Superoxide Dismutase (SOD) Activity in Liver (A) and Brain (B). Each bar represents the means±S.E.M. of 10 rats. Bars with *p<0.05, ***p <0.001, ****p <0.0001 are significantly different from the controls.

Effect of Quercetin and Naringin on Glutathione-S-Transferase Activity in Plasma and Red Blood Cell

Plasma GST activity differed significantly among treatment groups (Figure 3A). The negative control exhibited baseline activity, while the vehicle control showed a substantial increase relative to the negative control. Dichlorvos-only exposure caused a marked reduction in plasma GST activity, with a 58.2% decrease compared with the negative control and well below the vehicle control. The recovery group also showed reduced activity, recording a 43.0% decrease relative to the negative control, which was higher than dichlorvos alone but still below vehicle control levels. Co-administration with quercetin reversed the dichlorvos-induced reduction, increasing plasma GST activity to 35.7% above the negative control and exceeding both the dichlorvos-only and recovery groups. However, it remained slightly lower than the vehicle control. Dichlorvos + naringin partially restored GST activity, remaining 15.1% below the negative control but higher than dichlorvos-only. Antioxidant-only treatments caused modest increases. Quercetin-only increased plasma GST by 7.7% relative to the negative control, while naringin-only increased it by 5.2%, both lower than the vehicle control but above dichlorvos-only.

Red Blood Cell GST activity showed significant variation among groups (Figure 3B). The negative control recorded baseline activity, and dichlorvos-only exposure reduced activity by 16.9%. Co-treatment with quercetin further reduced erythrocyte GST, showing a 52.9% decrease relative to the negative control and below dichlorvos-only and vehicle control levels. In contrast, the dichlorvos + naringin treatment produced a smaller reduction of 16.0%, comparable to the dichlorvos-only treatment and higher than the dichlorvos + quercetin treatment. Antioxidant-only treatments affected erythrocyte GST differently: naringin alone increased GST by 9.8%, above dichlorvos-only, while quercetin alone decreased it by 30.6%, below both dichlorvos-only and negative control. The recovery group showed a 25.9% increase relative to the negative control, higher than those of the dichlorvos-only and co-treatment groups.

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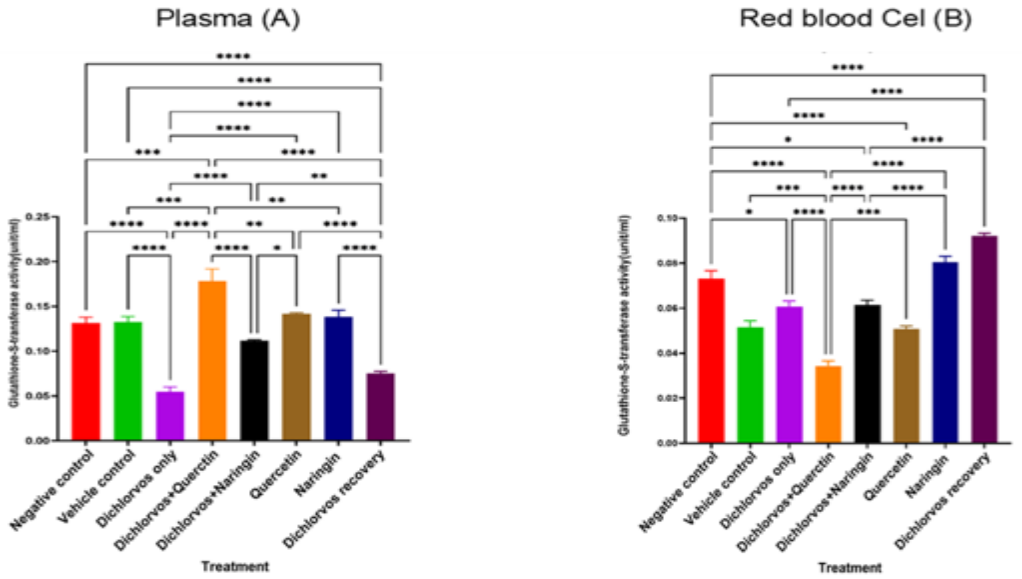

Figure 3: Effect of Quercetin and Naringin on Glutathione-S-Transferase (GST) Activity in Plasma (A) and Red Blood Cell (B). Each bar represents the means±S.E.M. of 10 rats. Bars with *p<0.05, **p<0.01, ***p <0.001, ****p <0.0001 are significantly different from the controls.

