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Evaluation of Biochemical Oxidative Stress Indices in Male Wistar Rats Treated with Swinol Tablets

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ABSTRACT: Drug consumption considerably contributes to organ damage and metabolic disorder, yet the precise biochemical effect of Swinol remain unknown. The objective of this paper was to evaluate the biochemical oxidative stress indices of male wistar rats treated with swinol tablet using appropriate standard methods. Results demonstrated a dose-dependent decline in antioxidant activity in the liver and kidney with increasing doses of swinol tablets, evidenced by decreased superoxide dismutase (SOD), catalase, glutathione (GSH), glutathione peroxidase (GPx), and glutathione S-transferase (GST). This connotes an impaired antioxidant defense in rats treated with Swinol tablets. Additionally, lipid peroxidation readings dramatically increased, suggesting heightened oxidative damage, particularly with greater Swinol doses. These studies show that continued administration of Swinol tablets increases oxidative stress by lowering antioxidant capacity and promoting lipid peroxidation, which may lead to organ malfunction. Further investigation is necessary to explore the long-term health risks connected with Swinol misuse.

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Drugs are substances that, when ingested, can cause physiological and psychological effects on the human body. They can be classified into several categories based on their chemical composition, therapeutic use, and potential for abuse. The dichotomy between therapeutic drugs, which are prescribed for health benefits, and recreational drugs, often associated with substance abuse, highlights the complex role drugs play in society (Rang *et al.*, 2024). Understanding the nature and effects of various drugs is crucial, especially considering the growing global concern about drug abuse and its consequences. Drug metabolism refers to the biochemical process through which the body transforms and eliminates drugs (Phang-Lyn and Llerena, 2023). This process primarily occurs in the liver and involves various enzymes that modify drugs to facilitate their excretion (Zhao *et al.*, 2021). Metabolism can affect a drug's potency and toxicity, impacting therapeutic outcomes and the potential for adverse effects (Gupta and Masand, 2004). Individual variations in drug metabolism can significantly influence how different people respond to medications, underscoring the importance of personalized medicine (Niederberger and Parnham, 2021; Zhao *et al.*, 2021). The liver plays a critical role in drug metabolism and detoxification (Vaja and Rana, 2020). Many drugs, particularly those that are ingested, are metabolized in the liver before

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being distributed to other tissues (Susa *et al.*, 2023). While this process is vital for detoxifying harmful substances, it can also lead to liver damage, especially with prolonged use of hepatotoxic drugs (Björnsson, 2016). Conditions such as drug-induced liver injury can result in elevated liver enzymes, jaundice, and even liver failure, necessitating careful monitoring of liver function during drug therapy (Pratt and Kaplan, 2000; Andrade *et al.*, 2019). Similarly, the kidneys are essential for the excretion of drugs and their metabolites. They filter blood, removing waste products and excess substances. Drug abuse can compromise kidney function, leading to acute or chronic kidney injury (Ogobuiro and Tuma, 2023). Certain drugs may induce nephrotoxicity, characterized by an elevation in serum creatinine and urea levels, which are critical indicators of renal function (Levey *et al.*, 2009). The preservation of kidney health is paramount, particularly in individuals using drugs that may adversely affect renal function. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them through antioxidant defenses (Devall *et al.*, 2012; Pizzino *et al.*, 2017). This condition is associated with various diseases, including those affecting the liver and kidneys. Drugs can exacerbate oxidative stress by promoting ROS production or depleting antioxidants, leading to cellular damage and inflammation (Valko *et al.*, 2007). The relationship between drug metabolism and oxidative stress is complex. While drug metabolism can generate reactive metabolites that contribute to oxidative stress, certain drugs also enhance antioxidant defenses (Pizzino *et al.*, 2017). Understanding this interplay is crucial for developing therapeutic strategies that minimize oxidative damage, particularly in patients undergoing chronic drug treatment.

Several biomarkers can indicate oxidative stress levels, including malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione (Ayala *et al.*, 2014; Weiss *et al.*, 1997; Weydert and Cullen, 2010). These indices provide valuable insights into the oxidative state of cells and tissues, helping researchers and clinicians assess the impact of drug exposure on overall health.

