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PROTECTIVE ROLE OF *SIDA CORDIFOLIA* IN MITIGATING TARTRAZINE INDUCED HEPATIC OXIDATIVE DAMAGE

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ABSTRACT

The present study investigates the antioxidant potential of aqueous and ethanolic extracts of *Sida cordifolia* against tartrazine-induced oxidative stress in albino rats. Tartrazine, a synthetic azo dye widely used in food and pharmaceutical products, has been reported to generate reactive oxygen species (ROS), leading to oxidative liver damage. Albino rats were divided into control, tartrazine-treated, extract-treated (aqueous and ethanolic), and protective groups (tartrazine + extract), and observations were recorded on the 7th, 14th, 21st, and 28th days of treatment. Key biochemical markers, lipid peroxidation (LPO), catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), were assessed to evaluate oxidative damage and the protective effects of *Sida cordifolia*. Tartrazine administration significantly increased LPO levels while decreasing the activities of CAT, GPx, and SOD, indicating the induction of oxidative stress and hepatic dysfunction. Treatment with *Sida cordifolia* extracts, particularly the ethanolic extract (EESC), restored antioxidant enzyme activities and reduced lipid peroxidation, suggesting strong hepatoprotective potential. The protective group receiving tartrazine along with EESC exhibited the most pronounced improvement, highlighting both preventive and therapeutic benefits. These findings demonstrate that *Sida cordifolia* mitigates tartrazine-induced oxidative liver injury by enhancing endogenous antioxidant defence mechanisms, thereby supporting its traditional medicinal use as a hepatoprotective agent.

KEYWORDS: *Sida cordifolia*, Tartrazine, Oxidative stress, SOD, GPx, CAT, Albino rats.

INTRODUCTION

Oxidative stress is a physiological condition that arises from an imbalance between the production of reactive oxygen species (ROS) and the ability of the antioxidant defence system to neutralise these reactive molecules (Ozougwu, 2012). Such an imbalance can lead to damage of essential cellular components, including lipids, proteins, and DNA, thereby disrupting normal cellular processes and contributing to tissue injury (Rani et al., 2016). The liver is particularly susceptible to oxidative stress due to its central involvement in metabolic activities, detoxification processes, and the biotransformation of xenobiotics. Persistent oxidative stress in hepatic tissue may initiate inflammatory responses, interfere with metabolic pathways, impair liver function, and ultimately contribute to the development of various liver diseases (Li et al., 2018).

Tartrazine, a synthetic azo dye commonly used as a colouring agent in beverages, processed foods, and pharmaceutical products because of its bright yellow colour, has been linked to several adverse biological effects (Kushwaha et al., 2012). Emerging evidence indicates that exposure to tartrazine can induce oxidative stress, inflammation, and hepatotoxicity (Visternicu et al., 2025). After ingestion, tartrazine undergoes metabolic reduction that generates free radicals capable of initiating lipid peroxidation, oxidising proteins, and depleting endogenous antioxidant systems (Amin et al., 2018). These toxicological effects highlight the importance of identifying protective agents that can mitigate oxidative damage induced by tartrazine (Hegazy et al., 2023).

Medicinal plants that are rich in natural antioxidants have attracted increasing scientific attention due to their potential to counteract oxidative stress and enhance endogenous defence mechanisms (Akbari et al., 2022). *Sida cordifolia*, a medicinal plant belonging to the family Malvaceae, has long been utilised in Ayurvedic medicine for the treatment of inflammatory, neurological, and metabolic disorders. The plant contains a variety of bioactive phytochemicals, including flavonoids, alkaloids, phenolic acids, and saponins, which have been reported to exhibit antioxidant, hepatoprotective, and anti-inflammatory activities (Dinda et al., 2015). These pharmacological properties suggest that *Sida cordifolia* may serve as a potential therapeutic agent in mitigating oxidative damage caused by synthetic chemicals and environmental toxicants (Kumar et al., 2019). Therefore, the present study aims to

evaluate the ameliorative effects of aqueous and ethanolic extracts of *Sida cordifolia* on tartrazine-induced oxidative stress in the liver of albino rats.

MATERIAL AND METHOD

CHEMICALS AND REAGENTS

Tartrazine, Thiobarbituric acid (TBA), Xanthine, Xanthine oxidase enzyme, Nitroblue tetrazolium (NBT), Reduced nicotinamide adenine dinucleotide (NADH), Hydrogen peroxide (H2O2), Ammonium molybdate, Reduced glutathione (GSH), Tert-butyl hydroperoxide (t-BHP), Ethanol (analytical grade), Distilled water, Trichloroacetic acid (TCA), Phosphate buffer, Sulfuric acid, Malondialdehyde (MDA) standard, Commercial antioxidant enzyme kits.