Effect of Quercetin and Naringin on Glutathione-S-Transferase Activity in Liver and Brain

Liver GST activity varied across treatment groups. Dichlorvos-only exposure reduced activity by 25.4% compared with the negative control and was below vehicle control levels. Co-treatment with dichlorvos + quercetin or dichlorvos + naringin partially restored liver GST activity relative to dichlorvos only but remained below the negative control. Quercetin-only treatment caused a smaller reduction (14.4%), whereas naringin-only treatment showed a 26.2% reduction relative to the negative control. The recovery group showed a marked increase in hepatic GST activity, 41.4% above the negative control and exceeding both the dichlorvos-only and co-treatment groups.

Brain GST activity differed markedly among groups. Dichlorvos only exposure reduced activity by 30.7% compared with the negative control. Co-administration with dichlorvos + quercetin partially restored activity, resulting in only a 6.5% reduction relative to the negative control, whereas dichlorvos + naringin showed a 9.6% reduction. Quercetin-only and naringin-only treatments increased brain GST activity by 18-23% above the negative control, higher than both dichlorvos-only and co-treatment groups. The recovery group also showed elevated GST activity, with a 21.9% increase relative to the negative control, comparable to the antioxidant-only treatment control.

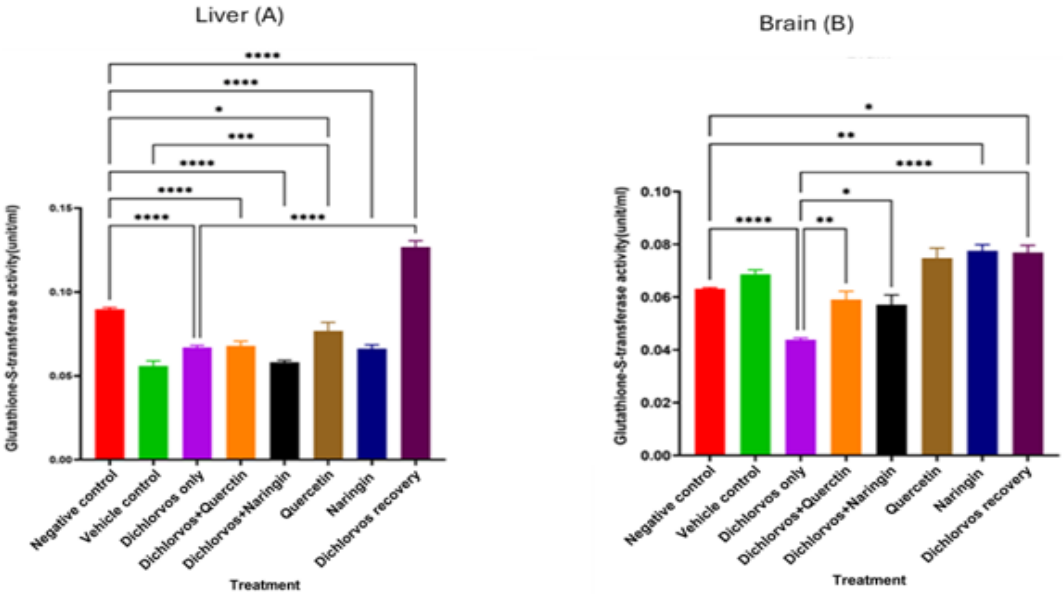

Figure 4: Effects of Quercetin and Naringin on Glutathione-S-Transferase Activity in Liver (A) and Brain (B). Each bar represents the means±S.E.M. of 10 rats. Bars with *p<0.05, **p<0.01, ***p <0.001, ****p <0.0001 are significantly different from the controls.

