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Hepatoprotective Properties of Psidium Guajava Fruit and Musa Parasidiaca Roots as a Di-Herbal Remedy in Wister Rats

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ABSTRACT:

Oxidative stress is a major factor in the development of chronic liver diseases, prompting interest in plant-based antioxidants. This study investigates the hepatoprotective and antioxidant effects of Psidium guajava fruit and Musa paradisiaca roots, individually and as a di-herbal remedy, against carbon tetrachloride (CCl_4)-induced liver toxicity in Wistar rats. Forty-two rats (n=6 per group) were used. Liver damage was induced with CCl_4 (1 ml/kg) for one month, followed by treatment with methanolic extracts of guava fruit and plantain roots (500 mg/kg individually; 500 mg/kg and 1000 mg/kg combined) for an additional month. Serum levels of ALT, AST, ALP, bilirubin, albumin, and total protein were measured alongside oxidative stress parameters (SOD, CAT, GSH, GPx, NO, MDA). In vitro antioxidant assays (DPPH, ABTS, FRAP, nitric oxide scavenging) were also performed. CCl_4 induction elevated liver enzymes and MDA levels while reducing antioxidant markers. Treatment with the extracts improved protein profiles, restored antioxidant enzyme activity, decreased lipid peroxidation, and demonstrated strong in vitro radical-scavenging activity. Findings indicate that the di-herbal combination offers potential synergistic hepatoprotective and antioxidant effects, supporting further mechanistic and histopathological investigation.

KEYWORDS:

Hepatoprotective, Psidium guajava, Musa parasidiaca, Di-herbal Remedy, Wister Rats.

1. Introduction

Hepatotoxicity refers to impairment or damage to the liver, resulting from an excessive accumulation of xenobiotics or drugs (1). The substances or chemicals responsible for liver damage are referred to as hepatotoxins or hepatoxicants (2). These hepatotoxicants are external compounds with significant clinical importance, encompassing instances such as dietary supplements, drug overdoses, herbal remedies, natural substances, and industrial chemicals (3). Even within recommended therapeutic doses, certain drugs can lead to liver injury. Hepatotoxicity can also arise from immunologically mediated responses that affect epithelial cells, liver vasculature, or reactive metabolites (4).

The liver is an organ susceptible to reactive oxygen species (ROS) attack; ultimately, oxidative stress is a major player in the initiation of liver damage. Furthermore, several investigations (on mice and humans) have shown that oxidative stress reduces the ability of mature hepatocytes to regenerate, leading to cirrhosis (5).

Recent studies (6-8) (Oyelola et al., 2021; Rajesh et al., 2022; Chen et al., 2023) have further emphasized that natural antioxidants from fruits and herbs offer hepatoprotective effects by modulating oxidative pathways and improving biochemical markers of liver function. Plants with antioxidant effects have shown a promising therapeutic effect on liver disorders in animal experiments (9).

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Guava, also known as Psidium guajava, is a popular tropical fruit grown in several different tropical and subtropical climates (10). Although it is a fruit commonly found in Nigeria, it is widely consumed as food and used in traditional medicine in other parts of the globe. Among other health benefits of guava, several studies (10-13) have indicated guava to be rich in antioxidant properties and exceptionally high vitamin C content.

On the other hand, Plantain (*Musa Parasidiaca*) is a perennial herbaceous plant found on every continent, including Africa. In medicine, the roots of plantain are employed as an antibiotic, an antidote, and an antiseptic agent. In addition, the roots are decocted and used to cure various ailments (11). Individually, both plants have been reported to possess hepatoprotective effects. However, despite their popularity in traditional practices, the combined use of P. *guajava* fruit and M. paradisiaca root extracts as a di-herbal therapy lacks scientific evidence. The rationale for combining *Psidium guajava* and *Musa paradisiaca* lies in their complementary phytochemical profiles—guava being rich in vitamin C and flavonoids, while plantain roots contain alkaloids and terpenoids known for anti-inflammatory actions. This di-herbal approach may provide a synergistic mechanism, enhancing both antioxidant and hepatoprotective potential beyond their individual effects.

This study, therefore, investigates the hepatoprotective and antioxidant properties of guava fruit and plantain root extracts, individually and in combination, against CCl_4-induced toxicity in Wistar rats.

2. Methodology

Collection and Extraction of Plant Materials

Guava fruit and Plantain roots were collected from a local farm in Keffi, Nasarawa state, Nigeria. They were both cleaned, dried, and ground into powder individually. To perform methanolic extraction, 400g of guava fruit powder was soaked in 1.5 L of absolute methanol for three days, then filtered. The procedure was iterated with the remaining powder residues. Subsequently, the methanolic extracts underwent concentration through rotary evaporation for a period of 24 hours. 600g of powdered roots from Plantain roots were blended with 2 liters of methanol. The resulting mixture underwent filtration through Whaltman filter paper no. 1. The obtained extract was concentrated through a rotary evaporation over a period of 24 hours. The residue was obtained and refrigerated until required.

Experimental Animals:

Forty-two (42) adult Wistar rats (160–200 g) were kept under standard laboratory conditions (25 ± 2°C; 12-hour light–dark cycle). They were acclimatized for two weeks with free access to food and water. Ethical approval was obtained from NSUK-ACUREC. Animals were randomly assigned to groups using a simple randomization procedure to minimize selection bias.

Experimental Design:

The CCl_4 dose was standardized to 1 ml/kg diluted in olive oil (1:1).
The 42 rats were assigned to seven groups (n=6):
- Group 1: Control (no CCl_4)
- Group 2: Negative control (CCl_4 only)
- Group 3: CCl_4 + 500 mg/kg guava extract
- Group 4: CCl_4 + 500 mg/kg plantain extract
- Group 5: CCl_4 + 250 mg/kg di-herbal combo
- Group 6: CCl_4 + 500 mg/kg di-herbal combo
- Group 7: CCl_4 + 100 mg/kg silymarin.

The silymarin dose of 100 mg/kg was selected based on published studies demonstrating consistent hepatoprotective and antioxidant efficacy at this concentration in carbon tetrachloride–induced liver injury models in rodents (63–65).
Carbon tetrachloride in olive oil was administered intraperitoneally. Meanwhile, all the animals were fed on vital feed and water (H_2O) ad libitum. Each group consisted of six rats; however, biochemical determinations were conducted in five replicates per group due to sample volume constraints and exclusion of technically compromised samples.

Extract Standardization:

The methanolic extracts of guava fruit and plantain roots were standardized based on their total phenolic and flavonoid contents, quantified using gallic acid and quercetin equivalents, respectively. These parameters served as marker indicators of extract potency, ensuring batch-to-batch reproducibility before biological evaluation.

Biochemical Assays:

Liver biomarkers (ALT, AST, ALP, albumin, total protein, and bilirubin) were analyzed using standard methods using standard kits from Randox Laboratory, UK, according to the instructions of the manufacturer. Oxidative stress parameters (SOD, CAT, GSH, GST, MDA, NO) were measured according to validated protocols.

