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**Anti Oxidant And Hepatoprotective Effect Of *Ludwigia Adscendens*,
Launaea Pinnatifida, And *Carica Papaya* Hydroalcoholic Extracts On
Paracetamol Induced Liver Injury In Rats****Sonika Gupta*¹, Rajesh Kumar Sharma**¹Research scholar, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, U.P, India²Associate Professor, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, U.P, India**Email: sonika_112002@yahoo.co.in****Article Information**

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Keywords*Ludwigia adscendens*,
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*histopathology etc***ABSTRACT**

Liver, a central organ for metabolism and detoxification, is highly susceptible to damage induced by oxidative stress and drug toxicity. The present study evaluated the phytochemical analysis, *in vitro* antioxidant potential, and *in vivo* hepatoprotective activity of hydroalcoholic extracts of *Ludwigia adscendens* (LA), *Launaea pinnatifida* (LP), and *Carica papaya* (CP). Preliminary phytochemical screening confirmed the presence of carbohydrates, alkaloids, terpenoids, tannins, phenols, saponins, glycosides, and flavonoids in all extracts. Antioxidant assays revealed that CP demonstrated the strongest free radical scavenging activity ($IC_{50} = 22.09 \mu\text{g/ml}$) close to that of the standard ascorbic acid ($15.56 \mu\text{g/ml}$), while LP exhibited the highest reducing power, followed by LA. Acute toxicity studies showed no mortality or adverse effects up to 2000 mg/kg, indicating safety of all extracts. In the paracetamol-induced hepatotoxicity model, the vehicle + paracetamol group exhibited significant increases in AST, ALT, ALP, bilirubin, lipid peroxidation (LPO), and concomitant decreases in superoxide dismutase (SOD) and glutathione (GSH). Treatment with CP markedly restored liver function markers and oxidative stress parameters toward normal, with effects comparable to silymarin, whereas LP and LA showed moderate hepatoprotection. Histopathological findings corroborated biochemical data, with CP-treated groups exhibiting the least hepatic damage. Overall, CP demonstrated the most promising hepatoprotective and antioxidant activity, followed by LP and LA, supporting their ethnomedicinal use in liver disorders.

INTRODUCTION:

The human liver is one of the most vital visceral organs, responsible for synthesis, metabolism, excretion, and detoxification of numerous endogenous and exogenous substances, including drugs (Kohen and Nyska, 2002). It is often referred to as the “fighting organ” because of its critical involvement in maintaining physiological balance (Muriel and Arauz, 2010). The liver carries out several essential functions such as storage, secretion, and particularly metabolism (Setty et al., 2007). Among these, detoxification of harmful substances is considered its most

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fundamental role (Nijveldt et al., 2003). However, excessive generation of reactive oxygen species (ROS) contributes to the onset of liver disorders such as hepatitis, fever, and hepatocellular carcinoma. Overproduction of ROS causes oxidative stress leading to liver damage, and therefore, plant-based antioxidants have attracted significant attention for their potential to prevent or alleviate such damage.

Medicinal plants remain a valuable source of bioactive compounds, and researchers continue to explore them for novel therapeutic agents. Several plants and their formulations are used in traditional and ethnomedicinal practices in India to treat drug-induced liver injury (Dash et al., 2007). One of the most widely recognized plant-derived hepatoprotective agents is silymarin, extracted from the seeds of *Silybum marianum* (milk thistle), which is used globally for liver protection (Fraschini et al., 2002).

Ludwigia adscendens subsp. *diffusa* (Forssk.) P.H.Raven, also known as *Ludwigia stolonifera* (Guill. & Perr.) P.H.Raven, is a prominent aquatic macrophyte distributed across canals and drains branching from the Nile River in Egypt (Saleh et al., 2019). Owing to its phytochemical diversity, it has been the subject of increasing interest for the discovery of novel bioactive compounds with unique structural and pharmacological properties.

Launaea pinnatifida (*L. pinnatifida*), also referred to as *Launaea sarmentosa* (Willd.), belongs to the family Asteraceae (Makwana and Pandya, 2019; Salih et al., 2013). Traditionally, it has been employed in folk medicine for the treatment of various ailments. In Ayurvedic literature, it is categorized under the controversial drug “Gojihva,” due to the leaf structure resembling a cow’s tongue (Khare, 2008). Although its medicinal potential is recognized, scientific exploration of this plant remains limited.

