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WMAK designed the study; WMAK and OEAA performed the experiments, AAMA, AMNQ and AMAA collected data, and WMAK, AYAY, HAJR, HAGA and MAMA wrote the first draft of the manuscript; MFHS and OAMA performed the statistical analysis; RHAA and ZYMA reviewed the draft of the manuscript; all authors approved manuscript for publication.

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Hepatoprotective Activity of Ethanolic Leaves Extract of *Vachellia origena* (Hunde) Kyal. and Boatwr. (Fabaceae) on Paracetamol-Induced Hepatotoxicity in Male Guinea Pigs

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Abstract:
Vachellia origena is a tree distributed in J. Saber, Alturba, Ibb, Dhamar, Sanaa, Haraz, Shibam, and Yafea. They have antibacterial, antifungal, and antioxidant properties. This study aimed to investigate the effect of *V. origena* ethanolic leaves extract on biochemical parameter activities and histopathological changes of the liver induced by paracetamol in male guinea pigs. A total of 28 male guinea pigs (350-650 g) were randomly assigned to seven groups of five guinea pigs each. Group I served as the control group. Group II received PCM (500 mg/kg) alone, Group III received PCM and proximol (0.8 mg/kg), Group IV received 100 mg/kg *V. origena* leaves extract alone, and Group V received 200 mg/kg *V. origena* leaves extract alone. Group VI was administered PCM (500 mg/kg) and 100 mg/kg of *V. origena* leaves extract. Meanwhile, group VII was administered with PCM (500mg/kg) and 200 mg/kg of *V. origena* leaves extract. The treatment period lasted for ten days, after which sera were harvested and assayed for serum liver indices using standard methods. The data obtained indicated that blood AST, ALT, ALP, and total bilirubin levels were elevated in the PCM-only group. It also resulted in a number of histopathological alterations. Treatment with the ethanolic leaf extract of *V. origena* (100 mg/kg and 200 mg/kg) reduced the amount of histopathological lesions in guinea pigs and shielded the liver from PCM-induced intoxication. Data from our study suggest that the ethanolic extract of the leaves of the plant *V. origena* has protective effects against PCM-induced liver toxicity.

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INTRODUCTION

The liver is an essential organ that serves several purposes (Khanam *et al.,* 2016). The liver is primarily important for innate immunity due to its massive endogenous macrophages, or Kupffer cells, and its ability to easily attract circulating leukocytes (Woolbright and Jaeschke, 2017). Increased intestinal permeability during different ailments can expose the liver to gut-derived microbes, and other pathological material through portal vein blood (Nicoletti *et al.,* 2019). Kupffer cells are designed to be extremely sensitive to these substances and are highly efficient at eliminating them (Woolbright and Jaeschke, 2017).

Paracetamol (PCM) is the most popular antipyretic and pain reliever, often referred to as acetaminophen N-(4-hydroxyphenyl)acetamide. It has been sold over the counter since 1955, either alone or in conjunction with other medications (Sheen *et al.,* 2002)**.** Nonetheless, in Western nations, PCM overdose continues to be the predominant cause of drug-induced liver damage (Lee, 2013). The primary cause of acute liver failure (ALF) is hepatotoxicity from PCM overdose, which accounts for over 50% of ALF cases in these countries (Yoon *et al.,* 2016). Liver damage caused by PCM is becoming a public health concern. A liver transplant is the only treatment that may be able to preserve a patient's life in extreme cases (Yang *et al.,* 2022).

The genus *Vachellia* Wight & Arn. (*Acacia* Mill.) is one of the largest genera in the family Fabaceae. It includes about 1350 species, which are grouped into three subgenera (*Acacia, Aculeiferum,* and *Phyllodineae*). The *Acacia* is essentially a tropical tree, but it also extends into the subtropics. Around 1000 species are found in Australia, and 170 species were found to be native to Africa and among them, 18 species are widespread and 152 are endemic to the African continent (Legesse, 2010; Farzana *et al.,* 2014), Eritrea, Ethiopia and Saudi Arabia (Al-Khulaidi *et al.,* 2024). The genus *Acacia* Mill is represented in Yemen by 32 species: 5 introduced and cultivated as ornamental trees (*A. auriculiformis, A. calcicola, A. cyanophylla, A. cyclops,* and *A. farnesiana*), 25 native to the mainland, including *A. origena,* and 2 endemic species to Socotra Island, *A. sarcophylla* and *A. pennivenia* (Al Khulaidi, 2013).

Vachellia origena Hunde (synonym: *Acacia origena*) (Nasser and Aref, 2014) is a flat-topped tree up to 12 m tall with a yellow-brown, papery peeling of layers; paired, straight spines; yellow-brown branchlets; bipinnate leaves; 10-25 pairs of leaflets; flowers in globular cream heads; and glabrous green-brown pods (Al Khulaidi, 2013). It is widespread on the escarpment above 1900 m and is also located on mountains around the high plateau from 2300 m to 2900 m; thus, it grows at altitudes higher than any other *Acacia* in Yemen (Al Khulaidi, 2013). Based on previous studies, *Vachellia origena* trees have medicinal value since they contain several phytochemicals, such as phenols, flavonoids, tannins, saponins, alkaloids, steroids, and carbonyls (Shaikh *et al.,* 2022); therefore, they are used medically to treat many diseases, such as antioxidants (Ibrahim *et al.,* 2023) and antibacterials (Mahmoud *et al.,* 2016). In conventional systems, *V. origena* is an interesting plant. Nevertheless, there have been no published scientific investigations on the hepatoprotective benefits of *V. origena*, and its chemical components might be helpful in the management of hepatotoxicity. The current study was conducted to examine the hepatoprotective effect of ethanolic extracts of the *V. origena* leaves against hepatotoxicity induced by paracetamol.