In Vitro Antioxidant Assays:

The DPPH, ABTS, FRAP, and nitric oxide scavenging assays followed established protocols with slight modifications. DPPH (2,2-diphenyl-1-picrylhydrazyl) Radical Scavenging assay was conducted following Brand-Williams *et al.* (1995) (13) with minor adjustments. ABTS antioxidant activity was determined as described by Re et al. (1999)(14). Ferric reducing antioxidant power (FRAP) was estimated spectrophotometrically following the procedure of Benzie and Strain 1996 (15). Nitric oxide generated from sodium nitroprusside (SNP) was measured according to the method of Marcocci *et al.* (1994) (16). Absorbance was read at the required wavelengths after incubation.

Statistical Analysis:

The analysis was performed using SPSS version 16 (Statistical Package for the Social Sciences). The groups' differences were tested for significance by one-way ANOVA followed by the Duncan post hoc test. Data were expressed as the Mean ± SD. P-values <0.05 were considered statistically significant.

3. Results

Total Phenol and Flavonoid present in Plantain roots and Guava fruits methanol extract.

The results of the quantification of Total Phenol and Flavonoid present in the methanol extract of Plantain roots and Guava fruits are presented in Table 1. The total phenol of guava fruits and plantain roots are 288.05 ± 0.01 and 54.1± 0.01, respectively, while their total flavonoid content is 43.30± 0.56 and 31.74± 0.80, respectively.

Table 1: Total Phenol and Total Flavonoid of Plantain roots and Guava fruits methanol extract

Extract	Total Phenol (mg/g GAE)	Total Flavonoids (mg/100g QUE)
Guava fruit	288.05 ± 0.01	43.30 ± 0.56
Plantain roots	54.10 ± 0.01	31.74± 0.80

Values are expressed as Mean ± Standard error of Mean (SEM) for three determinations.

Effect of Guava fruit and Plantain roots on the serum protein concentrations in the experimental groups.

The results of the effects of various concentrations of Guava fruit and Plantain roots individually and as a di-herb combo on the serum protein concentrations in the experimental groups are presented in Table 2. The results showed that CCl_4 induction significantly altered total protein and albumin levels compared to the control group. Treatment with guava fruit and plantain root extracts restored protein values closer to normal.

Table 2: Effect of Guava fruit and Plantain roots on the serum protein concentrations in the experimental groups

Group	Test (Unit)	Total Protein(g/dl)	Albumin (g/dL)	Direct Bilirubin (µmol/L)	Total Bilirubin (µmol/L)
1	Positive control	5.63 ± 0.31^{a}	3.35 ± 0.09^{a}	17.30 ± 0.75^{a}	21.40 ± 1.55^{a}
2	Negative control	7.49 ± 0.30^{b}	2.53 ± 0.16^{b}	19.80 ± 1.03^{b}	25.10 ± 1.61^{b}
3	500mg/kg Guava fruit	5.93 ± 0.19a	2.96 ± 0.09^{c}	20.30 ± 1.76^{c}	21.40 ± 2.04^{a}
4	500mg/kg Plantain roots	5.75 ± 0.23^{a}	2.88 ± 0.08^{c}	16.10 ± 0.77^{d}	18.60 ± 1.02^{c}
5	250mg/kg di-herbal	6.29 ± 0.18^{c}	3.18 ± 0.13^{d}	18.80 ± 1.00^{e}	19.80 ± 1.07^{c}
6	500mg/kg di-herbal	6.15 ± 0.35^{c}	2.89 ± 0.09^{c}	15.80 ± 0.46^{d}	17.90 ± 1.51^{c}
7	100mg/kg silymarin	5.61 ± 0.15^{a}	3.15 ± 0.06^{d}	16.70 ± 1.01^{a}	21.20 ± 1.35^{a}

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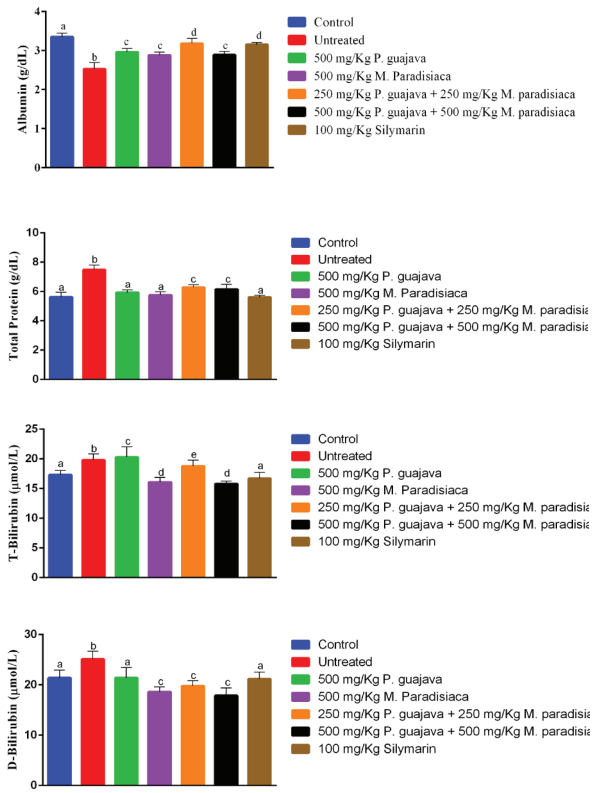
Figure 1: Effect of Guava fruit and Plantain roots on the serum protein concentrations in the experimental groups.



Effect on Liver Enzymes (ALT, AST, ALP):
CCl_4 significantly increased ALT, AST, and ALP levels, indicating severe hepatocellular damage. Treatment groups exhibited reductions in ALT and AST, but ALP levels remained elevated in all extract-treated groups. The results of the effect of Guava fruit and Plantain roots on the serum liver enzymes concentrations in the experimental groups are presented in Table 3.

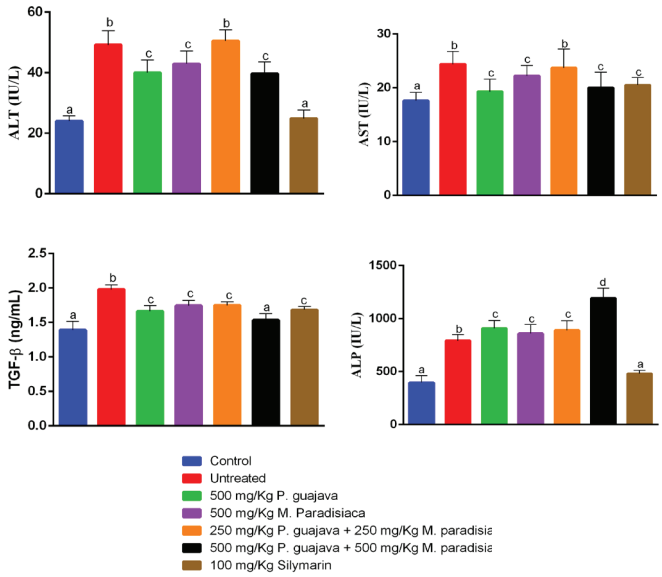
Effect on TGF-β:
TGF-β levels increased following CCl_4 administration, reflecting inflammatory and fibrotic signaling. Treatment with the 500 mg/kg di-herbal combination significantly reduced TGF-β levels. The results of the effect of Guava fruit and Plantain roots on TGF-β concentrations in the experimental groups are presented in Table 3.

