RESEARCH ARTICLE

Evaluation of Hepatoprotective Potential of Lamiaceae Family Plants in Rat Models of Alcohol, Paracetamol and Ranitidine-Induced Hepatotoxicity

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ABSTRACT
The whole plant of *Leucas zeylanica* (Lamiaceae) was tested for hepatoprotection in Wistar rats after paracetamol (PCM), ethyl alcohol (ALC), and ranitidine (RTD) produced hepato the albino mouse acute toxicity maximum dosage was 2000 mg/kg. Six animal groups were utilized in all models. Modelling followed Silymarin. MELZWP contains saponins, carbohydrates, flavonoids, tannins, and phenolic from *Leucas zeylanica* whole plant. LD50 experiments showed these extracts did not kill or alter mice at 2000 mg/Kg body weight. Silymarin and MELZWP dosages increased thiopental sleeping time, wet liver weight, and volume than PCM, ALC, and RTD-induced hepatotoxic mice. Albumin (ALB) and protein (PRO) increased whereas ALT, ALP, AST, CHO, BILT, and TG dropped. Steatosis, necrosis, and other histological abnormalities were disallowed. Saponins and flavonoids protect the liver, study finds.
Keywords: L. zeylanica, hepatoprotective, ranitidine, paracetamol, ethyl alcohol.
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INTRODUCTION

Homeostasis is maintained by the second-largest gland, the liver. Natural liver disease resembles drug- and chemical-induced liver damage[1]. Most liver damage is drug-related. More than 900 medicines, poisons, and plants can cause 20-40% fulminant hepatic failure[2]. Hepatic dysfunction causes most drug quits. Drug withdrawal hepatotoxicity can be decreased by early liver damage detection. Hepatotoxicity from drugs can cause asymptomatic liver enzyme elevation or fulminant liver failure.[3-4] Alcohol, ranitidine, paracetamol, tetracycline, hormonal oral contraceptives, anti-tubercular medicines, food preservatives, and agrochemicals damage the liver[5-6]. Multiple-medication liver disease affects medication metabolism differently. India's tenth greatest killer is liver disease, per WHO. Every fifth Indian may have liver disease. Cirrhosis is the 14th major cause of death worldwide and expected to reach 12th by 2020. The second leading cause of cancer death is HCC[7]. Herbal medicine has advanced in recent decades. It's popular in developing and developed countries for its natural ingredients and few side effects. Many incurable internal disorders are treatable with herbs. It stresses health [8]. Coumarins, lignans, alkaloids, essential oils, carotenoids, glycosides, phenols, flavonoids, lipids, organic acids, monoterpenes, and xanthenes protect the liver[9]. Raw plant medicines treat livers. Plant extracts from 25 species treat liver diseases[10]. Newly synthesised silybon protects, regenerates, and enhances liver function[11]. The whole plant was tested for *Leucas zeylanica*'s hepatoprotective effects in mice. A comprehensive literature research and ethnobotanical knowledge show that blended Leucas leaves heal eye, skin, nasal, wound, and painful problems like scabies and psoriasis. A decoction heals infant malaria and roundworms[12]. The entire plant is stomachic, carminative, and fragrant. Treats dyspepsia, flatulence, and acute/chronic anorexia. *Leucas zeylanica* leaves and flowers heal jaundice[13]. Antibacterial, anti-inflammatory, antidiabetic, antifungal, antioxidant, and larvicidal, *Leucas zeylanica* [14–19]. Hepatoprotection using *Leucas zeylanica* has not been studied despite its long history of treating hepatic diseases. We chose the entire *Leucas zeylanica* plant for the Wistar rat hepatoprotective effectiveness study employing different experimental paradigms.

MATERIAL AND METHODS

Plant Material

In Chamakuri Palem, West Godavari District, Andhra Pradesh, India, Botanical Survey of India taxonomists P.V. Prasanna, Scientist 'G'& HoO verified the entire plant from juvenile to mature. Our lab has voucher specimen BSI/DRC/2020-21/identification/Tech./68.

Washed, shade-dried, powdered.

Preparation of Ethanolic Extract

A dark greenish-brown product was created by macerating powdered plant materials in methanol (w/w) at the ambient temperature for one week, filtering, and concentrating under a decreasing pressure in a rotary evaporator (Evator,

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Table 1. Hepatoprotective characteristics of L. Zeylanica methanolic extracts on rats with paracetamol-induced hepatotoxicity.