MATERIALS AND METHODS

Collection and identification of plant

Green leaves of *V. origena* were collected from Waqash Village, Jiblah, Ibb City, Yemen. The identification and authentication of plant specimens were done by Dr. Esam Aqlan, Assistant Professor of Plant Taxonomy and

Flora, Biology Department, Faculty of Sciences, Ibb University, Yemen. A voucher specimen was deposited at the Biology Herbarium, Faculty of Sciences, Ibb University, Yemen, under the code CM202115.

Preparation of plant extract

The fresh plant material was harvested, properly cleaned with tap water to remove debris, and then dried in an oven set to 40°C until the leaves were brittle. The leaves were dried, then roughly crushed and ground in a blender into powder. 30 g of leave powder and 3000 mL of 70% ethanol were taken. The extraction was repeated 3 times, then the glass beaker was placed in the electric shaker for 24 hours, then the extract was filtered, and the water was removed by evaporating the extract in an electric oven at a temperature of 40°C to obtain the extract powder.

Preliminary phytochemical screening

Phytochemical screening was done following standard methods described in literature sources (Apoorva *et al.,* 2021).

Experimental protocol

The research proposal was initially submitted to the Department of Pharmacy, Aljazeera University, which referred it to the Ethical Review Committee of the Faculty of Medical Sciences, Aljazeera University, and ethical approval (Reference Number: 0112/on September 2024) was obtained for this study. We bought 28 male guinea pigs weighing between 350 and 650 grams from the local market, Ibb City, Yemen. The animals were kept in a controlled setting with a 12-hour light-dark cycle and room temperature so they could freely eat and drink ad libitum. The guinea pigs were allocated into seven groups at random, each with five animals, and each therapy was administered every day for 10 days. Paracetamol (PCM) and plant extracts at 100 and 200 mg/kg of body weight were administered orally. Guinea pigs in group I were considered the control group and received distilled water only. Group II received PCM (500 mg/kg) alone, Group III received PCM (500 mg/kg) and proximol (0.8 mg/kg), Group IV received 100 mg/kg *V. origena* ethanolic leaves extract alone, and Group V received 200 mg/kg *V. origena* ethanolic leaves extract alone. In Group VI, we were administered 500 mg/kg PCM and 100 mg/kg *V. origena* ethanolic leaves extract. Meanwhile, Group VII was administered 500 mg/kg PCM and 200 mg/kg *V. origena* ethanolic leaves extract. All animals were anesthetized with chloroform on day 11, and blood was collected.

Sample preparation

There is no heparin in the blood sample that is placed in tubes, so it can clot for 30 minutes at room temperature. Following that, the blood was centrifuged for 15 minutes at 3000 rpm to extract the serum. After being placed in sterile tubes, the serum samples were placed in a deep freezer to undergo biochemical examination. After the liver was removed, cleaned for histological analysis, and kept in 10% formalin.

Determination of biochemical parameters

The liver enzymes (AST, ALT, and ALP) and total bilirubin were measured by Roche Kits (Germany) (Tietz *et al.,* 1995).

Histological analysis

The liver histology was examined using standard histology procedures. After the animal was killed, the liver part was removed, cleaned in normal saline, and then cut into tiny pieces. The tissue was fixed in 10% formalin, dehydrated stepwise with ethanol solution (50% to 100% concentrations), and embedded in paraffin. Tissue sections of 4-µm thickness were created, fixed overnight, afterwards stained with hematoxylin and eosin (H&E), and examined with a light microscope (Olympus BX41, Japan).

Statistical analysis

The results of mean values ± standard deviation (S.D.) for each measure were used to express the data. One-way analysis of variance (one-way ANOVA) was used to analyze the data using SPSS (version 20). The results were considered significant at α 5%.

RESULTS

Phytochemical screening of *Vachellia origena* leaves

Qualitative tests for various phytochemical constituents were carried out on the leaf extracts, and the results were presented in Table1. The preliminary phytochemical screening of *V. origena* ethanolic leaves extracts showed the presence of flavonoids, tannins, alkaloids, steroids, and triterpenoids, while glycosides and saponins were absent.

Table 1. Phytochemical screening of alcoholic extracts of *V. origena* leaves.

Phytocjemical	Result
Flavonoids	+
Tannins	+
Alkaloids	+
Steroids	+
Glycosides	–
Triterpenoids	+
Saponins	–

(+) Present; (-) Absent

Effect of treatment of ethanolic extract of *V. origena* leaves on serum biochemical parameters

Our results presented in Table (2) showed that PCM administration significantly ($P < 0.05$) elevated the level of serum AST, ALT, ALP, and total bilirubin when compared with the control group. Treatments with silymarin (standard drug) and *V. origena* ethanolic leaves extract 100 and 200 mg/kg significantly decreased ($P<0.05$) the AST, ALT, ALP, and total bilirubin levels when compared with the control group (Figures 1 to 4).

Table 2. Effect of PCM and *V. origena* extract on biochemical parameters in guinea pigs with PCM-induced hepatotoxicity.

