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Hepatorenal Effects of *Kalanchoe pinnata* in High-Fat Diet–Induced Hyperlipidaemic Rats

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ABSTRACT

Background and Objective: Hyperlipidaemia is a critical metabolic disorder that predisposes individuals to hepatic and renal dysfunction through lipid accumulation, oxidative stress, and inflammation. Although *Kalanchoe pinnata* has been widely used in traditional medicine for treating various ailments, its role in protecting hepatic and renal function under high-fat dietary stress remains underexplored. This study investigated the effect of *Kalanchoe pinnata* on liver and renal biomarkers in high-fat diet-induced hyperlipidaemic albino rats. **Materials and Methods:** Thirty female albino rats (200-300 g) were randomly assigned into five groups (n = 6): normal control, negative control (HFD only), positive control (HFD+200 mg/kg simvastatin), and two treatment groups receiving 200 and 400 mg/kg *K. pinnata* extract, respectively. Hyperlipidaemia was induced using a high-fat diet composed of cholesterol (2%), cholic acid (1%), vanaspati ghee (20%), and coconut oil (6%). Treatments were administered orally for 21 days. Serum levels of ALT, AST, ALP, total protein, albumin, total and conjugated bilirubin, urea, and creatinine were measured on days 7, 14, and 21. Data were analyzed using IBM SPSS v27 with Tukey's *post hoc* test for multiple comparisons. A significance level of $p<0.05$ was considered statistically significant. **Results:** In the negative control group, liver enzymes were significantly elevated by day 21: ALT (7.05 U/L), AST (26.5 U/L), and ALP (55.0 U/L), while total protein (66 g/L) and albumin (37 g/L) were reduced. Treatment with 400 mg/kg *K. pinnata* significantly reduced ALT (11.9 U/L), AST (29.0 U/L), and ALP (53.5 U/L) ($p<0.05$), and restored total protein (78.5 g/L) and albumin (46 g/L). Similarly, total bilirubin and conjugated bilirubin were reduced from 5.9 µmol/L and 2.75 µmol/L in the HFD group to 6.2 µmol/L and 3.25 µmol/L, respectively, in the 400 mg/kg group. Renal biomarkers (urea and creatinine) showed no statistically significant differences among all groups across all time points ($p>0.05$), indicating no nephrotoxic effects. The 400 mg/kg dose consistently produced outcomes comparable to the simvastatin-treated group. **Conclusion:** *Kalanchoe pinnata* demonstrated potent, dose-dependent hepatoprotective effects in hyperlipidaemic rats, as evidenced by significant improvements in liver enzymes, protein synthesis markers, and bilirubin levels. The extract exhibited no signs of nephrotoxicity. These findings support the traditional use of *K. pinnata* and highlight its potential for further development as a complementary therapy in the management of lipid-associated hepatic dysfunction.

KEYWORDS

Kalanchoe pinnata, hyperlipidaemia, liver biomarkers, renal biomarkers, medicinal plants

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INTRODUCTION

Kalanchoe pinnata (syn. *Bryophyllum pinnatum*), a succulent plant belonging to the Crassulaceae family, is widely distributed in tropical and subtropical regions and is popularly referred to as the "'wonder plant" or "life plant" due to its ethnopharmacological relevance. Traditionally, it has been employed to treat a wide array of ailments, including wounds, ulcers, infections, and inflammatory conditions. Phytochemical analyses reveal the presence of bioactive compounds such as flavonoids, alkaloids, bufadienolides, triterpenes, glycosides, and phenolic acids, which contribute to its broad spectrum of pharmacological actions[1].

Preclinical studies have demonstrated that *K. pinnata* exhibits hepatoprotective and nephroprotective properties. Bopda *et al.*[2] have reported that ethanolic leaf extracts significantly reduced serum ALT levels and preserved hepatic histoarchitecture in CCl_4-induced liver injury. Similarly, Yadav and Dixit[3] confirmed its hepatocellular protective action through reductions in serum bilirubin and SGPT levels in rats. These findings suggest that *K. pinnata* may exert therapeutic effects through membrane stabilization, antioxidant activity, and enzymatic modulation.

In addition to its hepatotropic benefits, *K. pinnata* has also been reported to ameliorate nephrotoxicity. Experimental administration of *K. pinnata* attenuated gentamicin-induced renal damage, as evidenced by decreased urea and creatinine levels and reduced histological lesions such as glomerular congestion and tubular edema[4].

