

## ATTENUATION OF PARAQUAT-INDUCED NEPHROTOXICITY AND DYSFUNCTION IN MALE WISTAR ALBINO RATS

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**Background.** Paraquat (PQ) is a pesticide commonly used in the control of weed in agricultural practices worldwide. Exposure to PQ has adverse biochemical and physiological consequences to humans and animals. The mechanism of toxicity is linked to the generation of reactive oxygen species and subsequent lipid peroxidation. Presently, no single effective antidote to PQ toxicity has been established. Therefore, the need to continually investigate different treatment approaches is of paramount importance.

**Objective.** This study evaluated the capacity of selected dietary supplements to attenuate paraquat-induced kidney dysfunction and damages by determining some kidney function biomarkers and oxidative parameters.

**Methods.** Thirty-six Wistar albino rats were randomly separated into six groups. Each group (except Normal control) was intoxicated every other day with 1.5 mg/kg body weight of PQ and four groups (except PQ and Normal control groups) were treated daily with 40 mg/kg of garlic, glutathione and vitamin C for two weeks.

**Results.** The results showed significant ( $p < 0.05$ ) increases in concentration of kidney malondialdehyde, urea, creatinine, and blood lipid profiles. Also, significant decrease in concentrations of high-density lipoprotein cholesterol, kidney glutathione and total antioxidant capacity were presented by PQ control group compared to other PQ exposed groups treated with the antioxidant compounds.

**Conclusions.** PQ-induced changes indicated kidney dysfunction and damage. However, the administration of antioxidant supplements attenuated the PQ-induced biochemical and physiological dysfunction in the rats.

**Keywords:** paraquat; herbicide; nephrotoxicity; xenobiotics; antioxidants.

### Introduction

Paraquat (PQ) herbicide is a quaternary nitrogen compound (1,1'-dimethyl-4,4'-bipyridinium dichloride). It is a common non-selective contact herbicide used in agricultural practice worldwide [1, 2]. PQ is a known human and animal xenobiotic and it is highly active leading to several cases of acute poisoning and death [3, 4]. The toxicity of PQ necessitated the classification as moderately hazardous herbicide and class II poison for acute toxicity [5].

Studies have shown that oral ingestion of PQ induces generation of hydrogen peroxide anion, hydroxyl free radical as well as superoxide anions which cause lipid peroxidation with resultant cell membrane damage. These biochemical activities caused by oxidative free radicals are a common pathway for kidney damage and renal tubular necrosis. Aside from the potential for nephrotoxicity PQ exposure can result in hepatotoxicity and pulmonary fibrosis as well as systemic effects [6].

Systemic presence of PQ elicits generation of reactive oxygen species (ROS), accompanied by lipid peroxidation. This assertion is supported by epidemiological and clinical evidences which attribute mammalian biochemical and physiological changes

such as skin cancer and other tumors [7, 8], lung injuries [9], to PQ intoxication.

The increased advocacy for the use of herbicide in crop production makes it important to regularly ascertain the consequences of different levels of pesticides in the environment especially remnant of pesticides in food and water. Since PQ is one of the widely accepted herbicides, this study becomes imperative. PQ exerts its toxic effects by inducing oxidative stress on organisms. Different treatment measures have been adopted and yet no effective antidote has been found [9]. Due to the need to find an effective remedy to PQ-induced renal damage and dysfunction, this study used dietary supplements such as vitamin C, glutathione and garlic [10–13]. Vitamin C, glutathione and constituents of garlic exhibit antioxidant potentials that can reverse PQ-induced nephrotoxicity and dysfunction using male Wistar albino rats.

### Materials and Methods

#### Dietary supplements

The supplements used in this study were purchased from Orchard Pharmaceuticals, Ikenegbu

Owerri, Imo State, Nigeria. L-Glutathione (L-reduced) was manufactured by Raphe Pharmaceutiques Laboratoires, Dallas Texas USA. It is a certified supplement from nature lot#201604. Vitamin C (ascorbic acid) and Garlic tablet (*Allium sativum*) were manufactured in the USA for: Mason Vitamins, Inc. Miami Lakes, FL 33014, 1-888-860-5376 (www.MasonVitamins.com) The supplements were prepared in normal saline for oral administration.

### Study animals

Thirty-six male Wistar albino rats weighing  $150 \pm 10$  g were obtained from the Department of Veterinary Medicine, University of Nigeria Nsukka, Enugu State, Nigeria. The rats were kept in cages, maintained at a room temperature of  $25 \pm 2$  °C, 12 h light/dark cycle, and allowed free access to rat chow and water.

### Study design

After seven days of acclimatization, the rats were randomly allocated to six cages of six rats each, housed in the animal house of the Department of Biochemistry, Federal University of Technology, Owerri (FUTO). Each group was treated as follows:

Group 1 (normal control) received normal saline.

