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Curcumin Ameliorates The Hepatoxic Effects of Nitrites: A biochemical Experimental Study

Mohamed F. Assasa [1], Magdy Yousef Elsaied [2*]

Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.
Department of Physiology, Damietta Faculty of Medicine, Al-Azhar University, Damietta, Egypt.

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ABSTRACT

Background and aim: Sodium Nitrate is widely used all over the world and subjects are at risk of their toxic effects. Its use is inevitable and thus proper prophylaxis against its toxic effects is crucial. Curcumin is a medicinal plant with different uses, and it is suggested to produce prophylactic actions against nitrate toxicity. Here we tested the effects of acute oral exposure of $NaNO_2$ and potential ameliorative effects of pre-treatment by curcumin.

Methodology: An experimental study was designed by four groups of animals (each 10 rats). The first was the control group (animals received orally, 2ml/kg, body weight of olive oil (vehicle) daily); the second is the $NaNO_2$ where animals received 2ml/kg, body weight of olive oil and a single dose of $NaNO_2$ (60mg/kg, body weight). The third was the curcumin group (animals received a daily dose of 20mg/kg body weight of curcumin dissolved in 2ml/kg body weight of olive oil). The fourth group was the combination group, where animals received oral doses of curcumin as in the third group, followed by a single oral dose of NaNo2 after 4 weeks of treatment. 48 hours after oral $NaNO_2$, animals were sacrificed, and samples were collected for serum and tissue markers of hepatic injury, oxidative stress, and lipid profile.

Results: The use of a single oral dose of NaNo2 was associated with significant increase of hepatic injury indicators (e.g., ALT, AST, and ALP) when compared to control group. In addition, this group had dyslipidemia and a significant increase of oxidative stress indicators than the control group. The use of curcumin prior to administration of NaNO2 ameliorate these toxic effects but it did not abolish it, as there was a significant difference in combined than control and NaNO2 groups.

Conclusion: : A single oral dose of NaNO2 had a hepatotoxic effect. Curcumin had a prophylactic effect when administered prior to exposure to NaNO2. These actions are produced via modulation of antioxidant status.

Keywords: Hepatotoxicity; Turmeric; Nitrites; Liver Enzymes: Oxidative Stress; Lipid Peroxidation.

* Corresponding author
Email: Magdyyoussef11175@domazhermedicine.edu.eg

INTRODUCTION

Nitrates (specifically Sodium nitrite (NaNO2)) are widely used in industry (e.g., color fixation, food preservation, flavor enhancer, anti-microbials, and rancidity prevention). It is also used as a broncho- and Vaso-dilator at lower physiological doses [1-4]. However, acute exposure to higher disease or chronic exposure to low doses of nitrates and nitrites is associated with toxic effects on several organs. For example, single exposure to a single dose of (20-75 mg/kg body weight) could lead to organ damage in experimental animals. The adverse health effects include but are not limited to respiratory diseases, congenital birth defects, neurological insults, mutagenicity, and carcinogenicity [2, 5-8].

The liver is susceptible to exogenous and endogenous toxic substances. Hepatotoxicity was reported after exposure to $NaNO_2$. These toxic effects are expected to be exerted by mitochondrial injury and oxidative stress [9-11]. Thus, it is expected that any substance with phytochemical antioxidant properties could prevent $NaNO_2$-induced hepatotoxicity [12]. Turmeric (with active constituent curcumin) is a phytochemical bioactive substance, diverse use for its medicinal actions (For example, it had antioxidant, anti-inflammatory, antiangiogenetic and anticancer actions) [13-18].

At the same time, turmeric had no toxic effects, and it alleviates several toxicity-induced organ damages (e.g., cypermethrin, lead acetate, mercury, lindane, cadmium) [19-24]. However, data regarding its protective effects against $NaNO_2$-induced hepatotoxicity is scarce. Thus, the current work was designed to investigate if curcumin had a protective potential against hepatotoxicity induced by acute exposure to $NaNO_2$.