Groups	AST (U/L)	ALT (U/L)	ALP (U/L)	Total bilirubin (mg/dl)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Control	51.67±0.24	56.00±1.63	119.00±0.81	0.47±0.04
PCM only	77.33±1.69#	95.00±1.15#	364.67±7.13#	0.53±0.03#
PCM +Silymarin(100mg/kg)	60.67±0.94#*	85.00±0.81#*	216.00±1.41#*	0.52±0.01#
V. origena (100mg/kg)	48.00±0.16*	56.75±0.95*	116.00±0.16*	0.49±0.01*
V. origena (200mg/kg)	50.75±0.95*	55.75±0.95*	118.00±0.81*	0.48±0.01
PCM + *V. origena* (100mg/kg)	66.67±1.98#*	69.00±1.49#*	216.00±0.81#*	0.51±0.02
PCM + *V. origena* (200mg/kg)	62.67±1.09#*	62.00±1.32*	207.33±1.24#*	0.49±0.01

All value represents mean±SD of five animals. # $P < 0.05$ compared with the normal control value.
* $P < 0.05$ compared with PCN only values.

Effect of *V. origena* extracts on liver histopathology in PCM-induced hepatotoxicity in guinea pigs

The guinea pigs in the control group had no microscopic changes seen in their livers when examined under a microscope. Hepatocytes are polygonal cells having rounded nuclei, and some hepatic sinusoids have delicate Kupffer cell patterns. In addition, it appears to have normal lobular architecture with hepatocytes arranged in cords encircling the central vein (Figure 5, a, b, c). After ten days, the microscopic examination of the liver tissue intoxicated by PCM revealed a significant area of hemorrhagic necrosis surrounding the centrilobular region, along with inflammatory cell infiltration, portal vessel dilatation, and hyperplasia of the lining epithelium of the bile duct (Figure 5, d and e).

The microscopic analysis of the liver in groups treated with silymarin (100 mg/kg) demonstrated mild congestion of the central vein and necrosis of some liver cells (Figure 5, f). The examined livers of guinea pigs treated with 100 and 200 mg/kg *V. origena* treatment on PCM-intoxicated liver tissue showed mild sinusoidal congestion of the central vein and a moderate degree of necrosis in some liver cells (Figure 5, g and h).

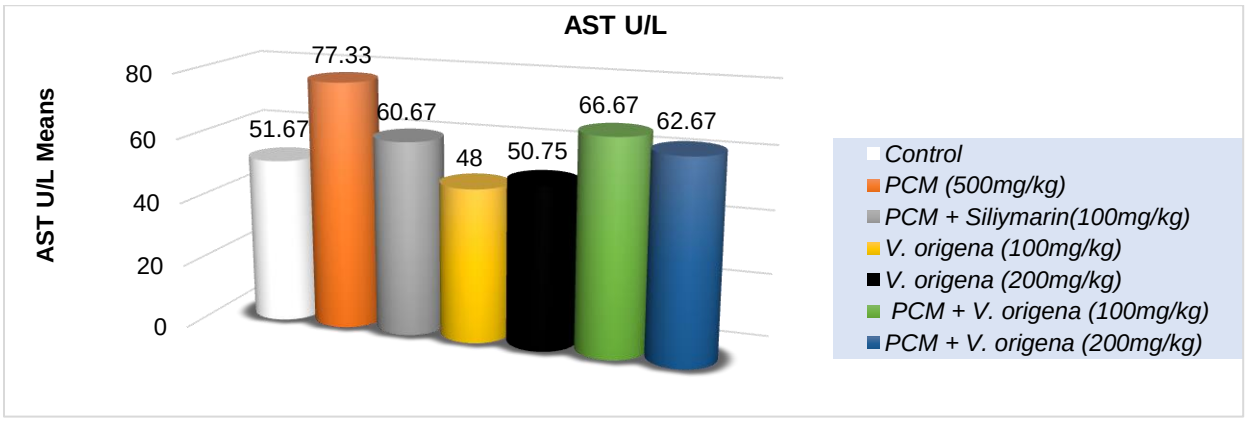

Fig. 1. Effect of PCM and *V. origena* extract on AST levels (U/L) in guinea pigs with PCM-induced hepatotoxicity.

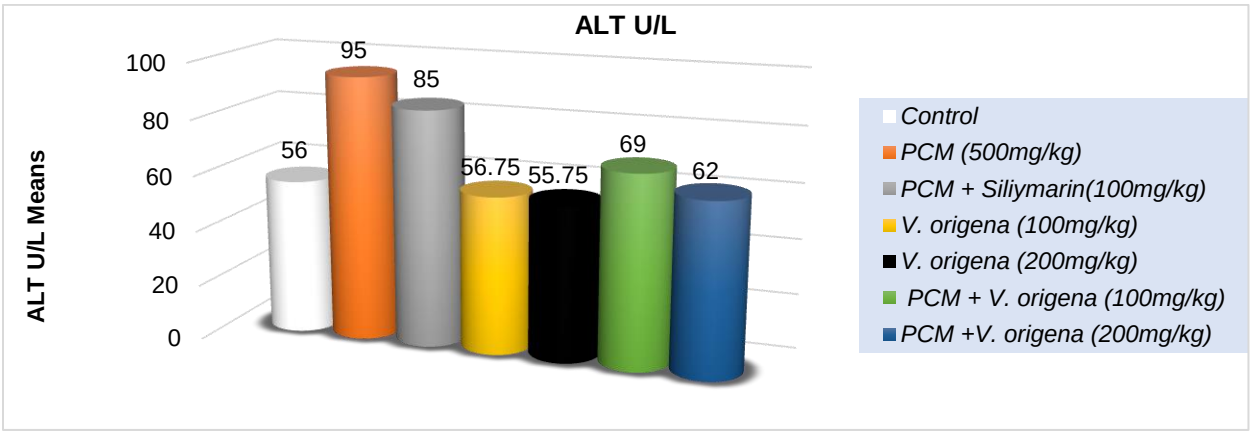

Fig. 2. Effect of PCM and *V. origena* extract on ALT levels (U/L) in guinea pigs with PCM-induced hepatotoxicity.