EXPERIMENTAL ANIMALS

Eight- to ten-week-old albino rats weighing 150–200 g were obtained from a certified local supplier. The animals were housed in standard polypropylene cages under controlled environmental conditions, including a temperature of 22 ± 2 °C, relative humidity of 50–60%, and a 12 h light/dark cycle. Prior to the commencement of the experiment, the rats were allowed to acclimatise to the laboratory environment for one week. During this period, they were provided with standard pellet diet and water *ad libitum*. All experimental procedures were conducted in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and were approved by the Institutional Animal Ethics Committee (IAEC) of Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, India.

COLLECTION OF PLANT MATERIAL

Sida cordifolia plants were collected from the campus of Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, Uttar Pradesh, India (PIN: 273009). The plant material was subsequently taxonomically identified and authenticated by the Department of Botany, Deen Dayal Upadhyaya Gorakhpur University.

PREPARATION OF PLANT EXTRACT

Fresh *Sida cordifolia* plants were thoroughly washed with distilled water to remove adhering dust and impurities. The cleaned plant material was shade-dried and subsequently pulverised into a fine powder using a mechanical grinder. For extraction, 500 g of the powdered material was mixed with the respective solvent in a 1:10 ratio (double-distilled water for the aqueous

extract and ethanol for the ethanolic extract) and subjected to extraction using a Soxhlet apparatus. The extraction process was carried out for 48 h. The resulting extracts were concentrated using a flash evaporator, and the dried residues were collected and stored in sterilised tubes under refrigerated conditions until further use. The aqueous and ethanolic extracts were designated as AESC (Aqueous Extract of *Sida cordifolia*) and EESC (Ethanolic Extract of *Sida cordifolia*), respectively.

EXPERIMENTAL PROTOCOL

The rats were randomly assigned to four experimental groups and exposed to different treatments of tartrazine, plant extract, or their combination for a period of 28 days, as described below.

Group I (Control): Animals received a standard pellet diet and distilled water only.

Group II (Tartrazine): Animals were administered tartrazine at a dose of 300 mg/kg body weight (bw) orally, dissolved in distilled water.

Group III (Tartrazine + AESC): Animals were administered tartrazine (300 mg/kg bw) along with AESC (400 mg/kg bw) orally, using distilled water as the vehicle.

Group IV (Tartrazine + EESC): Animals were administered tartrazine (300 mg/kg bw) in combination with EESC (400 mg/kg bw) orally, with distilled water as the vehicle.

All treatments were given daily for 28 consecutive days. The administered doses were selected based on previous studies (Hosieny et al., 2021).

BIOCHEMICAL ASSAYS

Lipid peroxidation was assessed as described by Placer et al. (1966). Superoxide dismutase (SOD) activity was measured according to Li (2012). Catalase (CAT) activity was analysed using the method of Sinha (1972). Glutathione peroxidase (GPx) activity was estimated following the standard protocol described by Pagila *et al*. (1984).

AUTOPSY SCHEDULE

Four animals from each group were autopsied on the 7th, 14th, 21st, and 28th day.

STATISTICAL ANALYSIS

Student t-test and two-way ANOVA were performed to determine the significance of the data.

RESULT

CATALASE ACTIVITY

The mean values of catalase activity in the liver of the control group were 3.743 ± 0.029, 3.935 ± 0.029, 4.065 ± 0.184, and 4.048 ± 0.145 U/mg protein after 7, 14, 21, and 28 days, respectively. In rats treated with Taz II (300 mg/kg bw/day), the mean catalase activities were 2.040 ± 0.022, 1.963 ± 0.037, 1.657 ± 0.008, and 1.392 ± 0.196 U/mg protein, representing a decrease of 45.52%, 50.10%, 59.24%, and 65.61%, respectively, relative to the control. In rats treated with Taz II + AESC, the mean catalase activities were 2.357 ± 0.247, 2.877 ± 0.206, 3.495 ± 0.112, and 3.617 ± 0.223 U/mg protein, showing an improvement of 15.54%, 46.60%, 110.91%, and 159.93%, respectively, compared to the Taz II group. In rats treated with Taz II + EESC, the mean catalase activities were 2.767 ± 0.065, 3.148 ± 0.101, 3.903 ± 0.152, and 3.992 ± 0.075 U/mg protein, showing an improvement of 35.64%, 60.35%, 135.59%, and 186.90%, respectively, compared to the Taz II group. Statistical analysis using the student's *t*-test indicated a significant ($p < 0.05$) decrease in catalase activity in rats treated with Taz II compared to the control rats. However, rats treated with Taz II + AESC and Taz II + EESC showed a significant ($p < 0.05$) increase in catalase activity compared to the Taz II group. Furthermore, two-way ANOVA revealed that both treatment type and exposure duration had a highly significant ($p < 0.01$) effect on catalase activity, indicating that administration of *Sida cordifolia* extracts caused a dose- and time-dependent restoration of catalase activity altered by tartrazine toxicity.