Carica papaya (*C. papaya*) L. is a major tropical and subtropical fruit crop, with global production exceeding 6.8 million tonnes in 2004 across nearly 389,990 hectares (FAO, 2004; Vij and Prashar, 2015). This plant is rich in bioactive compounds such as caffeic acid, rutin, myricetin, quercetin, α -tocopherol, papain, benzyl isothiocyanate (BITC), and kaempferol, which exhibit potent antioxidant properties (Kong et al., 2021). Beyond its nutritional value, *C. papaya* has been shown to possess diverse pharmacological activities, including antioxidant, anticancer, wound healing, digestive, and anxiolytic effects (Babalola et al., 2024).

Considering the medicinal relevance of these plants, the present study was designed to comparatively evaluate the hydroalcoholic extracts of *Ludwigia adscendens* (LA), *Launaea pinnatifida* (LP), and *Carica papaya* (CP) for their phytochemical constituents, antioxidant potential and *in vivo* hepatoprotective activity.

MATERIAL AND METHODS:

Collection and authentication of plant

The leaves of *Ludwigia adscendens*, *Launaea pinnatifida*, and *Carica papaya* were collected and authenticated under reference numbers 2023071, 2023072, and 2023073, respectively, at Government College Khimlasa, Sagar (M.P.), on 26-09-2023 by a plant taxonomist to confirm their identity and purity.

Extraction:

The leaves of *Ludwigia adscendens*, *Launaea pinnatifida* and *Carica papaya* were dried under shade and pulverized to a coarse powder. The powdered crude material was defatted with petroleum ether and then extracted successively with hydroalcoholic solvent using Soxhlet extractor. The extracts were concentrated using rotary vacuum evaporator to yield extract. These extracts were subsequently subjected to photochemical (Arora and Itankar, 2018). Extraction yield of extracts were calculated using the following equation below:

$$\text{Formula of Percentage yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100$$

Phytochemical screening:

The phytochemical analysis of *C. ternatea* was carried out using previously described protocols (Rashid et al., 2023). The Molish test was performed to identify carbohydrates. Alkaloid identification was conducted by using Mayer’s reagent, Hager’s reagent, Wagner’s reagent, and Dragendroff’s reagent. Flavonoid identification utilized concentrated HCl, and 5% FeCl₃ was added to the crude extract in the presence of distilled water. The presence of blue-black coloration or precipitation confirmed the presence of tannins. Steroid identification was performed by adding chloroform followed by concentrated H₂SO₄. The presence of red color in the chloroform layer ensures the presence of steroids.

In-vitro Anti-oxidant Activity

• DPPH Radical Scavenging Activity:

DPPH free radical scavenging assay was measured using DPPH (2,2-diphenyl-1-picryl hydrazyl) free radical test, by employing the method of Wong et al. 2006. The different concentrations of each of the extracts were prepared in methanol and were added to 3ml of 0.1mM methanolic solution of DPPH.

The tubes were shaken vigorously and allowed to stand for 30min at room temperature in dark. Changes in absorbance of samples were measured at 517nm. A control reading was obtained using methanol instead of the extract. Ascorbic acid was used as the standard control.

Percentage antioxidant activity of sample/standard was calculated by using formula:

$$\% \text{ Inhibition} = \left[\frac{\text{Ab of control} - \text{Ab of sample}}{\text{Ab of control}} \times 100 \right]$$

Results have also been reported as IC₅₀, which is the amount of antioxidant necessary to decrease the initial DPPH• concentration by 50%. All the tests were performed in triplicates and for IC₅₀ values the graph was plotted with the average of the three determinations.

• Reducing power assay:

The reducing power of the compound was evaluated according to Oyaizu, 1986. Different amounts of aqueous extracts were perched in aqueous solvent and diverse with 2.5ml of 0.2M phosphate buffer (pH 6.6), and 2.5ml of 1% K₃Fe(CN)₆. This mixture was incubated at 50°C for 20min, 2.5ml of 10% TCA was added to the blend and centrifuged at 3000rpm for 10 min. The upper layer of the solution (2.5ml) was assorted with distilled water (2.5ml) and FeCl₃ (0.5ml, 0.1%), and the absorbance was measured at 700nm. Increase in absorbance of the reaction mixture indicates increased reducing power. The experiment was conducted in triplicates and values are expressed as equivalents of ascorbic acid in µg / mg of extract.

In vivo study:

• Animals procurement:

Wistar rats of weighing 185±15 g were selected and procured from PBRI animal house. The animals were maintained under standard conditions of humidity, temperature (25±2 °C) and light (12 h light/dark). They were fed with standard rat pellet diet and water ad libitum.