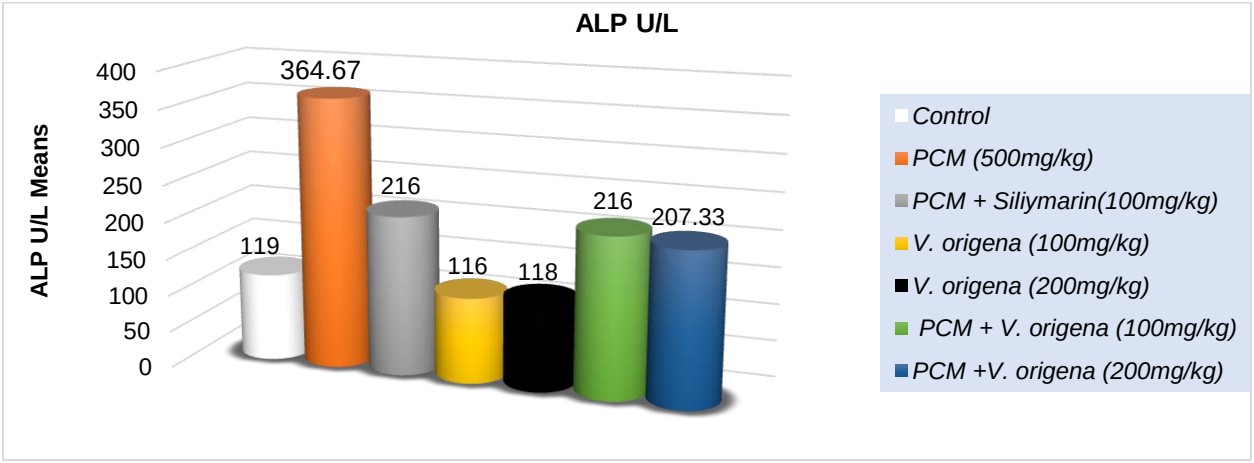

Fig. 3. Effect of PCM and *V. origena* extract on ALP levels (U/L) in guinea pigs with PCM-induced hepatotoxicity.

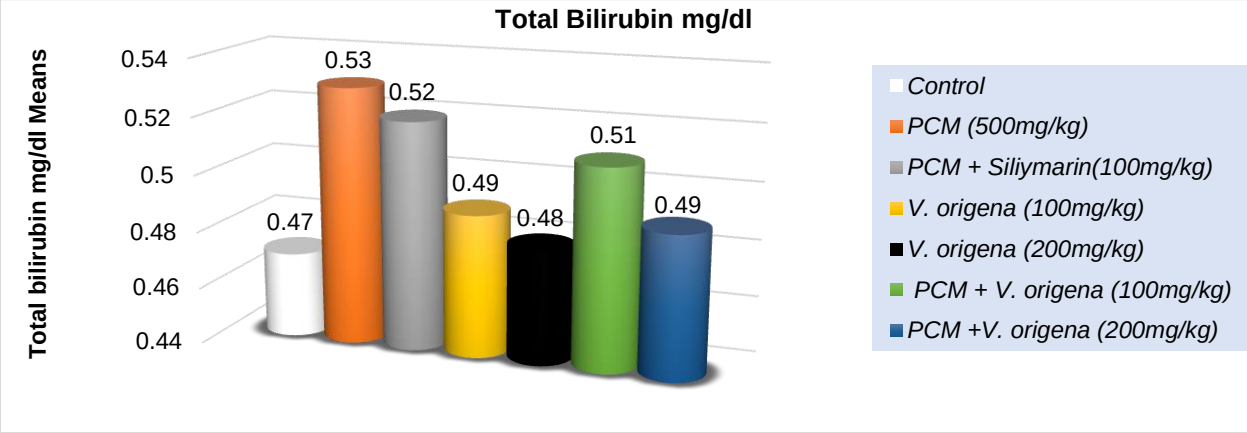

Fig. 4. Effect of PCM and *V. origena* extract on total bilirubin levels (mg/dl) in guinea pigs with PCM-induced hepatotoxicity.