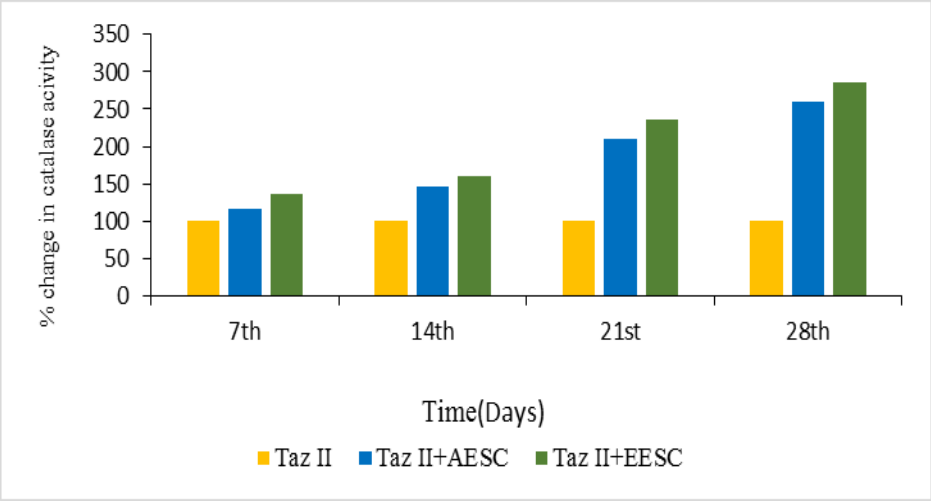

Figure 1: Protective effect of aqueous and ethanolic extract of *Sida Cordifolia* on catalase activity in the liver of rats. (Taz II:300mg/kg body weight/day, AESC: 400 mg/kg body weight/day, EESC:400mg/kg body weight/day).

Table 1: Effect on the activity of catalase in the liver of the rats exposed to Taz II, Taz II+AESC, and Taz II + EESC.

Time	Control	Taz II	Taz II+AESC	Taz II+EESC
7	3.743±0.029	2.040±0.022*	2.357±0.247	2.767±0.065
14	3.935±0.029	1.963±0.037*	2.877±0.206#	3.148±0.101#
21	4.065±0.184	1.657±0.008*	3.495±0.112#	3.903±0.152#
28	4.048±0.145	1.392±0.196*	3.6170.223#	3.992±0.075#

Each value represents the mean ± SEM of six rats in each group.

*Indicates significant ($p<0.05$) difference between control and tartrazine treated groups when student's t- test is applied between tartrazine treated and control groups.

# Indicates significant ($p<0.05$) difference between Taz II group and Taz II +AESC, Taz II and Taz II+EESC treated groups when student's t- test is applied between tartrazine treated and Taz II +AESC, Taz II and Taz II+EESC treated groups.

GLUTATHIONE PEROXIDASE ACTIVITY

The mean values of glutathione peroxidase activity in the liver of the control group were 5.422 ± 0.020, 5.430 ± 0.121, 5.457 ± 0.247, and 5.670 ± 0.065 U/mg protein after 7, 14, 21, and 28 days, respectively. In rats treated with Taz II (300 mg/kg bw/day), the mean glutathione peroxidase activities were 3.760 ± 0.025, 3.733 ± 0.098, 3.647 ± 0.052, and 2.528 ± 0.035 U/mg protein, representing a decrease of 30.65%, 31.24%, 33.18%, and 55.41%, respectively, relative to the control. In rats treated with Taz II + AESC, the mean glutathione peroxidase activities were 3.877 ± 0.049, 4.562 ± 0.034, 4.863 ± 0.129, and 5.122 ± 0.134 U/mg protein, showing an improvement of 3.11%, 22.17%, 33.33%, and 102.57%, respectively, compared to the Taz II group. In rats treated with Taz II + EESC, the mean glutathione peroxidase activities were 4.070 ± 0.060, 4.912 ± 0.209, 5.050 ± 0.029, and 5.375 ± 0.109 U/mg protein, showing an improvement of 8.24%, 31.57%, 38.46%, and 112.61%, respectively, compared to the Taz II group. Statistical analysis using the student's *t*-test indicated a significant ($p < 0.05$) decrease in glutathione peroxidase activity in rats treated with Taz II compared to the control rats. However, rats treated with Taz II + AESC and Taz II + EESC showed a significant ($p < 0.05$) increase in enzyme activity compared to the Taz II group. Furthermore, two-way ANOVA revealed that both treatment type and exposure duration had a highly significant ($p < 0.01$) effect on glutathione peroxidase activity, indicating that administration of *Sida cordifolia* extracts caused a dose- and time-dependent restoration of hepatic antioxidant defence against tartrazine-induced oxidative stress.