Group 2 (PQ control) received 1.5 mg/kg body weight (bw) of PQ.

Group 3 received 1.5 mg/kg bw of PQ and 40 mg/kg bw of vitamin C.

Group 4 received 1.5 mg/kg bw of PQ and 40 mg/kg bw of garlic.

Group 5 received 1.5 mg/kg bw of PQ and 40 mg/kg bw of glutathione.

Group 6 received 1.5 mg/kg bw of PQ and 40 mg/kg bw of vitamin C, glutathione, and garlic in the ratio of 1:1:1.

PQ was administered intraperitoneally at two days interval and other supplements orally administered daily for the two weeks. All rats were allowed free access to rat chow and clean water and no death was recorded for the two weeks duration of the study. This study was approved (FUTO/BCH/EC/2017/25) by the Ethics committee of the Department of Biochemistry, FUTO and it observed the guidelines of the National Institute of Health [14].

### Collection of tissue samples

After 14 days of study, blood samples were collected by ocular puncture into non-anticoagulant test tubes. Serum was obtained by allowing the blood samples to clot, centrifuged at  $3000 \times g$  for 15 min

and stored at 4 °C until used for analyses. Furthermore, the rats were sacrificed and kidney samples obtained and divided into two parts. A portion was washed in cold saline, homogenized in 1.15 % KCl in EDTA/pH 7.4, centrifuged for 20 min at  $250 \times g$  and aliquots of the supernatant used for biochemical assays. The other portions of the kidney sample were stored in 0.5 % formaldehyde for histopathology studies.

### Determination of some oxidative stress parameters

Malondialdehyde was determined by the method of Wallin *et al.* [15]. Four test tubes were prepared and aligned in a rack, and 0.1 ml of sample, 0.9 ml of distilled water, 0.5 ml of 25 % trichloroacetic acid (TCA) and 0.5 ml of 17 % TBA in 0.3 % NaOH were delivered into the test tubes. The mixture was incubated at 95 °C for 40 minutes and cooled in water bath afterward. Also, 0.1 ml of 20 % sodium dodecyl sulphate was added to the mixture. The concentration of malondialdehyde was determined from the absorbance read at 532 nm from the mixture and blank.

The concentration of glutathione was determined by the method described by Raja *et al.* [16]. Briefly: an equal amount of the homogenate was mixed with 10 % trichloroacetic acid and centrifuged to separate the proteins. Then 0.01 ml of the supernatant was pipetted, 2 ml of phosphate buffer (pH 8.4), 0.5 ml of 5, 5-dithiobis (2-nitrobenzoic acid), and 0.4 ml doubled distilled water was added to the test tubes. The mixture was vortexed and the absorbance was read within 15 minutes using a spectrophotometer. Absorbance of GSH was calculated from the standard calibration curve ( $y = mx$ ).

Total antioxidant activity was determined by the Ferric reducing ability of Plasma (FRAP) method by Benzie and Strain [17]. Initially, a working reagent comprising acetate buffer (pH 3.6), ferric chloride and tripyridyltriazine in the ratio of 10:1:1 respectively was prepared. To three test tubes containing 60  $\mu$ l of the sample, standard and blank, 1.8 ml of working reagent was added. The reaction mixture was mixed thoroughly and incubated at 37 °C for 10 minutes. The resulting blue-colored solution was read at 593 nm. The blank contained distilled water and the standard solution contains 1000  $\mu$ mol/l of ferrous sulfate.

Commercial test kits of BioSystems S.A. Costa Brava, 30. 08030 Barcelona (Spain) was used to determine serum creatinine and urea. Similarly, BioSystems, test kits were used to determine serum

triacylglycerides (TAG), cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL). Randox Laboratories Ltd (Antrim, United Kingdom) commercial test kits were used to determine serum nitric oxide and uric acid concentration.

### Histopathological studies

The fixed portions of kidney samples were dehydrated and allowed to undergo dealcoholization, infiltration and embedded in paraffin as shown by Okoro [18] with little modifications. Furthermore, the kidney samples were sectioned (serially) at an appropriate thickness, stained with hematoxylin and eosin [19]. Finally, a light microscope was utilized to examine tissue sections at a magnification of 100 $\times$  and 400 $\times$ .