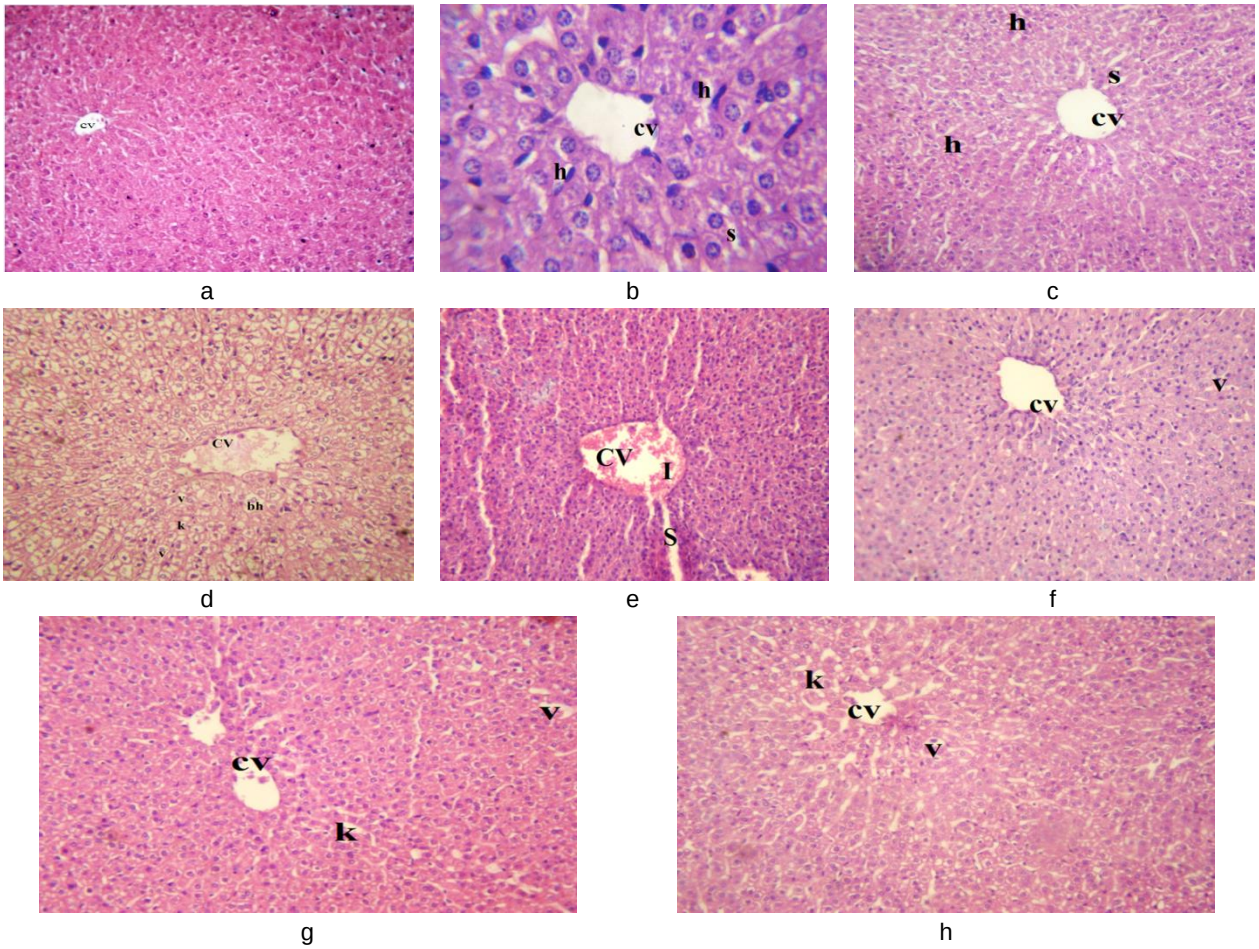

Fig.5. Histopathological study of liver tissue of guinea pigs.

(a) The liver architecture of the control group, which received distilled water for ten days, was normal (H&E stain ×100), **(b and c)** group administered 100 and 200 mg/kg of *V. origena*, the liver architecture was normal; the hepatocytes were polygonal cells with rounded nuclei, and there were a few hepatic sinusoids with finely arranged Kupffer cells (H&E stain ×100 and 200), **(d and e)** Liver tissue intoxicated with PCM had vacuolization (v), dilated and congested blood vessels (cv) with haemorrhage, hepatocytes that were ballooning (bh), inflammatory cell infiltration (i), nuclear pyknosis (k), and other signs of liver injury (H&E×100),**(f)** effect of 100 mg/kg silymarin treatment on PCM intoxicated liver tissue mild congestion of central vein(cv) and little vacuolization(v) compared to PCM only group (H&E×100), **(g and h)** impact of 100 and 200 mg/kg application of *V. origena* to liver tissue intoxicated by PCM revealed minimal histological alterations, including moderate central vein (cv) congestion, vacuolization (v), and nuclear pyknosis (k) (H&E×100).

DISCUSSION

Natural products have a broad spectrum of therapeutic effects and have been widely used in many disease conditions for many years (Iqbal and Ashraf, 2020; 2023; Almansory *et al.,* 2021; Iqbal, 2023a,b). However, ethnopharmacological information and scientific data are required to ensure safety and efficacy (Leung, 2006). Without undergoing systematic testing, several herbal medicines are marketed for human consumption, resulting in adverse effects (Ronald *et al.,* 2016).

The harmful effects of xenobiotics frequently target the liver. The liver is recognized to play a major role in detoxifying the harmful substances that enter the body (Naveen *et al.,* 2003). Therefore, the liver can serve as a gauge for xenobiotic toxicity. Thus, the levels of specific biochemical markers and the activity of particular enzymes characterize liver function. One enzyme that aids in the metabolism of protein is alanine aminotransferase (ALT). ALT levels rise and are released into the bloodstream when the liver is injured. Since this enzyme is mostly found in the liver and its levels are elevated during hepatocellular necrosis, its estimation is a more precise test for identifying liver defects. Another liver enzyme that helps make proteins is aspartate aminotransferase (AST). It is responsible for the reductive transfer of an amino group from aspartate to α-ketoglutarate, which results in the production of glutamate and oxaloacetate. AST is the mitochondrial enzyme principally found in the liver, skeletal muscles, and kidneys. Damage to any of these tissues can cause an elevated blood level. It also aids in distinguishing hepatocellular necrosis. The serum AST to ALT ratio can be used to discriminate liver damage from damage to other organs (Porth, 2015; Chen *et al.,* 2022).