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Effect of Quercetin and Naringin on Catalase Activity in Plasma and Red Blood Cells

Plasma catalase activity varied significantly across groups. The negative control recorded a baseline of 0.04157 U/ml, whereas the vehicle control decreased by 24.1% to 0.03154 U/ml. Dichlorvos-only exposure showed a slight increase above the negative control (0.04369 U/ml) and a 38.5% increase compared to the vehicle control. Co-treatment with dichlorvos + quercetin further elevated plasma catalase to 0.05498 U/ml, exceeding both controls. In contrast, dichlorvos + naringin reduced activity to 0.02439 U/ml, below the vehicle control. Quercetin-only treatment decreased plasma catalase to 0.02456 U/ml, while naringin-only increased it to 0.0537 U/ml, surpassing both controls. The recovery group showed a moderate increase (0.04713 U/ml), higher than the positive control but below the dichlorvos + quercetin co-treatment. RBC catalase activity was strongly suppressed by dichlorvos. The negative control had an activity of 0.4624 U/ml, while the vehicle control dropped sharply to 0.03597 U/ml (-92.2%). Dichlorvos-only exposure caused a similar reduction (-90%). Co-treatment with dichlorvos + quercetin further decreased RBC catalase (-94.8%), whereas dichlorvos + naringin partially restored activity (-83.4%), higher than both dichlorvos-only and vehicle control. Quercetin-only and naringin-only treatments led to reductions of 84.7% and 87.7%, respectively, relative to the negative control. The recovery group exhibited partial restoration, with activity at -41.6% relative to the negative control.

