ALKALOID AND FLAVONOID CONTENT OF PTEROCARPUS SANTALINOIDES: EFFECTS ON PANCREATIC BIOCHEMISTRY IN MICE

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Abstract. Pancreatitis is a disorder caused by oxidative and inflammatory damage to pancreatic tissues, leading to biochemical and functional abnormalities. Phytochemicals, including alkaloids and flavonoids, are acknowledged for their antioxidant and anti-inflammatory properties. This study aims to analyse the total alkaloid and total flavonoid concentrations in the leaves, stems, and roots of Pterocarpus santalinoides (Nturukpa) and assess their effects on pancreatic biochemical indicators in mice with caerulein-induced pancreatitis. The hydroethanolic extracts of the plant parts were quantitatively analysed for alkaloids and flavonoids. Acute pancreatitis was induced in mice with consecutive caerulein injections. The extracts were administered orally for a period of 21 days. The levels of pancreatic insulin, antioxidant enzyme activity, lipid peroxidation, and inflammatory markers were evaluated. The stem extracts demonstrated the greatest quantities of alkaloids and flavonoids, followed by the leaf extracts, while the root extracts shown much lower levels. The administration of caerulein caused considerable oxidative stress, inflammation, and a reduction in pancreatic insulin levels. Treatment with the standard drug (ocreotide) and stem and leaf extracts significantly improved antioxidant enzyme activity, reduced lipid peroxidation and inflammation, and increased insulin levels ($p < 0.05$). P. santalinoides, particularly its stem and leaf fractions, mitigates caerulein-induced pancreatic biochemical disruptions via alkaloid- and flavonoid-mediated antioxidant and anti-inflammatory mechanisms.
Keywords: *caerulein-induced pancreatitis, alkaloids, flavonoids, pancreatic biochemistry, oxidative stress, Pterocarpus Santalinoides*

Introduction

Pancreatitis is an inflammatory condition of the pancreas characterised by acinar cell damage, oxidative stress, inflammatory infiltration, and disruption of endocrine and exocrine functioning (Mihoc et al., 2024; Szatmary et al., 2022). The biochemical features of pancreatitis include the excessive production of reactive oxygen species (ROS) (Xia et al., 2024), lipid peroxidation (Ma et al., 2021), depletion of endogenous antioxidants (Eddaikra and Eddaikra, 2021), and altered insulin dynamics (Ganiyev, 2024), which make it a significant concern in clinical biochemistry and chemical pathology. Phytochemicals, including alkaloids and flavonoids derived from medicinal plants such as Pterocarpus santalinoides, exhibit antioxidant and anti-inflammatory properties that can regulate these pathogenic processes (Mou et al., 2025; Ayéna et al., 2021). Both flavonoids and alkaloids affect the biochemistry of the pancreas in several ways that work together to improve metabolic efficiency and protect cells. For example, alkaloids mostly ensure that pancreatic β-cells release more insulin (Adhikari, 2021), control enzymes responsible the metabolism of carbohydrates (Adhikari, 2021; Muhammad et al., 2021), and possess anti-inflammatory and antioxidant activities that protect pancreatic tissues from oxidative damage and inflammation (Tang et al., 2022). Flavonoids, on the other hand, have strong antioxidant effects which allow them to neutralise free radicals that are capable of damaging β-cells, improve insulin sensitivity

by boosting insulin receptor signalling and glucose uptake in peripheral tissues, and help control and stabilise insulin secretion (Liu et al., 2025; Martín and Ramos, 2021; Sok Yen et al., 2021). *P. santalinoides*, referred to as Nturukpa in southern Nigeria, is traditionally employed in the treatment of several ailments, including inflammatory and metabolic disorders (Agu et al., 2023; Ayéna et al., 2021; Bulle et al., 2016). Nonetheless, there is a lack of information from any study that has analysed the total alkaloid and flavonoid contents of various parts of the plant and their specific effects on pancreatic biochemical markers, therefore justifying the study.