Hyperlipidaemia, often resulting from diets rich in saturated fats, is a pathological condition that elevates plasma cholesterol and triglyceride levels. It is a known risk factor for cardiovascular diseases, type 2 diabetes, hepatic steatosis, and nephropathy[5]. Persistent hyperlipidaemia has been linked to oxidative stress, lipid peroxidation, and chronic inflammation, leading to hepatic and renal tissue injury[6]. These pathological changes are typically reflected in alterations of biochemical biomarkers including Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), and bilirubin for liver function, as well as serum creatinine and urea for renal function[7].

Despite numerous pharmacological claims surrounding *K. pinnata*, scientific validation of its efficacy in hyperlipidaemia-induced liver and kidney dysfunction remains insufficient, particularly in *in vivo* models mimicking high-fat dietary exposures. Existing literature has not fully explored its therapeutic potential in modulating biochemical markers of liver and renal health under such metabolic stress.

Therefore, the current study aims to evaluate the effect of *Kalanchoe pinnata* on liver and renal biomarkers in high-fat diet-induced hyperlipidaemic albino rats. This research intends to provide empirical evidence for the plant's protective role in diet-induced hepatorenal dysfunction, thereby expanding its pharmacological profile and supporting its traditional medicinal use.

MATERIALS AND METHODS

Plant collection, preparation and extraction: Fresh leaves of *Kalanchoe pinnata* were harvested in September, 2022 from the Emoh community in Abua/Odual Local Government Area, Rivers State, Nigeria. Only mature leaves without lesions were selected. The leaves were transported in plastic wrap to prevent desiccation and degradation. Botanical identification and authentication were conducted at the Department of Plant Science and Biotechnology, Rivers State University, Nigeria, and a voucher specimen was deposited under voucher number SUK-5279.

A total of 3.593 kg of *K. pinnata* leaves were cleaned and pulverized using a manual grinder. The maceration was performed by soaking the ground material in 196 mL of distilled water for 24 hrs at room temperature. The extract was filtered using Whatman No. 1 filter paper and then lyophilized. The resulting dry extract was stored in airtight containers and reconstituted in distilled water to the desired concentrations for oral administration, by previously established procedures[8].

Drug collection: Simvastatin tablets (used as a standard reference drug) were purchased from a certified pharmacy at Mile 3 Market, Port Harcourt, Rivers State, Nigeria. Appropriate dosages were calculated based on body weight and dissolved in distilled water for oral delivery.

Experimental animals and design: Thirty healthy female albino rats weighing between 200-300 g were obtained from the animal house of Rivers State University, Port Harcourt, Nigeria. The animals were housed in clean, ventilated stainless steel cages under standard laboratory conditions: a 12 hrs light/dark cycle, temperature of 22±2°C, and relative humidity of 55±5%. Rats were acclimatized for two weeks before experimentation and fed with commercially available rat chow (Top Feed®, Nigeria), composed of soybean meal, vegetable oil, maize grains, salt, limestone, di-calcium phosphate, vitamins, and mineral premix.

After acclimatization, rats were randomly assigned into five groups (n = 6 rats per group) as follows:

- **Group 1 (Normal control):** Standard feed+water (no treatment)
- **Group 2 (Negative control):** High-fat diet (HFD)+standard feed+water
- **Group 3 (Positive control):** HFD+200 mg/kg Simvastatin
- **Group 4 (Low dose *K. pinnata*):** HFD+200 mg/kg *K. pinnata* extract
- **Group 5 (High dose *K. pinnata*):** HFD+400 mg/kg *K. pinnata* extract

Simvastatin and *K. pinnata* extracts were administered orally using an intragastric feeding needle daily for 21 consecutive days.

Induction of hyperlipidemia: Hyperlipidaemia was induced in rats by feeding them a high-fat diet for 15 days before treatment initiation. The diet consisted of cholesterol (2%), cholic acid (1%), vanaspati ghee (20%), and coconut oil (6%) mixed in a ratio of 3:1 (v/v) to simulate atherogenic stress. Successful induction of hyperlipidaemia was confirmed by measuring serum lipid profiles using standard lipid assays.

Sample collection: Blood samples were collected from the tail vein of each rat at days 7, 14, and 21 to monitor progressive biochemical changes. On day 21, the rats were weighed and euthanized by placing them in a desiccator, and final cardiac blood samples were obtained. Serum was separated by centrifugation and stored at -20°C for biochemical analysis.

Statistical analysis of data: The IBM SPSS version 27.0 was used for statistical analysis. Results were expressed as Mean±Standard Deviation (SD). Statistical comparisons among groups were performed using One-way Analysis of Variance (ANOsVA), followed by Tukey's *post hoc* test for multiple comparisons. Statistical significance was set at $p \leq 0.05$.