### Statistical analysis

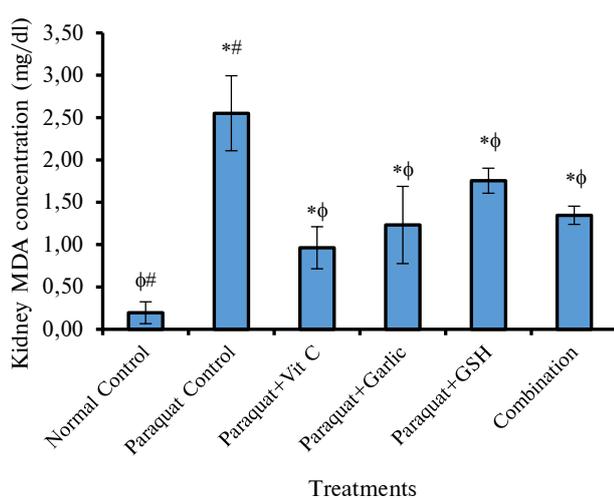
SPSS version 23 was used to analyze the data collected. The data were subjected to one-way analysis of variance (ANOVA) at  $p < 0.05$ . The results were expressed as mean  $\pm$  standard deviation of quadruple determination.

### Results

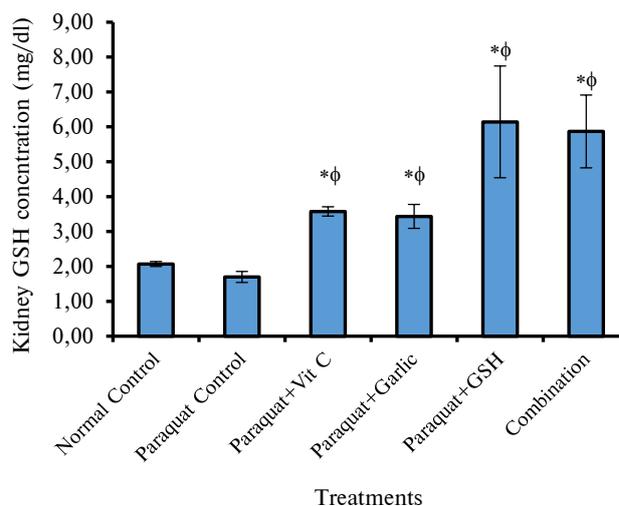
Fig. 1 shows a significant increase in the concentration of kidney malondialdehyde of animals exposed to PQ when compared to the normal control group which has the lowest concentration of

malondialdehyde. Treatment with supplements significantly reduced MDA concentration of animals exposed to PQ. The concentration of reduced glutathione (GSH) (Fig. 2), was lowest in PQ control group when compared to the normal control group. However, kidney concentration of GSH was significantly higher in vitamin C, GSH and combination groups compared to PQ control. The TAC (Fig. 3) was lowest in the PQ control group compared to the normal control group. The concentrations of kidney total antioxidant capacity were significantly increased in groups that received the supplements concomitantly. Aside from the concentration of nitric oxide (Fig. 7), the serum concentration of urea, creatinine and uric acid (Figs. 4 to 6) of PQ exposed rats were significantly increased compared to normal control rats. However, supplement treated groups presented urea, creatinine and uric acid concentrations which are within that of normal control rats.

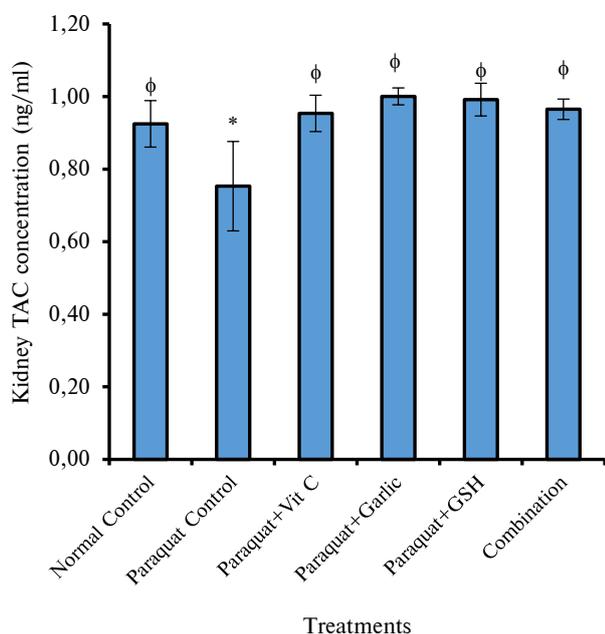
Rats administered PQ presented significantly increased serum cholesterol, triacylglyceride and low-density lipoprotein-cholesterol concentrations (Figs. 8 to 10). However, rats administered the supplements showed reduced concentration of some blood lipids with vitamin C and garlic groups presenting significantly reduced cholesterol, triacylglycerol, and LDL-cholesterol when compared to the PQ control group. Furthermore, HDL-cholesterol was significantly reduced in PQ control (Fig. 11) compared to the normal control and the supplement treated groups.