PCM-induced liver injury is a traditional paradigm for evaluating hepatoprotective efficacy (Kannan *et al.,* 2013). AST and ALT are mostly linked to liver parenchymal cells, although they have been detected in serum and other bodily tissues. In cases of acute liver injury, increased AST and ALT levels will be seen. Additionally, intrahepatic cholestasis and liver infiltrative disorders will cause the level of ALP to increase (Gaze, 2007; Lowe *et al.,* 2023). Large amounts of enzymes leaking into the circulation were linked to liver centrilobular necrosis. In a similar vein, our investigation confirmed the liver structural damage by seeing elevations in blood enzyme levels of ALT, AST, and ALP following PCM exposure. The hepatoprotective activity of *V. origena* is demonstrated by the restoration of these enzyme levels to the normal range. The maintenance of normal liver physiological activities that have been disrupted by hepatotoxins is a solid criterion for evaluating the quality of any hepatoprotective medication (Yadav and Dixit, 2003). Serum bilirubin levels and hepatic cell function were correlated. Serum bilirubin levels that are elevated during hepatotoxin treatment indicate a rate of erythrocyte breakdown brought on by liver damage (Kannan *et al.,* 2013). The bilirubin level in our research has returned to a normal level, suggesting that it possesses hepatoprotective properties. Excessive amounts of paracetamol and its metabolite NAPQI may oxidize and alkylate intracellular GSH and protein thiol groups, causing GSH depletion and increased lipid peroxidation, which in turn causes liver damage (Malhi *et al.,* 2006). In general, our body uses endogenous enzymes like SOD and catalase as part of an efficient defense system to neutralize or stop the harm caused by free radicals. The equilibrium between ROS production and antioxidant defense systems may be upset in acetaminophen-induced hepatotoxicity (Amresh *et al.,* 2007), causing oxidative stress, which in turn causes liver necrosis. In terms of nonenzymatic antioxidants, GSH plays a crucial role in identifying tissue that is vulnerable to oxidative stress by lowering hydrogen peroxide and xenobiotic toxicity (Kannan *et al.,* 2013). It has been demonstrated that decreased GSH is linked to increased

toxicity to substances, such as paracetamol (Hewawasam *et al.,* 2003; Sestili and Fimognari, 2020; Chidiac *et al.,* 2023).

The administration of *V. origena* ethanol extract with PCM to guinea pigs resulted in normalization and restoration of these liver enzymes to normal levels. The results of the present study were agreement with the results of previous research of other species of Acacia (Kannan *et al.,* 2013) showed that the treatment with methanolic extract of aerial parts of *A. nilotica* (250 mg/kg bw) orally showed that the administration of paracetamol increased the levels of serum activities of ALT, AST, ALP, and total bilirubin. The reduction of acetaminophen-induced lesions and relief of liver damage were confirmed by histopathological investigation. According to the study, the hepatoprotective activity of *A. nilotica* extract may depend on how well it lowers oxidative stress in a rat model of acetaminophen-induced liver injury. Sheshidhar et al. (2013), reported that there was a significant rise in AST, ALT and ALP values in the group that received paracetamol, indicating hepatic injury caused by paracetamol, whereas there was a reduction in these values in the group treated with the Silymarin and *Acacia catechu* (250 mg/kg p.o.) extract. *Acacia catechu* extract therapy dramatically reduced the levels of biochemical enzymes and liver histological alterations brought on by paracetamol. Thus, the ethanol extract of *Acacia catechu* was found to exhibit marked hepatoprotective activity ($P < 0.05$). The data of this study indicate that silymarin administration significantly alleviates levels of these enzymes and injury in the liver. It has been found that silymarin possesses potent scavenging capabilities for free radicals (Kren, 2005), as well as stabilizing cell membranes and regulating the intracellular contents of the reduced GSH. Furthermore, silymarin promotes the production of proteins and RNA, which speeds up liver damage recovery, repair, and renovation (Patel *et al.,* 2010; Vargas-Mendoza *et al.,* 2021; Jaffar *et al.,* 2024).

The hepatoprotective efficacy of the *V. origena* extract was further achieved through histological investigation. The results of biochemical investigations were consistent with the histopathological findings of liver tissues. According to light microscopic studies, the livers of the PCM-treated animals that were given silymarin and *V. origena* extract showed few alterations in comparison to the livers of the PCM-administered group. As a result, *V. origena* may help to reduce the liver damage brought on by PCM intoxication. Furthermore, the presence of several biologically active components may be the cause of the broad variety of biological activity found in many extracts from medicinal plants. The therapeutic properties of *V. origena* are often attributed to their different constituent phytochemicals, which are phenols, flavonoids, tannins, saponins, alkaloids, steroids, and carbonyls (Shaikh *et al.,* 2022), indicating that *V. origena* extract is able to inhibit PCM-induced hepatotoxicity.

