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EFFECT OF CARBON TETRACHLORIDE ON BIOCHEMICAL PARAMETERS IN BLOOD OF ALBINO RAT AFTER DRUG SUPPLEMENTATION

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Abstract

CCl4 is considered very toxic. Suspected carcinogenic to humans based on adequate evidence of carcinogenicity from animal studies. How does carbon tetrachloride affect children's health? The effects of carbon tetrachloride on child health have not been adequately studied. Carbon tetrachloride is an organic compound that can damage the liver by causing a state of oxidative stress. Carbon tetrachloride (CCl4) binds triacylglycerols and phospholipids throughout the subcellular fraction and causes lipid peroxidation in hepatocytes. CCl4 is a highly hepatotoxic xenobiotic and exposure to CCl4 directly causes hepatic necrosis and steatosis (Gu X and Manautou JE, Hodgman MJ, Garrard AR 2012). Mechanistic studies provide evidence that the metabolism of CCl4 to strongly reactive free radical metabolites by CYP2E1 plays an important role in the strategy mode of action. Metadoxin drug is known for its hepatoprotective potential and used in this study. Compataive effect of the plant extract of *Phyllanthus niruri* and *Urtica dioica* has been observed with the drug in albino rats for hepatoprotectant action.

Keywords: Liver function test, CCl4, Metadoxine, *Phyllanthus niruri*, *Urtica dioica*

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Introduction

The liver plays a crucial role in the body and is responsible for numerous vital processes. It's particularly dangerous because it's involved in every metabolic activity, but especially in getting rid of harmful infections and other xenobiotics. This is a quote from [Gu X and Manautou JE (2012),] rare drugs that cause liver failure due to drug-induced liver damage (DILI) are the leading reason for liver transplantation.

Alcohol, CCl4, and viral infections all produce hepatotoxicity in laboratory animals, and metadoxine (pyridoxine pyrrolidone carboxylate) has been shown to be effective in treating this condition. Metadoxine (pyridoxine pyrrolidone carboxylate) is an ion pair composed of pyridoxine (vitamin B6) and pyrrolidone carboxylate.

Alcoholic liver disease is treated well with metformin (Vonghia *et al.*, 2008). Ethanol's negative effects are mitigated, and acetaldehyde excretion is increased (Calabrese, 1995). Hepatocytes and hepatic stellate cells' glutathione stores can be preserved and ethanol- and acetaldehyde-induced lipid peroxidation, collagen deposition, and tumor necrosis factor (TNF) - production can be blocked with the help of metadoxin (Gutiérrez-Ruiz 2001). Methadoxine inhibits the decrease in hepatic adenosine triphosphate (ATP) concentration that occurs after oral administration of ethanol to rats, and it also recovers hepatic GSH levels. Several researchers have found this to be the case (Calabrese et al. 1995, Calabres et al. Metadoxine has also shown promise as a potential therapy for NASH. Factors that cause illness, such oxidative stress.

Animals given both CCl4 and metadoxin in a chronic control model of liver fibrosis showed reduced fibrosis and inflammation, with persistent levels of anti-prolyl hydroxylase antibodies (Annoni *et al.*1992). Therefore, this is the first study to look into how metadoxine may help protect rats from the hepatotoxicity caused by acetaminophen.

When metabolizing alcohol, the liver plays a crucial role and can be harmed by alcohol's byproducts such reactive oxygen species (ROS). Alcohol metabolism by CYP2E1 results in reactive oxygen species (ROS), which contributes to the development of ALD. Butura *et al*. discovered that introducing a CYP2E1 transgene into mice increased the expression of genes involved in oxidative stress and alcohol-induced liver damage. Adenovirus-mediated gene transfer to regulate CYP2E1 expression in mice results in elevated levels of oxidative stress and liver damage. Using an overexpressed CYP2E1 HepG2 cell line, the authors demonstrated that CYP2E1 suppresses the expression of antioxidants like glutathione (GSH), catalase (CAT), microsomal glutathione transferase 1 (MGST1), and -glutathione S-transferase (-GST) and promotes alcohol-induced oxidative stress.