MATERIALS AND METHODS

Chemicals: All chemicals were obtained from Sigma Aldrich Chemical Co. Inc. (St Louis, MO, USA), and prepared by pharmacist not included in the study.

Animals: Fourty male Wistar rats (180–220 g) were obtained from the Cairo Faculty of veterinary medicine animal house. They were kept in plastic cages, with free access to chow and water *ad libitum* for one week (at ambient temperature (25ºC) and relative humidity of ~ 50%), and 12 hours dark and light cycles, to permit acclimatization for climate. The handling of animals throughout the study was performed according to the United States National Research Council guidelines (8^{th} edition) for the care and use of laboratory animals [25]. In addition, the study protocol was approved by local research and ethics committee of the DFM, Al-Azhar University, Egypt.

Experimental design: Animals were divided into 4 equal groups (each including 10 rats): the first group (control group), where animals received 2ml/kg, body weight of olive oil (vehicle) daily by oral gavage. The second is the study Nitrous oxide group, where animals received 2ml/kg, body weight of olive oil and a single dose of NaNo2 (60mg/kg, body weight) as described by Ansari *et al.* [26]. The third is the curcumin group, where animals received a daily dose of 20mg/kg body weight of curcumin dissolved in 2ml/kg body weight of olive oil, as described by Tajik *et al.* [27]. The fourth group is the combination group, where animals received oral doses of curcumin as in the third group, followed by a single oral dose of NaNo2 after 4 weeks of treatment. Two days after the oral dose of NaNo2, animals were sacrificed and blood samples were collected directly from the portal vein in non-heparinized, test tubes, permitted to clot in room temperature, centrifuged at 3000g/minute and serum samples were collected in Eppendorf tubes and used directly for biochemical analysis (to determine liver function biomarkers, C-reactive protein, and lipid profile). The hepatic function indictors (ALT, AST, Alkaline phosphatases (ALP) were determined after the method described by Goodla *et al.* [12]. Albumin concentrations were estimated according to principle reported by Grant [28].

Determination of lipid profile (total cholesterol, Triglycerides, HDL, LDL) was achieved according to methods described by Bucolo and David [29] and Grant [28]. In addition, the high sensitivity C-reactive protein was measured by an enzyme-linked immunosorbent assay (ELISA) (rat C-reactive protein (CRP) ELISA Kit, e-Biosceince, Inc), according to manufacturer instructions. Samples of liver tissues were collected, rinsed in ice 1.15% KCl and stored at –20°C for estimation of oxidative stress biomarkers. The liver tissues were homogenized in 50 mmol/L of Tris-HCL buffer solution followed by centrifugation at 10000g/minute for 15 minutes at 4ºC. The supernatants were kept for at -20ºC till analysis. The oxidative stress markers, malondialdehyde (MDA), Catalase (CAT), superoxide dismutase (SOD), Glutathione (GSH) and glutathione peroxidase were determined according to methods described by Ohkawa et al. [30], Manubolu *et al.* [31], Misra and Fridovich [32](1972), Jollow *et al.* [33], and Rotruck *et al.* [34].

Statistical analysis: The collected data were represented by the arithmetic mean and standard deviation. Groups were compared by one way analysis of variance (ANOVA) with post-hoc analysis for comparison between two groups. The differences were considered significant at p value < 0.05.

RESULTS

In the current work, liver enzymes were significantly increased with a single oral dose of NaNO2. The effect was ameliorated by the prophylactic use of curcumin. But did not reach the values as in the control group. On the other side, albumin was significantly reduced in NaNO2 than the control group. The use of curcumin prevents this effect and there were no significant differences between the curcumin and control groups. The prophylactic use of curcumin ameliorates the effect but not to the normal levels (the combined group still have lower values than the control group) (Table 1). Table (2) presented the results of the lipid profile among the study groups. The use of NaNo2 was associated with a significant elevation of total cholesterol, triglycerides, LDL and CRP than the control group. No significant differences were recorded between curcumin and control groups. However, the use of prophylactic curcumin in combined group was associated with significant improvement of lipid profiles. However, there was a significant difference between combined and control groups.