Groups	Treatment	TST min	L. Wt. g/100g	L. Vol. ml/100g	ALT U/L	AST U/L	ALP U/L	BILT mg/dl	CHO mg/dl	TG mg/dl	PRO g/dl	ALB g/dl
Normal	Vehicle Dist. Water, p.o	67.83 ± 0.24	4.93 ± 0.48	5.97 ± 0.56	54.72 ± 0.48	119.11 ± 0.34	121.85 ± 0.07	0.36 ± 0.28	142.19 ± 1.07	43.18 ± 0.73	15.64 ± 0.37	5.52 ± 1.27
Toxicant	PCM 2g/Kg, p.o.	119.36 ± 0.42	5.87 ± 0.37	7.58 ± 1.05	129.12 ± 1.16	243.63 ± 1.57	252.18 ± 0.54	1.63 ± 0.36	251.19 ± 1.37	204.37 ± 0.89	8.35 ± 1.07	2.93 ± 1.07
Standard	Silymarin 100mg/kg, p.o.	74.85 ± 1.09***	4.82 ± 0.67***	5.88 ± 0.79***	62.52 ± 0.84***	123.18 ± 1.33***	137.55 ± 1.37***	0.49 ± 0.08***	156.19 ± 0.81***	52.54 ± 0.75***	14.82 ± 1.17***	5.16 ± 0.07***
MELZWP	Low dose 100mg/kg, p.o.	111.53 ± 1.48ns	5.62 ± 0.35ns	7.16 ± 0.48ns	119.35 ± 0.34*	221.53 ± 0.93*	228.77 ± 0.78*	1.52 ± 0.78ns	246.15 ± 0.78 ns	194.59 ± 1.18*	8.92 ± 0.93ns	2.99 ± 1.28ns
MELZWP	Medium dose 200mg/kg, p.o.	90.76 ± 1.32*	5.23 ± 0.75 ns	6.95 ± 1.18*	101.86 ± 1.13**	207.87 ± 0.76**	197.84 ± 0.89***	1.18 ± 0.67*	211.52 ± 0.92*	121.18 ± 1.03**	10.18 ± 1.08*	3.83 ± 0.57*
MELZWP	High dose 400mg/kg, p.o.	80.37 ± 0.71***	5.06 ± 0.83**	6.82 ± 0.57*	98.54 ± 0.58***	186.47 ± 0.71***	182.16 ± 1.21***	0.92 ± 0.49**	182.42 ± 0.06**	112.69 ± 1.01**	11.53 ± 1.14**	4.47 ± 0.76**

MELZWP-Methanolic extract of L. Zeylanica whole plant, n = 6, significant at P < 0.05*, 0.01**, and 0.001***, ns = not significant

Media Instrument Mfg. Following air-drying solvent removal, extract yield was determined.

Experimental Animal

The Hyderabad National Centre for Laboratory Animal Sciences provided 150-200 gm albino rats (Wistar strain) of both sexes and 16-25 g mice for research. All animals were acclimated to 26°C, 45–55% RH, and 12:12 light/dark cycle for 7 days after purchase. Mouse food was faked by Amrut Labs. Water and sanitation were constant. The Ramakrishna colony of Vaageswari College of Pharmacy in Karimnagar, Telangana, is IAEC-approved. Registered 1720/p.o/a/14/CPCSEA/IAEC/001/2019, all animal research met CPCSEA standards.

Chemicals and Drugs

Bengaluru gave 99.65% free paracetamol. In Hyderabad, TKM Pharma sold anaesthetic ether. Nice Laboratories in

Table 2: Hepatoprotective properties of L. Zeylanica methanolic extracts on alcohol-induced hepatotoxicity in rats.

Groups	Treatment	TST min	L. Wt. g/100g	L. Vol. ml/100g	ALT U/L	AST U/L	ALP U/L	BILT mg/dl	CHO mg/dl	TG mg/dl	PRO g/dl	ALB g/dl
Normal	Vehicle Dist. Water, p.o	65.48 ± 0.35	4.76 ± 0.48	5.87 ± 2.27	64.58 ± 2.86	116.37 ± 1.45	123.71 ± 2.37	0.56 ± 1.58	147.58 ± 1.35	47.54 ± 1.37	18.49 ± 1.08	5.26 ± 1.68
Toxicant	PCM 2g/Kg, p.o.	122.16 ± 0.42	4.48 ± 0.37	7.62 ± 1.05	124.32 ± 1.27	241.76 ± 1.38	238.49 ± 1.86	1.61 ± 1.67	257.49 ± 1.87	211.56 ± 1.90	4.57 ± 0.37	2.45 ± 11.86
Standard	Silymarin 100mg/kg, p.o.	77.38 ± 1.48***	4.02 ± 0.67***	5.81 ± 2.85***	63.24 ± 1.37***	121.86 ± 1.58***	131.72 ± 2.49***	0.68 ± 1.03***	152.48 ± 1.26***	65.48 ± 1.93***	17.59 ± 2.57***	5.18 ± 2.20***
MELZWP	Low dose 100mg/kg, p.o.	108.38 ± 1.48ns	5.42 ± 0.59 ns	7.22 ± 0.48 ns	122.45 ± 2.35ns	227.08 ± 1.38*	228.77 ± 1.08 ns	1.49 ± 1.46 ns	229.46 ± 1.48*	158.49 ± 1.67*	9.33 ± 1.63*	2.89 ± 1.31ns
MELZWP	Medium dose 200mg/kg, p.o.	92.38 ± 1.43*	5.23 ± 0.75ns	6.84 ± 1.37*	105.37 ± 2.07**	198.33 ± 1.34*	183.59 ± 2.42*	1.27 ± 1.40**	217.34 ± 1.43*	119.3 ± 2.44	10.76 ± 2.67**	3.41 ± 1.248
MELZWP	High dose 400mg/kg, p.o.	81.54 ± 0.73***	5.09 ± 1.38**	6.38 ± 2.57*	97.68 ± 2.48**	153.56 ± 1.27**	167.52 ± 1.46**	0.87 ± 1.22***	176.59 ± 1.67**	97.56 ± 0.35**	10.98 ± 1.07**	3.49 ± 1.10*

MELZWP-Methanolic extract of L. Zeylanica whole plant, n = 6, significant at P < 0.05*, 0.01**, and 0.001***, ns = not significant

Table 3: Hepatoprotective properties of L. Zeylanica methanolic extracts on ranitidine-induced hepatotoxicity in rats.