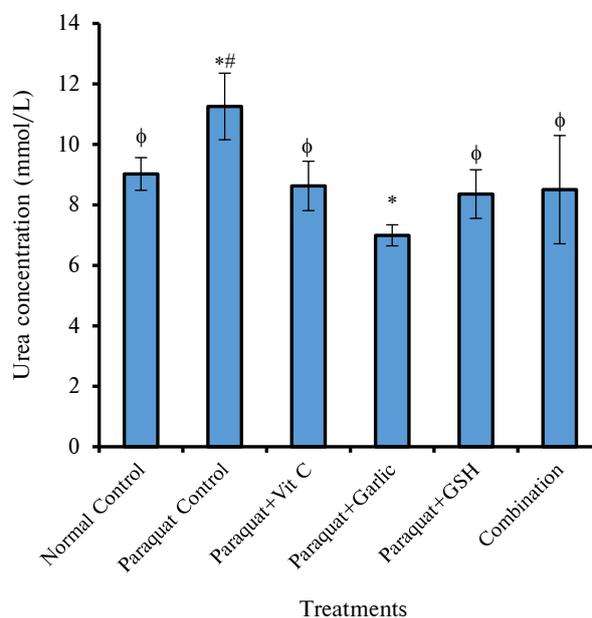
**Figure 1:** Concentration of kidney malondialdehyde (MDA) of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



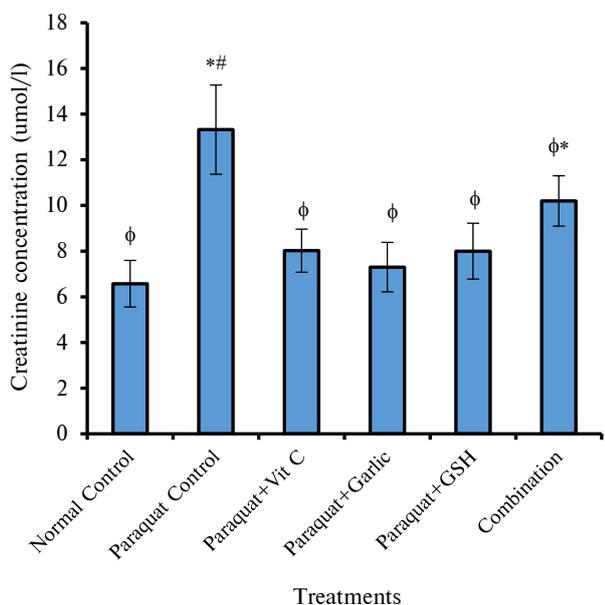
**Figure 2:** Concentration of kidney glutathione (GSH) of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



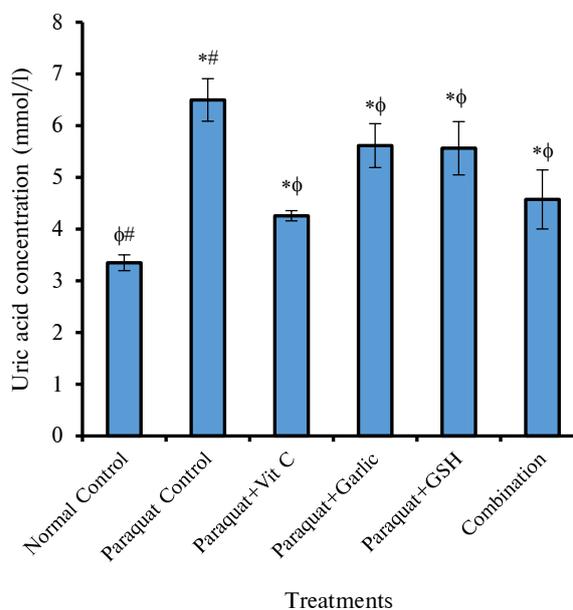
**Figure 3:** Concentration of kidney total antioxidant capacity (TAC) of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



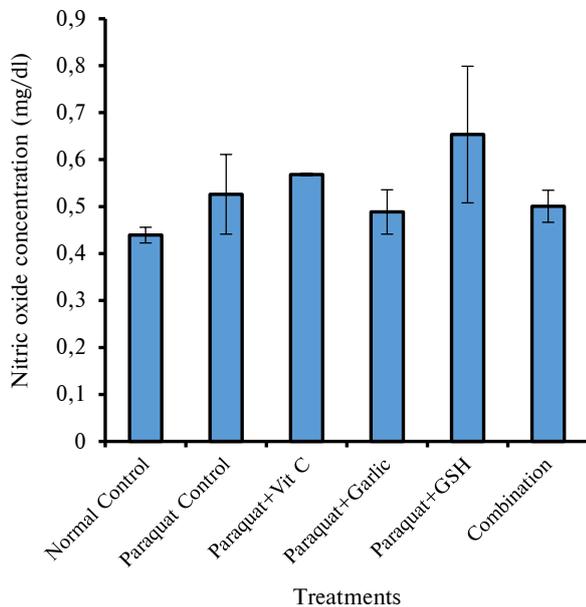
**Figure 4:** Concentration of urea of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