Results of the current work showed a significant increase of MDA in NaNO2 than control group in values of MDA. However, values of GSH, SOD, glutathione peroxidases and catalase were significantly reduced in NaNo2 than the control groups. The combined use of curcumin followed by NaNO2 was associated with significant improvement in these values. However, there is still a significant difference between combined and control groups (Table 3).

Table (1): Liver function indicators among study groups

		Control	NaNO2	Curcumin	Combined	F	P	Post Hoc, LSD		
ALT (U/L)	Mean±SD	46.20±8.13	86.10±10.99	39.40±5.20	58.10±6.36	66.05	<0.001*	P1<0.001*	P2=0.07	P3=0.002*
	Min. -Max.	30-62	70-105	32-52	49-71			P4<0.001*	P5< 0.001*	P6<0.001*
AST (U/L)	Mean±SD	132.50±21.34	191.00±16.70	130.50±20.58	151.00±13.22	23.62	<0.001*	P1<0.001*	P2=0.80	P3= 0.030*
	Min. -Max.	102-160	160-220	100-158	129-167			P4<0.001*	P5< 0.001*	P6= 0.017*
ALP (U/L)	Mean±SD	22.90±3.25	80.70±7.54	21.70±2.79	61.80±6.55	290.2	<0.001*	P1<0.001*	P2=0.62	P3=0.001*
	Min. -Max.	19-30	73-96	18-28	51-72			P4<0.001*	P5< 0.001*	P5< 0.001*
Albumin (g/dl)	Mean±SD	4.25±0.22	3.92±0.19	4.35±0.22	4.04±0.18	9.48	<0.001*	P1= 0.001*	P2=0.273	P3=0.025*
	Min. -Max.	3.90- 4.60	3.50-4.10	4.0- 4.70	3.70-4.30			P4<0.001*	P5= 0.19	P6= 0.001*

P1: NaNO2 vs Control; P2 Curcumin Vs control; P3 Combined versus control; P4: Curcumin vs NaNo2, P5 combined vs NaNO2 and P6 combined vs Curcumin.

Table (2): Lipid profile and CRP among study groups

		Control	NaNO2	Curcumin	Combined	F	P	Post Hoc, LSD		
TC (mg/dL)	Mean±SD	131.10±9.55	144.10±4.33	130.30±6.78	139.20±3.29	10.56	<0.001*	P1<0.001*	P2=0.78	P3=0.008*
	Min. -Max.	115-142	138-151	121-140	133-144			P4<0.001*	P5= 0.098	P6=0.004*
TG (mg/dl)	Mean±SD	57.30±11.35	76.40±12.99	56.20±11.79	65.60±14.09	5.50	0.003*	P1= 0.002*	P2= 0.85	P3= 0.15
	Min. -Max.	39-79	59-99	40-80	45-91			P4=0.001*	P5= 0.06	P6=0.10
HDL (mg/dl)	Mean±SD	44.90±4.17	25.10±3.54	44.80±4.26	32.70±5.12	50.77	<0.001*	P1<0.001*	P2=0.95	P3< 0.001*
	Min. -Max.	39-52	19-31	40-50	25-41			P4 <0.001*	P5< 0.001*	P6<0.001*
LDL (mg/dl)	Mean±SD	57.00±5.56	86.70±11.51	55.70±5.52	73.70±10.57	28.52	<0.001*	P1<0.001*	P2=0.74	P3< 0.001*
	Min. -Max.	49-68	72-108	48-67	59-89			P4 <0.001*	P5= 0.002*	P6<0.001*
CRP (ng/l)	Mean±SD	12.80±2.85	33.70±6.39	12.40±2.41	32.60±6.71	56.36	<0.001*	P1<0.001*	P2=0.85	P3< 0.001*
	Min. -Max.	9-19	27-48	10-17	25-48			P4 <0.001*	P5= 0.62	P6<0.001*

P1: NaNO2 vs Control; P2 Curcumin Vs control; P3 Combined versus control; P4: Curcumin vs NaNo2, P5 combined vs NaNO2 and P6 combined vs Curcumin.