• Acute toxicity studies:

Acute oral toxicity study of LA, LP, CP extracts and formulations were studied according to OECD-423 guidelines in mice. Four dose levels were selected for acute oral toxicity. 5 mg/kg, 50 mg/kg, 300 mg/kg and 2000 mg/kg were used as dose range.

• Paracetamol induced hepatotoxicity study:

Animal were divided into seven groups of six animals each group. The first group (Group1) received only normal saline 5 ml/kg for 7 days. Groups II animals were administered PCM (500

mg/kg) single dose on 7th day, Group III received silymarin 25 mg/kg (p.o) orally for 7 days once daily and PCM on 7th day and Group IV received *Ludwigia adscendens* 200mg/kg (LA) and PCM on 7th day, Group V received *Launaea pinnatifida* 200 mg/kg (LP) orally for 7 days and PCM on 7th day, Group VI received *Carica papaya* 200mg/kg (CP) orally daily for seven days orally daily for seven days and PCM on 7th day respectively. On the eight day after 24 h of respective treatments the blood samples were collected from retro orbital plexus for the estimation of biochemical marker enzymes (Simeonova et al., 2013).

Serum was separated by centrifugation at 2000 rpm for 10 min at 4°C in cooling microfuge. Liver function tests were performed by measuring the levels of serum enzymes: aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin. All determinations were carried out on day's 8–10 post administration.

All animals were sacrificed by cervical decapitation. Immediately after the sacrifice, the livers were isolated and washed with ice-cold saline. A small piece of the central lobe of liver of each rat was fixed in 10% [v/v], formalin solution for the histopathological examination.

The supernatant was used for determination of reduced glutathione (GSH) (Anderson, 1985) and marker enzymes namely, Malondialdehyde (MDA), and superoxide dismutase (SOD) (Kakkar, Das, & Viswanathan, 1984).

• Statistical Analysis

Results are provided as Mean ± SD (n=6). Results were analyzed statistically using one-way analysis of variance (ANOVA) followed by Bonferroni t-test. P < 0.05 was considered as level of significance while comparison between groups.

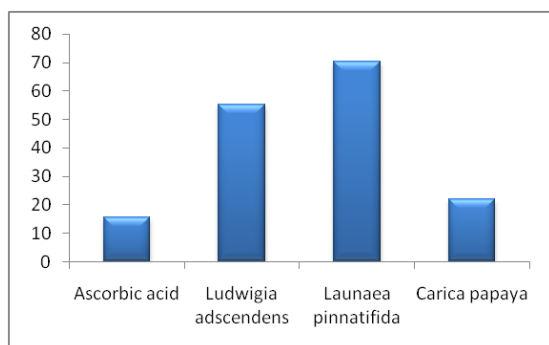
RESULTS:

In vitro antioxidant activity:

• DPPH radical scavenging activity:

Table 1 Comparative table of DPPH radical scavenging activity of samples

Sample name	IC 50 (µg/ml)
Ascorbic acid	15.569
<i>Ludwigia adscendens</i>	55.061
<i>Launaea pinnatifida</i>	70.230
<i>Carica papaya</i>	22.090

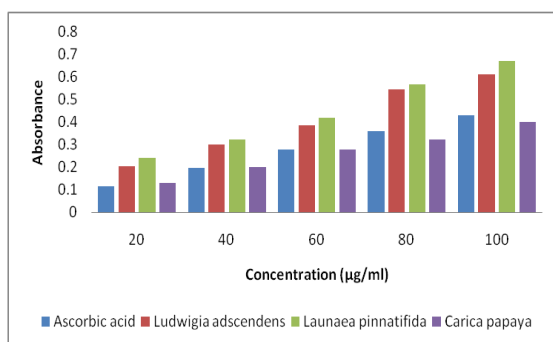


Graph 1 Comparative graph of DPPH radical scavenging activity of samples

• Reducing power scavenging activity:

Table 2 Reducing power scavenging activity:

Concentration (µg/ml)	Ascorbic acid	Ludwigia adscendens	Launaea pinnatifida	Carica papaya
20	0.115	0.202	0.239	0.131
40	0.196	0.299	0.323	0.201
60	0.276	0.387	0.418	0.276
80	0.361	0.545	0.565	0.322
100	0.43	0.612	0.669	0.401



Graph 2 Comparative graph of reducing power activity of samples

Paracetamol induced hepatotoxicity:

- Body weight changes during the study

Table 3 Body weight changes in normal control, inducer and Test samples LA, LP, CP (200 mg/kg bw), formulation and standard

Group No.	Treatment	Body weight (gm)	
		Initial	Final
I.	Normal Control (Vehicle treated)	188.83±6.43	210.83±4.36
II.	Vehicle + Paracetamol	205.33±3.01	186.67±7.37
III.	Standard Silymarin 25 mg/kg + Paracetamol	187.83±7.52	203.33±7.20 ^{ns}
IV.	LA (200 mg/kg)+ Paracetamol	191.00±2.68 ^{ns}	202.78±4.00 ^{ns}
V.	LP (200 mg/kg)+ Paracetamol	196.67±6.02 ^{ns}	209.33±1.37 ^{ns}
VI.	CP (200 mg/kg)+ Paracetamol	199.67±3.27 ^{ns}	213.50±4.85 ^{ns}

Values are expressed as MEAN±SD at n=6, One-way ANOVA followed by Bonferroni test, *P<0.050, **P<0.001 and ^{ns} non-significant compared to the Group II (Control).

- Liver enzyme parameters.

Table 4 Liver function test normal control, inducer and Test samples LA, LP, CP (200 mg/kg bw) and standard

Group No.	Group	Parameter			
		AST (IU/dL)	ALT (IU/dL)	ALP (IU/dL)	Bilirubin (mg/dL)
I	Normal Control (Vehicle treated)	53.03±1.273	33.27±3.798	125.83±4.875	0.40±0.025
II	Vehicle + Paracetamol	114.63±7.667	97.88±5.584	213.31±7.592	1.31±0.081
III	Standard Silymarin 25 mg/kg + Paracetamol	62.70±3.222**	44.83±5.115**	116.13±6.911**	0.57±0.043**
IV	LA (200 mg/kg)+ Paracetamol	94.33±6.022 ^{ns}	82.67±5.854 ^{ns}	159.67±7.941**	0.82±0.057**
V	LP (200 mg/kg)+ Paracetamol	89.12±7.787 ^{ns}	81.33±6.110 ^{ns}	145.20±4.441**	0.76±0.020**
VI	CP (200 mg/kg)+ Paracetamol	72.67±8.819**	64.71±8.573**	128.21±10.948**	0.65±0.076**

Values are expressed as MEAN±SD at n=6,

One-way ANOVA followed by Bonferroni test, *P<0.050, **P<0.001 and ^{ns} non-significant compared to the Group II (Control).

- Oxidative stress parameters

Table 5 Oxidative parameters SOD in normal control, inducer and Test samples LA, LP, CP (200 mg/kg bw) and standard

Group No.	Treatment	SOD (Unit/mg tissue)
I	Normal Control (Vehicle treated)	169.39±16.591
II	Vehicle + Paracetamol	85.38±3.839
III	Standard Silymarin 25 mg/kg + Paracetamol	162.80±5.476*
IV	LA (200 mg/kg)+ Paracetamol	117.71±24.691 ^{ns}
V	LP (200 mg/kg)+ Paracetamol	130.46±10.835 ^{ns}
VI	CP (200 mg/kg)+ Paracetamol	146.17±5.666 ^{ns}

Values are expressed as MEAN±SD at n=6,

One-way ANOVA followed by Bonferroni test, *P<0.050, **P<0.001 and ^{ns} non-significant compared to the Group II (Control).

Table 6 Oxidative parameters LPO in normal control, inducer and Test samples LA, LP, CP (200 mg/kg bw) and standard

Group No.	Treatment	LPO (nmol MDA/mg tissue)
I	Normal Control (Vehicle treated)	22.33±2.944
II	Vehicle + Paracetamol	79.43±8.060
III	Standard Silymarin 25 mg/kg + Paracetamol	30.33±5.428*
IV	LA (200 mg/kg)+ Paracetamol	57.67±8.430 ^{ns}
V	LP (200 mg/kg)+ Paracetamol	51.00±7.014 ^{ns}
VI	CP (200 mg/kg)+ Paracetamol	45.33±11.075 ^{ns}