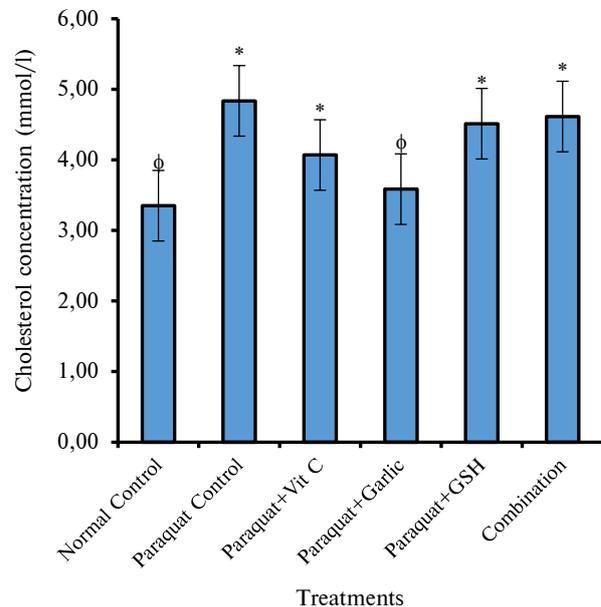
**Figure 5:** Concentration of creatinine of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



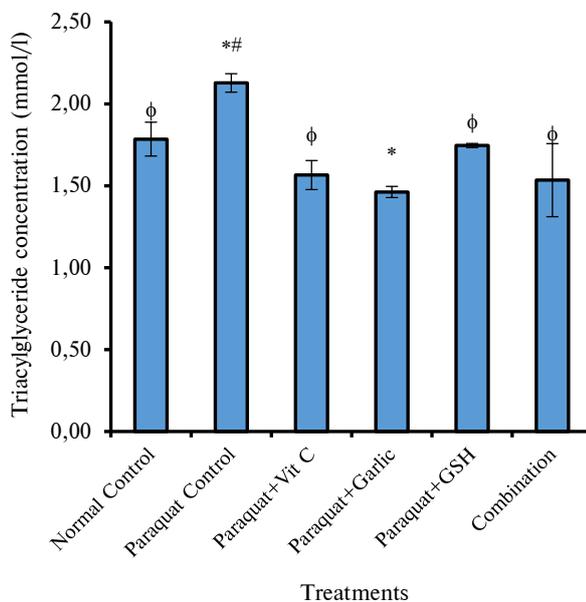
**Figure 6:** Concentration of uric acid of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



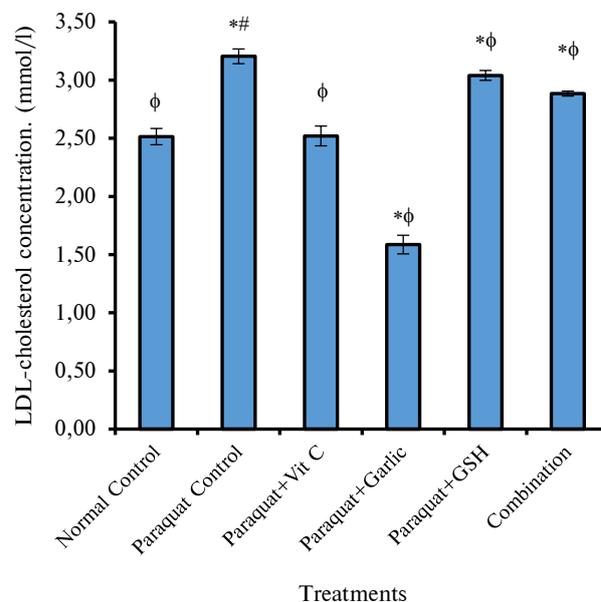
**Figure 7:** Concentration of nitric oxide of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



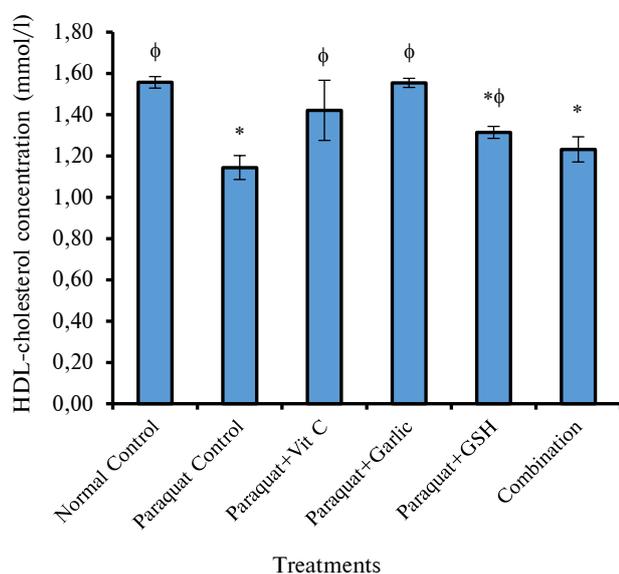
**Figure 8:** Cholesterol concentration of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