Table (3): Indicators of oxidative stress among study groups

		Control	NaNO2	Curcumin	Combined	F	P	Post Hoc, LSD		
MDA (umol/ Mg Protein)	Mean±SD	3.07±0.53	8.33±1.16	3.05±0.45	5.61±1.10	83.16	<0.001*	P1< 0.001*	P2=0.95	P3<0.001*
	Min. -Max.	2.1-4.1	5.9-9.6	2.20-3.80	4.20-8.10			P4<0.001*	P5<0.001*	P6<0.001*
GSH (umol/ Mg Protein)	Mean±SD	10.91±1.99	5.41±1.02	10.76±1.55	6.89±1.34	33.22	<0.001*	P1< 0.001*	P2=0.82	P3<0.001*
	Min. -Max.	7.9-13.5	3.9-7.1	8.60-13.10	4.9-9.3			P4<0.001*	P5=0.036*	P6<0.001*
SOD (U/ Mg Protein)	Mean±SD	48.82±4.41	17.70±3.11	48.70±3.02	28.60±3.20	195.27	<0.001*	P1< 0.001*	P2=0.93	P3<0.001*
	Min. -Max.	39-54	13-22	44-55	24-33			P4<0.001*	P5<0.001*	P6<0.001*
GPx (U/ Mg Protein)	Mean±SD	18.0±4.69	9.90±3.90	18.60±3.10	13.0±1.88	13.74	<0.001*	P1< 0.001*	P2=0.71	P3=0.003*
	Min. -Max.	7.0- 25.0	7-20	11-23	10.-15			P4<0.001*	P5=0.059	P=0.001*
CAT (U/mmol H2O2 consumed/mgProtein)	Mean±SD	801.90±29.01	383.0±62.90	799.50±27.73	608.9±35.47	231.24	<0.001*	P1< 0.001*	P2=0.89	P3<0.00*
	Min. -Max.	760-850	290-520	750-840	570-680			P4<0.001*	P5<0.001*	P<0.001*

P1: NaNO2 vs Control; P2 Curcumin Vs control; P3 Combined versus control; P4: Curcumin vs NaNo2, P5 combined vs NaNO2 and P6 combined vs Curcumin.

DISCUSSION

Humans are widely exposed to nitrites through different environmental routes (e.g., contaminated water). In addition, canned foods are significant sources of exposure and induced toxicities [35-38]. However, this exposure is unavoidable. Hence, the importance of prophylactic substances for those exposed to nitrites and nitrates. Here we tested the acute effects of a single dose of NaNO2 and possible ameliorative effects of curcumin. The results showed that the single oral dose is associated with significant changes in chemical indicators of liver injury. This could be attributed to significant changes in lipid profile and oxidative stress markers (i.e., the liver injury is mediated by toxic stress response). The use of curcumin for two weeks before acute exposure is associated with significant improvement of liver injury and oxidative stress indicators. The reported significant elevations of liver enzymes, ALT, AST, and ALP are markers of liver injury as reported in previous studies. In addition, the significant reduction of serum albumin may be related to destruction of hepatocytes and reported early in liver damage. The reduction of albumin synthesis could be explaining increased values of CRP due to switching of the direction of its synthesis [39-41].

Lipids are vital molecules for normal cellular function, structure, and homeostasis. The liver is a key player in the lipid's metabolism [42]. So, liver injury (acute or chronic) is expected to be reflected on the levels of lipids. This is confirmed by the results of the current work and these results agree with previous studies. The reduction in the lipids was suggested to be occurred by lipolysis, through stimulation of hormone sensitive lipase [43].

The use of curcumin was associated with significant amelioration of the toxic effects of NaNO2. Previous studies proved the ameliorative effects of curcumin on lipid profile (44).