Groups	Treatment	TST min	L. Wt. g/100g	L. Vol. ml/100g	ALT U/L	AST U/L	ALP U/L	BILT mg/dl	CHO mg/dl	TG mg/dl	PRO g/dl	ALB g/dl
Normal	Vehicle Dist. Water, p.o	68.39 ± 2.16	4.24 ± 1.68	5.38 ± 2.46	62.21 ± 2.22	118.33 ± 1.34	124.48 ± 2.67	0.75 ± 1.58	145.54 ± 1.37	47.54 ± 1.37	18.49 ± 1.08	5.56 ± 1.43
Toxicant	PCM 2g/Kg, p.o.	127.38 ± 1.47	3.94 ± 2.17	7.37 ± 1.21	122.12 ± 1.27	239.34 ± 1.42	242.41 ± 1.86	1.92 ± 1.38	275.41 ± 1.81	211.56 ± 1.90	5.67 ± 0.46	2.34 ± 11.86
Standard	Silymarin 100mg/kg, p.o.	74.34 ± 1.08***	4.31 ± 2.35***	5.73 ± 2.24***	78.20 ± 1.48	127.81 ± 1.68	121.39 ± 2.08	0.62 ± 1.67	164.43 ± 1.78	65.48 ± 1.93	18.79 ± 2.57	3.48 ± 2.28
MELZWP	Low dose 100mg/kg, p.o.	101.41 ± 1.12^{ns}	5.21 ± 1.67 ^{ns}	7.67 ± 0.67 ^{ns}	114.43 ± 2.33	232.34 ± 1.38	232.78 ± 1.08	1.53 ± 1.31	228.13 ± 1.48	158.49 ± 1.37	10.46 ± 1.67	2.83 ± 1.57
MELZWP	medium dose 200mg/kg, p.o.	91.32 ± 1.31*	5.46 ± 1.44^{ns}	6.71 ± 1.91*	107.37 ± 2.34	175.33 ± 1.33	163.59 ± 2.42	1.11 ± 1.46	222.31 ± 1.78	117.3 ± 2.17	10.76 ± 2.67	2.67 ± 1.24
MELZWP	High dose 400mg/kg, p.o.	83.59 ± 0.18***	5.29 ± 1.08**	6.49 ± 2.04*	92.45 ± 2.55	148.09 ± 1.21	156.53 ± 1.55	0.97 ± 1.34	173.67 ± 1.53	92.51 ± 0.48	11.38 ± 1.57	2.37 ± 1.75

The MELZWP-Methanolic extract of L. Zeylanica whole plant showed significant results ($P < 0.05$*, 0.01**, and 0.001***), with ns = not significant.

Cochin, India, supplied ranitidine and ethanol. Bangalore Micro labs supplied silymarin. All test chemicals are drug-grade.

Phytochemical Test

Tannins, flavonoids, alkaloids, saponins, and steroids varied little in dry extract. Initial phytochemical extract values were typical [20-21]

LD50 Testing for Acute Toxicity

Critical Toxicity

OECD 423[22] limits acute toxicity assessments to 2000 mg/kg, p.o. Ganapathy et al.[23-24].S, Shivhare et al. advise. Those in control received only vehicle (3 ml/kg, p.o.). The test extract was injected p.o. at 100, 1000, and 2000 mg/kg like the other groups. We monitored the animals for four hours after medication and regularly afterward. Monitored were hyperactivity, salivation, ataxia, tremors, diarrhoea, lethargy, convulsions, sleep, and coma after drug use, deaths were followed for 14 days. The acute (2000 mg/kg, p.o.) and hepatotoxic (100, 200, 400 mg/kg) effects of MELZWP were

Liver Damage by Paracetamol

This procedure divided 150–200 g Wister rats into six groups of six [25-26]. Group A cars only. The B group received 2 gm/p.o. paracetamol. O.G. 100 mg/kg. C likes Silymarin. Animals D, E, and F received low, medium, and high MELZWP. B, C, D, E, and F received 2 gm/Kg p.o paracetamol in 3 days. E, F, and D received 100, 200, and 300mg/kg MELZWP days 4–10. All Day 11 animal groups Sleeping on thiopentone. Ether anesthetised. Retroorbital ether blood poisoning. Weighing, saline-washing, and fixing liver histopathology samples in 10% formaldehyde.