Ethical statement: Handling and treatment of the rats were in conformance with the guidelines of the National Institute of Health for Laboratory Animal Care and Use. All animals in this study adhered to the Institutional Animal Ethical Committee according to guidelines given by the Committee for Control and Supervision of Experiments on Animals (CPCSEA). This study received approval from the Ethical Committee of Rivers State University.

RESULTS AND DISCUSSION

Effect of *Kalanchoe pinnata* on liver weight: From the result in Fig. 1, liver weight increased in the negative control group, from 5.10 g at day 7 to 5.36 g by day 21, compared to the normal control group, which maintained lower liver weights throughout (4.65 to 4.06 g). The 200 mg/kg and 400 mg/kg *K. pinnata* group exhibited a marked reduction by day 21 (4.85 g), down from 7.16 g at day 14. These findings indicate that *K. pinnata* may exert hepatorestorative effects in a dose- and time-dependent manner. Similar hepatoprotective outcomes have been reported in studies using *Kalanchoe pinnata*, where its antioxidant and anti-inflammatory phytochemicals, such as flavonoids and phenolic acids, contributed to liver tissue recovery in hepatotoxic models[4].

Effect of *Kalanchoe pinnata* Alanine Aminotransferase (ALT) levels: As shown in Fig. 2, ALT levels were highest in the 400 mg/kg *K. pinnata* group, peaking at 15.2 U/L on day 7 and reducing to 11.9 U/L by day 21. In contrast, the positive control recorded a continuous decline from 12.5 to 4.6 U/L across the same period. The negative control dropped from 11.35 to 7.05 U/L, suggesting partial spontaneous resolution. These results suggest that while *K. pinnata* did not suppress ALT more effectively than the standard treatment, it contributed to a gradual restoration of hepatocyte membrane integrity. A comparable reduction in ALT activity due to plant extract therapy has been reported by Son *et al.*[9] which attributed the hepatoprotective effects to the antioxidant-rich profile of medicinal plants like *Vernonia amygdalina* and *Piper guineense*.

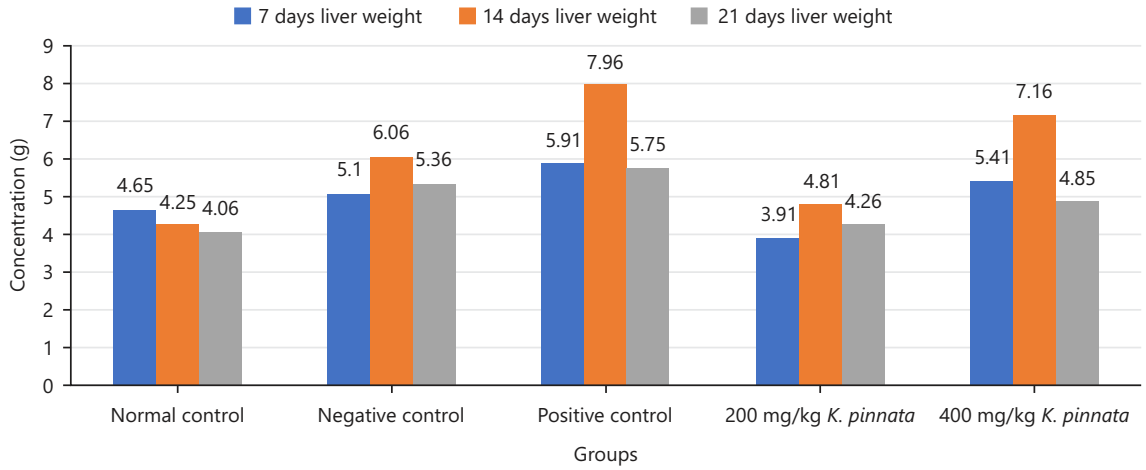

Fig. 1: Liver weights of experimental rats treated with *K. pinnata* for 7, 14 & 21 days