The oxidative stress induced by NaNO2 is consistent with previous studies. NaNO2 is a highly reactive compound, that could oxidize, reduce or nitrolyze compounds. It also transformed into different compounds

(e.g., nitrous acid, nitric oxide, and nitrites) 61; and reported oxidative stress can be explained by these compounds. The use of curcumin could neutralize or ameliorate these oxidative stress as it had anti-oxidative actions. anti-oxidative actions play a hepatoprotective action, as reported previously [45-47].

Previous reports indicated that the pre-treatment of animals with curcumin before exposure to toxic agents results in significant improvement of the oxidative stress and its biomarkers (e.g, MDA). Thus, curcumin play a role against NaO2-induced cellular damage [44,48].

This action of curcumin had been confirmed in earlier studies and against different toxic agents (Heavy metals, lead acetate paracetamol, and lindane) on different organs. The antioxidative ability of curcumin is further evidenced by increased levels of glutathione and activities of antioxidant enzymes (superoxide dismutase, glutathione peroxidase and catalase) in the livers of the treated rats [20, 48-51].

To summarize, the current work proved the hepatoxic effects of a single oral dose of NaNO2 and indicated the protective (ameliorative) effects of curcumin against these hepatotoxic effects. These actions are produced via modulation of antioxidant status.

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REFERENCES

1. Lundberg JO, Carlström M, Weitzberg E. Metabolic Effects of Dietary Nitrate in Health and Disease. Cell Metab. 2018 Jul 3;28(1):9-22. doi: 10.1016/j.cmet.2018.06.007.
2. Ansari FA, Ali SN, Arif H, Khan AA, Mahmood R. Acute oral dose of sodium nitrite induces redox imbalance, DNA damage, metabolic and histological changes in rat intestine. PLoS One. 2017 Apr 6;12(4):e0175196. doi: 10.1371/journal.pone.0175196.
3. Omar SA, Webb AJ, Lundberg JO, Weitzberg E. Therapeutic effects of inorganic nitrate and nitrite in cardiovascular and metabolic diseases. J Intern Med. 2016 Apr;279(4):315-36. doi: 10.1111/joim.12441.
4. Lidder S, Webb AJ. Vascular effects of dietary nitrate (as found in green leafy vegetables and beetroot) via the nitrate-nitrite-nitric oxide pathway. Br J Clin Pharmacol. 2013 Mar;75(3):677-96. doi: 10.1111/j.1365-2125.2012.04420.x.
5. Quist AJL, Inoue-Choi M, Weyer PJ, Anderson KE, Cantor KP, Krasner S, et al. Ingested nitrate and nitrite, disinfection by-products, and pancreatic cancer risk in postmenopausal women. Int J Cancer. 2018 Jan 15;142(2):251-261. doi: 10.1002/ijc.31055.
6. Lin W, Hou J, Guo H, Li L, Wang L, Zhang D, Li D, Tang R. The synergistic effects of waterborne microcystin-LR and nitrite on hepatic pathological damage, lipid peroxidation and antioxidant responses of male zebrafish. Environ Pollut. 2018 Apr;235:197-206. doi: 10.1016/j.envpol.2017.12.059.
7. Jensen FB, Gerber L, Hansen MN, Madsen SS. Metabolic fates and effects of nitrite in brown trout under normoxic and hypoxic conditions: blood and tissue nitrite metabolism and interactions with branchial NOS, Na+/K+-ATPase and hsp70 expression. J Exp Biol. 2015 Jul;218(Pt 13):2015-22. doi: 10.1242/jeb.120394.
8. Til HP, Kuper CF, Falke HE. Nitrite-induced adrenal effects in rats and the consequences for the no-observed-effect level. Food Chem Toxicol. 1997 Mar-Apr;35(3-4):349-55. doi: 10.1016/s0278-6915(97)00122-1.