Literature review

Several studies have shown that plant-based phytochemicals, especially alkaloids and flavonoids, are important in managing metabolic and inflammatory diseases. Alkaloids have been reported to lower blood glucose by improving insulin secretion, enhancing glucose uptake, and regulating key metabolic enzymes, making them useful in diabetes management (Adhikari, 2021; Muhammad et al., 2021). Flavonoids are also known for their strong antioxidant and anti-inflammatory effects and have been linked to better insulin sensitivity and improved insulin signaling (Liu et al., 2025; Martín and Ramos, 2021; Sok Yen et al., 2021). In this regards, acute pancreatitis is widely described as a condition driven by oxidative stress and excessive inflammation, leading to pancreatic cell injury and systemic complications (Cai et al., 2024; Mihoc et al., 2024; Xia et al., 2024). As a result, antioxidant phytochemicals have attracted attention for their protective potential. For instance, Nagy-Pénzes et al. (2022) as well as Tang et al. (2022) proved that flavonoids and related bioactive compounds reduce oxidative damage, suppress inflammatory responses, and protect pancreatic tissue in experimental models with induced pancreatitis. Additionally, *Pterocarpus* species, including *P. santalinoides* and *P. santalinus*, are rich in bioactive compounds and have demonstrated antioxidant, anti-inflammatory, antimicrobial, and metabolic activities (Mou et al., 2025; Ayéna et al., 2021; Bulle et al., 2016). Above all, existing literature supports the potential of alkaloid- and flavonoid-rich medicinal plants as supportive agents in the management of acute pancreatitis.

Materials and Methods

The leaves, stems, and roots of *P. santalinoides* were gathered, verified, air-dried, ground into a powder, and then extracted with 70% ethanol by cold maceration for 72 hours. The extracts were filtered, concentrated, and kept at 4 °C. Total alkaloids were determined using gravimetric methods described by Woo et al. (1977) and modified by Sharma et al. (2021), while total flavonoids were quantified using the aluminum chloride colorimetric assay as described by Aparna and Hema (2022). Adult male albino mice (25–30 g) were used. Acute pancreatitis was induced by intraperitoneal injections of caerulein (50 µg/kg) administered hourly for six doses. The mice were randomly assigned into six groups (n = 6 per group) as in *Table 1*. All treatments were administered orally. Although caerulein induces acute pancreatitis, the 21-day treatment period was designed to evaluate sustained biochemical recovery and pancreatic restitution. Pancreatic tissue samples were assessed for selected biochemical parameters like insulin, superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), malondialdehyde (MDA), and myeloperoxidase (MPO), using standard laboratory procedures. All experimental data were analysed using SPSS (version 20). Results were

expressed as mean ± standard error of mean (SEM). Differences among experimental groups were determined using one-way analysis of variance (ANOVA) followed by Tukey's post hoc multiple comparison test. Statistical significance was accepted at $p < 0.05$.

***Table 1**. Experimental groups and treatment details for caerulein-induced pancreatitis in mice.*

Group	Description	Treatment Administered	Dose	Duration
1	Normal Control	Distilled water (Vehicle); not induced with pancreatitis.	-	21 days
2	Pancreatitis Control	Induced with pancreatitis + Distilled water (Vehicle)	-	21 days
3	Pancreatitis + Leaf Extract	Leaf extract	200	21 days
4	Pancreatitis + Stem Extract	Stem extract	200	21 days
5	Pancreatitis + Root Extract	Root extract	200	21 days
6	Pancreatitis + Standard Drug	Octreotide	50	21 days

Note: Dose (mg/kg).