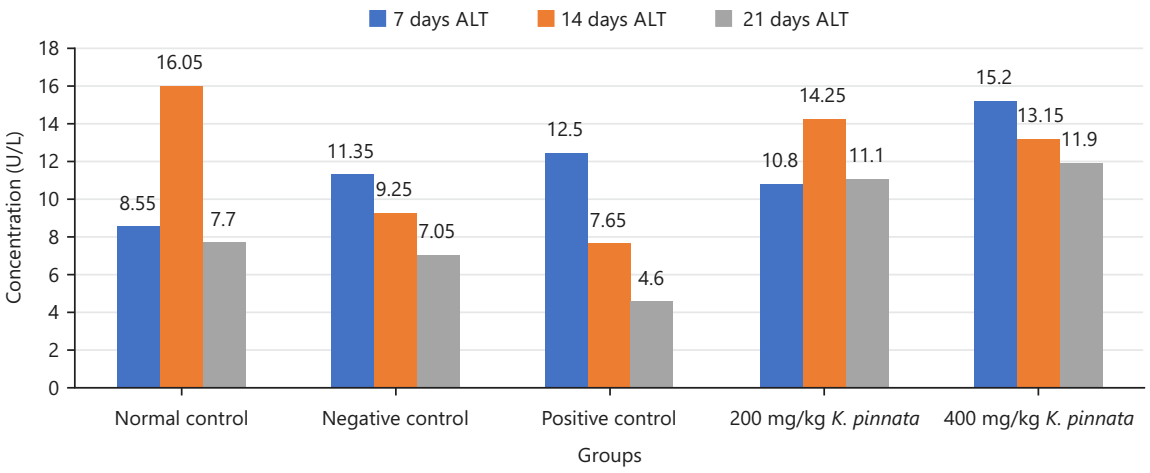

Fig. 2: ALT concentrations of experimental rats treated with *K. pinnata* for 7, 14 & 21 days

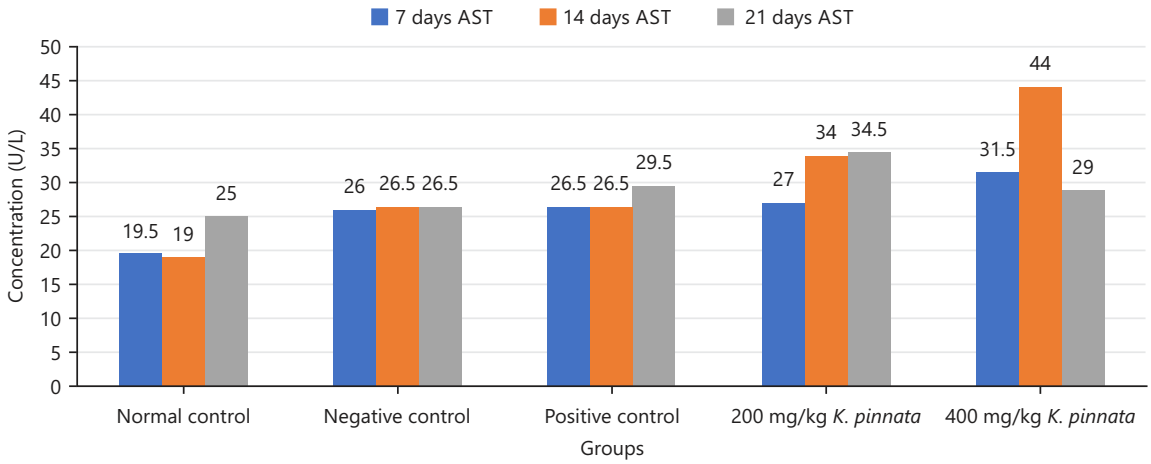

Fig. 3: AST concentrations of experimental rats treated with *K. pinnata* for 7, 14 & 21 days