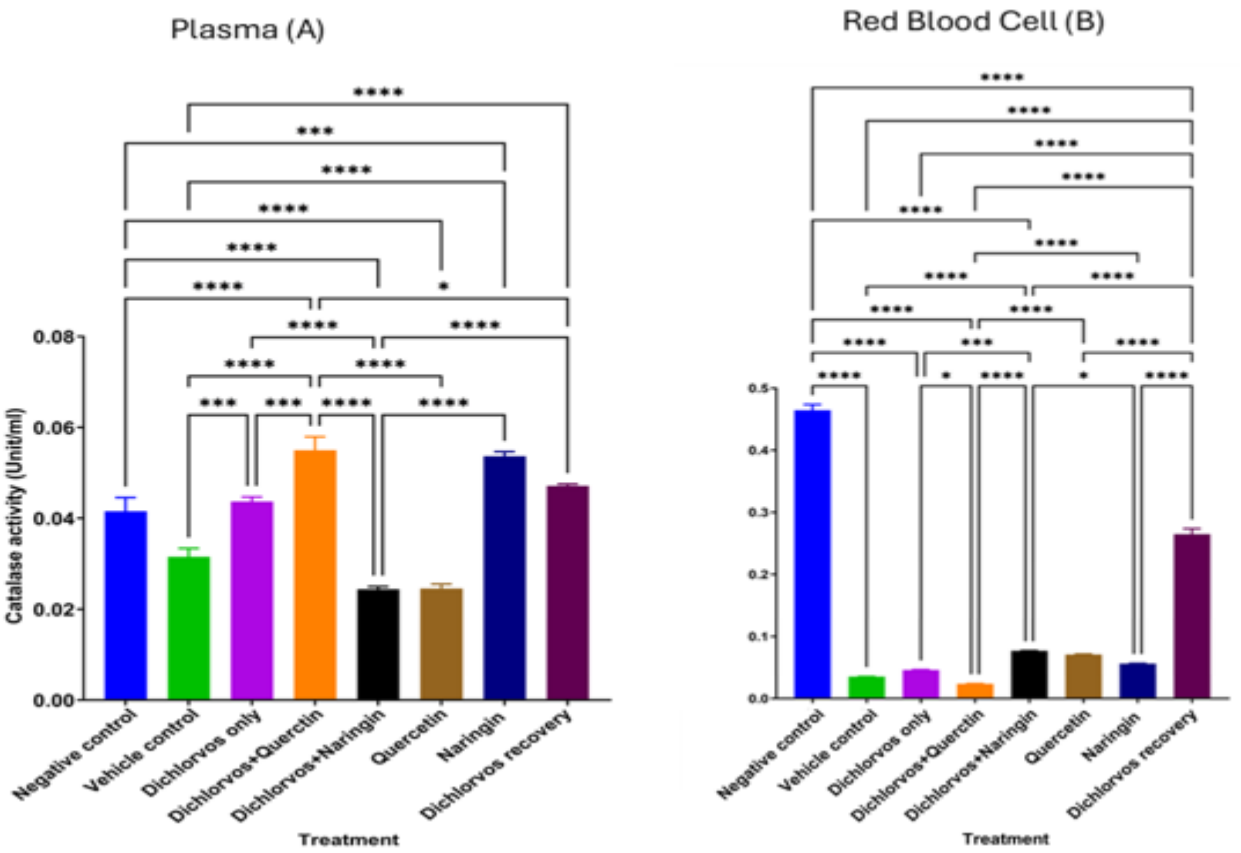

Figure 5: Effect of Quercetin and Naringin on Catalase Activity in Plasma (A) and Red Blood Cell (B). Each bar represents the means±S.E.M. of 10 rats. Bars with *p<0.05, ***p <0.001, ****p <0.0001 are significantly different from the controls.

Effect of Quercetin and Naringin on Catalase Activity in Brain and Liver

In the brain, catalase activity in the negative control was 1.62 U/ml. Vehicle control decreased to 0.4623 U/ml (-71.5%), and dichlorvos-only treatment further reduced it to 0.344 U/ml (-78.8%). Co-treatment with dichlorvos + quercetin markedly increased activity to 2.302 U/ml, surpassing both controls and the dichlorvos-only group. Dichlorvos + naringin restored activity to 1.276 U/ml, above dichlorvos-only and vehicle control but below the negative control. Quercetin alone increased brain catalase to 2.216 U/ml, whereas naringin alone decreased it to 0.6702 U/ml. The recovery group exhibited the highest activity at 2.59 U/ml. In the liver, catalase activity in the negative control was 1.95 U/ml. Vehicle control decreased to 0.7177 U/ml (-63.2%), and dichlorvos-only treatment reduced it to 1.19 U/ml (-38.8%). Co-treatment with dichlorvos + quercetin significantly increased activity to 4.17 U/ml, exceeding all other groups. Dichlorvos + naringin restored activity moderately to 1.23 U/ml. Quercetin alone slightly decreased liver catalase to 1.06 U/ml, while naringin alone maintained near-baseline activity at 1.82 U/ml. The recovery group showed 2.46 U/ml, above the negative control but below the dichlorvos + quercetin co-treatment.