Material and Methods

The male albino rats (Rattus norvegicus) of wistar strain utilized in the experiments were from a colony maintained by

the Zoology Department's anima house at Agra College, Agra, and ranged in weight from 120 to 25 grams. The albino rats were kept in polypropylene cages with dimensions of 45x25x15cm, with the temperature kept at 25°C, the humidity kept at 6510%, and a regular 24-hour light/dark cycle maintained. The acclimated animals were separated into seven groups—control, CCl4 treated, CCl4+metadoxine treated, CCl4+*Phyllanthus niruri*, CCl4+Urtica dioica, and CCl4+*Phyllanthus niruri* + *Urtica dioica*—and housed in seven different cages over the course of the seven, fifteen, thirty, forty-five, and sixty-day experiment. Goldmohar brand feed and water were provided ad libitum to keep them healthy.

After receiving CCl4 (70mg/kg.b.wt) and metadoxine (200mg/kg.b.wt), the rats were observed for a set amount of time. Both *Phyllanthus niruri* and *Urtica dioica* plant extracts (10 ml/kg body weight) were administered. All medications and injections were administered orally with a syringe and bent canula tip. Doses were administered for a total of 60 days. All of the albino rats were killed with minimal sedation.

The alanine aminotransferase (AST) and alanine aminotransferase (ALT) levels were estimated using the Reitman and Frankel method, and the alkaline phosphatase levels were estimated using the Kind and King method; all data were analyzed statistically using software and the analysis of variance (ANOVA).

Result and Discussion

Biotransformation of acetaminophen to the active liver metabolite NAPQI by several isozymes of the cytochrome P450 system is assumed to be the cause of acetaminophen-induced liver injury (Hodgman MJ, Garrard AR, 2012). Hepatic transaminases are enzymes produced in the liver that are released into the bloodstream when cellular tissue malfunctions. The presence of enzymes in the blood shows the severity of liver injury when there is an elevation of both ALT and AST in the liver (Plaa GL, Charbonneau M, 2008).

ALP is a tissue-general enzyme found in many organs. The breakdown of liver cell membranes and damage to the hepatobiliary machinery have both been linked to a rise in ALP levels in the blood (Muthulingam 2008, and Giannini et al. 2005).

One way to evaluate elimination is by measuring total bilirubin in the blood. Abnormally high blood bilirubin levels and impaired liver function are hallmarks of hepatobiliary illness and severe hepatocellular dysfunction (Giannini et al., 2005).

This study demonstrated that oral treatment of acetaminophen induced liver impairment in rats, as evidenced by an elevation of serum bilirubin levels and an increase in alanine aminotransferase (ALT), aspartate aminotransferase (ALP), and ALT activities. The aggregate of people. Our results show that metadoxin prevents the reduction in serum enzyme levels (AST, ALT, and ALP) that characterizes acetaminophen-induced hepatotoxicity in rats. There are two components involved in the formation of GSH: pyridoxine (vitamin B6) and pyrrolidone carboxylate, which may explain why metadoxine has antioxidant effects. Toxic effects of a transfluthrin-based liquid mosquito repellent were also seen in albino rats (Biswas *et al*.2023) *Tamrandus indica* and vitamin D supplementation were found to have a mitigating impact on the elevation of fluoride-induced biochemical parameters in albino rats, as reported by Yadav *et al*., 2022.

Glutamic acid's cyclic lactam, pyrrolidone carboxylic acid, hydrolyzes directly into glutamic acid. It plays a key role in the synthesis and degradation of glutathione (GSH) as an intermediary in the -glutamyl cycle (Woolbright *et al.*, 2010; Jaeschke *et al.*, 2010; Addolorato 2003; Kumar *et al*., 2012). Multiple in vivo and laboratory experiments have shown that metadoxin has a protective effect on the liver. Metadoxin was shown to have anti-fibrotic and even anti-necrotic activities by Anony *et al*. (1992) during the chronic ligation phase of caused liver injury in rats.