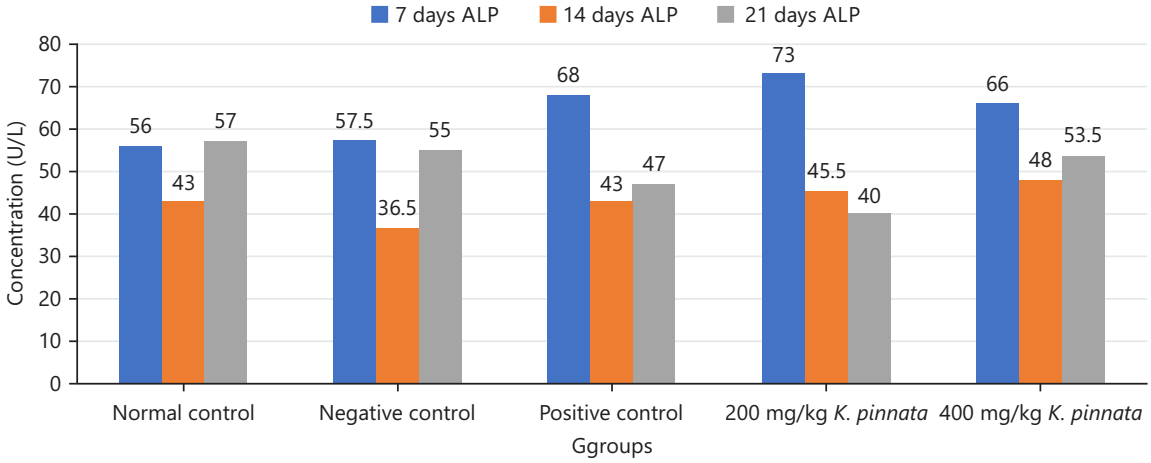

Fig. 4: ALP concentrations of experimental rats treated with *K. pinnata* for 7, 14 & 21 days

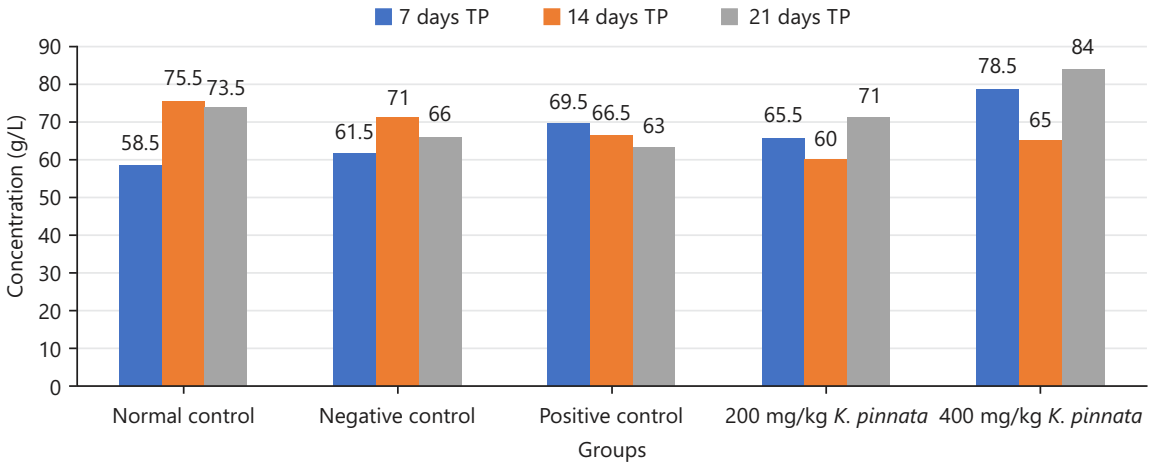

Fig. 5: Total Protein concentrations of experimental rats treated with *K. pinnata* for 7, 14 & 21 days

Effect of *Kalanchoe pinnata* on Aspartate Aminotransferase (AST) levels: According to Fig. 3, AST values were consistently elevated in the negative control group (26-26.5 U/L), while the 400 mg/kg *K. pinnata* group showed an initial surge to 44 U/L at day 14, followed by a reduction to 29 U/L at day 21. This suggests that although AST elevation initially worsened, prolonged treatment may help reverse hepatic stress. Tokofai *et al.*[10] showed that polyphenolic plant extracts ameliorate AST levels in hepatotoxic models, supporting the relevance of *K. pinnata* in hepatoprotection.

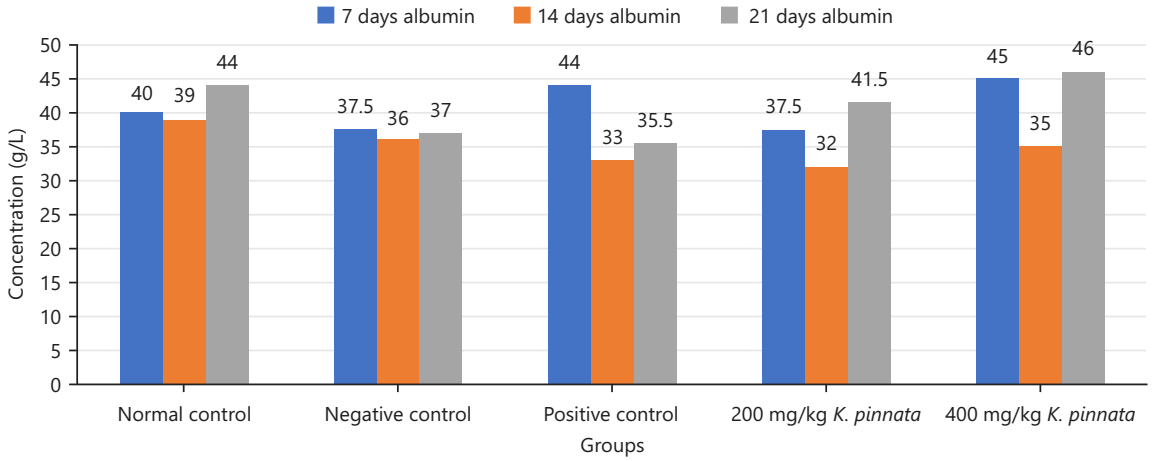

Fig. 6: Serum Albumin concentrations of experimental rats treated with *K. pinnata* for 7, 14 and days