Liver Damage from Alcohol

Six 150–200-g Wistar rats were separated into six groups [27]. Group A was given vehicle, Group B Alcohol (3.76 g/Kg daily in 2 equal dosages), and Group C Silymarin (100 mg/Kg p.o) as a benchmark The Group D, E, and F animals got low, medium, and high MLZWP for 25 days. B–F received 3.76 g/Kg alcohol p.o. for 25 days. Groups D, E, and F received 100, 200, and 400mg/kg MELZWP from 1–10 and 11–25 days.

Ranitidine Liver Harm

Six 150-200 g Wistar rat groups were studied [28]. A received vehicle, B received Ranitidine (50 mg/Kg i.m.), and C received Silymarin (100 mg/Kg p.o.) as a comparison. For 10 days, B–F received 50mg/kg i.m. Ranitidine. Animals D, E, and F got low, medium, and high MELZWP for 21 days. On day 22, animals were anaesthetised with ether after monitoring thiopentone sodium sleeping time in all groups. Ether poisoning damaged retroorbital puncture blood. Hepatopathology samples were weighed, saline-washed, and stored in 10% formaline.

Statistical Study

Triple SEM. Data analysis used one-way ANOVA and Dunnett's multiple comparisons. PRISM and INSTAT calculated-Graph Pad.

RESULTS

The whole plant methanolic extract of *Leucas zeylanica* contains saponins, polysaccharides, flavonoids, tannins, and phenolic in a preliminary phytochemical research. Oral methanolic extracts of the whole *Leucas zeylanica* plant (MELZWP) were given to albino mice at varied dose Methanolic extract did not affect behaviour or mortality at 2000 mg/kg. Post-toxicity testing examined dose-dependent effects at low, medium, and high levels.

Liver Injury from Paracetamol

This study assessed normal control rats' physical and metabolic markers and thiopentone sleeping time (TST).

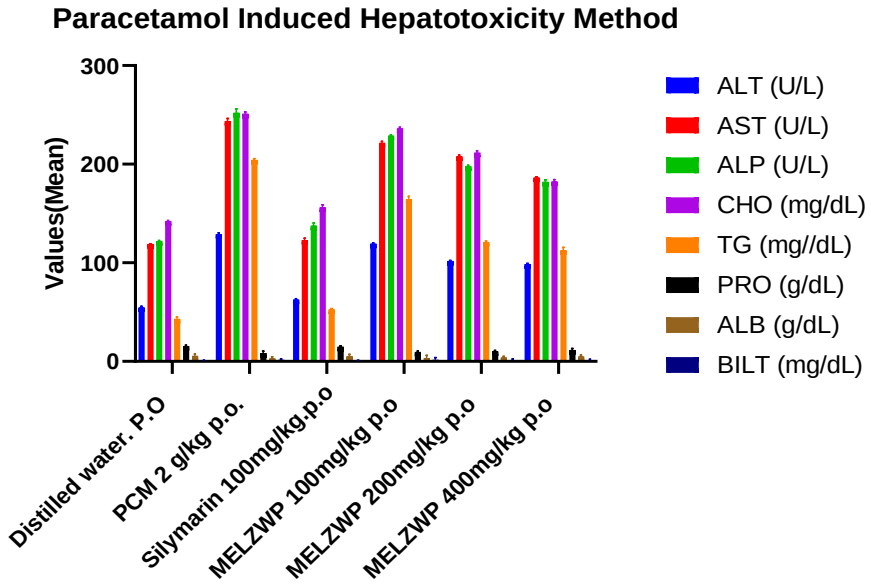

Figure 1: Biochemical parameters of L. Zeylanica methanolic extracts treated with paracetamol-induced hepatotoxicity in rats.