The bile duct ligation group had greater hepatic glycogen storage capacity and enzyme storage capacity. Results like these agree with those found by Gutiérrez-Ruiz et al. Metadoxin has been shown to inhibit lipid peroxidation and preserve the GSH pool in cultured hepatocytes and stellate liver cells that have been exposed to ethanol (Gutiérrez-Ruiz 2001). Multiple in vivo and laboratory experiments have shown that metadoxin has a protective effect on the liver. Metadoxine was reported to have anti-fibrotic and even anti-necrotic characteristics in bacterial cells responsible for liver injury in mice by Annoni *et al.* (1992). The bile duct ligation group had greater hepatic glycogen storage capacity and enzyme storage capacity. The protective effects of metadoxine on the liver against ischemia and reperfusion in rats were studied by Feher *et al.* in 2009. Alcoholic adiposity is eliminated, AMP-activated protein kinase activity is increased, and fat formation and CYP2E1 activation in the liver of rats are prevented when metadoxin and garlic oil are administered together (Ki SH *et al.*, 2007).

Because they contain a wide variety of useful secondary metabolites (phytochemicals), medicinal plants have been validated as legitimate therapeutic agents. Plants with therapeutic characteristics are utilized as ingredients in health and medical products. After being exposed to carbon tetrachloride, the antioxidant activities of Phyllostachys phylloxera and nettle plant extracts were found to be significantly more effective at protecting the liver than metadoxine (Kandis *et al*., 2010). The results differ significantly from the control group after being exposed to rice straw smoke. The toxic effect in liver is modulated by honey supplementation as shown in Tables and graphs below-

Table-1 and Fig. 1Effect of CCl4 on alkaline phosphatide with supplementation of drug metadoxine and plant extract *Phyllanthus niruri* and *Urtica dioica* for 7, 15, 30, 45 and 60 days in Albino rat

Experimental Sets	7 days (Mean±S.Em.)	15 days (Mean±S.Em.)	30 days (Mean±S.Em.)	45 days (Mean±S.Em.)	60 days (Mean±S.Em.)
Control	110+1.20	110+1.20	110+1.20	110+1.20	110+1.20
CCl4	127+1.10	148+2.30	166+1.67	156+1.99	186+2.55
CCl4+Metadoxine	152+1.15	149+2.05	142+1.22	126+1.0	157+1.25
CCl4+ *Phyllanthus niruri*	154+1.02	135+1.09	145+1.33	138+1.88	158+1.21
CCl4+ *Urtica dioica*	157+1.05	130+1.90	141+1.10	115+1.86	124+1.15
CCl4+ *Phyllanthus niruri*+ *Urtica dioica*	172+1.23	131+1.08	133+1.0	124+1.20	102+1.30