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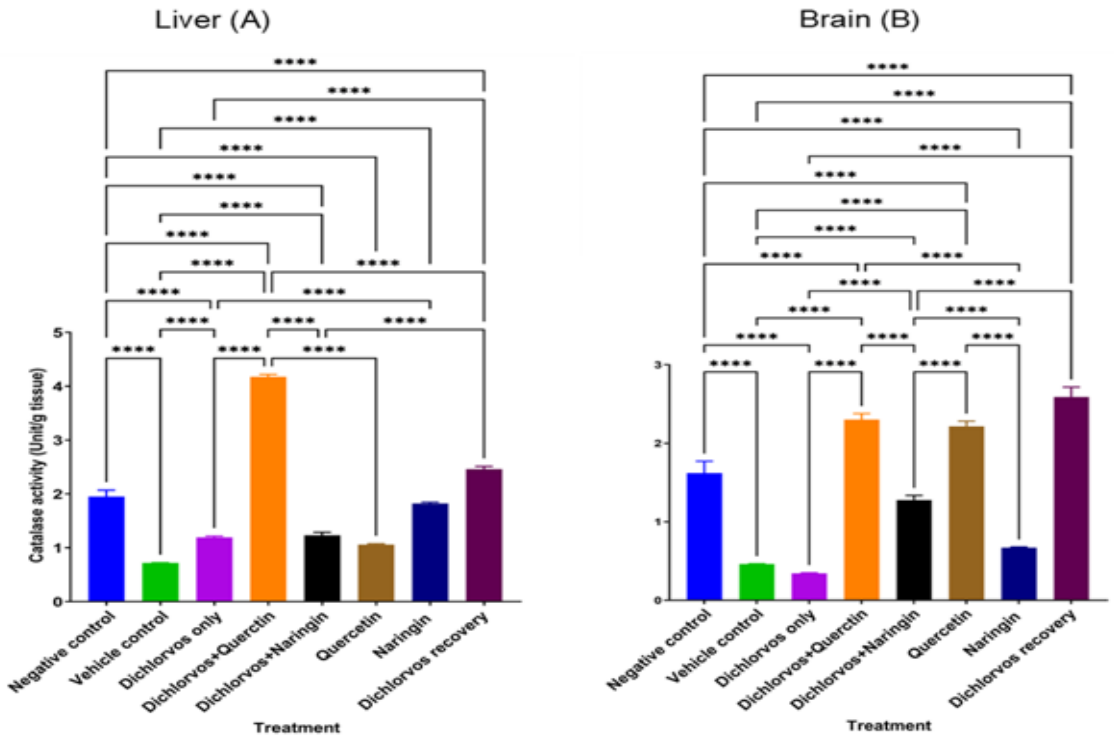

Figure 6: Effect of Quercetin and Naringin on Catalase Activity in Liver (A) and Brain (B). Each bar represents the means±S.E.M. of 10 rats. Bars with ****p, <0.0001 are significantly different from the controls.

DISCUSSION

Organophosphate pesticides, such as dichlorvos, remain a significant public health concern due to their widespread use and potent toxicity (Ambali, 2011; Karami-Mohajeri & Abdollahi, 2011). Dichlorvos is rapidly absorbed and metabolized, generating reactive oxygen species (ROS) that overwhelm endogenous antioxidant defenses and disrupt cellular homeostasis (Shadnia, 2007; Bas, 2011; Akinyoola, 2012). Oxidative stress is widely recognized as a central mechanism of organophosphate-induced cytotoxicity, leading to functional impairments in multiple organs, including the liver, brain, and hematopoietic tissues (Tuzmen, 2008; Zhang, 2022).

In this study, dichlorvos exposure significantly altered enzymatic antioxidant defenses in plasma, erythrocytes, liver, and brain. The sharp reduction in plasma SOD activity, alongside an increase in erythrocyte SOD, suggests a compensatory systemic response to oxidative stress. Brain and liver SOD activities showed moderate increases, indicating tissue-specific oxidative responses. Catalase activity was markedly suppressed in RBCs and neural tissue, whereas plasma and liver catalase exhibited partial or variable changes, reflecting differential tissue vulnerability to hydrogen peroxide accumulation. GST activity was also significantly reduced across all tissues, confirming impaired phase II detoxification pathways critical for xenobiotic clearance. Collectively, these findings corroborate previous studies demonstrating that dichlorvos induces systemic oxidative stress and compromises both enzymatic antioxidant defenses and detoxification systems (Hou, 2014; Qi, 2017; Soliman, 2023).