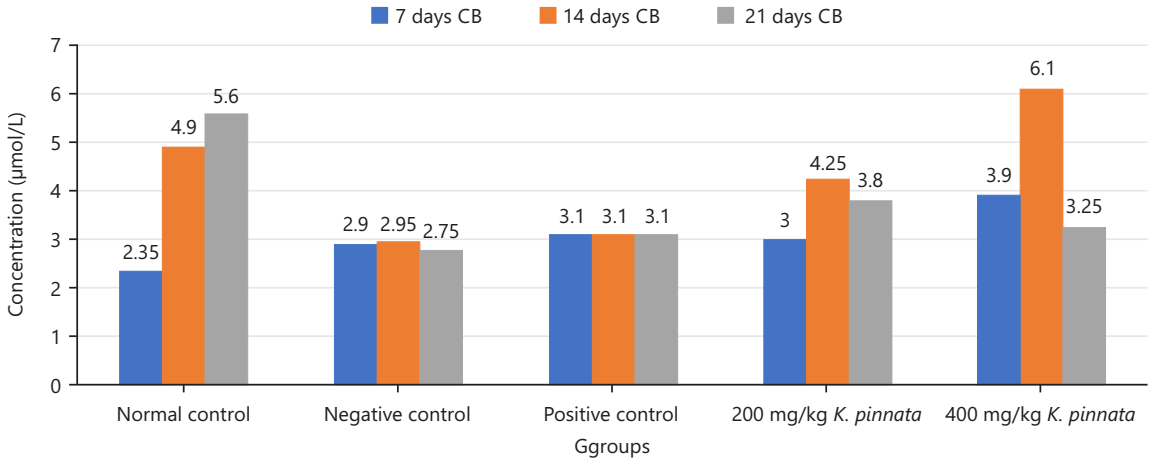

Fig. 7: Conjugated bilirubin concentrations of experimental rats treated with *K. pinnata* for 7, 14 and days

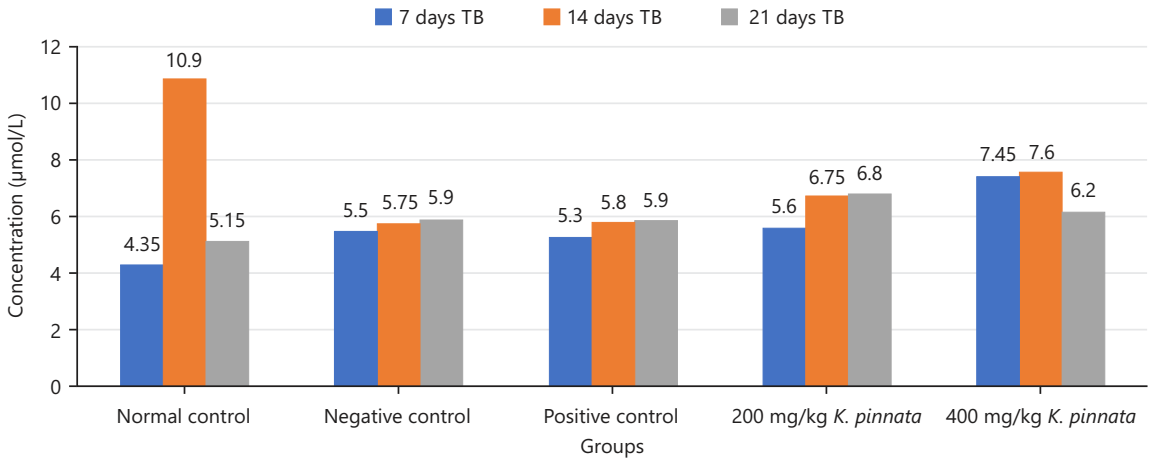

Fig. 8: Total bilirubin concentrations of experimental rats treated with *K. pinnata* for 7, 14 and 21 days

Effect of *Kalanchoe pinnata* on Alkaline Phosphate (ALP) levels: Figure 4 demonstrates that ALP levels in the negative control group hovered between 55-57.5 U/L. The 400 mg/kg *K. pinnata* group showed a drop from 66 U/L at day 7 to 53.3 U/L by day 21, closely mirroring normal control values (57 U/L at day 21). These results suggest that *K. pinnata* may enhance bile flow and reduce cholestatic stress. This agrees with the findings[11] which reported ALP normalization with plant-based flavonoids acting as bile duct modulators.