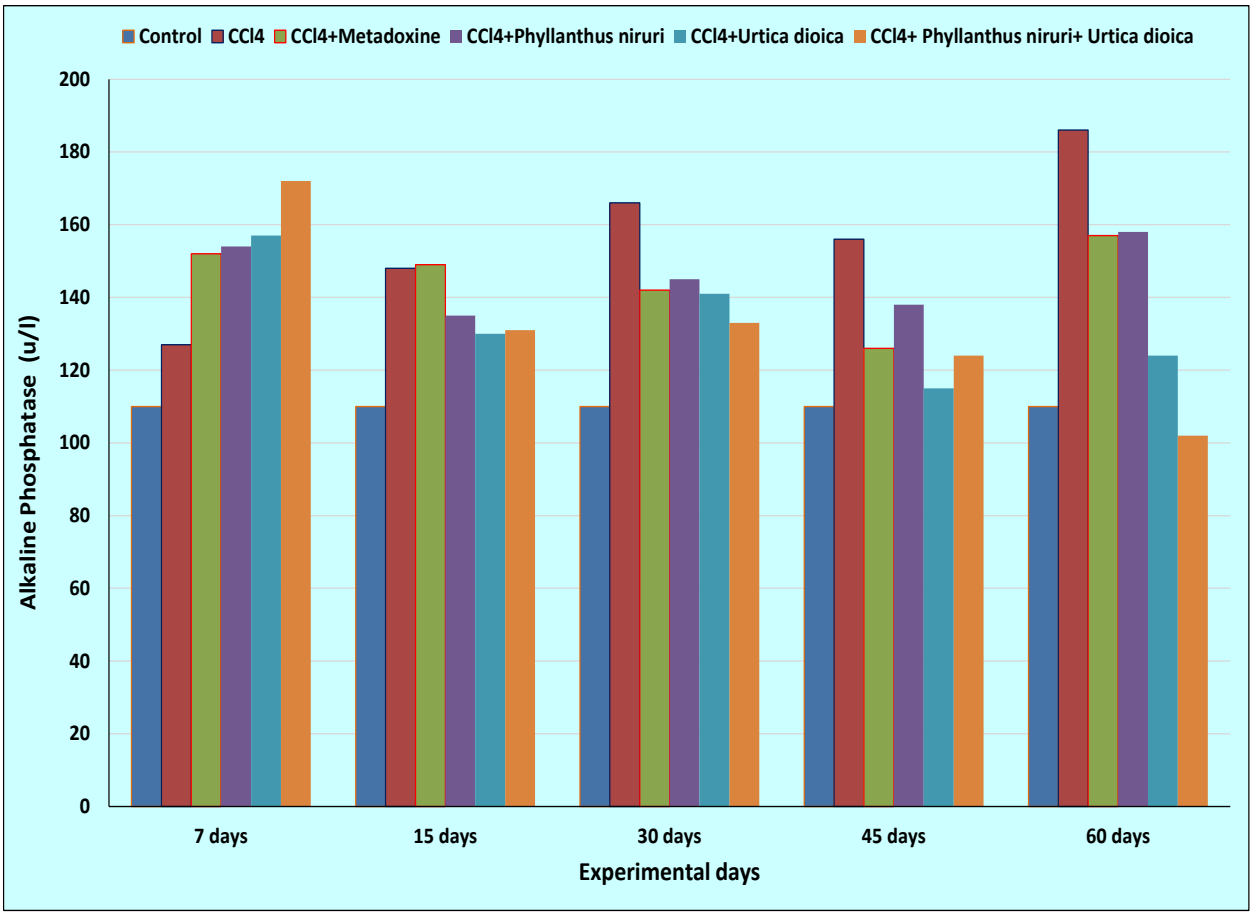


Table-2 and Fig. 2 Effect of CCl4 on AST with supplementation of drug metadoxine and plant extract *Phyllanthus niruri* and *Urtica dioica* for 7, 15, 30, 45 and 60 days in Albino rat

Experimental Sets	7 days (Mean±S.Em.)	15 days (Mean±S.Em.)	30 days (Mean±S.Em.)	45 days (Mean±S.Em.)	60 days (Mean±S.Em.)
Control	88+0.90	88+0.90	88+0.90	88+0.90	88+0.90
CCl4	175+2.50	114+2.10	125+2.88	135+2.80	136+2.15
CCl4+Metadoxine	108+2.03	110+1.30	138+1.80	102+2.10	188+2.25
CCl4+ *Phyllanthus niruri*	102+1.98	112+1.15	133+1.90	116+2.30	124+1.90
CCl4+ *Urtica dioica*	99+2.10	98+1.03	125+2.13	114+2.20	128+1.90
CCl4+ *Phyllanthus niruri+ Urtica dioica*	92+1.99	106+1.02	110+1.20	115+2.21	104+1.35