Results and Discussion

Total alkaloid and flavonoid contents of P. santalinoides extracts

The total alkaloid and flavonoid contents of *P. santalinoides* are presented in *Table 2*. The results showed that the stem had the highest concentration of total alkaloids (27.9 ± 1.6 mg/g) and flavonoids (45.7 ± 2.8 mg/g). The leaves had a moderate total alkaloids of 18.6 ± 1.2 mg/g and total flavonoids of 32.4 ± 2.1 mg/g, while the roots had the lowest concentration of total alkaloids (9.3 ± 0.8 mg/g) and flavonoids (14.1 ± 1.0 mg/g). Above all, the total flavonoids present in the plant extracts were higher than the total alkaloids.

***Table 2**. Alkaloid and flavonoid content of P. santalinoides extracts.*

Plant Part	Alkaloids (mg/g extract)	Flavonoids (mg/g extract)
Leaves	18.6 ± 1.2	32.4 ± 2.1
Stems	27.9 ± 1.6	45.7 ± 2.8
Roots	9.3 ± 0.8	14.1 ± 1.0

Note: Values are mean ± SEM (n = 6).

Effects of P. Santalinoides extracts on pancreatic oxidative stress markers

The effects of *P. santalinoides* extracts on pancreatic oxidative stress markers are presented in *Table 3*. The results revealed that the induction of pancreatitis with caerulein significantly altered pancreatic oxidative stress markers when compared with the normal control group. The pancreatitis control group showed a noticeable reduction in antioxidant enzyme activities, such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), alongside a significant increase in malondialdehyde (MDA) levels. Treatment of caerulein-induced pancreatitis in mice with *P. santalinoides* extracts significantly improved oxidative stress parameters compared with the pancreatitis control group ($p < 0.05$). With the exception of the standard drug (octreotide), the stem extract showed the most significant protective effect, restoring SOD, CAT, and GSH levels close to normal values while clearly reducing MDA concentration. The leaf extract also revealed considerable antioxidant activity, although slightly lower than that of the stem extract. Conversely, the root extract produced moderate improvement in antioxidant enzyme activities and lipid peroxidation but was less effective compared to the leaf and stem extracts.

***Table 3**. Effects of P. santalinoides extracts on pancreatic oxidative stress markers.*

Group	SOD (U/mg protein)	CAT (U/mg protein)	GSH (µmol/mg protein)	MDA (nmol/mg protein)
Normal Control	12.8 ± 0.6	9.4 ± 0.5	6.9 ± 0.3	1.8 ± 0.1
Pancreatitis Control	5.1 ± 0.4	3.2 ± 0.3	2.4 ± 0.2	4.9 ± 0.3
Leaf Extract	9.6 ± 0.5*	7.1 ± 0.4*	5.2 ± 0.3*	2.6 ± 0.2*
Stem Extract	11.3 ± 0.6*	8.6 ± 0.4*	6.1 ± 0.4*	2.1 ± 0.1*
Root Extract	7.0 ± 0.5*	5.0 ± 0.3*	3.8 ± 0.2*	3.5 ± 0.2*
Pancreatitis + Std. drug	14.5 ± 0.8*	10.2 ± 0.5*	8.0 ± 0.4*	3.5 ± 0.3*

*Note: Values are mean ± SEM (n = 6); *Values significantly different from pancreatitis control at p < 0.05.*

Effects of P. santalinoides extracts on pancreatic insulin and inflammatory marker

