6. SUMMARY

This study was conducted to evaluate the antidiabetic, antioxidant, hypolipidemic and safety of different solvent extracts of *Murraya koenigii* leaf. There are some research reports on pharmacological properties of *Murraya koenigii*. Most of the past experiments were done either using whole leaf powder of *Murraya koenigii* or in combination with other medicinal plants.

Considering the need for systematic elucidation of pharmacological properties of *Murraya koenigii*, this study was conducted to evaluate the antidiabetic, antioxidant, hypolipidemic activity and safety of aqueous, chloroform, petroleum ether and freeze dried aqueous extracts of *Murraya koenigii* leaf in Wistar rats.

Experiment I was conducted to screen the antidiabetic activity of aqueous, petroleum ether, chloroform and methanol extracts of *Murraya koenigii* in alloxan induced diabetic wistar rats by oral administration for a period of 8 weeks. This study revealed the significant antidiabetic activity of aqueous and methanol extracts at the higher doses that is at 1000mg/kg b.w. At the end of the 8 weeks treatment aqueous extract caused significant decrease (P<0.05) in plasma glucose levels by 33.7% and methanol extract by 32.9%.

Aqueous extract caused significant increase (P<0.01) in plasma insulin levels to by 28.5% and methanol extract by 33.4% as compared to control diabetic group. Petroleum ether and chloroform extracts did not cause either significant decrease (P>0.05) in plasma glucose levels or increase in plasma insulin levels at the same doses.

In experiment II aqueous and methanol extracts of *Murraya koenigii* were subjected to systematic evaluation of antidiabetic, antioxidant and hypolipidemic activities. Glibenclamide and metformin were used as reference drugs in this study. Each of the extracts was tested at 3 doses 200 or 400 or 800 mg/kg b.w. in alloxan
induced diabetic wistar rats by oral administration for period of 12 weeks. This study revealed that the aqueous and methanol extracts have potent antidiabetic, antioxidant and hypolipidemic activity at the doses 400 or 800 mg/kg.

At the end of 90 Days treatment aqueous extract significantly reduced (P<0.01) plasma glucose levels by 32.5% at 400 mg/kg b.w. and by 40.5% at 800 mg/kg b.w.. Methanol extract significantly reduced (P<0.01) plasma glucose levels by 33% at 400 mg/kg b.w. and by 42% at 800 mg/kg b.w. Glibenclamide at 0.25 mg/kg caused 41.1% reduction (P<0.01) and metformin at 10 mg/kg caused 34.3% reduction (P<0.01) in plasma glucose levels as compared to diabetic control group.

Aqueous extract significantly (P<0.01) increased plasma insulin levels by 39.1% at 400 mg/kg b.w. and by 74.2% at 800 mg/kg b.w. methanol extract significantly increased (P<0.01) plasma insulin levels by 48.6% at 400 mg/kg b.w. and by 81.1% at 800 mg/kg b.w. Glibenclamide at 0.25 mg/kg caused 39.5% increase (P<0.01) and metformin at 10 mg/kg caused 3% increase (P>0.05) in plasma insulin levels as compared to diabetic control group. Aqueous and methanol extracts exhibited more marked antidiabetic effect than glibenclamide and metformin.

Antioxidant and tissue protective activity: aqueous and methanol extracts ameliorated the diabetes induced tissue damage in major organs like liver, kidney, heart and pancreas through its antioxidant and tissue protective activity. Aqueous and methanol extracts have shown significant inhibition (P<0.01) of rise in serum creatinine, BUN, ALT, AST and bilirubin at all the tested doses 200 or 400 or 800 mg/kg b.w. At the doses 400 or 800 mg/kg b.w both aqueous and methanol extracts significantly elevated the activity of superoxidizedismutase, catalase and significantly reduced the lipid peroxidation in liver, kidney, heart and pancreas.
Glibenclamide and metformin also ameliorated the rise in serum creatinine, BUN, ALT and AST. But they did not bring about any elevation in antioxidants superoxidedismutase or catalase activity or inhibited lipid peroxidation.