Table 3: Effect of Guava fruit and Plantain roots on the serum concentration of liver enzymes and TGF-β in the experimental groups

Group	Test (Unit)	ALP (IU/L)	ALT (IU/L)	AST (IU/L)	TGF-β (ng/mL)
1	Positive control	395.6 ± 66.4^a	24.02 ± 1.80^a	17.60 ± 1.56 ^{a}	1.39 ± 0.12^a
2	Negative control	792.40 ± 57.55^b	49.17 ± 4.69^b	24.40 ± 2.33^b	1.98 ± 0.07^b
3	500mg/kg Guava fruit	907.60 ± 75.63^c	40.05 ± 4.19^c	19.30 ± 2.32^c	1.66 ± 0.08^c
4	500mg/kg Plantain roots	859.30 ± 86.80^c	42.90 ± 4.31^c	22.20 ± 1.95^c	1.74 ± 0.07^c
5	250mg/kg di-herbal	889.60 ± 90.48^c	50.50 ± 3.73^b	23.70 ± 3.49^b	1.75 ± 0.05^c
6	500mg/kg di-herbal	1192.80 ± 95.29^d	39.70 ± 3.91^c	20.00 ± 2.89^c	1.54 ± 0.09^a
7	100mg/kg silymarin	480.40 ± 32.58^a	24.86 ± 2.86^a	20.50 ± 1.40^c	1.68 ± 0.05^c

Values that have the same superscript are not significantly different @ p < 0.05 down the table.

Figure 2: Effect of Guava fruit and Plantain roots on the liver enzymes and TGF-β in experimental groups



Effect of Guava fruit and Plantain roots on antioxidant parameters

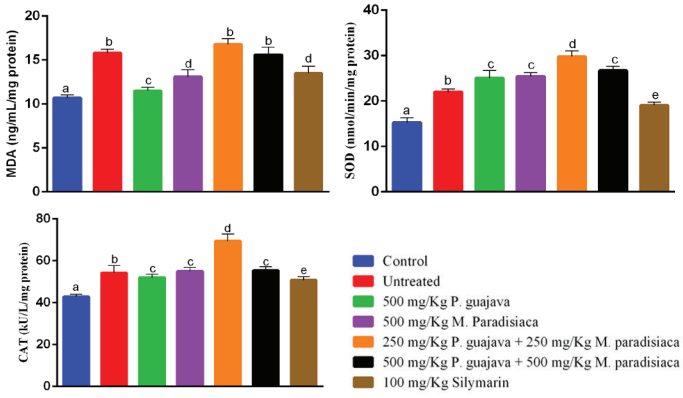
The results of the effect of Guava fruit and Plantain roots on the antioxidant parameters, such as MDA, SOD, and CAT concentrations in the experimental groups, are presented in Table 4. CCl_4 increased MDA levels and reduced SOD and CAT activity. Treatment with guava and plantain extracts significantly reversed these changes, with the di-herbal groups producing the greatest improvement.

Table 4: Concentration of antioxidant parameters

Group	Test (Unit)	MDA (nmol/L)	SOD (nmol/min/mg protein)	CAT (kU/L/mg protein)
1	Positive control	10.70 ± 0.33^{a}	22.00 ± 0.65^{c}	54.33 ± 3.37 ^{c}
2	Negative control	15.80 ± 0.45^{d}	15.27 ± 1.09^{a}	42.89 ± 1.11^{a}
3	500mg/kg Guava	11.50 ± 0.41^{b}	25.10 ± 1.63^{d}	51.97 ± 1.58^{b}
4	500mg/kg Plantain roots	13.10 ± 0.80^{c}	25.41 ± 0.86^{d}	55.01 ± 1.85^{c}
5	250mg/kg di-herb	16.80 ± 0.64^{d}	29.80 ± 1.27^{e}	69.40 ± 3.44^{d}
6	500mg/kg di-herb	15.60 ± 0.86^{d}	26.72 ± 0.98^{c}	55.43 ± 1.78^{c}
7	100mg/kg silymarin	13.50 ± 0.81^{c}	19.09 ± 0.68^{b}	50.79 ± 1.65^{b}

Values with different superscripts down the column are statistically significant at $p < 0.05$

Figure 3: Effect of Guava fruit and Plantain roots on antioxidant parameters



Effect on GST, GSH, and Nitrite:

The results of the effect of Guava fruit and Plantain roots on the antioxidant parameters such as GST, GSH, and Nitrite concentrations in the experimental groups are presented in Table 5. CCl_4 reduced GST and GSH levels while increasing Nitrite, indicating oxidative stress. The di-herbal extract at 250 mg/kg produced the greatest improvement in antioxidant markers.

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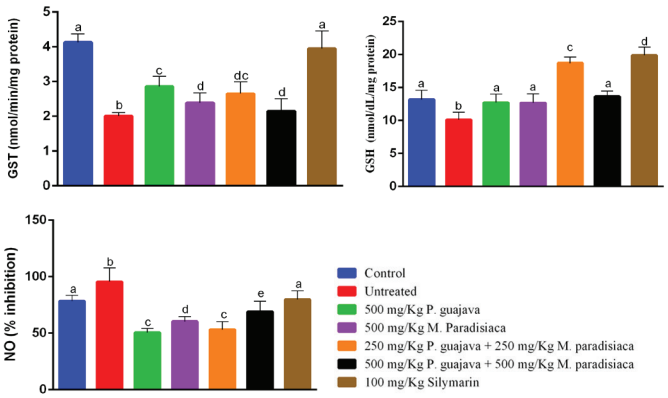
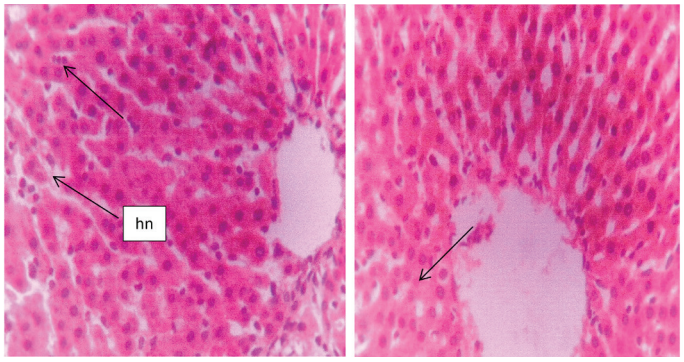
Figure 4: Effect of Guava fruit and Plantain roots methanol extract on GSH, GST, and Nitrite.