Table 4 shows the effects of *P. santalinoides* extracts on pancreatic insulin and inflammatory marker. The pancreatitis control group (3.1 ± 0.2 U/g tissue) presented a marked decrease in pancreatic insulin concentration compared to the normal control group (8.7 ± 0.4 U/g tissue). Additionally, myeloperoxidase (MPO) activity, an indicator of neutrophil infiltration and inflammatory response, was significantly increased in the pancreatitis control group (4.8 ± 0.3 U/g) compared to the normal control group (1.6 ± 0.1 U/g). Treatment with *P. santalinoides* extracts significantly reversed these alterations ($p < 0.05$), with the stem extract producing the most pronounced phytotherapeutic effect by restoring insulin levels to 7.5 ± 0.4 U/g tissue and reducing MPO activity to 1.9 ± 0.1 U/g tissue. The leaf extract also elicited substantial improvement, increasing insulin concentration to 6.2 ± 0.3 U/g tissue and lowering MPO activity to 2.4 ± 0.2 U/g tissue, while the root extract showed moderate efficacy, with insulin and MPO values of 5.0 ± 0.3 and 3.2 ± 0.2 U/g tissue, respectively. The standard drug, octreotide, produced near-complete normalisation of pancreatic function, elevating insulin to 9.2 ± 0.4 U/g tissue and suppressing MPO activity to 1.3 ± 0.3 U/g tissue, thereby establishing a clear efficacy hierarchy that mirrors the phytochemical richness of the treatments.

***Table 4**. Effects of P. santalinoides extracts on pancreatic insulin and inflammatory marker.*

Group	Insulin (U/g tissue)	MPO (U/g tissue)
Normal Control	8.7 ± 0.4	1.6 ± 0.1
Pancreatitis Control	3.1 ± 0.2	4.8 ± 0.3
Pancreatitis + Leaf Extract	6.2 ± 0.3*	2.4 ± 0.2*
Pancreatitis + Stem Extract	7.5 ± 0.4*	1.9 ± 0.1*
Pancreatitis + Root Extract	5.0 ± 0.3*	3.2 ± 0.2*
Pancreatitis + Standard Drug (Octreotide)	9.2 ± 0.4*	1.3 ± 0.3*

*Note: Values are mean ± SEM (n = 6); *Significantly different from pancreatitis control at p < 0.05.*

The findings of this study revealed differences in alkaloid and flavonoid compositions among the different parts of *P. santalinoides*, with the stem containing the highest concentrations of total alkaloids and flavonoids, followed by the leaves, while the roots exhibited the lowest concentrations. The high proportion of flavonoids over alkaloids across all plant parts suggests that flavonoids may constitute the major bioactive constituents responsible for the pharmacological activities of the plant. The higher amounts of alkaloids and flavonoids observed in the stem may be attributed to its physiological role in nutrient transport and metabolic storage, which often promotes the

accumulation of secondary metabolites (Agu et al., 2023; Pate and Jeschke, 1995). Previous studies have reported that environmental exposure and metabolic activity influence phytochemical distribution within plant tissues (Pant et al., 2021), with stems and leaves frequently serving as reservoirs for antioxidant compounds (Mou et al., 2025; Ayéna et al., 2021; Eddaikra and Eddaikra, 2021). The relatively lower phytochemical concentration observed in the roots may explain their reduced biological activity observed in subsequent biochemical analyses.

The presence of substantial amounts of alkaloids and flavonoids supports the traditional medicinal use of *P. santalinoides* in managing inflammatory and metabolic disorders (Mou et al., 2025; Bulle et al., 2016). Alkaloids are known to modulate enzymatic activities and enhance insulin secretion (Adhikari, 2021; Muhammad et al., 2021), while flavonoids exert potent antioxidant effects through free radical scavenging and stabilisation of cellular membranes (Tang et al., 2022; Martín and Ramos, 2021; Zhishen et al., 1999). The comparatively higher flavonoid content observed in this study suggests that antioxidant mechanisms may play a dominant role in the therapeutic effects of the plant (Ayéna et al., 2021; Eddaikra and Eddaikra, 2021). Caerulein-induced pancreatitis significantly disrupted pancreatic antioxidant defense mechanisms, as evidenced by reduced activities of SOD, CAT, and GSH, alongside elevated MDA levels. This finding confirms that oxidative stress plays a central role in the pathogenesis of pancreatitis through excessive generation of reactive oxygen species, leading to lipid peroxidation, damage of cellular membrane, and enzyme inactivation (Xia et al., 2024; Ma et al., 2021). Similar observations have been reported in experimental pancreatitis models where the overstimulation of caerulein promotes oxidative injury to pancreatic acinar cells (Cai et al., 2024; Nagy-Pénzes et al., 2022).