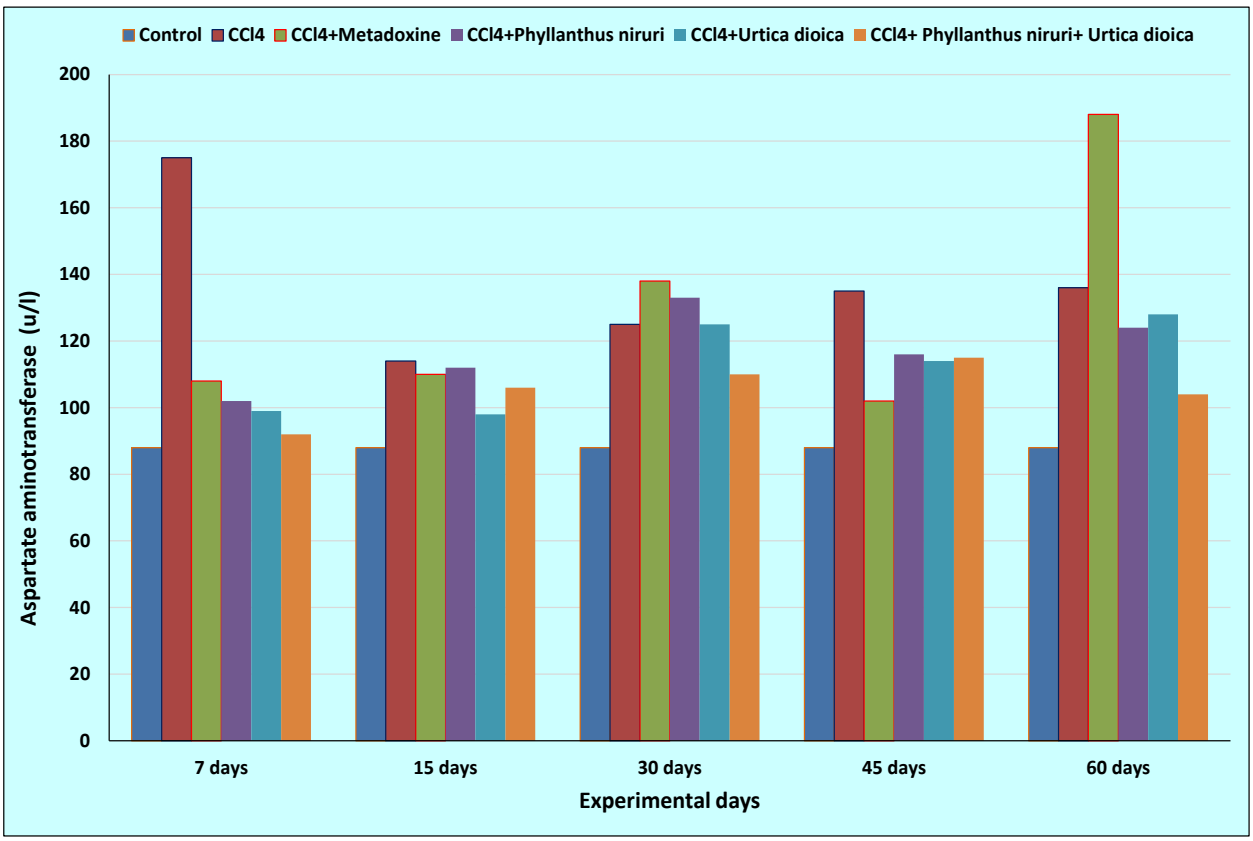
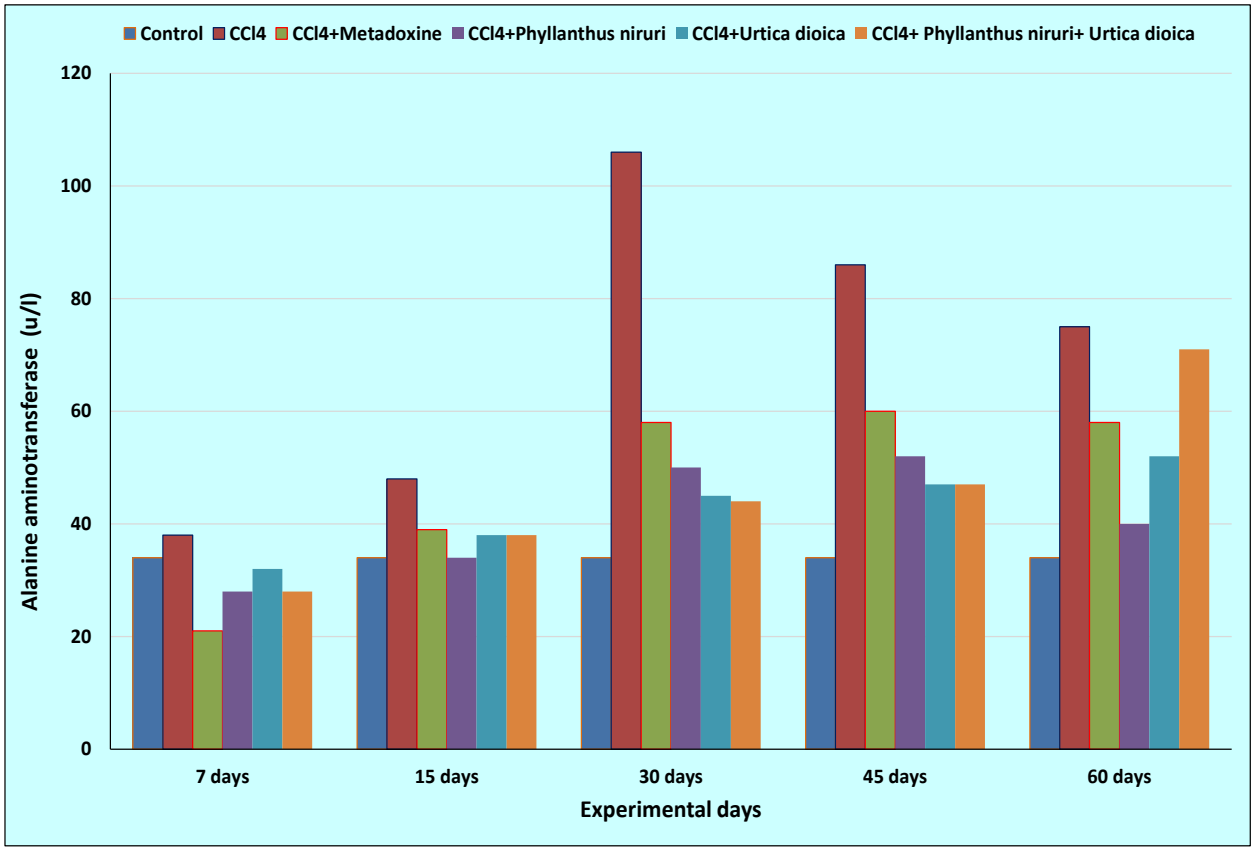


