



Faculty of Science Zoology Department

# Physiological and Molecular Studies on The Protective Effect of Resveratrol in Male Rats Exposed to Sulfoxaflor.

By

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#### **Summary and conclusion**

The current study is aimed to assess the molecular and physiological alterations in male albino rats that treated with different doses of sulfoxaflor. The oral  $LD_{50}$  was calculated according to the Miller and Tainter method and found to be 3755.3 mg/kg.b.wt.

Sulfoxaflor, has been used by humans for crop preservation, considered the main reason for its widespread distribution and causes a number of adverse effects in man and animals. Chronic or acute exposure to sulfoxaflor causes cancers, birth defects, sterility, immunotoxicity, neurological, and developmental toxicity.

Oxidative stress plays an important role in pathogenesis of sulfoxaflor induced toxicity in several tissues such as liver and kidney. Evidences suggest that sulfoxaflor exposure stimulates intracellular production of reactive oxygen species (ROS) and lipid peroxidation, which leads to tissue damage.

In this study, sixty adult male albino rats  $(130 \pm 10 \text{ g})$  were utilized and divided into six equal groups as follows:

GP<sub>I</sub>: Normal control group (C); rats were kept without any treatments.

 $GP_{II}$ : Resveratrol group (RSV); rats treated orally by gavage once per day with resveratrol in a dose of 20 mg/kg.b.wt., for four weeks.

 $GP_{III}$ : Sulfoxaflor with low dose group (L-SFX); normal male rats were received orally low dose of sulfoxaflor (187.7 mg/kg.b.wt.), for four weeks per day.

 $GP_{IV}$ : Resveratrol and Sulfoxaflor with low dose group (RSV + L-SFX); normal male rats were given resveratrol by oral gavage daily with (20mg/kg.b.wt.) and L-SFX sulfoxaflor (187.7 mg/kg.b.wt.), for four weeks.

 $GP_V$ : Sulfoxaflor with high dose group (H-SFX); normal male rats were treated orally with sulfoxaflor in a high dose (375.5 mg/kg.b.wt.), for four weeks per day.

 $GP_{VI}$ : Resveratrol and Sulfoxaflor with high dose group (RSV + H-SFX); normal male rats were received resveratrol (20 mg/kg.b.wt.) and H-SFX (375.5 mg/kg.b.wt.) by oral gavage, for four weeks per day.

At the propitiate experimental periods, rats from each group were sacrificed and blood samples were drawn, then liver and kidney tissues were immediately collected for experiments. The levels of serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT), albumin, urea, and creatinine and total antioxidant concentration (TAC) levels were measured in serum blood.

Tissue supernatants of liver and kidney were isolated for estimated the levels of lipid peroxidation as malondialdehyde (MDA), reduced glutathione (GSH), Glutathione disulfide (GSSG), nitric oxide (NO) in the different groups.

The results were statistically analyzed by One-way (ANOVA) and Tukey's post hoc test was used to evaluate the relationship between the groups at conventional probability levels (P < 0.05).

Results revealed that the administration of SFX at two selected doses leading to an elevation of ALT, AST, LDH, gamma glutamyl transferase GGT, urea, and creatinine with a concomitant reduction in albumin and Total antioxidant (TAC) levels. In addition, the levels of MDA, GSSG, NO in liver and kidney tissues were increased with a decrease in GSH levels.

RSV administration improved the condition by reversing the oxidative stress and reducing SFX toxicity. Rats treated with RSV revealed a decrease in the serum levels of ALT, AST, LDH, gamma glutamyl transferase GGT, urea, and creatinine with an elevation in albumin and Total antioxidant (TAC) levels to normal levels. Moreover, there was a decrease in the MDA, GSSG, and NO in liver and kidney tissues with a concomitant enhancement in GSH levels. Histological studies revealed that SFX caused a damage of histological structure of liver including pyknosis, necrosis, and hemorrhage and also induced a damage of histological structure of kidney such as a degeneration of glomruli, pyknosis, and exfoliated cells in lumen of tubules of kidney tissues of male rats. RSV showed an improvement in the histological change induced by SFX.

Molecular studies indicated that SFX induced DNA damage at both selected dose which was revealed by comet assay and DNA fragmentation. Results revealed that RSV has an effective impact on DNA.

In conclusions, in the light of biochemical results, histological and molecular studies of the current study showed that supplementation of resveratrol may be a plausible way to reduce the toxicity mediated by sulfoxaflor due to its direct ROS scavenging activity.