**Figure 9:** Triacylglyceride concentration of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments



**Figure 10:** Low-density lipoprotein (LDL)-cholesterol concentration of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments

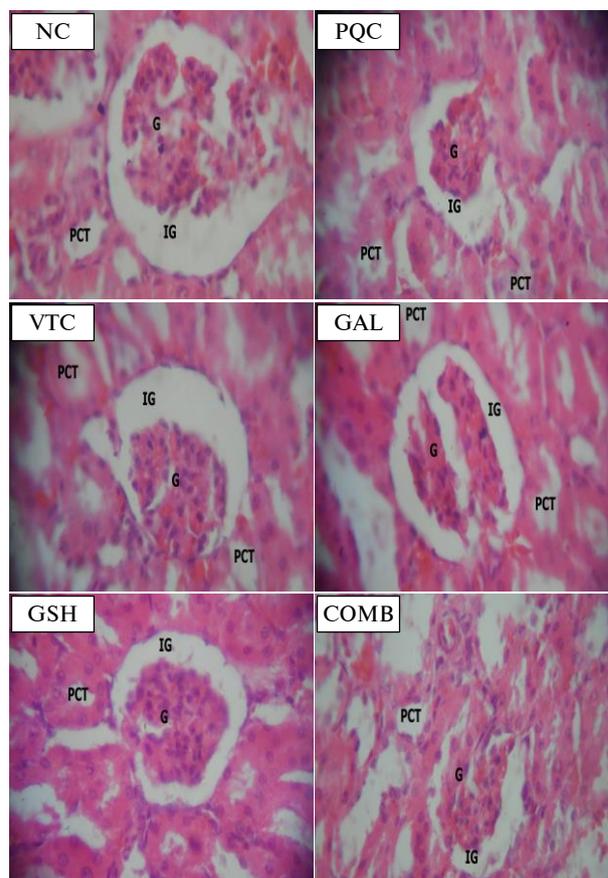


**Figure 11:** High-density lipoprotein(HDL)-cholesterol concentration of albino Wistar rats exposed to paraquat and treated with supplements. Bars represent mean  $\pm$  standard deviation of quadruple determinations; \*,  $\phi$ , # – statistical difference between groups ( $p < 0.05$ ): \* – compared to the Normal control group,  $\phi$  – compared to paraquat control, # – compared to supplement treatments

The kidney sections are presented in Fig. 12: NC: section shows a renal corpuscle with normal glomerulus (G), intraglomerular space (IG) and proximal convoluted tubule (PCT). PQC: section shows renal tissue with shrunken glomerulus (G) and widened intraglomerular space (IG) and proximal convoluted tubules(PCT). VTC: section shows slightly shrunken glomerulus (G) and intraglomerular space (IG) and a mild increase in proximal convoluted tubule (PCT). GAL: section shows renal corpuscle with normal glomerulus (G) and intraglomerular space (IG), proximal convoluted tubules (PCT) also appeared normal. GSH: section presents slightly shrunken glomerulus (G) and slightly widened intraglomerular space (IG), the proximal convoluted tubule (PCT) appeared normal. COMB: section shows renal corpuscle with slightly shrunken glomerulus (G), slightly dilated intraglomerular space (IG) and proximal convoluted tubules (PCT) slightly dilated.

### Discussion

Kidney is involved in the body's regulation of numerous biochemical activities especially the excretion of waste and toxic substances. In the current study, the use of garlic, glutathione and vitamin C to protect cells and tissues from PQ-induced toxicity



**Figure 12:** Kidney sections of Wistar albino rats exposed to paraquat and treated with nutritional supplements

highlights the significant role of antioxidants in mitigating the damaging effects of oxidative stress on (kidney) tissues. There were differences in the concentration of kidney malondialdehyde, total antioxidant capacity, glutathione on the supplement treated groups when compared to the PQ-exposed/untreated control group.