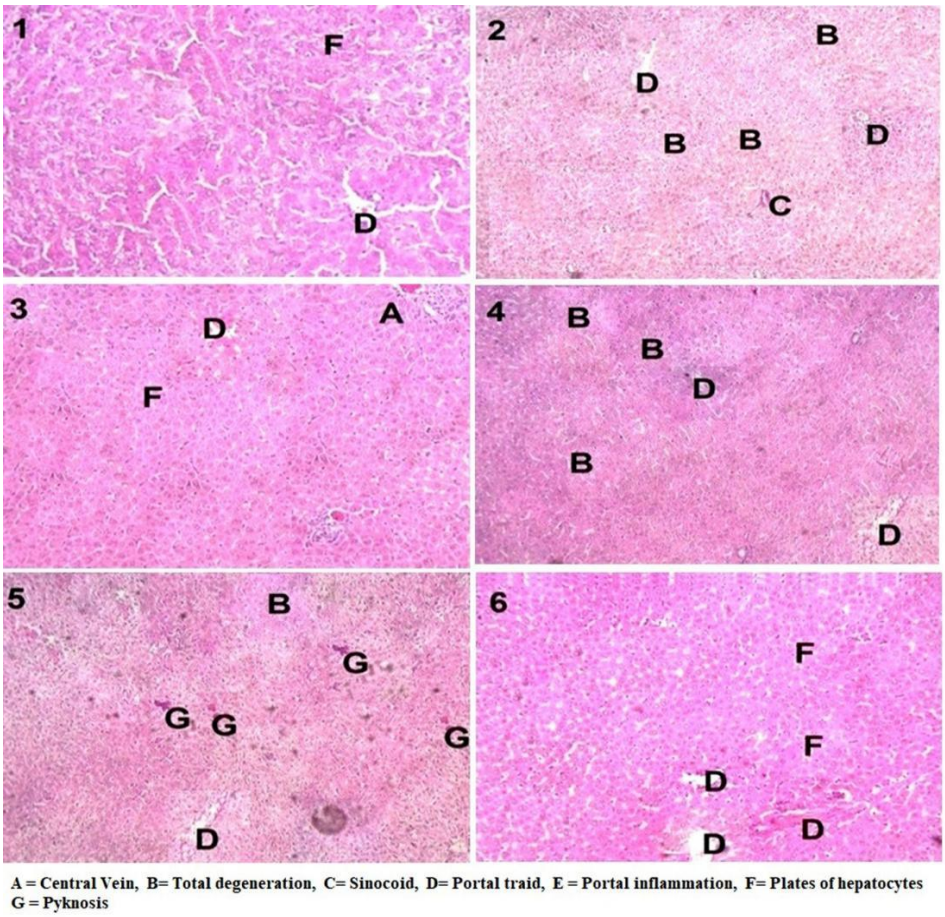

Figure 2: MELZWP dosages affect liver histopathology in paracetamol-induced hepatotoxicity. (1=normal control, 2=toxicant control, 3=silymarin, 4=MELZWP 100mg/kg, 5=200mg/kg, 6=400mg/kg).

Limits: TST: 67.830.04 minutes, wet liver weight: 4.93± 0.48 g/100 g, and volume: 5.97±0.56 ml/100 g. ALT, ALP, AST, BILT, ALB, CHO, protein, and TG are in Table 1. Normal liver structure and cell organization in control rats. Control livers in Figure 2 are healthy.

TST, physical, and metabolic effects of paracetamol on rats

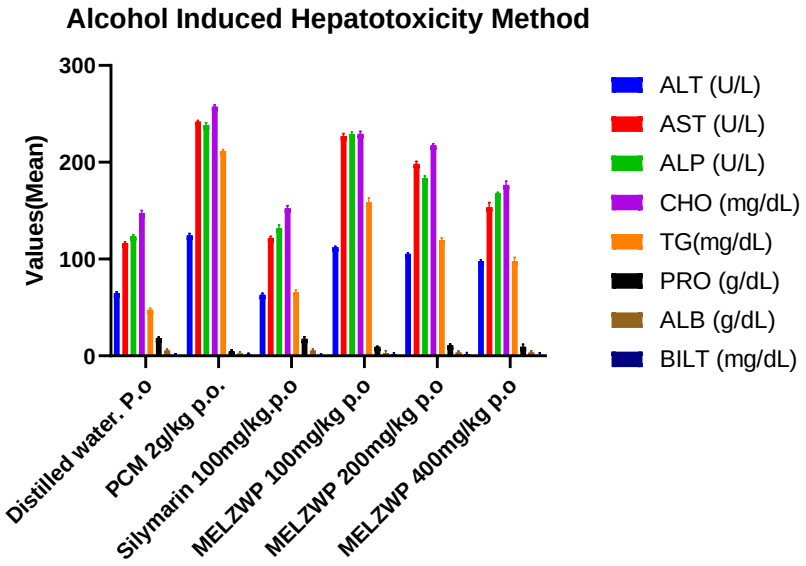

Figure 3: Biochemical characteristics of L. Zeylanica methanolic extracts treated with alcohol that caused hepatotoxicity in rats.