9. Sherif IO, Al-Gayyar MM. Antioxidant, anti-inflammatory and hepatoprotective effects of silymarin on hepatic dysfunction induced by sodium nitrite. Eur Cytokine Netw. 2013;24(3):114-21. doi: 10.1684/ecn.2013.0341.
10. Kiani A, Yousefsani BS, Doroudian P, Seydi E, Pourahmad J. The mechanism of hepatotoxic effects of sodium nitrite on isolated rat hepatocytes, Toxicol Environ Health Sci 2017; 9 (3): 244‑250. https://doi.org/10.1007/s13530-017-0327-z
11. Kawanishi T, Ohno Y, Sunouchi M, Onoda K, Takahashi A, Kasuya Y, Omori Y. Studies on nitrosamine formation by the interaction between drugs and nitrite. II. Hepatotoxicity by the simultaneous administration of several drugs and nitrite. J Toxicol Sci. 1981 Nov;6(4):271-86. doi: 10.2131/jts.6.271.
12. Goodla L, Manubolu M, Pathakoti K, Jayakumar T, Sheu JR, Fraker M, Tchounwou PB, Poondamalli PR. Protective Effects of *Ammannia baccifera* Against CCl_4-Induced Oxidative Stress in Rats. Int J Environ Res Public Health. 2019 Apr 23;16(8):1440. doi: 10.3390/ijerph16081440.
13. Farkhondeh T, Samarghandian S, Azimi M, Shahri AMP. Protective Effects of Curcumin Against Nephrotoxic Agents. Cardiovasc Hematol Disord Drug Targets. 2019;19(3):176-182. doi: 10.2174/1871529X18666180905160830.
14. Di Meo F, Filosa S, Madonna M, Giello G, Di Pardo A, Maglione V, Baldi A, Crispi S. Curcumin C3 complex®/Bioperine® has antineoplastic activity in mesothelioma: an in vitro and in vivo analysis. J Exp Clin Cancer Res. 2019 Aug 16;38(1):360. doi: 10.1186/s13046-019-1368-8.
15. Calibasi-Kocal G, Pakdemirli A, Bayrak S, Ozupek NM, Sever T, Basbinar Y, Ellidokuz H, Yigitbasi T. Curcumin effects on cell proliferation, angio-genesis and metastasis in colorectal cancer. J BUON. 2019 Jul-Aug; 24(4):1482-1487. PMID: 31646795.
16. Kuhad A, Pilkhwal S, Sharma S, Tirkey N, Chopra K. Effect of curcumin on inflammation and oxidative stress in cisplatin-induced experimental nephrotoxicity. J Agric Food Chem. 2007 Dec 12;55(25):10150-5. doi: 10.1021/jf0723965.
17. Hongsibsong S, Stuetz W, Sus N, Prapamontol T, Grune T, Frank J. Dietary exposure to continuous small doses of α-cypermethrin in the presence or absence of dietary curcumin does not induce oxidative stress in male Wistar rats. Toxicol Rep. 2014;1:1106-1114. doi: 10.1016/j.toxrep.2014.10.025.
18. Fu Z, Chen X, Guan S, Yan Y, Lin H, Hua ZC. Curcumin inhibits angiogenesis and improves defective hematopoiesis induced by tumor-derived VEGF in tumor model through modulating VEGF-VEGFR2 signaling pathway. Oncotarget. 2015 Aug 14;6(23):19469-82. doi: 10.18632/oncotarget.3625.
19. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Mol Pharm. 2007 Nov-Dec;4(6):807-18. doi: 10.1021/mp700113r.
20. Singh R, Sharma P. Hepatoprotective Effect of Curcumin on Lindane-induced Oxidative Stress in Male Wistar Rats. Toxicol Int. 2011 Jul;18(2):124-9. doi: 10.4103/0971-6580.84264.
21. Sharma P, Aslam Khan I, Singh R. Curcumin and Quercetin Ameliorated Cypermethrin and Deltamethrin-Induced Reproductive System Impairment in Male Wistar Rats by Upregulating The Activity of Pituitary-Gonadal Hormones and Steroidogenic Enzymes. Int J Fertil Steril. 2018 Apr; 12(1):72-80. doi: 10.22074/ijfs.2018.5160.
22. Samarghandian S, Azimi M, Farkhondeh T, Samini F. Anti-oxidative effects of curcumin on immobilization-induced oxidative stress in rat brain, liver and kidney. Biomed Pharmacother. 2017 Mar;87:223-229. doi: 10.1016/j.biopha.2016.12.105.