Swinol tablets are often used for their analgesic and antipyretic properties (National Center for biotechnology Information, 2024). However, misuse can lead to serious side effects, including gastrointestinal issues, liver damage, and addiction. Understanding the proper dosage and potential risks is essential for ensuring safe use and minimizing the likelihood of abuse (Gupta and Masand, 2004). The objective of this paper is to evaluate the biochemical oxidative stress indices in rats treated with Swinol tablets.

MATERIALS AND METHOD

Reagents and Chemicals: All reagents and chemicals used were of analytical grade.

Animals: Twenty male Wistar rats weighing between 120 and 150 g were obtained from the animal house of the Department of Anatomy, Delta State University, Abraka, and were housed in large spacious cages and maintained under laboratory conditions of temperature, humidity and 12 hour day: 12 hour night cycle; and fed with a standard laboratory diet (grower's mash) and water ad libitum throughout the duration of the experiment. The animals were acclimatized to laboratory conditions for two weeks prior to the commencement of the experiment.

Experimental design: The twenty male rats divided into four groups of five rats each, and treated for 42 days as follows:

Group A = Normal control.
Group B= Rats + 0.014 mg/ kg body weight of swinol tablets.
Group C= Rats + 0.029 mg/ kg body weight of swinol tablets.
Group D= Rats + 0.057 mg/ kg body weight of swinol tablets.

Collection of Tissues: After 42 days of treatment, the animals in groups A – D were fasted for 12 hours, anaesthetized and sacrificed by decapitation and blood was collected for serum separation. The serum was separated by centrifugation at 3000 rpm and analyzed for the various biochemical parameters.

Assessment of Oxidative Stress Markers: The assay for superoxide dismutase (SOD) activity was done by the method of Misra and Fridovich (1972). Catalase levels were determined according to the method of Aebi (1974) by the depletion rate of H2O2 at 240 nm in a reaction buffer. Total reduced glutathione (GSH) was estimated according to the method described by Moron *et al.* (1979). Determination of glutathione peroxidase activity was earned out by the method of Ellman (1959). The method Habig *et al.* (1974) was adopted for the determination of glutathione-S-transferase activity. Estimation of Lipid peroxidation was done according to the method described by Niehius and Samuelsson (1968).

Data Analysis: The data were statistically analysed using the GraphPad Prism 8 software and evaluated by one-way ANOVA followed by Tukey's post hoc. $P < 0.05$ was considered to be statistically significant.

RESULT AND DISCUSSION

Analysis of Oxidative Stress Indices in Wistar Rats Exposed to Swinol tablet: The table 1 presents the effects of Swinol tablets on oxidative stress indices in Wistar rats, measured through various biomarkers. Superoxide dismutase (SOD) and catalase levels in both liver and kidney showed a significant decline in response to increasing doses of Swinol, indicating a reduction in antioxidant capacity. Lipid peroxidation (LPO) levels, an indicator of oxidative damage, increased with higher Swinol doses in the liver and kidney. Table 2 illustrates the effects of swinol tablets on glutathione (GSH), glutathione peroxidase (GPx), and glutathione S-transferase (GST) levels in the liver and kidneys of Wistar rats. The control group displayed the highest levels of GSH, GPx, and GST, indicating optimal antioxidant capacity. Swinol treatment resulted in a dose-dependent decline in GSH, GPx and GST levels in both organs, particularly at higher doses.

Table 1: effects of swinol tablets on oxidative stress indices in Wistar rats

	SOD (Liver)	SOD (Kidney)	LPO (Liver)	LPO (Kidney)	Catalase (Liver)	Catalase (Kidney)
Control	70.00±5.39^{a}	60.20±4.32^{a}	42.81±2.56^{a}	52.29±3.13^{a}	40.16±4.23^{a}	28.69±1.87^{a}
Swinol 0.014mg/kg	51.80±4.09^{b}	38.40±2.07^{b}	48.42±3.58^{a}	43.23±3.09^{a}	33.51±3.15^{b}	24.01±2.87^{a}
Swinol 0.029mg/kg	38.20±3.90^{b}	30.40±2.30^{b}	76.12±3.85^{b}	66.11±2.79^{b}	27.77±3.57^{b}	18.04±3.71^{b}
Swinol 0.057mg/kg	23.00±2.24^{c}	28.00±2.12^{b}	77.46±3.85^{b}	84.50±3.91^{c}	23.15±1.44^{c}	17.10±1.15^{a}

The result is expressed in mean ± standard deviation. Values having different superscript are significantly different at $p<0.05$.