The results of the present study provided the first experimental evidence that *V. origena* ethanol extract maintain the liver enzymes such as AST, ALT, ALP, as well as total bilirubin concentrations from gradually increasing after induction by PCM and they were kept mean normal values in comparison with positive control which induced by PCM and caused liver cell damage.

CONCLUSION

According to the results of this study, it is concluded that PCM-induced liver injury leads to hepatotoxicity. The treatment of guinea pigs with *V. origena* ethanolic leaves plant and silymarin showed a significant protective effect against PCM-induced liver injury, which was reflected in the biochemical and histological parameters, providing evidence of the beneficial effect of *V. origena* extract in mitigating the chronic PCM intoxication in male guinea pigs. The ethanolic extracts of the leaves of the plant *V. origena* contain nephroprotective ingredients (flavonoids, tannins, alkaloids, steroids, and triterpenoids) that protect from PCM-induced hepatic damage.

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CONFLICT OF INTEREST

Authors hereby declare that they have no conflict of interest.

REFERENCES

Al Khulaidi, A.A., 2013. Flora of Yemen. The sustainable natural resource management project (SNRMP II), EPA and UNDP, Republic of Yemen.

Al-Khulaidi, A., Rabei, S.H., Al-Gifri, A., 2024. The genus *Acacia S.L.* (Fabaceae) in Yemen. Sci. J. Damietta Fac. Sci., 14(2): 90-97.

Almansory, A.H., Al-Shaibani, E.A.S., Shediwah, F.M.H., Ibrahim, H. M., 2021. The Effect of Cisplatin and 5-Fluorouracil versus *Aloe perryi* extracts on Rat Liver and Kidney Tissues. PSM Vet. Res., 6(3): 59-73.

Amresh, G., Rao, C.V., Singh, P.N., 2007. Antioxidant activity of *Cissampelos pareira* on benzo (a) pyrene-induced mucosal injury in mice. Nutr. Res., 27(10): 625–632.

Apoorva, M., Suryawanshi, P., Vidyasagar, G.M., 2021. Phytochemical screening for secondary metabolites and nutraceutical value of *Sesbania grandiflora* (L) Pers leaf extract. Indo Global J. Pharm. Sci., 11(1): 28-32.

Chen, W., Wang, W., Zhou, L., et al. 2022. Elevated AST/ALT ratio is associated with all-cause mortality and cancer incident. J. Clin. Lab. Anal., 36: e24356.

Chidiac, A.S., Buckley, N.A., Noghrehchi, F., Cairns, R., 2023. Paracetamol (acetaminophen) overdose and hepatotoxicity: mechanism, treatment, prevention measures, and estimates of burden of disease. Expert Opin. Drug. Metab. Toxicol., 19(5): 297–317.

Farzana, M.U.Z.N., Al Tharique, I., Sultana, A., 2014. A review of ethnomedicine, phytochemical and pharmacological activities of *Acacia nilotica* (Linn) Willd. J. Pharmacogn. Phytochem., 3(1): 84-90.

Gaze, D.C., 2007. The role of existing and novel cardiac biomarkers for cardioprotection. Curr. Opin. Invest. Drugs., 8(9): 711–717.

Hewawasam, R.P., Jayatilaka, K.A.P.W., Pathirana, C., Mudduwa, L**.**K.B., 2003. Protective effect of *Asteracantha longifolia* extract in mouse liver injury by carbon tetrachloride and paracetamol. J. Pharm. Pharmacol., 55(10): 1413–1418.

Ibrahim, H.M., Humaid, A.A., Thabit, A.A.M., Rizq, E.A., Al-awadhi, B., 2023. Phytochemical screening, antioxidant and antimicrobial activities of *Acacia origena* Hunde. J. Chem., Biol. Phys. Sci., 13(3): 308-321.

Iqbal, M.N., Ashraf, A., 2020. Milk thistle (*Silybum marianum*) as a Promising Chemoprotective Agent for Liver Therapy. PSM Biol. Res., 5(1): 55-57.

Iqbal, M.N., Ashraf, A., 2023. Bioactivity of *Moringa oleifera*: Therapeutic Agent in Human Bacterial Infections. PSM Microbiol., 8(3): 91-93.

Iqbal, M.N., 2023a. Palm Fruit (*Phoenix dactylifera* L.): Bioactive potential and Source of Nutraceuticals for Health Promotion. Int. J. Altern. Fuels. Energy., 7(1): 25-7.

Iqbal, M.N., 2023b. *Moringa oleifera*: A Potential Source for the Discovery and Development of New Drugs. PSM Microbiol., 8(3): 94-6.

Jaffar, H.M., Al-Asmari, F., Khan, F.A., Rahim, M.A., Zongo, E., 2024. Silymarin: unveiling its pharmacological spectrum and therapeutic potential in liver diseases-a comprehensive narrative review. Food Sci. Nutr., 12(5): 3097-3111.

Kannan, N., Sakthivel, K.M., Guruvayoorappan, C., 2013. Protective Effect of *Acacia nilotica* (L.) against Acetaminophen-Induced Hepatocellular Damage in Wistar Rats. Adv. Pharmacol. Sci., 2013: 987692.

Khanam, F., Iqbal, M.N., Ashraf, A., Yunus, F.N., Alam, S., Muhammad, A., Xiao, S., Toor, S., Mumtaz, H., 2016. Evaluation of Changes in Liver Enzymes in Broiler Chicks (Gallous domesticus). PSM Vet. Res., 01(1): 26-31.