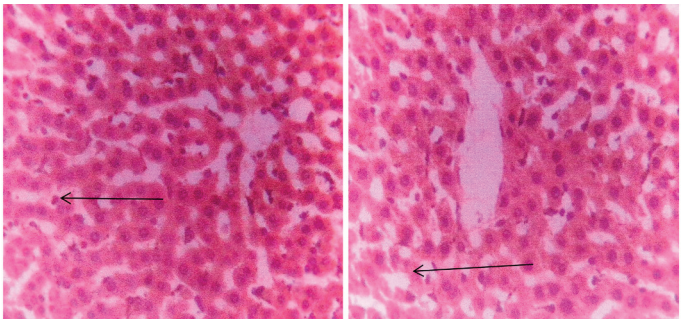


Histopathological Findings

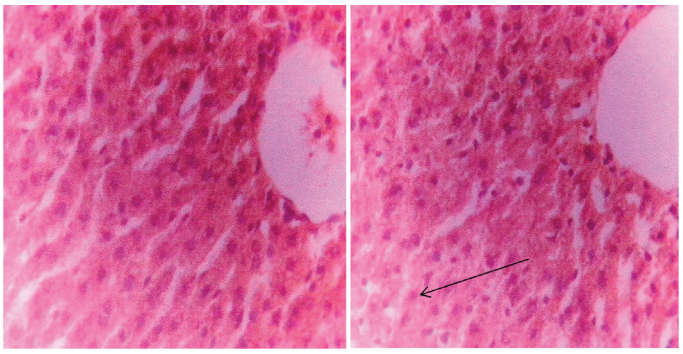
Qualitative histopathological examination revealed normal hepatocytes in control rats. CCl_4-treated rats showed hepatic necrosis (HN), inflammatory cell hyperplasia (LH), and sinusoidal congestion (SC). Treatment groups demonstrated partial restoration of hepatic architecture with mostly normal hepatocytes and only mild residual lesions. These findings support biochemical evidence of hepatocellular recovery and explain persistent ALP elevation due to delayed biliary or vascular normalization.



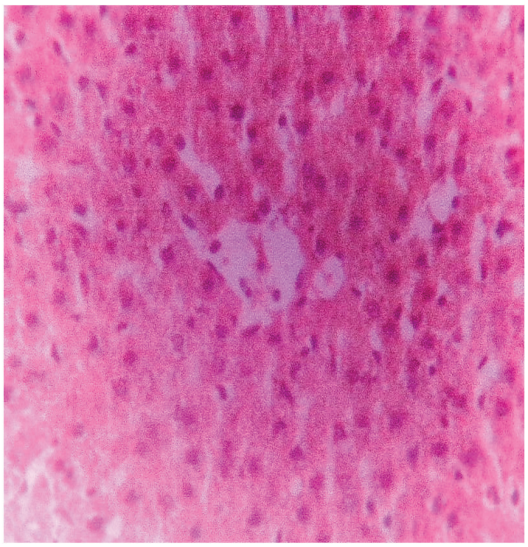
G1 shows sc with slight lh, f2 shows slight hn



D3 shows slight LH, e1 shows slight HN



B3 shows normal hepatocytes, a2 show slight hn



C2 shows normal hepatocytes.
Codes
Hn is hepatic necrosis
LH is a hyperplasia of inflammatory cells
Sc is sinusoidal congestion

4. Discussion

Over the years, phytochemicals have been explored in managing several diseases in folklore medicine (16). The ameliorative properties of several medicinal plants have been related to bioactive principles like phenolic, flavonoids, saponins, and alkaloids (17). In the context of this research, both guava fruit and plantain roots were found to contain flavonoids and phenols. Phenols are known for their noteworthy antioxidant properties, while flavonoids, owing to their specific chemical structure, are identified as the most potent among the phenolic compounds with antioxidant activity (18). The findings of the constituent phytochemicals of plantain roots of this study agree with the studies of (19) and (11). For guava fruit, the findings of this study agree with the study of Atik et al (2019)(20). A correlation between phenolic content and antioxidant activities on fruits and vegetables

has been previously reported (21); (22). Phenolic compounds recovery was largely dependent on the nature and polarity of the solvent. This is because a wide range of phenols are soluble in aqueous methanol mixtures. The TPC and TFC are similar and in line with several studies, such as Thuaytong and Anprung 2011, Lin & Yin (2012), Saeed et al. 2019 and Odubanjo et al. 2022(21,23–25).

The DPPH radical scavenging activity of antioxidants is largely dependent on their hydrogen-donating ability (26). In this study, Guava fruit and Plantain roots exhibited radical scavenging activities against DPPH radical. This was evident in the extracts' proton-donating abilities, making them potential subjects as primary antioxidants against free radicals and reactive oxygen species. Guava fruit showed the most free radical scavenging property in a dose-dependent manner when compared with Ascorbic acid, which is the standard. This agrees with the study of (27) and Lim et al 2006 (28). The results of plantain roots in this study are in line with the work of (Abdel Ghany et al. 2018, 29) for the pseudostem exudate of *M. paradisiaca,* DPPH scavenging % increased with increasing exudate concentrations.

Antioxidant activity has been proposed to be related to reducing power (26). Therefore, Guava fruit and Plantain roots possess antioxidant properties by reducing iron (Fe^{2+}) II to iron III (Fe^{3+}), but not better than the reference compound. This trend was also observed in the Nitric oxide (NO) and ABTS (2,2'-azinobis (3-ethylbenzothiaoline-6-sulfonate) assay and showed free radical scavenging property in a dose-dependent manner, and this is in line with several studies (30–35). The ability of guava fruit and plantain roots to chelate iron and scavenge DPPH, nitric oxide radicals is attributed mainly to the presence of phenolic compounds (35,36). These strong *in vitro* antioxidant properties of the extract of guava fruit and plantain roots may be a result of the functional groups of the compounds present in the extract. Factors modulating these antioxidant activities include the number of hydroxyl groups, methoxy esters, carbohydrate moieties, and phenolic units (37).

After careful evaluation of the individual compounds, the redox property and antioxidant effects of the compounds were found to be related to their functional group characteristics, the amount and positions of hydroxyl groups in their structures (35). Furthermore, the activity of phenolic compounds was suggested to be a synergistic effect on antioxidant capacity when they are together (36,38–40)

The concentration of albumin, bilirubin, and total protein can be used to ascertain different types of liver damage (41). Bilirubin is a product of haemoglobin catabolism with important biological and diagnostic values (42). The significant increase in both the serum total and direct bilirubin in the negative control induced with CCl_4 compared to the positive control suggests that there was a defect in liver function on induction, and this might be a result of haemolysis and impairment of the secretion of conjugated bilirubin into the bile duct in the liver of the rats induced with $CC1_4$. The results also revealed a significant decrease ($p<0.05$) across treatment groups 3, 4, 5, and 6, respectively, compared to the negative control. This suggests that the extracts at different concentrations were able to improve the liver damage, which is in line with the studies of Nirmila *et al*, 2012, and Osman et al., 2011(44,45). For both direct and total bilirubin, Group 6 (500mg/kg guava fruit + 500mg/kg plantain roots) was significantly lower ($p<0.05$) than group 7(100mg/kg silymarin) and positive control, this may suggests that treatment was able to reverse haemolysis and impairment of bilirubin and thus combing the extract might have a positive synergistic effect as evident in the results.

A significant decrease ($p<0.05$) in Albumin concentration in the negative group compared to the positive control suggests that there may be a reduction in the hepatocyte mass due to disease, and this suggests that the functionality of the immune cells has been compromised, and the severity and risk of infections are increased. Therefore, a significant increase ($p<0.05$) in albumin concentration across all the treatment groups suggests that immune function is boosted, hepatocyte volume increased, and the severity of the risk of infection has been mitigated. This agrees with the study by (11), plantain roots increased albumin content of arsenic oxidative damage in rats, and Osman et al. 2011 (45) showed that the ethanolic extract of guava leaf decreased the level of albumin in CCl_4-induced hepatotoxicity.

