The present study focuses on the authentication of claims made about *Pergularia daemia* as an anti-inflammatory and diuretic agent in traditional system of medicine. The experimental work performed in this dissertation consists of two parts. The first part of the study was carried out in Lipschitz test (diuretic activity) and in different inflammatory (acute, sub-acute and chronic) animal models for assessing effectiveness of 50% ethanolic extract (PDE), petroleum ether fraction (PDP), ethyl acetate fraction (PDEA), n-butanol fraction (PDB) and water fraction (PDW) of *P. daemia* and were subjected to phytochemical screening. In second part, efficacious and potent fractions of *P. daemia* were selected to find possible mode of action with identification of phytoconstitute/s responsible for activity using HPTLC, preparative TLC and IR spectroscopy.

The whole plant was extracted with 50% alcohol and fractioned with petroleum ether, ethyl acetate, n-butanol and water and subjected to phytochemical analysis. Preliminary phytochemical investigations revealed the presence of alkaloids, carbohydrates, steroids, flavonoids, glycoside, triterpenoids, phenolic compounds and tannins in 50% alcoholic ethanolic extract of *P. daemia*. Acute toxicity study was performed for 50% alcoholic extract according to the acute toxic classic method (as per OECD guidelines). N mortality was observed up to 2000 mg/kg.

In anti-inflammatory activity, all the fractions except PDP were effective in carrageenan-induced paw edema (acute inflammation), formaldehyde-induced paw edema (sub-acute inflammation), cotton pellet granuloma and adjuvant-induced arthritis (chronic inflammation) with highest activity in PDB (100 and 200 mg/kg) followed by PDW (100 and 200 mg/kg), in rats. On the contrary, PDP was found effective only in acute inflammation and devoid of effectiveness in sub-acute and chronic inflammation.

In carrageenan-induce paw edema, all fractions at dose 100 mg/kg and 200 mg/kg showed significant reduction in the edema. Mechanistic studies showed that PDB (100 and 200 mg/kg) and PDW (100 and 200 mg/kg) orally decreased the level of malondialdehyde in paw edema by increasing activities of antioxidant enzymes such as SOD and GPx, in liver and decreasing TNF-α activities in paw edema. Further, the effect of PDB and PDW were evaluated on proliferative phase of inflammation in cotton pellet granuloma and air-pouch model. PDB and PDW in both
Summary

doses produced reduction in weight of granuloma induced by cotton pellet, with maximum effect was found in n-butanol fraction 200 mg/kg and water fraction 200 mg/kg. Both fractions were found effective in air pouch granuloma model by decreasing the exudation and granuloma formation. In addition, we found that PDB and PDW produce reduction in leucocytes count and neutrophil number within the air pouch membrane. In the mechanistic studies, test fractions showed reduction in MPO level, TNF-α and NO\(^x\) level in air pouch granuloma model.

In Adjuvant-induced arthritis (AIA), n-butanol and water fraction of \(P.\ daemia\) significantly attenuated primary lesions (paw edema in injected paw) and secondary lesions. Similarly, both test fractions were able to reduce serum CRP and RF levels, the markers for systemic inflammation and antibody formation, increased in AIA-induced animals. Administration of Freund’s adjuvant induced significant decrease in body weight, serum A/G ratio, Hb and increases arthritic index, ESR, pain score and percent lymphocytes. These changes were significantly prevented by the pre-treatment with prednisolone, PDB and PDW.

In present investigation, we found that administration of PDW (100 and 200 mg/kg) showed gastric irritation with increases in ulcer incidence and lesion area, while PDB exhibited negligible ulcerogenic activity. On the contrary, in soyabean lipoxygenase inhibition study, PDB (IC\(_{50}\) 572.6 μg/ml) demonstrated significant inhibitory activity as compared to PDW with IC\(_{50}\) > 1000 μg/ml.

In mechanistic studies, test fractions prevented migration of leucocytes in mouse peritonitis model and neutrophil adhesion at site of inflammation in neutrophil adhesion study. In addition, n-butanol and water fraction prevented increased vascular permeability induced by acetic acid with significant mast cell stabilizing activity and without membrane stabilization activity. Further the results obtained in the present study indicate that the test fractions from \(P.\ daemia\) exhibit antioxidant activities in various \textit{in vitro} antioxidant experiments.

Diuretic activity of plant was assessed in rats with furosemide as a standard drug using Lipschitz's test. Between fractions, petroleum ether fraction failed to produce diuresis, while n-butanol (200 and 400 mg/kg) and water (200 and 400 mg/kg) fraction were found to have highest activity. Administration of both fractions leads to diuresis with increase in Na\(^+\) and K\(^+\) level without altering Na\(^+\)/K\(^+\) and Cl\(^-\)/Na\(^+\) + K\(^+\) ratio and slight decrease in pH. Despite change in urinary excretion of
electrolytes, the plasma Na⁺, K⁺ level and hematocrit were not affected by any of the fractions. The n-butanol and water fraction did not show renal toxicity or any adverse effect during the study period. Results showed that diuresis produces by both fractions is saluretic rather than aquaretic.

Phytochemical analysis of n-butanol fraction showed presence of triterpenoids like α, β – amyrin, lupeol, ursolic acid, β-sitosterol and β-stigmasterol, while water fraction showed presence of flavonoids (2.03 mg of catechin equivalents/ g of dry extract) and phenolic compounds (15.62 mg of gallic acid/ g of dry extract).

In conclusion, present finding demonstrate that the *P. daemia* exhibits antiinflammatory and diuretic activity. Figure 7.1 and 7.2 illustrated the possible mechanism/s involve in anti-inflammatory and diuretic action of *P. daemia*, respectively.