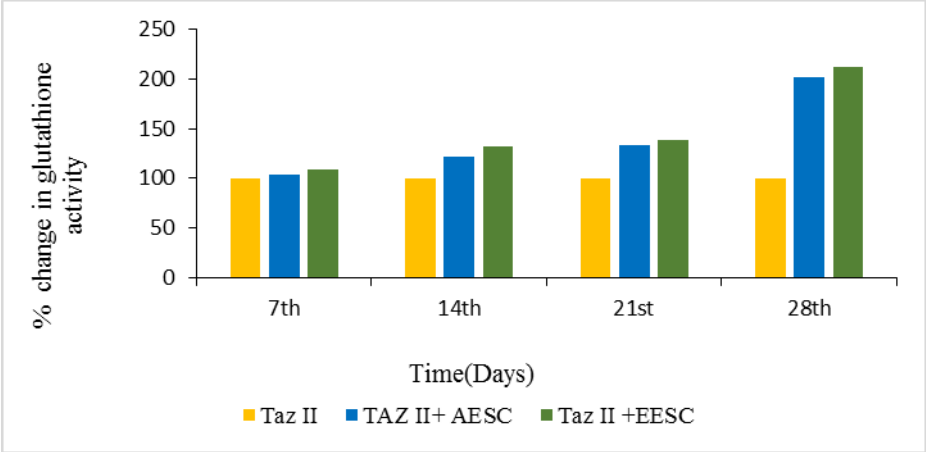

Figure 2: Protective effect of aqueous and ethanolic extract of *Sida Cordifolia* on glutathione activity in the liver of rats. (Taz II:300mg/kg body weight/day, AESC: 400 mg/kg body weight/day, EESC:400mg/kg body weight/day).

Table 2: Effect on the activity of glutathione in the liver of the rats exposed to Taz II, Taz II+AESC, Taz II + EESC.

Time	Control	Taz II	Taz II +AESC	Taz II+ EESC
7	5.422±0.020	3.760±0.025*	3.877±0.049	4.070±0.060#
14	5.430±0.121	3.733±0.098*	4.562±0.034#	4.912±0.209#
21	5.457±0.247	3.647±0.052*	4.863±0.129#	5.050±0.029#
28	5.670±0.065	2.528±0.035*	5.122±0.134#	5.375±0.109#

Each value represents the mean ± SEM of six rats in each group.

*Indicates significant ($p<0.05$) difference between control and tartrazine-treated groups when student's t- test is applied between tartrazine-treated and control groups.

# Indicates significant ($p<0.05$) difference between Taz II group and Taz II +AESC, Taz II and Taz II+EESC treated groups when student's t- test is applied between tartrazine-treated and Taz II +AESC, Taz II and Taz II+EESC treated groups.

SUPEROXIDE DISMUTASE ACTIVITY

The mean values of superoxide dismutase (SOD) activity in the liver of the control group were 6.372 ± 0.077, 6.503 ± 0.080, 6.603 ± 0.079, and 6.668 ± 0.032 U/mg protein after 7, 14, 21, and 28 days, respectively. In rats treated with Taz II (300 mg/kg bw/day), the mean SOD activities were 4.887 ± 0.039, 3.913 ± 0.191, 3.330 ± 0.134, and 2.763 ± 0.099 U/mg protein, representing a decrease of 23.33%, 39.82%, 49.57%, and 58.55%, respectively, relative to the control. In rats treated with Taz II + AESC, the mean SOD activities were 5.305 ± 0.247, 5.531 ± 0.067, 5.727 ± 0.047, and 5.912 ± 0.023 U/mg protein, showing an improvement of 8.56%, 41.33%, 71.92%, and 113.96%, respectively, compared to the Taz II

group. In rats treated with Taz II + EESC, the mean SOD activities were 5.477 ± 0.065, 5.651 ± 0.076, 5.910 ± 0.016, and 6.320 ± 0.320 U/mg protein, showing an improvement of 12.08%, 44.41%, 77.51%, and 128.73%, respectively, compared to the Taz II group. Statistical analysis using the student's *t*-test indicated a significant ($p < 0.05$) decrease in SOD activity in rats treated with Taz II compared to the control rats. However, rats treated with Taz II + AESC and Taz II + EESC showed a significant ($p < 0.05$) increase in SOD activity compared to the Taz II group. Furthermore, two-way ANOVA revealed that both treatment type and exposure duration had a highly significant ($p < 0.01$) effect on SOD activity, indicating that administration of *Sida cordifolia* extracts caused a dose- and time-dependent restoration of SOD activity suppressed by tartrazine toxicity.