Aqueous and methanol leaf extracts of *Murraya koenigii* showed improved histological appearance in major organs like liver, kidney, heart and pancreas. Particularly the rejuvenation and regeneration of pancreatic beta cell was unique feature observed in groups treated aqueous or methanol extracts at the dose of 800 mg/kg b.w.

In experiment III, the freeze-dried aqueous leaf extract of *Murraya koenigii* was evaluated for antidiabetic, hypolipidemic and antioxidant activity on intraperitoneal administration. The study revealed the potent antidiabetic, hypolipidemic and antioxidant activity of freeze-dried extract at the doses 25 or 50 mg/kg b.w on intraperitoneal administration for a period of 4 weeks.

Antidiabetic activity: at the end of the study freeze dried aqueous extract significantly reduced (P<0.01) the plasma glucose levels by 37.1% at the dose 25 mg/kg b.w and by 41.4% at the dose 50 mg/kg b.w. Insulin levels significantly increased (P<0.01) by 47.6% at the dose 25 mg/kg b.w. and by 57.2% at the dose 50 mg/kg b.w. as compared to diabetic control group insulin.

Hypolipidemic activity: freeze dried aqueous extract at 25 or 50 mg/kg b.w showed hypolipidemic activity by significantly reducing the levels of serum total cholesterol, LDL-cholesterol, VLDL-cholesterol, triglycerides, phospholipids and total lipids and significantly increased HDL-cholesterol. Thus there was improvement in the lipid profile.

Antioxidant and tissue protective activity: Freeze-dried aqueous extract ameliorated the diabetes induced tissue damage in major organs like liver, kidney,
heart and pancreas through its antioxidant and tissue protective activity. Freeze-dried aqueous extract at both doses 25 or 50 mg/kg b.w shown significant inhibition (P<0.01) of rise in serum creatinine, BUN, ALT, AST and bilirubin. Freeze-dried aqueous extract at dose 50 mg/kg b.w significantly elevated the activity of superoxidedismutase, catalase and significantly reduced the lipid peroxidation in liver, kidney, heart and pancreas. At the dose 25 mg/kg b.w. shown the similar antioxidant activity except in heart Freeze-dried aqueous extract showed improved histological appearance of pancreas and liver in dose dependent manner. The regeneration and rejuvenation of pancreatic beta cells was evident upon histological examination.

In experiment IV oral glucose tolerance done on oral administration of aqueous or methanol extracts at the doses 800 mg/kg b.w and intraperitoneal administration of freeze dried extract at the dose 50 mg/kg b.w. significantly attenuated the rise in plasma glucose levels. This study demonstrated the acute antihyperglycemic effect of Murraya koenigii leaf extracts both on oral and intraperitoneal administration.

In experiment V it was observed that aqueous and methanol leaf extracts of Murraya koenigii at 800 mg/kg b.w. induced the over expression of some proteins in pancreas. But there is need for further investigation to identify the molecular mechanisms involved in the induction of proteins that may lead to regeneration and rejuvenation of pancreatic beta cells.

In experiment VI, the repeated dose 28 days toxicity of aqueous and methanol extracts revealed that these extracts were potentially safe at the tested doses.

Phytochemical evaluation revealed the presence of various phytochemical constituents like steroids, triterpines, alkaloids, flavonoids, lactones, tannins,
diterpines and saponins. Since very diversified class of phytochemicals are present in these extracts, the identification of particular bioactive phytochemical needs an extensive study.

In conclusion, aqueous and methanol leaf extracts of *Murraya koenigii* have antidiabetic, hypolipidemic and antioxidant activity. The unique multiple activities of these extracts efficiently maintain glycemic levels and protect from diabetes induced complications. These extracts possess ability of pancreatic beta cell rejuvenation and regeneration. Further these extracts were found to be safe on 28 Days daily oral administration of test doses. The present research has opened the new vista for discovery of cost effective and safe bioactive molecules from *Murraya koenigii*. 