23. Liu W, Xu Z, Li H, Guo M, Yang T, Feng S, Xu B, Deng Y. Protective effects of curcumin against mercury-induced hepatic injuries in rats, involvement of oxidative stress antagonism, and Nrf2-ARE pathway activation. Hum Exp Toxicol. 2017 Sep;36(9):949-966. doi: 10.1177/0960327116677355.

24. Akinyemi AJ, Onyebueke N, Faboya OA, Onikanni SA, Fadaka A, Olayide I. Curcumin inhibits adenosine deaminase and arginase activities in cadmium-induced renal toxicity in rat kidney. J Food Drug Anal. 2017 Apr;25(2):438-446. doi: 10.1016/j.jfda.2016.06.004.

25. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals. 8th ed. Washington (DC): National Academies Press (US); 2011. PMID: 21595115.

26. Ansari FA, Ali SN, Khan AA, Mahmood R. Acute oral dose of sodium nitrite causes redox imbalance and DNA damage in rat kidney. J Cell Biochem. 2018 Apr;119(4):3744-3754. doi: 10.1002/jcb.26611.

27. Tajik H, Tamaddonfard E, Hamzeh-Gooshchi N. The effect of curcumin (active substance of turmeric) on the acetic acid-induced visceral nociception in rats. Pak J Biol Sci. 2008 Jan 15;11(2):312-4. doi: 10.3923/pjbs.2008.312.314.

28. Grant GH. Amino Acids and Proteins. In: Fundamentals of Clinical Chemistry (1987).

29. Bucolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. Clin Chem. 1973 May;19(5):476-82.

30. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem. 1979 Jun;95(2):351-8. doi: 10.1016/0003-2697(79)90738-3.

31. M Manubolu M, Goodla L, Ravilla S, Thanasekaran J, Dutta P, Malmlöf K, Obulum VR. Protective effect of Actiniopteris radiata (Sw.) Link. against CCl4 induced oxidative stress in albino rats. J Ethnopharmacol. 2014 May 14;153(3):744-52. doi: 10.1016/j.jep.2014.03.040.

32. Misra HP, Fridovich I. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. J Biol Chem. 1972 May 25;247(10):3170-5.

33. Jollow DJ, Mitchell JR, Zampaglione N, Gillette JR. Bromobenzene-induced liver necrosis. Protective role of glutathione and evidence for 3,4-bromobenzene oxide as the hepatotoxic metabolite. Pharmacology. 1974;11(3):151-69. doi: 10.1159/000136485.

34. Rotruck JT, Pope AL, Ganther HE, Swanson AB, Hafeman DG, Hoekstra WG. Selenium: biochemical role as a component of glutathione peroxidase. Science. 1973 Feb 9;179(4073):588-90. doi: 10.1126/science.179.4073.588.

35. El-Toony MM, Eid G, Algarni H. Estimation of hazardous materials in water and their toxicity levels in Mahayel Aseer, Kingdom of Saudi Arabia. Environ Monit Assess. 2019 Nov 29;191(12):779. doi: 10.1007/s10661-019-7820-6.

36. Zhang Q, Xu P, Qian H. Assessment of Groundwater Quality and Human Health Risk (HHR) Evaluation of Nitrate in the Central-Western Guanzhong Basin, China. Int J Environ Res Public Health. 2019 Nov 1;16(21):4246. doi: 10.3390/ijerph16214246.

37. Ainerua MO, Erhunmwunse N, Tongo I, Ezemonye L. Food toxicity assessment of selected canned foods in Nigeria. Toxicol Res. 2019 Nov 26;36(1):45-58. doi: 10.1007/s43188-019-00001-9.