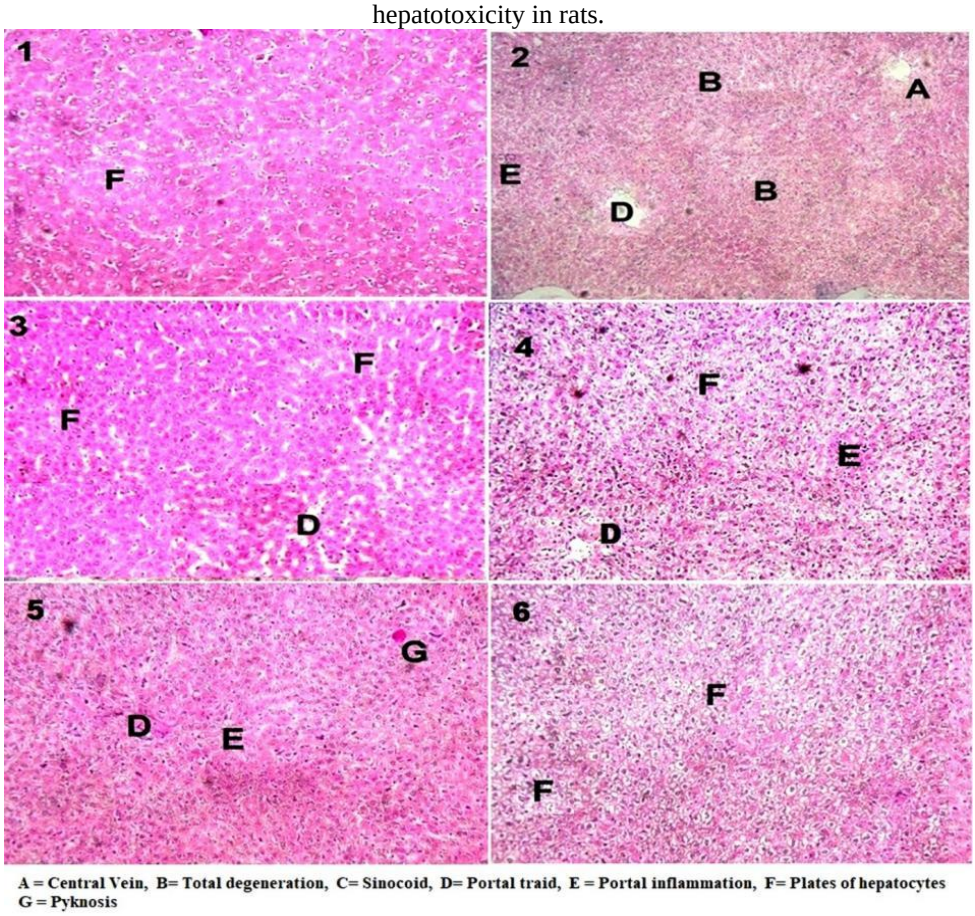

Figure 4. Alcohol-induced hepatotoxicity hepatic histopathology at different MELZWP dosages. (1) Normal control, (2) toxicant control, (3) silymarin, (4) MELZWP 100mg/kg, (5) 200mg/kg. 6. MELZWP 400mg/kg).

Paracetamol-treated rats showed greater TST (119.36 ± 0.42 min) and liver weight (5.87 ± 0.37), compared to controls. Wet liver volume per 100 g is 7.58 ±1.05 ml. Increased ALT, ALP, AST, BILT, CHO, TG. ALB/PRO bad. Table 1 and Figure 1 show all results. Vacuolar degradation, vascular obstruction, and mild inflammatory cell infiltration were seen in paracetamol-treated livers (Figure 2).

Silymarin alters TST, physical, and biochemical indicators in paracetamol-induced hepatotoxic rats.

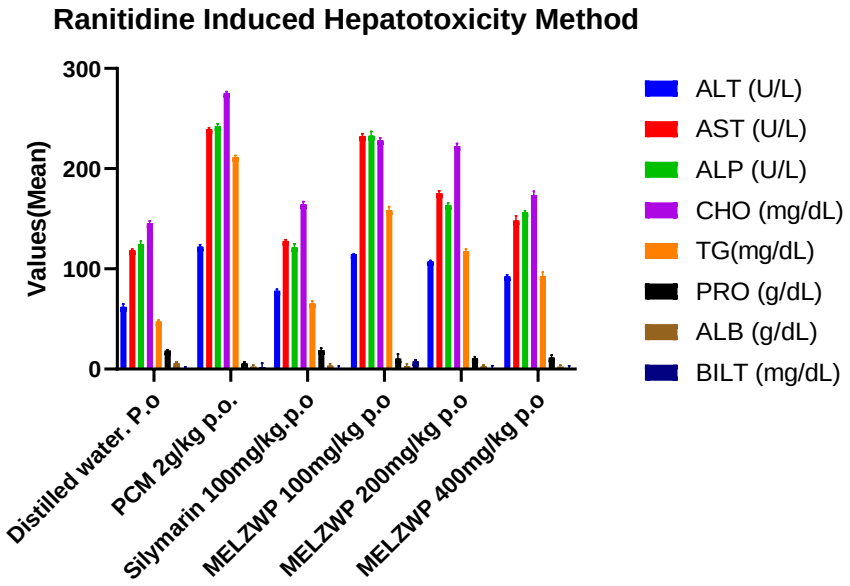

Figure 5: Biochemical parameters of L. Zeylanica methanolic extracts treated with ranitidine-induced hepatotoxicity in rats.