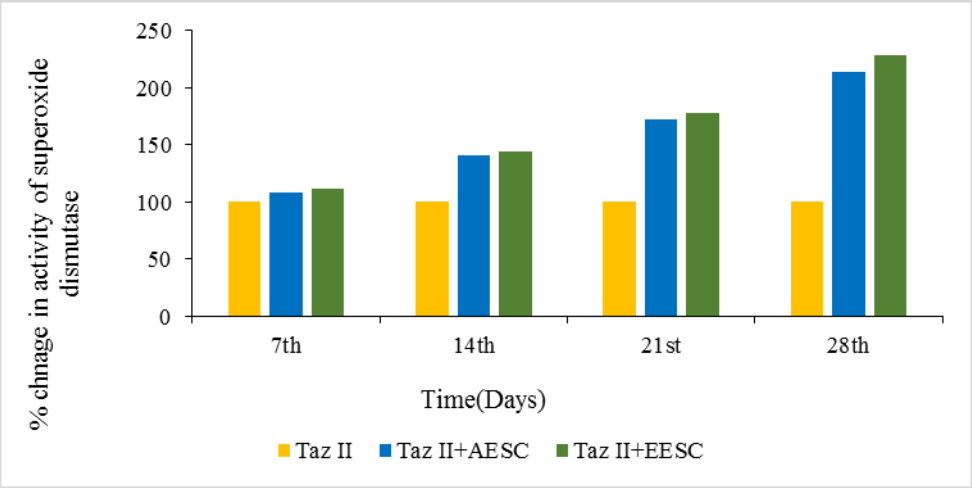

Figure 3: Protective effect of aqueous and ethanolic extract of *Sida Cordifolia* on superoxide dismutase activity in the liver of rats. (Taz II:300mg/kg body weight/day, AESC: 400 mg/kg body weight/day, EESC:400mg/kg body weight/day).

Table 3: Effect on the activity of superoxide dismutase in the liver of the rats exposed to Taz II, Taz II+AESC, Taz II + EESC.

Time	Control	Taz II	Taz II +AESC	Taz II + EESC
7	6.372±0.077	4.887±0.039*	5.305±0.247	5.477±0.065$^{\#}$
14	6.503±0.080	3.913±0.191*	5.531±0.067$^{\#}$	5.651±0.076$^{\#}$
21	6.603±0.079	3.330±0.134*	5.727±0.047$^{\#}$	5.910±0.016$^{\#}$
28	6.668±0.032	2.763±0.099*	5.912±0.023$^{\#}$	6.320±0.320$^{\#}$

Each value represents the mean ± SEM of six rats in each group.

*Indicates significant ($p<0.05$) difference between control and tartrazine treated groups when student's t- test is applied between tartrazine treated and control groups.

#Indicates significant ($p<0.05$) difference between Taz II group and Taz II +AESC, Taz II and Taz II+EESC treated groups when student's t- test is applied between tartrazine treated and Taz II +AESC, Taz II and Taz II+EESC treated group

LIPID PEROXIDATION LEVELS (LPO)

The mean values of lipid peroxidation levels in the liver of the control group were 1.470 ± 0.009, 1.435 ± 0.007, 1.400 ± 0.008, and 1.393 ± 0.006 nmol MDA/mg protein after 7, 14, 21, and 28 days, respectively. In rats treated with Taz II (300 mg/kg bw/day), the mean lipid peroxidation levels were 2.218 ± 0.173, 3.512 ± 0.052, 3.833 ± 0.040, and 4.527 ± 0.105 nmol MDA/mg protein, representing an increase of 50.95%, 144.79%, 173.79%, and 225.09%, respectively, relative to the control. In rats treated with Taz II + AESC, the mean lipid peroxidation levels were 2.070 ± 0.247, 2.130 ± 0.023, 1.890 ± 0.029, and 1.697 ± 0.054 nmol MDA/mg protein, showing a decrease of 6.67%, 39.35%, 50.69%, and 62.50%, respectively, compared to the Taz II group. In rats treated with Taz II + EESC, the mean lipid peroxidation levels were 2.097 ± 0.065, 1.963 ± 0.005, 1.795 ± 0.020, and 1.638 ± 0.074 nmol MDA/mg protein, showing a decrease of 5.45%, 44.11%, 53.18%, and 63.81%, respectively, compared to the Taz II group. Statistical analysis using the student's *t*-test indicated a significant ($p < 0.05$) increase in lipid peroxidation levels in rats treated with Taz II compared to the control rats. However, rats treated with Taz II + AESC and Taz II + EESC showed a significant ($p < 0.05$) decrease in lipid peroxidation compared to the Taz II group. Furthermore, two-way ANOVA revealed that both treatment type and exposure duration had a highly significant ($p < 0.01$) effect on lipid peroxidation, indicating that administration of *Sida cordifolia* extracts caused a dose- and time-dependent reduction in oxidative stress induced by tartrazine toxicity.

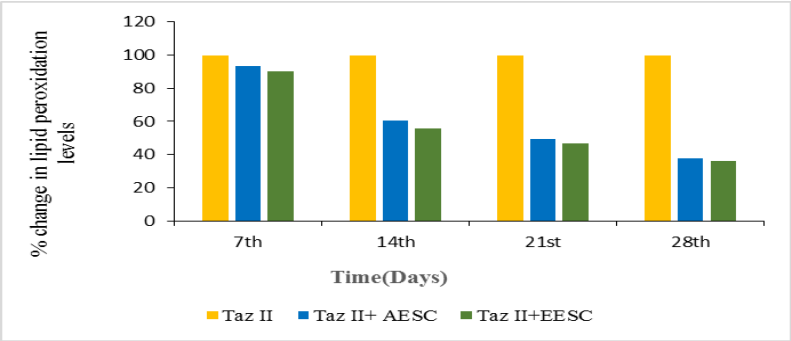

Figure 4: Protective effect of aqueous and ethanolic extract of *Sida Cordifolia* on level of lipid peroxidation in the liver of rats. (Taz II:300mg/kg body weight/day, AESC: 400 mg/kg body weight/day, EESC:400mg/kg body weight/day).