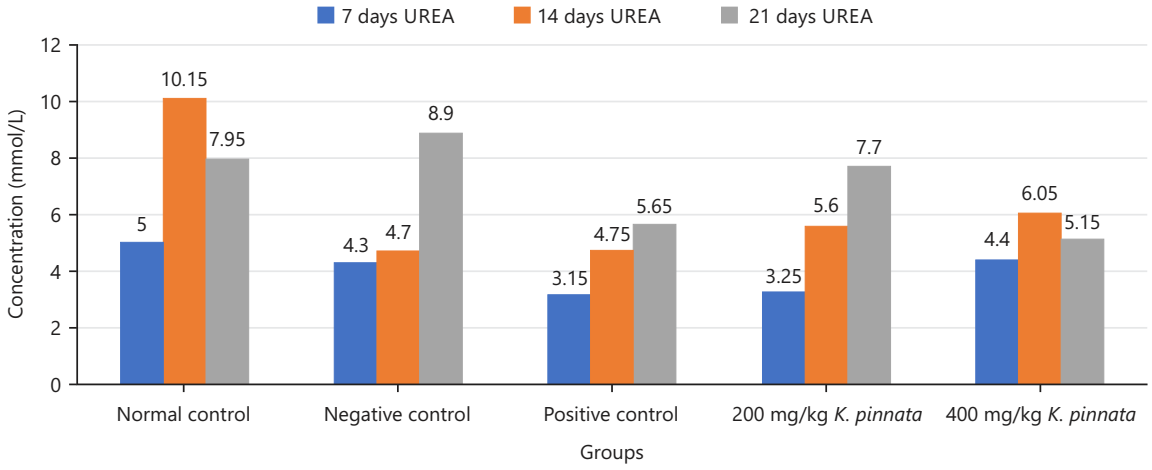

Fig. 9: Effect of *Kalanchoe pinnata* on urea biomarkers in high-fat diet-induced hyperlipidemic albino rats after 7, 14 and 21 days

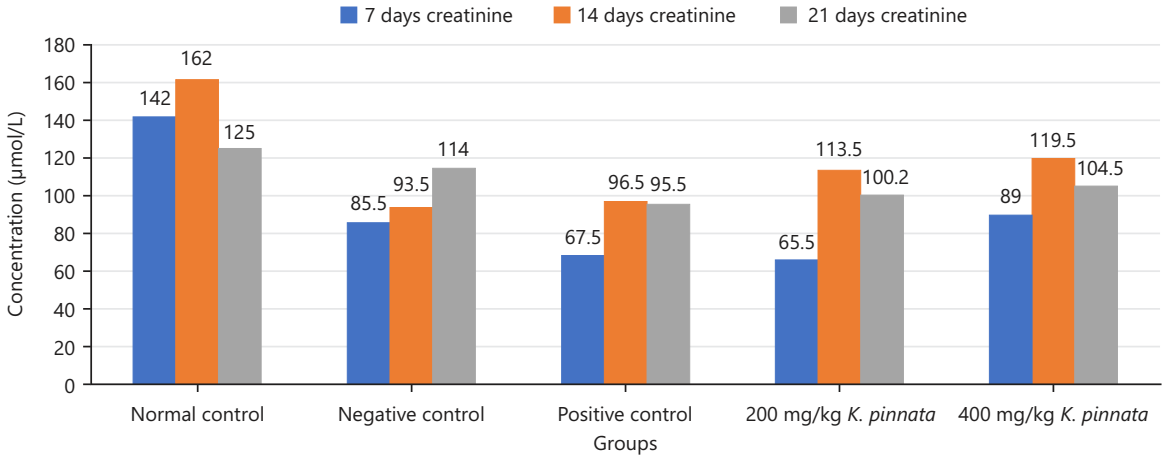

Fig. 10: Effect of *Kalanchoe pinnata* on creatinine biomarkers in high-fat diet-induced hyperlipidemic albino rats after 7, 14, and 21 days

Effect of *Kalanchoe pinnata* on total protein concentration: From Fig. 5, total protein levels were highest in the 400 mg/kg group by day 21 (84 g/L), surpassing both the normal control (73.5 g/L) and positive control (63 g/L). This increase suggests enhanced hepatic synthetic function, supporting the potential of *K. pinnata* to promote hepatocyte regeneration. Botanical extracts containing saponins and flavonoids restore liver protein synthesis via their anti-inflammatory pathways[12].