38. Menard C, Heraud F, Volatier JL, Leblanc JC. Assessment of dietary exposure of nitrate and nitrite in France. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2008 Aug; 25 (8): 971-88. doi: 10.1080/02652030801946561.

39. Freitag AF, Cardia GF, da Rocha BA, Aguiar RP, Silva-Comar FM, Spironello RA, et al. Hepatoprotective Effect of Silymarin (Silybum marianum) on Hepatotoxicity Induced by Acetaminophen in Spontaneously Hypertensive Rats. Evid Based Complement Alternat Med. 2015; 2015: 538317. doi: 10.1155/2015/538317.

40. 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 Nov 2;16(11):26087-124. doi: 10.3390/ijms161125942.

41. Lin L, Zhou F, Shen S, Zhang T. Fighting Liver Fibrosis with Naturally Occurring Antioxidants. Planta Med. 2018 Dec;84(18):1318-1333. doi: 10.1055/a-0757-0008.

42. Arain SQ, Talpur FN, Channa NA, Ali MS, Afridi HI. Serum lipid profile as a marker of liver impairment in hepatitis B Cirrhosis patients. Lipids Health Dis. 2017 Mar 1;16(1):51. doi: 10.1186/s12944-017-0437-2.

43. Ozen H, Kamber U, Karaman M, Gül S, Atakişi E, Özcan K, Atakişi O. Histopathologic, biochemical and genotoxic investigations on chronic sodium nitrite toxicity in mice. Exp Toxicol Pathol. 2014 Oct;66(8):367-75. doi: 10.1016/j.etp.2014.05.003. Epub 2014 Jun 17. PMID: 24947405.

44. Qin S, Huang L, Gong J, Shen S, Huang J, Ren H, Hu H. Efficacy and safety of turmeric and curcumin in lowering blood lipid levels in patients with cardiovascular risk factors: a meta-analysis of randomized controlled trials. Nutr J. 2017 Oct 11;16(1):68. doi: 10.1186/s12937-017-0293-y.

45. Rezzani R, Franco C, Rodella LF. Curcumin as a Therapeutic Strategy in Liver Diseases. Nutrients. 2019 Oct 17;11(10):2498. doi: 10.3390/nu11102498.

46. Farzaei MH, Zobeiri M, Parvizi F, El-Senduny FF, Marmouzi I, Coy-Barrera E, et al. Curcumin in Liver Diseases: A Systematic Review of the Cellular Mechanisms of Oxidative Stress and Clinical Perspective. Nutrients. 2018 Jul 1;10(7):855. doi: 10.3390/nu10070855.

47. Ghosh S, Bhattacharyya S, Rashid K, Sil PC. Curcumin protects rat liver from streptozotocin-induced diabetic pathophysiology by counteracting reactive oxygen species and inhibiting the activation of p53 and MAPKs mediated stress response pathways. Toxicol Rep. 2015 Jan 2;2:365-376. doi: 10.1016/j.toxrep.2014.12.017.

48. Sudjarwo SA, Sudjarwo GW, Koerniasari. Protective effect of curcumin on lead acetate-induced testicular toxicity in Wistar rats. Res Pharm Sci. 2017 Oct;12(5):381-390. doi: 10.4103/1735-5362.213983.

49. Ahmad MM, Rezk NA, Fawzy A, Sabry M. Protective effects of curcumin and silymarin against paracetamol induced hepatotoxicity in adult male albino rats. Gene. 2019 Sep 5;712:143966. doi: 10.1016/j.gene.2019.143966.

50. Mohajeri M, Rezaee M, Sahebkar A. Cadmium-induced toxicity is rescued by curcumin: A review. Biofactors. 2017 Sep 10;43(5):645-661. doi: 10.1002/biof.1376.

51. Garcia-Nino WR, Pedraza-Chaverrí J. Protective effect of curcumin against heavy metals-induced liver damage. Food Chem Toxicol. 2014 Jul;69:182-201. doi: 10.1016/j.fct.2014.04.016.

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