Table 4: Effect on the lipid peroxidation level in the liver of the rats exposed to Taz II, Taz II+AESC, and Taz II + EESC.

Time (Day)	Control	Taz II	TazII+AESC	Taz II+EESC
7	1.470±0.009	2.218± 0.173*	2.070 ± 0.247	2.097 ± 0.065
14	1.435±0.007	3.512± 0.052*	2.130 ± 0.023#	1.963 ± 0.005#
21	1.400±0.008	3.833± 0.040*	1.890 ± 0.029#	1.795 ± 0.020#
28	1.393±0.006	4.527± 0.105*	1.697 ± 0.054#	1.638 ± 0.074#

Each value represents the mean ± SEM of six rats in each group.

* Indicates significant ($p<0.05$) difference between control and tartrazine treated groups when student's t- test is applied between tartrazine treated and control groups.

# Indicates significant ($p<0.05$) difference between Taz II group and Taz II +AESC, Taz II and Taz II+EESC treated groups when student's t- test is applied between tartrazine treated and.

DISCUSSION

Assessment of oxidative stress parameters in liver tissue is of considerable importance because the liver is highly susceptible to reactive oxygen species (ROS) owing to its central role in metabolism, detoxification, and xenobiotic biotransformation (Zhu et al., 2012). Oxidative stress arises when the production of ROS exceeds the antioxidant defence capacity of the organism, resulting in cellular and molecular damage. This imbalance plays a critical role in the development and progression of various liver disorders, including viral hepatitis, alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD), fibrosis, cirrhosis, and hepatocellular carcinoma (Li et al., 2015). Excessive ROS generation can initiate inflammatory responses, activate hepatic stellate cells leading to fibrosis, impair bile secretion, and ultimately disturb hepatic homeostasis.

Free radicals are highly reactive molecules characterised by the presence of unpaired electrons. Major biologically relevant radicals include hydroxyl radicals, singlet oxygen, superoxide anions, nitrate radicals, and carbonate radicals, which may further generate potent oxidants such as hydrogen peroxide (H_2O_2) (Di Meo & Venditti, 2020). These reactive species can damage vital cellular macromolecules, including lipids, proteins, and DNA. Polyunsaturated fatty acids in cellular membranes are particularly vulnerable to oxidative attack, resulting in a process known as lipid peroxidation. One of the major end products of lipid peroxidation is malondialdehyde (MDA), which is widely used as a biomarker of

oxidative stress. Elevated levels of MDA reflect increased lipid degradation and oxidative tissue damage (Ray Halder & Bhattacharyya, 2014; Yaman & Ayhanci, 2021).

To counteract ROS-mediated damage, biological systems employ a complex antioxidant defence network consisting of enzymatic and non-enzymatic components. Key antioxidant enzymes include superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). SOD catalyses the dismutation of superoxide radicals into H_2O_2, which is subsequently converted into water and oxygen by CAT and GPx. In addition, GPx reduces lipid hydroperoxides using reduced glutathione (GSH) as a cofactor, thereby maintaining cellular redox balance and protecting membrane integrity (Ighodaro & Akinloye, 2018; Nandi et al., 2019). Alterations in the activity of these antioxidant enzymes, together with increased MDA levels, are indicative of compromised antioxidant defence and ongoing oxidative stress.

Tartrazine, a synthetic azo dye, undergoes microbial reduction in the gastrointestinal tract to produce aromatic amines, which may interact with dietary nitrates or nitrites and promote ROS generation (Moutinho et al., 2007). Several experimental studies have demonstrated that tartrazine exposure leads to enhanced lipid peroxidation and elevated MDA levels, accompanied by a reduction in the activities of SOD, CAT, and GPx. These changes indicate severe oxidative damage and depletion of endogenous antioxidant systems (Moutinho et al., 2007; Himri et al., 2011; Abd-Elhakim et al., 2019). Mechanistically, ROS-mediated depletion of GSH destabilises SOD, while accumulation of H_2O_2 damages proteins and enzymatic structures, further impairing antioxidant activity (Ighodaro & Akinloye, 2018). Prolonged oxidative stress may ultimately disrupt membrane stability, induce cellular degeneration, and impair metabolic processes (Erdemli et al., 2025). Moreover, oxidative stress has also been associated with impaired pancreatic function, decreased insulin secretion, and enhanced fatty acid oxidation, which generates additional H_2O_2 and exacerbates lipid peroxidation (Erdamli et al., 2021).