In this study the significant increase in malondialdehyde indicates increased lipid peroxidation in groups exposed to PQ, thereby implicating PQ as an agent of oxidative stress. This result corroborates previous findings which states that free radicals interact with the polyunsaturated fatty acids present in the phospholipid portion of the cell membrane [20] provoking tissue injury [21]. Similarly, the significantly decreased glutathione (GSH) concentration further indicates exposure of rats to PQ-induced oxidative stress. The decrease of GSH concentration might be due to its overwhelming utilization to neutralize excessively produced free radicals [22]. The low GSH concentration agrees with the significant reduction measured for TAC in PQ exposed groups. This confirms the role of free radical generation and

attenuation of antioxidant levels in PQ-intoxicated rats and this can result in renal injury. This is in agreement with the findings that PQ alters the oxidative state indices in exposed animals [23]. The continued exposure to PQ as seen in pesticide remnants in foods and water [24] and as applied in this study is pathogenesis to diverse adverse biochemical changes in kidneys of animals, which could lead to renal dysfunction [25].

Rats administered the supplements showed significantly reduced concentration of malondialdehyde. Similarly, the concentration of GSH and TAC have significantly increased in all supplements treated groups. These findings are in agreement with studies that showed that vitamin C ameliorated a pesticide (deltamethrin)-induced toxicity [26] and garlic partially prevented PQ-induced impairment of renal function [27]. Vitamin C is an important non-enzymatic antioxidant known to protect cells of the body against oxidants. The inclusion of vitamin C as one of the supplements in the present study was due to previous reports which indicated that PQ and some xenobiotics induce low vitamin C levels, and this causes renal toxicity [28, 29]. The present study shows that vitamin C treated group presented significantly reduced MDA, urea, creatinine, uric acid, triacylglyceride, and LDL-cholesterol. Parameters such as GSH, TAC, and HDL-cholesterol were significantly increased in Vitamin C group compared to PQ control.

The significantly increased urea and creatinine concentrations in PQ control rats indicate pathology associated with tissue breakdown [30–32]. These two parameters are biomarkers of renal toxicity [33] and the increase indicate renal damage associated with increased urea production. This is in line with previous reports [34, 35]. However, garlic supplementation showed the significant ameliorative potential to the abnormal urea and creatinine production as presented by rats in the garlic group. However, rats supplemented with vitamin C presented the most significant reduction in uric acid in all PQ exposed groups. The fluctuation in nitric oxide concentration showed none significant variation compared to the normal control.

The variations in blood lipid concentration corroborate studies which indicate that toxicants induce reactive oxygen species (ROS) generation. And this elicits oxidative damage that results in various fluctuations of pathophysiological processes and disease induction [36, 37]. The adverse fluctuations in the lipid profile in the present study affirm the observed increase in MDA concentration in PQ exposed rats which indicate oxidative stress induced by

oxygen-derived free radicals. This oxidative state causes disturbance in the pro-oxidant and antioxidant balance, which may cause functional cell damage and adverse biological reactions such as dyslipidemia [38]. Antioxidants, as provided by the supplements, can prevent, protect and repair free-radical-mediated damage. Garlic is an important source of allicin, an organosulfur compound, which changes quickly into various sulfur-containing compounds such as diallyl tetrasulfide, diallyl trisulphide, disulfide derivatives, etc. capable of scavenging hydroxyl radicals, preventing lipid peroxidation and altering antioxidant and membrane-bound enzymes in toxicant-exposed rats [39]. The decreased HDL-cholesterol indicates the adverse effect of PQ-induced dyslipidemia which disturbs biological functions of HDL-cholesterol [40]. However, the HDL-cholesterol concentration showed no significant difference between control and supplement treated groups, implying that the supplements may have enhanced clearance of bad cholesterol from the system. HDL-cholesterol functions by transporting excess cholesterol derived from peripheral tissues to the liver and exchanges proteins and lipids with chylomicrons and VLDL.

The results of this study indicate that PQ induced some adverse histological changes in kidney of exposed rats. Examination of the kidney section of PQ control (PQC) showed significant alteration in the glomerulus, intraglomerular space and proximal convoluted tubules. These could lead to tubular degeneration and glomerular disruption, and eventually necrosis. These results are similar to previous studies that indicated that PQ can induce kidney damage and dysfunctions [4, 33, 41]. Kidney histology results further support the dysfunction as observed in increased serum creatinine concentration which indicated a decrease in kidneys glomerular filtration rate (GFR). This will ultimately impair renal function with a consequential reduction in the rate of renal clearance. This may further increase the systemic concentration of PQ, increase the toxicity, and cause other organ dysfunctions [42, 43].

## Conclusions

This study demonstrated that exposure to PQ herbicide can induce nephrotoxicity by a mechanism associated with the generation of hydroxyl free radical, hydrogen peroxide anion and superoxide anion, which result in exhaustion of cellular NADPH and lipid peroxidation of cellular membranes of kidneys. The adverse biochemical consequences of PQ poisoning indicated that provision of antioxidants

stimulates some level of amelioration. It was in this regard that this study administered garlic, vitamin C and glutathione as antioxidant supplements to PQ-

exposed rats. These supplements acted as potent agents for the attenuation of PQ-induced renal dysfunction and pathological damages.