The assessment of protein concentration in the liver could be used to ascertain the secretory and synthetic functions (46). In this study, total protein (TP) concentrations in the negative control group induced with $CC1_4$ significantly increased

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($p<0.05$) compared to the positive control. This suggests liver damage, thereby making it nearly impossible for the body to process and metabolize protein for utilization. Also, this might be because of increased gamma globulin, indicating the presence of inflammatory diseases and immune disorders, further confirming liver damage. There was a significant decrease across all treatment groups compared to the negative control. It can be deduced that since guava fruit and plantain roots at all treatment concentrations significantly decreased the elevated TP in CCl_4-induced hepatotoxicity, they were able to improve the disease state. This is in line with the study Abbas et al. 2016, and Mohan et al. 2015 (46,47) that revealed P. *guajava* and M.*paradisiaca* extract decreased total protein, respectively. However, the individual groups of the extract, i.e, Group 3 (500mg/kg P. *guajava*) and Group 4 (500mg/kg M.*paradisiaca*), had an optimum effect compared to the di-herbal group (5 and 6).

Alanine aminotransaminases (ALT) and aspartate aminotransferases (AST) are well-known enzymes used as biomarkers to predict possible toxicity to the liver (48). The results from this study showed that on induction with CCl_4 (Negative control), the serum levels of ALT and AST increased significantly ($p<0.05$) when compared with the positive control. For ALT, the most effective treatment was group 6 (500mg/kg guava fruit and 500 mg/kg plantain root di-herb), which significantly ($p<0.05$) decreased ALT compared to the negative control. For AST, the most effective treatment is group 3 (500 mg/kg guava fruit), followed by group 6 (500 mg/kg guava fruit and 500 mg/kg plantain roots di-herb). This suggests that the di-herb combo might have a synergistic effect, as evident in the results. Nirmila et al. 2012 and Oyewole et al. 2015 (11,43)showed that plantain roots reduced ALT and AST levels, whereas Roy and Das (2010 also showed a decrease in AST and ALT levels by guava(49).

The result showed that CCl_4 induction (Negative control) elevated the ALP level significantly ($p<0.05$) in the serum compared to the positive control, while treatment at all concentrations of guava fruit and plantain roots further increased the ALP concentrations. This suggests that guava fruit and plantain roots were not able to protect or restore the integrity of the cell components of the liver. This was also observed in a study by Sambo et al. 2019 where the aqueous extract of guava fruit further increased the level of ALP, suggesting hepatoxicity; however, ALP is not specific to the liver, it is also found in bones, bile ducts, etc(50). Therefore, elevations in total ALP may arise from extra-hepatic tissue activity rather than persistent hepatic injury. Without isoenzyme differentiation, it is not possible to attribute the increased ALP solely to the liver. Histological evidence of mild sinusoidal congestion and inflammatory infiltration supports delayed structural recovery rather than ongoing hepatocellular injury.

Furthermore, the kinetics of ALP clearance differ substantially from those of transaminases. Unlike ALT and AST, which respond rapidly to injury and recovery, ALP has a longer circulating half-life and often normalizes more slowly, especially when the pattern of injury has cholestatic components (51). Thus, the observed persistence of elevated ALP alongside improved ALT/AST likely reflects delayed enzyme resolution rather than ongoing liver damage. Interpretation of liver injury patterns also requires more than ALP alone. Classification frameworks emphasize that cholestatic or mixed patterns typically present with disproportionate ALP elevation, whereas hepatocellular injury is driven primarily by ALT/AST changes (52). In this study, the improvement of ALT/AST and other biochemical parameters suggests hepatocellular recovery despite the isolated ALP elevation.

We acknowledge that, as a limitation, ALP isoenzyme fractionation was not performed. Future studies should include isoenzyme profiling or repeated ALP measurements at later time points to clarify the source of ALP elevation and strengthen mechanistic interpretation.

While having a normal level of human transforming growth factor-beta 1 (TGF-β) indicates a healthy immune system, high levels of this growth factor can indicate several diseases and conditions, such as chronic Liver diseases, chronic inflammatory response syndrome, cancer, tumor cells, fibrosis, and many more. In this study, the induction of CCl_4 significantly increased ($p<0.05$) the levels of TGF-β compared to the positive control; however, it was significantly ($p<0.05$) reduced in group 6 (500 mg/kg di-herbal combo) compared to the negative control group. This suggests that the guava fruit and plantain roots di-herbal combo can boost the immune system, and it could also indicate the amelioration of the disease condition. This is in line with the study by El-Said et al. 2022 (53) on plantain leaves and Shady et al. 2022 (54) on guava seeds, decreasing the level of TGF-β.

Glutathione (GSH), a liver-concentrated tripeptide, serves as a crucial thiol-reducing agent in regulating redox processes. Beyond its role as a free radical scavenger, GSH is implicated in determining outcomes between survival, necrosis, and apoptosis. Moreover, it influences the functionality of signal transduction and transcription factor molecules. In this study, there was a significant ($p<0.05$) decrease in GST and GSH concentration on induction with CCl_4 (Negative control) compared to the positive control; however, guava fruit and plantain roots di-herbal combo or individually significantly increased GST and GSH compared to the negative control. The most effective treatment was Group 5 (250mg/kg di-herb), which significantly increased GST and GSH compared to the negative control. This suggests that the di-herbal combo of guava fruit and plantain roots confers free radical scavenging property. These results agree with Hung et al. 2006 (55) and Suneetha et al.2010 (56), who showed that CCl_4-treated rats significantly decreased the GSH content in the liver. Nitrite levels were elevated in the negative control, indicating increased oxidative stress and nitric oxide production. Treatments with guava fruit and plantain roots, either alone or in combination, reduced nitrite levels, suggesting a potential ability to attenuate nitric oxide production and oxidative stress. This agrees with the studies by Cavichioli et al. 2022 and Rao et al. 2016 (57).

CCl_4 multiorgan toxicity is linked to a depleted antioxidant defense because of excessive O_2 and H_2O_2 generation (58). It is interesting to note that research has linked liver damage to oxidative stress (59). The increase in SOD, CAT, and MDA activity seen in this study on induction with CCl_4 is consistent with earlier research (49,60) and consequent to its increase in liver tissue in response to the liberation of reactive oxygen species. This suggests that products of free radical reactions might be involved in the pathogenesis and/or progression of medical cholestasis, and that these molecules might attempt to minimise the liver injury. Both SOD and Catalase are antioxidant enzymes that help neutralize reactive oxygen species (ROS). Treatments with guava fruit and plantain roots increased the levels of SOD and Catalase significantly ($p<0.05$) compared to the negative control. This suggests treatments might enhance antioxidant enzyme activity and protect against oxidative stress. Suneetha et al. 2010 (56) and Osman et al. 2011 (45) showed a decrease after induction with CCl_4 in SOD and CAT, and an increase after treating with guava leaves. A study by (Vijayakumar et al. 2008, 61) showed that plantain significantly increased CAT and SOD, respectively. The most effective treatment that significantly decreased SOD and CAT is the di-herbal groups (5 and 6), suggesting the di-herbal combo has a positive synergistic effect, as seen in the result. However, there was a significant decrease in MDA following treatment with group 3 (500mg/kg *P. guajava*) compared with the negative control and even better than silymarin 100mg. This shows it is effective against lipid peroxidation in the hepatocyte membrane. This result agrees with data from Osman et al. 2011, where guava significantly reduces MDA, and there is no significant difference between treatment and positive control (62).