Kren, V., 2005. Silybin and silymarin: New effects and applications. Biomed Papers, 149: 29-41.

Lee, W.M., 2013. Drug-induced acute liver failure. Clin. Liver Dis., 17(4): 575–86.

Legesse, N., 2010. A selection of ethiopia's indigenous trees: Biology, uses and propagation techniques. Addis Ababa University Press, Addis Ababa, Ethiopia.

Leung, P.C., 2006. A practical way of research in Chinese medicine. Ann. Acad. Med. Singapore., 35: 770–772.

Lowe, D., Sanvictores, T., Zubair, M., et al. 2023.Alkaline Phosphatase. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

Mahmoud, M.F., Alrumman, S.A., Hesham, A., 2016. Biological activities of some *Acacia* spp. (Fabaceae) against new clinical isolates identified by ribosomal RNA gene-based phylogenetic analysis. Pak. J. Pharm. Sci*.,* 29(1): 221-229.

Malhi, H., Gores, G.J., Lemasters, J.J., 2006. Apoptosis and necrosis in the liver: a tale of two deaths. Hepatol., 43(2): S31–S44.

Nasser, R.A., Aref, I.M., 2014. Fuelwood characteristics of six *Acacia* species growing wild in the southwest of Saudi Arabia as affected by geographical location. Bio Resour., 9: 1212–1224.

Naveen, A., Premendran, J., Venkatanarayana1, N., 2003. Evaluation of hepatoprotective activity of aqueous extract of *Ricinus communis* in Wistar rats. Int. J. Basic. Clin. Pharmacol., 18203/2319.

Nicoletti, A., Ponziani, F.R., Biolato, M., Valenza, V., Marrone, G., Sganga, G., Gasbarrini, A., Miele, L., Grieco, A., 2019. Intestinal permeability in the pathogenesis of liver damage: From non-alcoholic fatty liver disease to liver transplantation. World J. Gastroenterol., 25(33): 4814-4834.

Patel, N., Corcoran, G.B., Joseph, C., Ray, S.D., 2010. Silymarin modulates doxorubicin-induced oxidative stress, Bcl-Xl and p53 expression while preventing apoptotic and necrotic cell death in the liver. Toxicol. Applied Pharmacol., 245: 143-152.

Porth, C.M., 2015. Essentials of pathophysiology, 4th Ed. *Lippincott Williams &Wilkins*, New York, pp: 727-730.

Ronald, K., Sam, O., Charles, K., Sheila, M.B., 2016. Herbal medicine use and linked suspected adverse drug reactions in a prospective cohort of Ugandan inpatients. BMC Compl. Altern. Med., 16: 145.

Sestili, P., Fimognari, C., 2020. Paracetamol-Induced Glutathione Consumption: Is There a Link With Severe COVID-19 Illness? Front. Pharmacol., 11: 579944.

Shaikh, I.A., Muddapur, U.M., Bagewadi, Z.K., Chiniwal, S., Ghoneim, M.M., Mahnashi, M.H., Alsaikhan, F., Yaraguppi, D., Niyonzima, F.N., More, S.S., Mannasaheb, B.A., Al Ali, A., Asiri, A., Khan, A.A., Iqubal, S.M.S., 2022. Characterization of bioactive compounds from *Acacia Concinna* and *Citrus Limon*, silver nanoparticles production by *A. concinna* extract, and their biological properties. Mol., 27(9): 2715.

Sheen, C.L., Dillon, J.F., Bateman, D.N., Simpson, K.J., MacDon, T.M., 2002. Paracetamol-related deaths in Scotland, 1994–2000. Br. J. Clin. Pharmacol., 54(4): 430–432.

Sheshidhar, G.B., Yasmeen, A.M., Arati, C., Sangappa, V.K., Pundarikaksha, H.V., Manjula, R., 2013. Evaluation of hepatoprotective activity of ethanolic extract of *Acacia catechu* wild in paracetemol induced hepatotoxicity in albino rats. Int. J. Pharm, Biol. Sci., 264-270.

Tietz, N.W., 1995. Clinical guide to laboratory tests. 3rd ed. Philadelphia, PA: WB Saunders Co. Pp. 622-626.

Vargas-Mendoza, N., Angeles-Valencia, M., Morales-González, Á., Morales-Martínez, M., Madrigal-Bujaidar, E., Álvarez-González, I., Fregoso-Aguilar, T., Delgado-Olivares, L., Madrigal-Santillán, E.O., Morales-González, J.A., 2021. Effect of Silymarin Supplementation in Lung and Liver Histological Modifications during Exercise Training in a Rodent Model. J. Funct. Morphol. Kinesiol., 6(3): 72.

Woolbright, B.L., Jaeschke, H., 2017. The impact of sterile inflammation in acute liver injury. J. Clin. Transl. Res., 3(Suppl 1):170–88.

Yadav, N.P., Dixit, V.K., 2003. Hepatoprotective activity of leaves of *Kalanchoe pinnata* Pers. J. Ethnopharmacol., 86(2-3): 197–202.

Yang, T., Wang, H., Wang, X., Li, J., Jiang, L., 2022. The dual role of innate immune response in acetaminophen-induced liver injury. Biol. (Basel), 11: 1057.

Yoon, E., Babar, A., Choudhary, M., Kutner, M., Pyrsopoulos, N., 2016. Acetaminophen-induced hepatotoxicity: A comprehensive update. J. Clin. Transl. Hepatol., 4: 131–142.