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#### **ЗМЕНШЕННЯ НЕФРОТОКСИЧНОСТІ ТА ДИСФУНКЦІЇ, ІНДУКОВАНИХ ПАРАКВАТОМ, У САМЦІВ ЩУРІВ-АЛЬБІНОСІВ ЛІНІЇ WISTAR**

**Проблематика.** Паракват (PQ) – це пестицид, який широко застосовується у світовій сільськогосподарській практиці для боротьби з бур'янами. Він має несприятливі біохімічні та фізіологічні наслідки для людини і тварин. Механізм токсичної дії пов'язаний з утворенням активних форм кисню та подальшим перекисним окисненням ліпідів. На сьогодні не встановлено жодного ефективного антидоту проти токсичності параквату. Тому необхідність постійного вивчення різних підходів до лікування набуває першорядного значення.

**Мета.** У цьому дослідженні через визначення деяких біомаркерів функції нирок і параметрів окиснення оцінювалась здатність вибраних біологічно-активних добавок зменшувати індуковані паракватом дисфункцію та ураження нирок.

**Методика реалізації.** Тридцять шість щурів-альбіносів лінії Wistar було випадковим чином розділено на шість груп. Кожну групу (за винятком контрольної) через день піддавали інтоксикації паракватом із розрахунку 1,5 мг PQ/кг маси тіла, а чотирьом групам (крім PQ і контрольної) протягом двох тижнів щодня вводили екстракт часнику, глутатіон і вітамін С у кількості 40 мг/кг маси тіла.

**Результати.** Результати дослідження показали достовірне ( $p < 0,05$ ) підвищення концентрації малонового діальдегіду в нирках, сечовини, креатиніну та ліпідного профілю крові. Також було відзначено достовірне зниження концентрації холестерину ліпопротеїдів високої щільності, глутатіону нирок і загального антиоксидантного потенціалу в контрольній групі PQ порівняно з іншими PQ-інтоксикованими групами, яким вводили антиоксидантні композиції.

**Висновки.** Зміни, викликані паракватом, вказували на дисфункцію та ураження нирок. Однак застосування антиоксидантних добавок зменшувало індуковану паракватом біохімічну та фізіологічну дисфункцію в щурів.

**Ключові слова:** паракват; гербіцид; нефротоксичність; ксенобіотики; антиоксиданти.

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#### **УМЕНЬШЕНИЕ НЕФРОТОКСИЧНОСТИ И ДИСФУНКЦИИ, ИНДУЦИРОВАННЫХ ПАРАКВАТОМ, У САМЦОВ КРЫС-АЛЬБИНОСОВ ЛИНИИ WISTAR**

**Проблематика.** Паракват (PQ) – это пестицид, который широко применяется в мировой сельскохозяйственной практике для борьбы с сорняками. Он имеет неблагоприятные биохимические и физиологические последствия для человека и животных. Механизм токсического действия связан с образованием активных форм кислорода и последующим перекисным окислением липидов. На сегодняшний день не установлено ни одного эффективного антидота против токсичности параквата. Поэтому необходимость постоянного изучения различных подходов к лечению приобретает первостепенное значение.

**Цель.** В этом исследовании через определение некоторых биомаркеров функции почек и параметров окисления оценивалась способность выбранных биологически-активных добавок уменьшать индуцированные паракватом дисфункцию и поражение почек.

**Методика реализации.** Тридцать шесть крыс-альбиносов линии Wistar были случайным образом разделены на шесть групп. Каждую группу (за исключением контрольной) через день подвергали интоксикации паракватом из расчета 1,5 мг PQ/кг массы тела, а четырем группам (кроме PQ и контрольной) в течение двух недель ежедневно вводили экстракт чеснока, глутатион и витамин С в количестве 40 мг/кг массы тела.

**Результаты.** Результаты исследования показали достоверное ( $p < 0,05$ ) повышение концентрации малонового диальдегида в почках, мочевины, креатинина и липидного профиля крови. Также было отмечено достоверное снижение концентрации холестерина липопротеидов высокой плотности, глутатіона почек и общего антиоксидантного потенціалу в контрольній групі PQ по сравнению с другими PQ-интоксикованными группами, которым вводили антиоксидантные композиции.

**Выводы.** Изменения, вызванные паракватом, указывали на дисфункцию и поражение почек. Однако применение антиоксидантных добавок уменьшало индуцированную паракватом биохимическую и физиологическую дисфункцию у крыс.

**Ключевые слова:** паракват; гербицид; нефротоксичность; ксенобіотики; антиоксиданти.