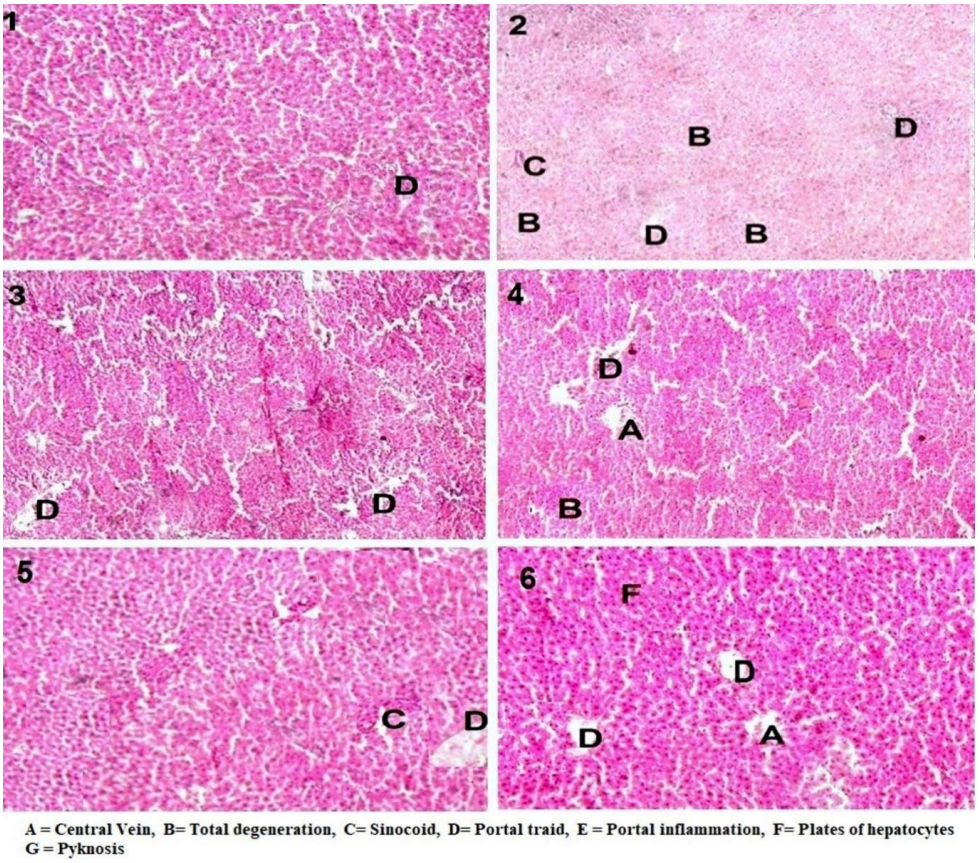

Figure 6. MELZWP dosages affect liver histology in ranitidine-induced hepatotoxicity. (1) Normal control, (2) toxicant control, (3) silymarin, (4) MELZWP 100mg/kg, (5) 200mg/kg. 6. MELZWP 400mg/kg).

Compared to the toxicant control, animals treated with conventional silymarin had a significantly decreased TST (74.85 ± 1.09 min). Physical measurements show a wet liver weight of 4.82 ± 0.67 g/100 g and volume of 5.88 ± 0.79 ml/100 g. AST, ALT, ALP, BILT, CHO, and TG fall while ALB and PRO rise. Table 2 displays results. Normal silymarin liver histology with little microvascular fatty alterations and central venous congestion is shown in Figure 2.

MELZWP affects TST, physical, and biochemical indicators in paracetamol-induced hepatotoxic rats.

MELZWP caused dose-dependent hepatoprotection in rats, with lower TST (111.53 ± 1.48 min at low, 90.78 ± 1.32

min at medium, and 80 Wet liver weight (g/100 g) at low, medium, and high doses compared to toxicant Low dose yielded 7.16 ± 0.48 ml/100 g wet liver volume, medium dose 6.95 ± 1.18, and high dose 6.82 ± 0.83. ALT, AST, ALP (U/L), BILT, CHO, and TG fall while ALB and PRO (g/dL) rise. Table 1 and Figure 1 show details.

Liver Histopathology, MELZWP

Figure 2 shows vacuolar degeneration, blocked arteries, and moderate inflammatory cell infiltration in the 100 mg/kg MELZWP with paracetamol group. Perivascular oedema and occluded arteries decreased in the paracetamol-treated MELZWP medium dose (200 mg/kg) group. Figure 2 shows liver vacuolar degeneration and arterial blockage with 400 mg/kg MELZWP alcohol.

Liver Damage from Alcohol

In normal control rats, thiopentone-induced sleeping time (TST) was 65.48 ± 0.35 minutes, according to physical/biochemical indications. Moist livers have a weight of 4.76±0.48 g/100 g and a volume of 5.87±2. ALT, ALP, AST, BILT, ALB, CHO, PRO, and TG are in Table 2. Lobules were normal in liver slices.

Alcohol's TST, physique, and metabolism effects on Wister rats

significantly higher liver weight (4.48 ± 0.37 g/100 g), volume (7.62±1.05 ml/100 g), biochemical indicators (ALT, ALP, AST, BILT, CHO, and TG), and ALB and PRO values compared to normal Histology showed

Hepatotoxicity from Ranitidine

Normal control rats showed thiopentone-induced sleep duration (TST) of 68.39 ±2.16 min, with physical wet liver weight (4.24 ± 1.68 g/100 g), volume (5.38 ± 2.46 ml/100 g), and biochemical markers (AST, ALT, ALP, albumin, protein, cholesterol, and total) in single hepatocyte cords in liver Sinusoidal cells have Kupffer cells, although binucleate cells seldom have central nuclei.

Ranitidine alters rat TST, physical, and metabolic indicators.

Ranitidine administration led to enhanced TST (127.38 min), physical measurements (wet liver weight 3.93 ± 2.17 g/100 g, wet liver volume 7.37 ±1.21 ml/100), and elevated AST, ALT, ALP, CHO, BILT, and TG. Table 3 and picture 5 show considerable ALB and PRO reductions. Lymphocytic infiltration, hydropic degeneration, and cell necrosis were found in liver histology.

Silymarin affects ranitidine-induced hepatotoxic rats' TST, physical, and biochemical markers.