5. Conclusion

The present study demonstrates that *Psidium guajava* fruit extract and *Musa paradisiaca* root extract possess significant hepatoprotective and antioxidant activities against CCl_4-induced liver injury in Wistar rats. Both extracts improved liver function biomarkers, reduced oxidative stress, and enhanced endogenous antioxidant defenses. Notably, the combined di-herbal extract at 500 mg/kg produced the most pronounced protective effects, suggesting a synergistic interaction between the phytochemicals of both plants.

These findings support the traditional use of *P. guajava* and *M. paradisiaca* in managing liver disorders and highlight their potential for development as complementary therapeutic agents. However, further studies incorporating expanded dose–response assessments and molecular investigations are recommended to validate these results and better understand the mechanisms involved.

6. Limitations and Recommendations

This study has several limitations that should be acknowledged. First, the relatively short study duration and modest sample size may have restricted the full expression of biochemical recovery or injury patterns, particularly for biomarkers such as ALP, which have slower clearance kinetics. Longer observation periods with larger cohorts will be essential to determine whether the biochemical alterations observed here persist or resolve with extended treatment.

Second, the study did not investigate the

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molecular mechanisms underlying the observed effects. Although the findings suggest potential hepatoprotective and antioxidant activity, the precise pathways involved remain unclear. Future work should therefore explore oxidative stress signaling, inflammatory mediators, and apoptotic pathways, and evaluate mitochondrial and enzymatic responses using both in vitro and in vivo models.

Third, although the extract was confirmed to contain broad classes of phytochemicals, the specific bioactive constituents responsible for the biological effects were not isolated or quantified. Isolation, purification, and characterization of these active compounds will be crucial for identifying the molecules responsible for the therapeutic effects and for optimizing dosage and treatment regimens.

Additionally, Histopathological evaluation was qualitative; quantitative scoring and photomicrographs were not included. Future studies should incorporate standardized histological grading and molecular pathway investigations.

Finally, total ALP activity was measured without isoenzyme fractionation, making it difficult to distinguish hepatic from extra-hepatic sources of elevation. Isoenzyme profiling should therefore be included in subsequent research to clarify the origin of ALP changes.

Furthermore, comprehensive toxicity studies—both in vitro and in vivo—are recommended to establish the safety profile of *Psidium guajava* and *Musa paradisiaca* extracts at varying concentrations, especially if they are to be considered for therapeutic development.

References

1. Navarro VJ, Senior JR. Drug-Related Hepatotoxicity. New England Journal of Medicine. 2006 Feb 16;354(7):731–9.

2. Willett KL, Roth RA, Walker L. Workshop Overview: Hepatotoxicity Assessment for Botanical Dietary Supplements. Toxicological Sciences. 2004 May;79(1):4–9.

3. Papay JI, Clines D, Rafi R, Yuen N, Britt SD, Walsh JS, et al. Drug-induced liver injury following positive drug rechallenge. Regulatory Toxicology and Pharmacology. 2009 Jun;54(1):84–90.

4. Singh SK, Kesari AN, Rai PK, Watal G. Assessment of glycemic potential ofMusa paradisiaca stem juice. Indian Journal of Clinical Biochemistry. 2007 Sep;22(2):48–52.

5. Cichoż-Lach H. Oxidative stress as a crucial factor in liver diseases. World Journal of Gastroenterology. 2014;20(25):8082.

6. Rudrapal M, Khairnar SJ, Khan J, Dukhyil AB, Ansari MA, Alomary MN, et al. Dietary Polyphenols and Their Role in Oxidative Stress-Induced Human Diseases: Insights Into Protective Effects, Antioxidant Potentials and Mechanism(s) of Action. Frontiers in Pharmacology. 2022 Feb 14;13(1).

7. Caldas APS, Coelho OGL, Bressan J. Cranberry antioxidant power on oxidative stress, inflammation and mitochondrial damage. International Journal of Food Properties. 2018 Jan 1;21(1):582–92.

8. Yau Yan L. ANTIOXIDANT PROPERTIES OF GUAVA FRUIT: COMPARISON WITH SOME LOCAL FRUITS. Sunway Academic Journal [Internet]. 2006 [cited 2025 Sep 22];3:9–20. Available from: http://eprints.sunway.edu.my/28/1/lim3.pdf

9. Hartati R, Nadifan HI, Fidrianny I. Crystal Guava (*Psidium guajava* L. "Crystal"): Evaluation of *In Vitro* Antioxidant Capacities and Phytochemical Content. The Scientific World Journal. 2020 Sep 1;2020:1–7.

10. Bouchoukh, Imane , Hazmoune, Tahar , Boudelaa, Mokhtar, Bensouici, Chawki , Zellagui, Amar . Anticholinesterase and antioxidant activities of foliar extract from a tropical species: *Psidium guajava* L. (Myrtaceae) grown in Algeria. Current Issues in Pharmacy and Medical Sciences. 2019 Sep 1;32(3):160–7.

11. Israel Oyewole O. Hepatorenal Protective Activities of Plantain Root (Musa paradisiaca) on Arsenic-induced Oxidative Damage in Rat. Advances in Biochemistry. 2015;3(2):30.

12. Yadav N, Chattopadhyay S, Pal A, Chanda D, Gupta A. Hepatoprotective effects and safety evaluation of coumarinolignoids isolated from Cleome viscosa seeds. Indian Journal of Pharmaceutical Sciences. 2010;72(6):759.

13. Brand-Williams W, Cuvelier ME, Berset C. Use of a Free Radical Method to Evaluate Antioxidant Activity. LWT - Food Science and Technology [Internet]. 1995 Jan [cited 2025 Sep 22];28(1):25–30. Available from: https://www.sciencedirect.com/science/article/pii/S0023643895800085

14. Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C. Antioxidant activity applying an improved ABTS radical cation decolorization assay. Free Radical Biology and Medicine. 1999 May;26(9-10):1231–7.

15. Marcocci L, Maguire JJ, Droy-Lefaix MT, Packer L. The nitric oxide-scavenging properties of Ginkgo biloba extract EGb 761. Biochemical and Biophysical Research Communications [Internet]. 1994 Jun 15 [cited 2025 Sep 22];201(2):748–55. Available from: https://pubmed.ncbi.nlm.nih.gov/8003011/

16. Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, Linder T, Wawrosch C, Uhrin P, et al. Discovery and resupply of pharmacologically active plant-derived natural products: A review. Biotechnology Advances. 2015 Dec;33(8):1582–614.

17. Yakubu MT, Sunmonu TO, Lewu FB, Ashafa AOT, Olorunniji FJ, Eddouks M. Medicinal Plants Used in the Management of Diabetes Mellitus 2015. Evidence-Based Complementary and Alternative Medicine. 2015;1–2.