Co-administration of the flavonoids quercetin and naringin substantially mitigated the deleterious effects of dichlorvos. Both compounds restored SOD, catalase, and GST activities across all examined tissues, although the degree of protection varied. In plasma, quercetin reversed GST suppression, resulting in nearly a 40% increase, while naringin partially restored plasma SOD and GST, suggesting stronger systemic antioxidant activity in the naringin-treated groups. In erythrocytes, naringin co-treatment produced the highest SOD activity, whereas quercetin co-treatment resulted in modest reductions, highlighting tissue-specific differences in efficacy. In the liver and brain, quercetin demonstrated superior recovery of SOD and catalase activities, whereas naringin provided moderate but consistent restoration, particularly for GST. These observations suggest that flavonoids act through dual mechanisms: direct ROS scavenging and stabilization or upregulation of endogenous antioxidant enzymes (Ozcan, 2015; Akande, 2017).

Flavonoid-only treatments revealed intrinsic baseline effects. Both quercetin and naringin significantly increased SOD activity in the liver and brain, exceeding control levels and reflecting enzyme-inducing properties. However, plasma SOD decreased with flavonoid-only treatment, suggesting potential negative feedback regulation in circulating compartments. Catalase responses were tissue-dependent: quercetin strongly restored brain and liver catalase but decreased RBC catalase, whereas naringin moderately increased plasma and liver catalase, highlighting organ-specific pharmacodynamics influenced by bioavailability and molecular structure (Zhang, 2013; David, 2016).

Recovery groups demonstrated delayed but substantial compensatory responses. Several tissues, including liver and brain, showed enzyme activities rebounding above negative control

levels after cessation of dichlorvos exposure, reflecting delayed upregulation of antioxidant defenses. However, plasma GST and RBC catalase remained below baseline, indicating incomplete recovery in circulating compartments and suggesting that continued antioxidant support may be necessary to fully restore systemic redox balance.

Overall, the comparative trends of SOD, GST, and catalase across plasma, RBCs, liver, and brain underscore both systemic and organ-specific oxidative perturbations induced by dichlorvos, as well as the broad-spectrum protective effects of quercetin and naringin. Dichlorvos consistently suppressed plasma GST and RBC catalase while eliciting compensatory SOD elevations in erythrocytes and moderate increases in liver and brain, reflecting tissue-dependent oxidative responses. Co-treatment with flavonoids restored or enhanced antioxidant enzyme activities, with quercetin exerting pronounced effects in the liver and brain, and naringin providing robust systemic and RBC protection. Flavonoid-only treatments further demonstrated intrinsic enzyme-inductive properties, particularly in neural and hepatic tissues, while recovery groups exhibited partial or delayed rebounds in enzyme activity. These results indicate that quercetin and naringin confer broad-spectrum antioxidant protection, mitigating dichlorvos-induced oxidative damage by restoring endogenous enzyme function and reinforcing detoxification pathways (Middleton, 2000; Chtourou, 2014; Poonam, 2012; Singh, 2024).

In conclusion, dichlorvos exposure induces significant oxidative stress and multiorgan toxicity, primarily through suppression and dysregulation of key antioxidant and detoxifying enzymes, including SOD, catalase, and GST. This study demonstrates that quercetin and naringin effectively mitigate these adverse effects, restoring enzymatic activities across plasma, erythrocytes, liver, and brain in a tissue- and enzyme-specific manner. Quercetin provided pronounced neuroprotective and hepatoprotective effects, particularly on catalase and SOD, while naringin offered robust systemic and erythrocyte antioxidant support. The protective actions of these flavonoids likely involve a combination of direct free radical scavenging, stabilization and enhancement of endogenous antioxidant enzymes, and facilitation of detoxification processes. The observed tissue-specific responses underscore the complexity of oxidative damage and highlight the importance of selecting protective compounds based on their bioactivity and organ-targeting potential. These findings indicate that quercetin and naringin are promising natural therapeutic agents for counteracting organophosphate-induced toxicity.

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