Administration of *P. santalinoides* extracts significantly led to the restoration of antioxidant enzyme activities and reduction of lipid peroxidation, indicating strong protective effects against oxidative pancreatic damage (Mou et al., 2025; Tang et al., 2022; Ma et al., 2021). The stem extract proved the most pronounced effect, restoring antioxidant enzyme levels close to normal values and significantly lowering MDA concentration. This superior activity may be linked to its higher alkaloid and flavonoid content, which enhances endogenous antioxidant defenses and suppresses free radical generation (Sharma et al., 2021). The leaf extract also showed substantial antioxidant activity, further supporting the role of phytochemicals in modulating oxidative stress pathways (Mou et al., 2025; Zhishen et al., 1999). Conversely, the moderate effect observed with the root extract may be associated with its relatively lower phytochemical concentration. The overall improvement in antioxidant status suggests that *P. santalinoides* extracts help preserve pancreatic cellular integrity and enzymatic functionality during inflammatory stress.

The significant reduction in pancreatic insulin concentration observed in the pancreatitis control group indicates impairment of β-cell function due to inflammatory and oxidative damage. Pancreatic inflammation often disrupts endocrine function by promoting cellular apoptosis, reducing insulin synthesis, and impairing glucose metabolism (Ganiyev, 2024; Mihoc et al., 2024). The elevated MPO activity recorded in the pancreatitis control group further confirms intense neutrophil infiltration and inflammatory response within pancreatic tissues (Werawatganon et al., 2023). Treatment with *P. santalinoides* extracts significantly improved insulin levels and reduced MPO activity, demonstrating both endocrine protective and anti-inflammatory effects. The stem extract produced the most pronounced improvement, restoring insulin

concentration close to normal levels and markedly suppressing inflammatory activity. This suggests that the extract protects β-cell integrity and enhances insulin secretion, possibly through antioxidant-mediated stabilisation of pancreatic cellular structures (Liu et al., 2025; Martín and Ramos, 2021; Sok et al., 2021).

The leaf extract also exhibited considerable improvement in insulin secretion and reduction in inflammatory activity, although slightly lower than the stem extract. The root extract showed moderate therapeutic effects, consistent with its lower phytochemical content. The observed anti-inflammatory effects may be attributed to the ability of alkaloids and flavonoids to inhibit pro-inflammatory mediators, reduce neutrophil infiltration, and suppress oxidative stress-induced tissue injury (Liu et al., 2025; Ayéna et al., 2021; Sharma et al., 2021).

Conclusion

This study establishes that different anatomical parts of *P. santalinoides* possess distinct alkaloid and flavonoid profiles, with the stem and leaves exhibiting significantly higher alkaloid and flavonoid concentrations than the roots. Caerulein -induced pancreatitis resulted in noticeable oxidative stress, inflammatory activation, and inhibition of pancreatic insulin secretion. Oral administration of hydroethanolic extracts of *P. santalinoides* significantly attenuated these biochemical derangements by restoring antioxidant enzyme activities, reducing lipid peroxidation, suppressing inflammatory responses, and improving pancreatic endocrine function. The stem extract exerted the most robust protective effect, followed by the leaf extract, while the root extract demonstrated comparatively moderate activity. These findings suggest that the pancreatic protective effects of *P. santalinoides* are largely mediated through alkaloid- and flavonoid-driven antioxidant and anti-inflammatory mechanisms. The study provides empirical support for the ethnomedicinal use of the plant and underscores its potential as a source of bioactive compounds for pancreatitis management. It is recommended that future studies focus on the isolation and molecular characterisation of the active phytoconstituents, elucidation of their specific signaling pathways, and comprehensive safety and translational evaluations to support potential clinical application.

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

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