18. Bamidele TO, Enemali MO, Ijeomah AU. HEPATOPROTECTIVE ACTIVITY OF ETHANOL EXTRACT OF PURPLE ONION BULB (Allium cepa Linn) ON CCl4 INDUCED HEPATOTOXICITY IN WISTAR RATS [Internet]. Ftstjournal.com. FUW Trends in Science & Technology Journal; 2018 [cited 2025 Sep 22]. Available from: https://www.ftstjournal.com/

19. Amutha K, Selvakumari U. Wound healing activity of methanolic stem extract ofMusa paradisiaca Linn.(Banana) in Wistar albino rats. International Wound Journal. 2014 Sep 16;13(5):763–7.

20. Atik N, Muda I, Rahmadi AR, Achadiyani A, Djunaedi DD. PHYTOCHEMICAL SCREENING AND HISTOLOGY APPEARANCE OF ACUTE ORAL TOXICITY STUDY ON ETHANOL EXTRACT OF PSIDIUM GUAJAVA LINN. FRUIT IN MICE. Asian Journal of Pharmaceutical and Clinical Research [Internet]. 2019 Jan 7 [cited 2025 Sep 22];12(1):351. Available from: https://repository.unmul.ac.id/bitstream/handle/123456789/8407/document(2).pdf?sequence=1

21. Saeed A, Marwat MS, Shah AH, Na R, Zain-Ul-Abidi S, Akbar S, et al. Assessment of total phenolic and flavonoid contents of selected fruits and vegetables. Indian Journal of Traditional Knowledge (IJTK), [Internet]. 2019;18(4):686–93. Available from: http://op.niscpr.res.in/index.php/IJTK/article/view/28999

22. Pellegrini N, Serafini M, Colombi B, Del Rio D, Salvatore S, Bianchi M, et al. Total antioxidant capacity of plant foods, beverages and oils consumed in Italy assessed by three different in vitro assays. The Journal of Nutrition [Internet]. 2003 Sep 1;133(9):2812–9. Available from: https://pubmed.ncbi.nlm.nih.gov/12949370/

23. Thuaytong W, Anprung P. Bioactive Compounds and Prebiotic Activity in Thailand-Grown Red and White Guava Fruit (Psidium guajava L.). Food Science and Technology International. 2011 Jun;17(3):205–12.

24. Lin CY, Yin MC. Renal Protective Effects of Extracts from Guava Fruit (Psidium guajava L.) in Diabetic Mice. Plant Foods for Human Nutrition. 2012 May 12;67(3):303–8.

25. Odubanjo VO, Shodehinde SA, Adedeji FA, Daniel JA, Olayinka AA, Akinnusi PA, et al. Starch Content, Antioxidant Activity and Inhibition of Starch Hydrolyzing Enzymes by Unripe Musa paradisiaca and Musa acuminata. Science Letters. 2022 Jun 14;10(2):67–75.

26. Oboh, G. and Rocha, J. (2007) Antioxidant in Foods A New Challenge for Food Processors. In Leading Edge Antioxidants Research, Nova Science Publishers Inc., New York, 35-64. - References - Scientific Research Publishing [Internet]. Scirp.org. 2020 [cited 2025 Sep 22]. Available from: https://www.scirp.org/reference/referencespapers?referenceid=2747009

27. Gull J, Sultana B, Anwar F, Naseer R, Ashraf M, Ashrafuzzaman M. Variation in Antioxidant Attributes at Three Ripening Stages of Guava (Psidium guajava L.) Fruit from Different Geographical Regions of Pakistan. Molecules. 2012 Mar 14;17(3):3165–80.

28. Lim, Y. Y., Lim, T. T., & Tee, J. J. Antioxidant properties of guava fruit: comparison with some local fruits. Sunway Academic Journal ; 2006.

Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
http://dx.doi.org/10.21622/AMPDR.2026.06.1.1693

29. Abdel Ghany TM, Ganash M, Alawlaqi MM, Al-Rajhi AMH. Antioxidant, Antitumor, Antimicrobial Activities Evaluation of Musa paradisiaca L. Pseudostem Exudate Cultivated in Saudi Arabia. BioNanoScience [Internet]. 2018 Dec 6;9(1):172–8. Available from: https://link.springer.com/article/10.1007/s12668-018-0580-x

30. SOWMYA BH, ANANDHI DU. Quantification of Total Phenolics, Flavonoids and Evaluation of in vitro Free Radical Scavenging Activities in Psidium guajava L. Indian Journal of Pharmaceutical Sciences. 2020;82(4).

31. Ademiluyi AO, Oboh G, Ogunsuyi OB, Oloruntoba FM. A comparative study on antihypertensive and antioxidant properties of phenolic extracts from fruit and leaf of some guava (Psidium guajava L.) varieties. Comparative Clinical Pathology [Internet]. 2016 Mar 1;25(2):363–74. Available from: https://link.springer.com/article/10.1007%2Fs00580-015-2192-y

32. Ashok Kumar BS, Lakshman K, Jayaveea KN, Sheshadri Shekar D, Saleemulla Khan, Thippeswamy BS, et al. Antidiabetic, antihyperlipidemic and antioxidant activities of methanolic extract of Amaranthus viridis Linn in alloxan induced diabetic rats. Experimental and Toxicologic Pathology. 2012 Jan;64(1-2):75–9.

33. Loganayaki N, Rajendrakumaran D, Manian S. Antioxidant capacity and phenolic content of different solvent extracts from banana (Musa paradisiaca) and mustai (Rivea hypocrateriformis). Food Science and Biotechnology. 2010 Oct;19(5):1251–8.

34. Thaipong K;Boonprakob U;Cisneros-Zevallos L;Byrne DH. Hydrophilic and lipophilic antioxidant activities of guava fruits. The Southeast Asian journal of tropical medicine and public health [Internet]. 2018;36 Suppl 4. Available from: https://pubmed.ncbi.nlm.nih.gov/16438219/

35. Chen HY, Yen GC. Antioxidant activity and free radical-scavenging capacity of extracts from guava (Psidium guajava L.) leaves. Food Chemistry. 2007 Jan;101(2):686–94.

36. Azofeifa G, Quesada S, Boudard F, Morena M, Cristol JP, Pérez AM, et al. Antioxidant and Anti-inflammatory in Vitro Activities of Phenolic Compounds from Tropical Highland Blackberry (Rubus adenotrichos). Journal of Agricultural and Food Chemistry. 2013 Jun 10;61(24):5798–804.

37. Medina, M., et al. (2014) Health Promotion and Chronic Disease Prevention What Are Family Health Teams Doing Saúde Debate, 38, 69-82. - References - Scientific Research Publishing [Internet]. Scirp.org. 2016. Available from: https://www.scirp.org/reference/referencespapers?referenceid=1948011

38. Kumar S, Pandey AK. Chemistry and Biological Activities of Flavonoids: An Overview. The Scientific World Journal. 2013;2013(162750):1–16.