Effect of *Kalanchoe pinnata* on albumin levels: As shown in Fig. 6, serum albumin decreased in the negative control group to 37 g/L by day 21, while it improved in the 400 mg/kg group to 46 g/L, exceeding the normal control (44 g/L). These findings affirm the capacity of *K. pinnata* to stimulate albumin synthesis and restore liver protein metabolism. This is supported by a previous study[13] that reported improved albumin levels in streptozotocin-induced hepatic injury after phytochemical-rich extract treatment.

Effect of *Kalanchoe pinnata* on conjugated bilirubin (CB) levels: Figure 7 shows that conjugated bilirubin remained low in the negative control group (~2.75 µmol/L) but peaked in the 400 mg/kg group at day 14 (6.1 µmol/L) before its reduction to 3.25 µmol/L at day 21. This reduction suggests enhanced conjugation and excretion mechanisms, possibly driven by phytochemicals stimulating detoxifying enzymes. This aligns with earlier findings indicating that flavonoid-based plant extracts promote detoxification enzyme activity and bilirubin clearance[14].

Effect of *Kalanchoe pinnata* on total bilirubin (TB) levels: The TB levels, as shown in Fig. 8, were highest in the 400 mg/kg group on day 7 (7.45 g/L) and dropped to 6.2 g/L by day 21. While this remained higher than the normal control (5.15 g/L), the downward trend suggests partial hepatic recovery. Similar trends were observed in a study[4], which found that phytochemicals enhance bilirubin metabolism and membrane stabilization in hepatic injury.

Effect of *Kalanchoe pinnata* on urea and creatinine levels: From the trend observed in Fig. 9 and 10, the 400 mg/kg group showed fluctuating urea levels: 4.4 g/L at day 7, a peak at 10.15 g/L by day 14, and a reduction to 7.95 g/L by day 21. Although this suggests some renal stress mid-treatment, the final value is close to the negative control (7.7 g/L), indicating that *K. pinnata* does not induce chronic nephrotoxicity. Creatinine values also showed no significant deviation across groups. As shown in Fig. 10, the 400 mg/kg group remained relatively stable (89 → 104.5 g/L), statistically similar to the normal control group (125 g/L at day 21). The data confirm the renal safety of *K. pinnata*, consistent with nephroprotective findings in related phytochemical studies[15,16].

CONCLUSION

This study demonstrates that *Kalanchoe pinnata* possesses significant hepatoprotective and non-nephroprotective effects in a high-fat diet-induced hyperlipidaemic rat model. Repeated administration of *K. pinnata* at both 200 mg/kg and 400 mg/kg doses led to dose- and time-dependent restoration of key hepatic biomarkers, including ALT, AST, ALP, total protein, albumin, and bilirubin, suggesting improved hepatic integrity and function. Notably, the 400 mg/kg treatment group showed performance comparable to the standard drug group (Simvastatin) in several parameters, especially by day 21. Renal markers such as serum urea and creatinine showed no significant elevations in the treatment groups, indicating that *K. pinnata* did not exert nephrotoxic effects at the administered doses. While the renal parameters did not show marked improvement, maintaining near-normal levels supports a nephron-neutral or renally safe profile. These findings validate the traditional use of *K. pinnata* in the management of metabolic and organ-related disorders. The observed biochemical modulations are likely attributable to its rich content of flavonoids, saponins, and other bioactive compounds known for antioxidant, membrane-stabilizing, and anti-inflammatory activities.

SIGNIFICANCE STATEMENT

This study shows that *Kalanchoe pinnata* has the possibility of use as adjunct therapy for hyperlipidaemia and its effects on the liver and kidney and is an addition to research on the therapeutic potencies of plant. Further research is recommended to elucidate the mechanisms of action of *Kalanchoe pinnata* at the molecular level, including its influence on oxidative stress markers, lipid profile, and histological structure of hepatic and renal tissues. Dose optimization studies, long-term safety profiling, and pharmacokinetic evaluations should also be conducted to support its potential development as a complementary therapy for hyperlipidaemia-associated organ dysfunction.

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