Table-3 and Fig. 3 Effect of CCl4 on ALT with supplementation of drug metadoxine and plant extract *Phyllanthus niruri* and *Urtica dioica* for 7, 15, 30, 45 and 60 days in Albino rat

Experimental Sets	7 days (Mean±S.Em.)	15 days (Mean±S.Em.)	30 days (Mean±S.Em.)	45 days (Mean±S.Em.)	60 days (Mean±S.Em.)
Control	34+0.95	34+0.95	34+0.95	34+0.95	34+0.95
CCl4	38+0.66	48+0.98	106+1.12	86+0.90	75+0.95
CCl4+Metadoxine	21+0.33	39+0.66	58+1.0	60+0.67	58+0.30
CCl4+ *Phyllanthus niruri*	28+0.65	34+0.67	50+0.90	52+1.1	40+0.32
CCl4+ *Urtica dioica*	32+0.50	38+0.88	45+0.80	47+0.83	52+0.65
CCl4+ *Phyllanthus niruri+ Urtica dioica*	28+0.33	38+0.80	44+0.85	47+0.33	71+0.88

NS- Non-significant (p>0.05), *- Significant (p<0.05), **- Highly Significant (p<0.01), ***- Very Highly Significant (p<0.001)



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Reference

Gu X, Manautou JE. (2012), Molecular mechanisms underlying chemical liver injury. Expert Rev Mol Med.;14:e4.

Hodgman MJ, Garrard AR (2012), A review of acetaminophen poisoning. Crit Care Clin; 28:499–516.