In the present study, co-administration of tartrazine with aqueous (AESC) or ethanolic (EESC) extracts of *Sida cordifolia* significantly reduced lipid peroxidation and restored the activities of SOD, CAT, and GPx in liver tissues. The observed reduction in MDA levels suggests inhibition of oxidative chain reactions and protection of membrane lipids, whereas

the increased activities of antioxidant enzymes indicate restoration of endogenous redox defence mechanisms.

These findings are consistent with earlier reports demonstrating the hepatoprotective and antioxidant properties of *Sida cordifolia*. Rejitha, Prathibha, and Indira (2012) reported that ethanolic extracts of *Sida cordifolia* restored hepatic SOD, CAT, and GPx activities and reduced MDA levels in alcohol-intoxicated rats. In a subsequent study, the same authors demonstrated that the extract activates the Nrf2 signalling pathway, which enhances the transcription of glutathione-related antioxidant genes and improves redox homeostasis (Rejitha et al., 2015). Additional evidence from Dhalwal et al. (2005) revealed strong free radical scavenging, anti-lipid-peroxidation, and superoxide-neutralising activities of root and stem extracts. Similarly, Kubavat and Asdaq (2009) reported increased SOD and CAT activities in cardiac tissue under oxidative stress conditions. Ahmad et al. (2014, 2015) also observed reduced lipid peroxidation and improved antioxidant status in diabetic rats treated with *Sida cordifolia* extracts.

The antioxidant activity of *Sida cordifolia* is largely attributed to the presence of bioactive phytochemicals such as flavonoids, phenolic acids, alkaloids, and saponins. These compounds possess hydrogen-donating, metal-chelating, and radical-scavenging properties, which enable them to neutralise ROS and inhibit oxidative reactions (Auddy et al., 2003). The enhanced activities of SOD, CAT, and GPx observed in the presence of AESC and EESC suggest that the extracts not only directly scavenge ROS but also stimulate endogenous antioxidant enzyme synthesis (Ighodaro & Akinloye, 2018; Wang et al., 2018).

Overall, both aqueous and ethanolic extracts of *Sida cordifolia* effectively attenuate tartrazine-induced oxidative stress through two complementary mechanisms: direct scavenging of reactive oxygen species and inhibition of lipid peroxidation, as well as enhancement of enzymatic antioxidant defence systems. These combined actions contribute to the preservation of hepatic structure and function under conditions of toxicant-induced oxidative stress.

CONCLUSION

In conclusion, the findings of the present study demonstrate that tartrazine induces hepatotoxicity primarily through oxidative stress–mediated mechanisms. The results further indicate that *Sida cordifolia* exerts a significant protective and restorative effect against

tartrazine-induced hepatic damage, which may be attributed to its phytochemical-rich composition and potent antioxidant properties. The consistent improvement observed across multiple biochemical parameters and experimental time points enhances the reliability of the findings. Collectively, these results suggest that *Sida cordifolia* may serve as a promising natural therapeutic agent for mitigating oxidative damage associated with exposure to synthetic food additives.

REFERENCE

1. Abd-Elhakim YM, Hashem MM, El-Metwally AE, Anwar A, Abo-El-Sooud K, Moustafa GG, Ali HA. Comparative haemato-immunotoxic impacts of long-term exposure to tartrazine and chlorophyll in rats. Int Immunopharmacol, 2018; 63: 145–154.
2. Ahmad M, Prawez S, Sultana M, Raina R, Kumar P, Verma AAA, Pankaj NK. Antidiabetic effect of Sida cordifolia (aqueous extract) on diabetes induced in Wistar rats using streptozotocin and its phytochemistry. *Group*, 2015; 329(23): 321–326.
3. Ahmad M, Prawez S, Sultana M, Raina R, Pankaj NK, Verma PK, Rahman S. Anti-hyperglycemic, anti-hyperlipidemic and antioxidant potential of alcoholic extract of Sida cordifolia (aerial part) in streptozotocin-induced diabetes in Wistar rats. *Proc Natl Acad Sci India B Biol Sci*, 2014; 84(2): 397–405.
4. Akbari B, Baghaei-Yazdi N, Bahmaie M, Mahdavi Abhari F. The role of plant-derived natural antioxidants in reduction of oxidative stress. *BioFactors*, 2022; 48(3): 611–633.
5. Auddy B, Ferreira M, Blasina F, Lafon L, Arredondo F, Dajas F, et al. Screening of antioxidant activity of three Indian medicinal plants traditionally used for the management of neurodegenerative diseases. *J Ethnopharmacol*, 2003; 84(2–3): 131–138.
6. Dhalwal K, Deshpande YS, Purohit AP, Kadam SS. Evaluation of the antioxidant activity of Sida cordifolia. *Pharm Biol*, 2005; 43(9): 754–761.
7. Di Meo S, Venditti P. Evolution of the knowledge of free radicals and other oxidants. *Oxid Med Cell Longev*, 2020; 2020: 9829176.
8. Erdemli ME, Gul M, Altinoz E, Aksungur Z, Yildiz S, Yildirim S, Guler MC. Oxidative and apoptotic effects of tartrazine exposure on rat pancreatic tissue. *J Food Biochem*, 2021; 49(2): e14628.
9. Erdemli Z, Zayman E, Gokturk N, Gul M, Demircigil N, Levent AB, Erman Erdemli M. The protective effects of thymoquinone against tartrazine-induced pancreatic injury and its impact on oxidative stress, caspase-3, blood glucose, insulin and cholesterol levels. *Arch Physiol Biochem*, 2025; 1–11.