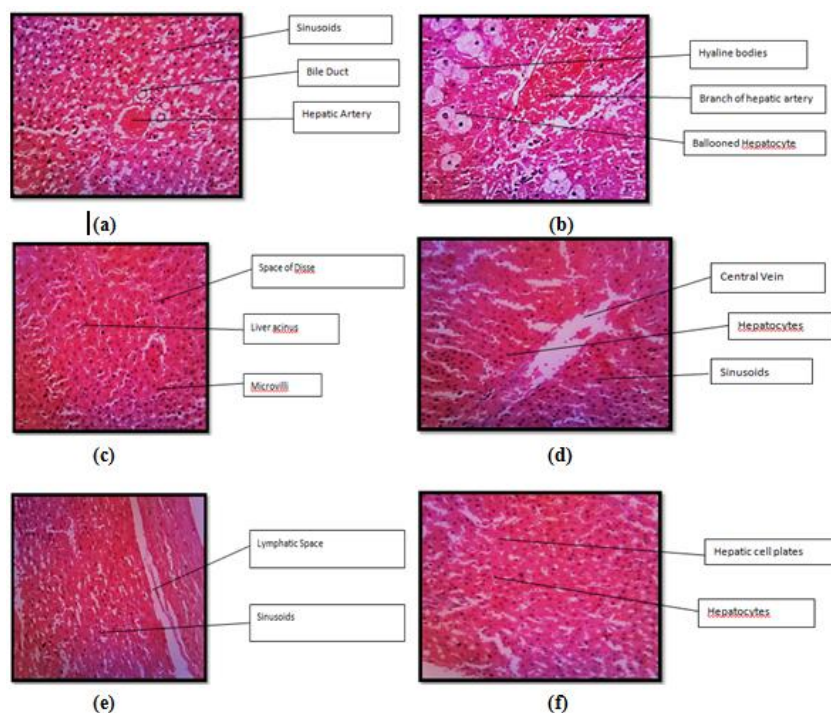
Values are expressed as MEAN±SD at n=6, One-way ANOVA followed by Bonferroni test, *P<0.050, **P<0.001 and ^{ns} non-significant compared to the Group II (Control).

Table 7 Oxidative parameters GSH in normal control, inducer and Test samples LA, LP, CP (200 mg/kg bw) and standard

Group No.	Treatment	GSH (nmol/mg tissue)
I	Normal Control (Vehicle treated)	0.91±0.132
II	Vehicle + Paracetamol	0.29±0.011
III	Standard Silymarin 25 mg/kg + Paracetamol	0.79±0.090**
IV	LA (200 mg/kg)+ Paracetamol	0.57±0.092 ^{ns}
V	LP (200 mg/kg)+ Paracetamol	0.61±0.026 ^{ns}
VI	CP (200 mg/kg)+ Paracetamol	0.64±0.065*

Values are expressed as MEAN±SD at n=6, One-way ANOVA followed by Bonferroni test, *P<0.050, **P<0.001 and ^{ns} non-significant compared to the Group II (Control).

Histology



- a) Group I: Normal control showed normal tissue histology
- b) Group II: Paracetamol induced manifested by large number of inflammatory cells infiltration, hyaline bodies and ballooned hepatocyte
- c) Group III: Standard treated rats showing normal hepatocytes with sinusoids
- d) Group IV: LA treated rats showing mild inflammation in central vein with fatty liver, larger sinusoids
- e) Group V: LP treated rats showing lymphatic

- f) Group VI: CP treated rats showing vacuolization of the cytoplasm of hepatocyte and disarrangement of hepatic parenchyma

DISCUSSION:

The phytochemical screening of *Ludwigia adscendens* hydroalcoholic extract showed the presence of carbohydrates, alkaloids, terpenoids, tannins, phenols, saponins, glycosides, and flavonoids, while *Launaea pinnatifida* extract revealed mainly carbohydrates, alkaloids,

terpenoids, tannins, phenols, saponins, glycosides, and flavonoids. Furthermore, *Carica papaya* extract also showed the presence of proteins, carbohydrates, alkaloids, terpenoids, tannins, phenols, saponins, glycosides, and flavonoids.

The comparative evaluation of antioxidant activity through DPPH radical scavenging and reducing power assays revealed distinct differences among the tested samples. Ascorbic acid, used as the standard antioxidant, exhibited the strongest free radical scavenging activity with the lowest IC₅₀ value of 15.569 µg/ml, indicating high potency. Among the plant extracts, *Carica papaya* showed the most promising antioxidant potential with an IC₅₀ value of 22.090 µg/ml, which was comparatively close to the standard. *Ludwigia adscendens* demonstrated moderate activity with an IC₅₀ of 55.061 µg/ml, while *Launaea pinnatifida* exhibited the least activity among the tested samples with an IC₅₀ of 70.230 µg/ml.