39. Aparadh VT, Naik VV, Karadge BA. ANTIOXIDATIVE PROPERTIES (TPC, DPPH, FRAP, METAL CHELATING ABILITY, REDUCING POWER AND TAC) WITHIN SOME CLEOME SPECIES [Internet]. 2012 [cited 2025 Sep 22]. Available from: https://rosa.uniroma1.it/rosa04/annali_di_botanica/article/view/9958

40. Ibrahim M, Muhammad N, Naeem M, Deobald AM, Kamdem JP, Rocha JBT. In vitro evaluation of glutathione peroxidase (GPx)-like activity and antioxidant properties of an organoselenium compound. Toxicology in Vitro. 2015 Aug;29(5):947–52.

41. Liang N, Kitts D. Antioxidant Property of Coffee Components: Assessment of Methods that Define Mechanisms of Action. Molecules. 2014 Nov 19;19(11):19180–208.

42. Adebayo A. Protective Properties of Citrullus lanatus on Carbon Tetrachloride Induced Liver Damage in Rats. European Journal of Medicinal Plants. 2014;4(8):979–89.

43. Hopkins PN, Wu L, Hunt SC, James BC, Vincent G, Williams RR. Higher Serum Bilirubin Is Associated With Decreased Risk for Early Familial Coronary Artery Disease. 1996 Feb 1;16(2):250–5.

44. Nirmala M, Girija K, Lakshman K, Divya T. Hepatoprotective activity of Musa paradisiaca on experimental animal models. Asian Pacific Journal of Tropical Biomedicine. 2012 Jan;2(1):11–5.

45. Osman M, Ahmed M, Mahfouz S, Elaby S. Biochemical Studies on the Hepatoprotective Effects of Pomegranate and Guava Ethanol Extracts. New York Science Journal. 2011;4(3):27–41.

46. Khizar A, Ghazala HR, Hina Z, Tariq MJ. Evaluation of Hepatic activity of various morphological

parts of Musa paradisiaca L. African Journal of Pharmacy and Pharmacology. 2016 May 22;10(19):419–29.

47. Mohan M, Shashank B, Priya A. Protective effect of Psidium guajava L. leaves ethanolic extract on doxorubicin-induced nephrotoxicity in rats. Indian Journal of Natural Products and Resources [Internet]. 2014;5(2):129–33. Available from: https://nopr.niscpr.res.in/bitstream/123456789/29070/1/IJNPR%205%282%29%20129-133.pdf

48. Rahmat A, Bakar M, Hambali Z. The effects of guava (*Psidium guajava) consumption on total antioxidant and lipid profile in normal male youth*. African Journal of Food, Agriculture, Nutrition and Development. 2011 Nov 9;6(2).

49. Roy CK, Das AK. Comparative evaluation of different extracts of leaves of Psidium guajava Linn. for hepatoprotective activity. Pakistan journal of pharmaceutical sciences [Internet]. 2010 Jan;23(1):15–20. Available from: https://pubmed.ncbi.nlm.nih.gov/20067861/

50. Sambo N, Garba SH, Timothy H. Effect of the aqueous extract of *Psidium guajava* on erythromycin-induced liver damage in rats. Nigerian Journal of Physiological Sciences [Internet]. 2010 Mar 16;24(2):171–6. Available from: https://www.ajol.info/index.php/njps/article/view/52928

51. Iluz-Freundlich D, Zhang M, Uhanova J, Minuk GY. The relative expression of hepatocellular and cholestatic liver enzymes in adult patients with liver disease. Annals of Hepatology. 2020 Mar;19(2):204–8.

52. Lala V, Minter DA, Zubair M. Liver Function Tests [Internet]. Nih.gov. StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482489/

53. Karim Samy El-Said, Hussein S, Alrashdi BM, Mahmoud HA, Ibrahim MA, Elbakry M, et al. Musa sp. Leaves Extract Ameliorates the Hepato-Renal Toxicities Induced by Cadmium in Mice. Molecules. 2022 Jan 16;27(2):559–9.

54. Shady NH, Abdullah HS, Maher SA, Albohy A, Elrehany MA, Mokhtar FA, et al. Antiulcer Potential of Psidium guajava Seed Extract Supported by Metabolic Profiling and Molecular Docking. Antioxidants. 2022 Jun 23;11(7):1230.

55. Hung MY, Timothy Yu-Chi Fu, Ping Hsiao Shih, Lee CP, Yen GC. Du-Zhong (Eucommia ulmoides Oliv.) leaves inhibits CCl4-induced hepatic damage in rats. 2006 Aug 1;44(8):1424–31.

56. Suneetha B, Prasad K, Sujatha D.

57. Rao M, Ahmad BA, Mohd KS. IN VITRO NITRIC OXIDE SCAVENGING AND ANTI INFLAMMATORY ACTIVITIES OF DIFFERENT SOLVENT EXTRACTS OF VARIOUS PARTS OF Musa paradisiaca. Malaysian Journal of Analytical Science [Internet]. 2016 Jan 1;20(5):1191–202. Available from: https://www.researchgate.net/publication/327344928_IN_VITRO_NITRIC_OXIDE_SCAVENGING_AND_ANTI_INFLAMMATORY_ACTIVITIES_OF_DIFFERENT_SOLVENT_EXTRACTS_OF_VARIOUS_PARTS_OF_Musa_paradisiaca

58. Marchionatti AM, Perez AV, Diaz de Barboza GE, Pereira BM, Tolosa de Talamoni NG. Mitochondrial dysfunction is responsible for the intestinal calcium absorption inhibition induced by menadione. Biochimica et biophysica acta [Internet]. 2008 Feb;1780(2):101–7. Available from: https://pubmed.ncbi.nlm.nih.gov/18053815/

59. Farombi E, Akintunde J, Nzute N, Adedara I, Arojojoye O. Municipal landfill leachate induces hepatotoxicity and oxidative stress in rats. Toxicology and Industrial Health. 2011 Sep 21;28(6):532–41.

60. Sirisha K, Goverdhan P, Hima G, Madhavi M. Kalam Sirisha et al / Int. J Pharm Phytopharmacol Res. 2013;3(3):190–5.

61. Vijayakumar S, Presannakumar G, Vijayalakshmi NR. Antioxidant activity of banana flavonoids. Fitoterapia [Internet]. 2008 Jun;79(4):279–82. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0367326X08000464

62. Osman M, Ahmed M, Mahfouz S, Elaby S. Biochemical Studies On The Hepatoprotective Effects Of Pomegranate And Guava Ethanol Extracts. New York Science Journal [Internet]. 2011;4(3):27–39. Available from: https://www.sciencepub.net/newyork/ny0403/04_4647ny0403_27_39.pdf

63. Mourelle M, Muriel P, Favari L, Franco TT. PREVENTION OF CCL_4-INDUCED LIVER CIRRHOSIS BY SILYMARIN. 1989 May 6;3(3):183–91.

64. Ramachandra R, Subramanian S, Govindasamy S. Protective role of silymarin on

Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
http://dx.doi.org/10.21622/AMPDR.2026.06.1.1693

liver damage induced by carbon tetrachloride in rats. Indian J Exp Biol. 2007;45:1053–7.

65. Abenavoli L, Izzo AA, Milić N, Cicala C, Santini A, Capasso R. Milk thistle (Silybum marianum): A concise overview on its chemistry, pharmacological, and nutraceutical uses in liver diseases. Phytotherapy Research. 2018 Aug 6;32(11):2202–13.