Silymarin therapy considerably lowered TST (74.34 ±1.08 min) compared to toxicant control groups. We measured a moist liver weight of 4.31 ± 2.35 g/100 g and volume of 5.73 ± 2.24 ml/100 g. AST, ALT, ALP, BILT, CHO, and TG fall while ALB and PRO rise. See Table 3 and Figure 5 for results. Histology showed no microvascular fatty alterations and modest central venous congestion.

MELZWP affects TST, physical, and metabolic indicators in ranitidine-induced hepatotoxic Wister rats.

MELZWP treatment yielded dose-dependent hepatoprotection, with TST reductions of 101.41±1.12 min at low, 91.32±1.31 min at medium, and 83.59 ± 0.18 mi at high dose, compared to toxic Wet liver weight (g/100 g) of 5.21 ± 1.67, 5.46 ± 1.44 Wet liver volume (ml/100 g), hepatic and vacuolar degeneration.

Alcohol-induced hepatotoxic rats' biochemical, TST, and physical characteristics are modulated by silymarin.

In rats treated with silymarin, TST decreased (77.38±1.48 min), moist liver weight (4.02±0.67g/100 g) and volume (5.81±2.85) decreased, while PRO and ALB rose compared to toxic rats. All data are in Table 2 and Figure 3. Figure 4 shows liver histology without microvascular fatty alterations and mild central venous congestion.

MELZWP impacts physical, biochemical, and alcohol TST indicators. Damaged rat liver

Treatment with MELZWP exhibited dose-dependent hepatoprotective effects, lowering TST by 108.38 ±1.48 min at low dosage, 92.38 ±1.43 min at medium dose, and 81.54±0.73 min Increased ALT, AST, ALP (U/L), BI Pro, and ALB were observed with low dosage wet liver weight (g/100 g) of 5.42 ±0.59, medium dose 5.23±0.75, and low dose 5.09 Table 2 shows details.

Melzwp and Liver Histopathology

Low-dose MELZWP (100 mg/kg) + alcohol reduced inflammatory cell infiltration, bleeding, and perivascular oedema (Figure 1). The alcohol-treated MELZWP medium dose (200 mg/kg) group had moderate inflammatory cell infiltration and perivascular oedema. MELZWP 400 mg/kg with alcohol caused mild vacuolar degeneration, perivascular oedema, and hepatic haemorrhage (Figure 4).

biochemical markers (AST, ALT, ALP, U/L), BILT, CHO, and TG decreased while PRO and ALB increased. See Table 3.

MELZWP liver

With 100 mg/kg MELZWP, ranitidine-treated patients have the most liver cell and lymphocytic infiltration. At 200 mg/kg MELZWP, ranitidine induced blood sinusoidal dilatation, moderate Kupffer cell changes, and lymphocytic infiltration. Ranitidine with MELZWP 400 mg/kg reduced Kupffer cell, lymphocytic, and hydropic degeneration (Figure 6).

DISCUSSION

Saponins, carbohydrates, flavonoids, tannins, and phenolics were found in *Leucas zeylanica* methanolic extract in preliminary phytochemical testing. At 2000 mg/Kg MELZWP extract LD50, no deaths occurred. In rats, continuous paracetamol, alcohol, and ranitidine therapy boosted marker enzymes because AST, ALT, and ALP are kept in liver cells and higher serum levels signal liver cell injury. MELZWP decreased ALT, AST, ALP, BILT, CHO, and TG and raised PRO and ALB, suggesting it may prevent alcohol, paracetamol, and ranitidine-induced hepatotoxicity in all three chronic drug-induced hepatotoxicity models, thiopentone sodium prolongs sleep. Barbiturates and hepatic insufficiency prolong thiopentone inactivation [27-28]. Reduced thiopentone-induced sleeping period protected rats' livers from alcohol, paracetamol, and ranitidine toxicity with MELZWP. Every toxicant control model gains liver weight and volume. *Leucas zeylanica* methanolic extract reduced liver weight and volume in silymarin and MELZWP groups, demonstrating hepatoprotective effects. Thiopentone-induced drowsiness

and moist liver weight and volume are inhibited by the extract. Liver sections treated with 400 mg/kg ethanolic extract showed mild perivascular oedema and occluded arteries in alcohol-induced hepatotoxicity. Aqueous extract enhanced alcohol-induced histological changes and perivascular oedema, but high dosage MELZWP decreased them. Paracetamol-induced hepatotoxicity caused vacuolar degeneration and vascular congestion in the animal. Silymarin-treated patients had no liver histology, microvascular fatty changes, or moderate central venous congestion. Paracetamol produced minor vacuolar degeneration, perivascular oedema, and liver slice haemorrhage at 400 mg/kg methanolic extract [29-31]. Methanolic extract 400 mg/kg decreased ranitidine-induced hepatotoxicity's hydropic degeneration, lymphocyte infiltration, and kupffer cell alterations.

CONCLUSION

The experimental animal's liver is protected from alcohol, paracetamol, and ranitidine-induced functional, physical, biochemical, and histological changes by MELZWP. At 200 and 400 mg/kg, MELZWP was more hepatoprotective than silymarin (100 mg/Kg p.o). The liver may be dose-dependently protected by *Leucas zeylanica* methanolic extract phytoconstituents.

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