The reducing power assay is a reliable indicator of the electron-donating ability of compounds, which reflects their potential antioxidant activity. In this study, all tested extracts (*Ludwigia adscendens*, *Launaea pinnatifida*, and *Carica papaya*) as well as the standard ascorbic acid exhibited a concentration-dependent increase in reducing power, indicating enhanced antioxidant activity with increasing concentration.

Among the extracts, *Launaea pinnatifida* showed the highest reducing power at all concentrations, reaching an absorbance of **0.669 at 100 µg/ml**, which was higher than both *Ludwigia adscendens* (**0.612**) and *Carica papaya* (**0.401**). This suggests that *Launaea pinnatifida* possesses a relatively stronger electron-donating capacity compared to the other extracts tested. *Ludwigia adscendens* also demonstrated significant reducing activity, while *Carica papaya* showed comparatively lower reducing power, though still higher than the standard at lower concentrations.

Overall, the findings suggest that the antioxidant potential of these plants is multifaceted. *Carica papaya* appears to be more effective in direct free radical scavenging, whereas *Launaea pinnatifida* demonstrates stronger reducing power, reflecting greater electron-donating capacity. *Ludwigia adscendens* exhibited moderate activity in both assays. These complementary results emphasize the importance of employing multiple antioxidant assays to comprehensively evaluate the potential of plant extracts.

The acute oral toxicity study of *Ludwigia adscendens* (LA), *Launaea pinnatifida* (LP) and

Carica papaya (CP) extracts in Wistar rats, administered at doses of 5, 50, 300, and 2000 mg/kg, revealed No mortality or signs of toxicity were observed in any group during the 14-day observation period. All animals survived until the end of the study, indicating that the LD₅₀ of each test sample is greater than 2000 mg/kg. Additionally, the body weight of all animals increased gradually across all dose groups, suggesting normal growth and no adverse effects on metabolic functions. This absence of lethality and the steady increase in body weight across treated groups confirm the safety of LA, LP, and CP, at the tested dose range.

Paracetamol-induced hepatotoxicity is commonly associated with reduced appetite, altered metabolism, and consequent weight loss in experimental animals. In the present study, the vehicle + paracetamol group (Group II) demonstrated a significant reduction in body weight compared to the normal control, confirming the systemic toxicity induced by paracetamol. Conversely, treatment with standard silymarin (25 mg/kg) and all plant extracts (*Ludwigia adscendens*, *Launaea pinnatifida*, and *Carica papaya*) at 200 mg/kg restored body weight towards normal levels.

Paracetamol administration (Group II) resulted in a marked elevation of serum AST, ALT, ALP, and bilirubin levels compared to the normal control, reflecting extensive hepatic injury and leakage of intracellular enzymes into circulation. Treatment with silymarin significantly reversed these alterations, reaffirming its hepatoprotective potential. Among the extracts, *Carica papaya* showed the strongest protective effect, with AST, ALT, ALP, and bilirubin values approaching those of the standard, followed by *Launaea pinnatifida* and *Ludwigia adscendens*. The significant reduction of ALP and bilirubin in all extract-treated groups indicates preservation of hepatic membrane integrity and bile secretion.

Oxidative stress plays a central role in paracetamol-induced liver injury, primarily through reactive metabolite (NAPQI) formation, which depletes glutathione and enhances lipid peroxidation. In the current study, the paracetamol group exhibited a marked decrease in SOD and GSH, along with a significant rise in LPO levels, confirming oxidative damage. Silymarin treatment significantly normalized these parameters, highlighting its potent free radical scavenging activity. Among the extracts, *Carica papaya* again demonstrated the strongest antioxidant effect, significantly improving GSH levels and reducing lipid peroxidation, though SOD recovery was moderate. *Launaea pinnatifida*

and *Ludwigia adscendens* also exhibited protective effects, but to a lesser degree.

CONCLUSION:

The study highlights the hepatoprotective and antioxidant potential of *Ludwigia adscendens*, *Launaea pinnatifida*, and *Carica papaya* hydroalcoholic extracts against paracetamol-induced hepatotoxicity. All extracts were found to be safe up to 2000 mg/kg in acute toxicity studies. Among the tested plants, *Carica papaya* exhibited the strongest antioxidant and hepatoprotective activity, significantly improving liver enzyme levels, enhancing antioxidant defenses (GSH, SOD), and reducing lipid peroxidation, with effects comparable to silymarin. These findings validate the traditional use of these plants in managing liver ailments and suggest that *Carica papaya*, in particular, holds strong potential for development as a natural hepatoprotective agent.

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