10. Hegazy AA, Abdel Haliem WAH, El-Bestawy EM, Ali GME. Brief overview about tartrazine effects on health. *Eur Chem Bull*, 2023; 12: 4698–4707.
11. Himri I, Bellahcen S, Souna F, Belmakki F, Aziz M, Bnouham M, Zoheir J, Berkia Z, Aziz M, Saalaoui E. A 90-day oral toxicity study of tartrazine, a synthetic food dye, in Wistar rats. *Int J Pharm Pharm Sci*, 2011; 3(3): 159–169.
12. Hosieny NA, Eldemerdash M, Ahmed SM, Zayed M. Toxic effects of food azo dye tartrazine on the brain of young male albino rats: role of oxidative stress. *Zagazig J Forensic Med Toxicol*, 2021; 19(1): 60–73.
13. Ighodaro OM, Akinloye OA. First line defence antioxidants – superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): their fundamental role in the entire antioxidant defence grid. *Alexandria J Med*, 2018; 54(4): 287–293.
14. Kubavat BB, Asdaq SMB. Role of Sida cordifolia L. leaves on biochemical and antioxidant profile during myocardial injury. *J Ethnopharmacol*, 2009; 124(1): 162–165.
15. Li S, Tan HY, Wang N, Zhang ZJ, Lao L, Wong CW, Feng Y. The role of oxidative stress and antioxidants in liver diseases. *Int J Mol Sci*, 2015; 16(11): 26087–26124.
16. Li X. Improved pyrogallol autoxidation method: a reliable and cheap superoxide-scavenging assay suitable for all antioxidants. *J Agric Food Chem*, 2012; 60(25): 6418–6424.
17. Moutinho ILD, Bertges LC, Assis RVC. Prolonged use of the food dye tartrazine (FD&C yellow No. 5) and its effects on the gastric mucosa of Wistar rats. *Braz J Biol*, 2007; 67: 141–145.
18. Nandi A, Yan LJ, Jana CK, Das N. Role of catalase in oxidative stress- and age-associated degenerative diseases. *Oxid Med Cell Longev*, 2019; 2019: 9613090.
19. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. *J Lab Clin Med*, 1967; 70(1): 158–169.
20. Placer ZA, Cushman LL, Johnson BC. Estimation of product of lipid peroxidation (malonyl dialdehyde) in biochemical systems. *Anal Biochem*, 1966; 16(2): 359–364.
21. Ray Halder S, Bhattacharyya M. Oxidative stress: lipid peroxidation products as predictors in disease progression. *J Exp Integr Med*, 2014; 4(3).
22. Rejitha S, Prathibha P, Indira M. Amelioration of alcohol-induced hepatotoxicity by the administration of ethanolic extract of Sida cordifolia Linn. *Br J Nutr*, 2012; 108(7): 1256–1263.

23. Rejitha S, Prathibha P, Indira M. Nrf2-mediated antioxidant response by ethanolic extract of Sida cordifolia provides protection against alcohol-induced oxidative stress in liver by upregulation of glutathione metabolism. *Redox Rep*, 2015; 20(2): 75–80.
24. Singh R, Sheoran IS. Enzymic browning of whole wheat meal flour. *J Sci Food Agric*, 1972; 23(1): 121–125.
25. Varlı M, Yavaş MC, Cantürk Tan F, Tur K, Basmacı G. Toxic effects of tartrazine and the protective role of curcumin on liver function and DNA integrity in male rats. *Food Sci Nutr*, 2025; 13(12): e71213.
26. Visternicu M, Săvucă A, Rarinca V, Burlui V, Plavan G, Ionescu C, et al. Toxicological effects of tartrazine exposure: a review of in vitro and animal studies with human health implications. *Toxics*, 2025; 13(9): 771.
27. Wang Y, Branicky R, Noë A, Hekimi S. Superoxide dismutases: dual roles in controlling ROS damage and regulating ROS signaling. *J Cell Biol*, 2018; 217(6): 1915–1928.
28. Yaman SO, Ayhanci A. Lipid peroxidation. *Accenting Lipid Peroxidation*, 2021; 1: 1.
29. Zhu R, Wang Y, Zhang L, Guo Q. Oxidative stress and liver disease. *Hepatol Res*, 2012; 42(8): 741–749.