Vonghia L, Leggio L, Ferrulli A, Bertini M, Gasbarrini G, Addolorato G, (2008), Acute alcohol intoxication. Eur J Intern Med., 19:561–7.

Calabrese V, Ragusa N, Rizza V., (1995) Effect of pyrrolidone carboxylate (PCA) and pyridoxine on liver metabolism during chronic ethanol intake in rats. Int J Tissue React.,17:15–20.

Gutiérrez-Ruiz MC, Bucio L, Correa A, Souza V, Hernández E, Gómez-Quiroz LE, (2001) Metadoxine prevents damage produced by ethanol and acetaldehyde in hepatocyte and hepatic stellate cells in culture. Pharmacol Res., 44:431–6.

Calabrese V, Calderone A, Ragusa N, Rizza V., (1996) Effects of metadoxine on cellular status of glutathione and of enzymatic defence system following acute ethanol intoxication in rats. Drugs Exp Clin Res., 22:17–24.

Felicioli R, Saracchi I, Flagiello AM, Bartoli C., (1980) Effects of pyridoxine-pyrrolidon-carboxylate on hepatic and cerebral ATP levels in ethanol treated rats. Int J Clin Pharmacol Ther Toxicol., 18:277–80.

Annoni G, Contu L, Tronci MA, Caputo A, Arosio B., (1992) Pyridoxol L,2-pyrrolidon-5 carboxylate prevents active fibroplasia in CCl4-treated rats. Pharmacol Res., 25:87–93.

Plaa GL, Charbonneau M., (2008) Detection and evaluation of chemically induced liver injury. In: Hayess AW, editor. Principles and Methods of Toxicolog. 5th ed. Massachussets: CRC Press; pp. 1465–507.

Muthulingam M., (2008), Antihepatotoxic effects of boerhaavia diffusa L. on antituberculosis drug, rifampicin induced liver injury in rats. J Pharmacol Toxicol., 3:75–83.

Giannini EG, Testa R, Savarino V., (2005), Liver enzyme alteration: A guide for clinicians. CMAJ., 172:367–79.

Woolbright BL, Jaeschke H., (2010), Mechanisms of acetaminophen-induced liver necrosis. In: Hinson JA, Roberts DW, James LP, editors. Adverse Drug Reactions. Kanzas: Springer; pp. 369–405.

Addolorato G, Ancona C, Capristo E, Gasbarrini G., (2003) Metadoxine in the treatment of acute and chronic alcoholism: A review. Int J Immunopathol Pharmacol., 16:207–14.

Kumar A, Bachhawat AK., (2012), Pyroglutamic acid: Throwing light on a lightly studied metabolite. Curr Sci. 102:288–97.

Fehér J, Váli L, Blázovics A, Lengyel G., (2009), The beneficial effect of metadoxine (pyridoxine-pyrrolidone-carboxylate) in the treatment of fatty liver diseases. Clin Exp Med. 3:65–79.

Ki SH, Choi JH, Kim CW, Kim SG., (2007), Combined metadoxine and garlic oil treatment efficaciously abrogates alcoholic steatosis and CYP2E1 induction in rat liver with restoration of AMPK activity. Chem Biol Interact., 169:80–90.

Kandis H, Karapolat S, Yildirim U, Saritas A, Gezer S, Memisogullari R. (2010), Effects of Urtica dioica on hepatic ischemia-reperfusion injury in rats. Clinics (Sao Paulo)., 65(12):1357-61.

Biswas S., Vishwakant, A P Singh, P Sagar, (2022), "Toxic Effect of Transfluthrin Based Liquid Mosquito Repellent on The Liver Enzymes in Rattus norvegicus (Berkenhout)" Journal of Science Innovations and Nature of Earth, Vol. 2(4), page- 41-45.

Yadav S., P.K. Singh, P. Sagar and H. N. Sharma, (2022), Ameliorative Effect of *Tamarindus indica* and Vitamin D Supplementation On Fluoride Induced Biochemical Parameters in Albino Rat. Int J Pharm Sci.,13(3), b57-63.

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