Table 2: effects of swinol tablets on glutathione (GSH), glutathione peroxidase (GPx), and glutathione S-transferase (GST) levels in Wistar rats

	GSH (Liver)	GSH (Kidney)	GPx (Liver)	GPx (Kidney)	GST (Liver)	GST (Kidney)
Control	10.38±1.45^{a}	6.23±1.18^{a}	12.04±1.96^{a}	9.38±1.01^{a}	9.03±1.68^{a}	5.59±0.96^{a}
Swinol 0.014mg/kg	9.31±1.78^{a}	5.42±0.82^{b}	11.06±1.23^{a}	7.50±1.05^{a}	8.98±1.30^{a}	4.73±0.54^{a}
Swinol 0.029mg/kg	7.47±1.45^{b}	5.39±0.69^{b}	10.78±1.06^{b}	5.24±0.46^{b}	7.75±1.01^{b}	2.28±0.65^{b}
Swinol 0.057mg/kg	7.56±1.14^{b}	3.88±0.77^{c}	9.38±1.49^{c}	3.64±0.79^{c}	6.84±0.51^{b}	1.91±0.49^{b}

The result is expressed in mean ± standard deviation. Values having different superscript are significantly different at $p<0.05$.

The findings in Tables 1 and 2 demonstrate a distinct dose-dependent effect of Swinol tablets on oxidative stress indicators in Wistar rats. A significant decrease in the antioxidant enzymes superoxide dismutase (SOD) and catalase indicates that Swinol compromises the antioxidant defense mechanism, especially in the liver and kidneys. These enzymes are essential for alleviating oxidative stress by neutralizing reactive oxygen species (ROS) (Hayyan *et al.*, 2016). The reduction in their activity signifies heightened vulnerability to oxidative damage, corroborated by the increasing levels of lipid peroxidation (LPO). LPO serves as an indicator of oxidative damage to cell membranes, with its elevation correlating to increased oxidative stress, which is associated with cellular damage and inflammation (Ayala *et al.*, 2014). Table 2 illustrates the reduction of glutathione (GSH) and its related enzymes, glutathione peroxidase (GPx) and glutathione S-transferase (GST), highlighting the diminished antioxidant capability due to Swinol exposure. GSH is essential for detoxifying detrimental oxidative metabolites, while GPx and GST are responsible for neutralizing lipid peroxides and other oxidative byproducts (Forman *et al.*, 2014). A dose-dependent decrease in these indicators further underscores the pro-oxidant action of Swinol, indicating that elevated dosages surpass the capacity of endogenous antioxidant mechanisms. These results agree with the general concept of oxidative stress, where an imbalance between ROS generation and antioxidant defenses leads to oxidative damage, leading to tissue malfunction and perhaps disease development (Sies *et al.*, 2017). The observed effects of Swinol, especially at larger dosages, imply that its chronic administration may pose a danger to organ health by reducing the body's natural antioxidant defenses.

Conclusion: The findings indicate that prolonged exposure to Swinol tablet may surpass the body's inherent antioxidant defenses, resulting in heightened oxidative stress associated with cellular damage and possible organ malfunction. Therefore, Swinol's usage, particularly at higher dosages, may offer health hazards by compromising oxidative equilibrium and increasing tissue harm. Further study may be necessary to examine the long-term health repercussions and the underlying processes of this oxidative damage.

Declaration of Conflict Of Interest: The authors disclose no conflict of interest.

Declaration of Data Availability Statement: Data are accessible upon request from the corresponding author.

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