Summary

Diabetes provides a major challenge to the present population globally. It is a major threat to global public health that is rapidly reaching epidemic scale. According to the World Health Organization (WHO), at least 171 million people worldwide have diabetes. This figure is likely to more than double by 2030 to reach 366 million. It is postulated that most of this increase will occur as a result of a 150% rise in developing countries (Wild et al., 2004). This estimate is likely to be even higher taking into consideration population growth, ageing, urbanization, declining levels of physical activity, which – combined with unbalanced diet – increases the risk of obesity linked to the onset of Type 2 diabetes. Diabetes lowers the average life expectancy by up to 15 years, increases cardiovascular disease risk two to four fold, and is the leading cause of renal, neuronal and retinopathy diseases (Roglic et al., 2005). In addition to these human costs, the estimated financial costs of diabetes are staggering. India is the number one, among the top 10 countries, in the incidence of diabetes. In India, approximately 31.7 million people suffered from diabetes in 2000 and it is estimated that about 79.4 million people will be diabetic by 2030.

India has an ancient heritage of traditional medicine for the treatment of human ailments. The Western Ghats in Karnataka (Siddrabetta of Tumkur district) and Kerala states were well known as hubs of medicinal plants.

An ethanobotanical survey and interactions with various Vidyas of Siddarabetta region of Karnataka State, India, we have selected 15 medicinal plants used for the treatment of diabetes. The proposed study is made to give a scientific evidence of their usage of these plants in the traditional systems of medicine.
The thesis work was presented in seven chapters

Chapter 1

This chapter describes about the study of the disease Diabetes mellitus and treatment option, including information about Indian Scenario of diabetes. It also dealt the scope of various alternative system of medicine available for the treatment of diabetes and their merits and demerits. It also describes the status of medicinal plants in the treatment of diabetes in the traditional system. At the end of the chapter, the scope and objectives of the present study was discussed.

Chapter 2

This chapter presents the literature survey of selected15 medicinal plants for the antidiabetic study (which are being used for the treatment of Diabetes mellitus by the local vidyas of Siddarabetta region) and method of preparation of their extracts (ethanolic and aqueous) with their percentage yields. The selected plants are Madhuca indica (bark), Ancardium occidentalis (bark), Basella alba (aerial parts), Echinaps echinatus (aerial parts), Holoptetea integrifolia (bark), Mangifera indica (kernels), Caesalpinia bounduc (Kernels), Limonia acidissima (bark), Bauhinia varigata (bark), Spondias mangifera (bark), Erythrina variegate (bark), Amaranthus viridis (areal parts), Pondanus odoratus (aerial parts), Ichnocarpus frutescens (aerial parts) and Cressa critica (aerial parts)
Chapter 3

This chapter includes the antioxidant activity of selected plants by using different \textit{in vitro} methods such as 2,2-diphenyl-1-picryl hydrazyl (DPPH), nitric oxide radical, scavenging of 2,2'-azino-bis (3-ethylbenz-thiazoline-6-sulfonic acid) diammonium salt (ABTS) radical cation assay, hydrogen peroxide. Further, total antioxidant capacities of all the 15 plants extracts were determined. From the data the following aqueous extracts of \textit{Erythrina variegata} (EVAE), \textit{Madhuca indica} (MIAE), \textit{Ichnocarpus frutescens} (IFAE), \textit{Holoptetae integrifolia} (HIAE), \textit{Basella alba} (BAAE), \textit{Echinaps echinatus} (EEAE), \textit{Limonia acidissima} (LAAE), \textit{Ancardium occidentalis} (ACAE) and the ethanolic extracts of \textit{Erythrina variegata} (EVEE), \textit{Madhuca indica} (MIEE), \textit{Ichnocarpus frutescens} (IFEE), \textit{Holoptetae integrifolia} (HIEE), \textit{Basella alba} (BAEE), \textit{Echinaps echinatus} (EEEE), \textit{Limonia acidissima} (LAEE) and \textit{Ancardium occidentalis} (ACEE) exhibited the ability to scavenge different free radicals by exhibiting low IC$_{50}$ values.

Chapter 4

This chapter deals with the \textit{in-vitro} antidiabetic activity, mainly alpha-amylase and alpha-glucosidase enzyme inhibition activities of all the extracts of the selected plants. The major outcome of this study reveals that both the extracts of \textit{Erythryna varigata}, \textit{Madhuca indica}, \textit{Pandanus odoratissimus}, \textit{Ichnocarpus frutescens}, \textit{Ancardia occidentalis}, \textit{Mangifera indica}, \textit{Cressa critica} have exhibited potent inhibition of alpha-amylase and alpha-glucosidase enzyme activity. In addition, only aqueous extract of \textit{Caesalpinia boundac} was able to inhibit both the enzymes. However, both extracts of \textit{Holoptetea integrifolia} showed
only alpha-amylase inhibition, whereas *Amaranthus viridis* exhibited only alpha-glucosidase inhibition property with low IC$_{50}$ values.

**Chapter 5**

This chapter includes the toxicity study conducted as per OECD guidelines for all the plant extracts of selected 15 plants. In the present study, acute toxicity was tested up to a dose of 3 g/kg (four to eight times more than the tested/therapeutic dose). Even at this high-dose, the extracts did not exhibit any signs or symptoms of toxicity and death.

**Chapter 6**

This chapter describes the *in vivo* pharmacological screening on normoglycemic rats (single dose one day study and OGTT study) of 15 selected plants extracts. Based on free radical scavenging activity (Chapter 3), *in-vitro* anti diabetic activity (Chapter 4) and improvement in glucose tolerance in normoglycemic rats. The four plants viz., *Erythryna varigata*, *Madhuca indica*, *Ichnocarpus frutescens* and *Pandanus odoratissimus* were selected to evaluate antidiabetic potential in alloxan-induced diabetic rats (single dose one day study, OGTT study, multiple dose 15 day study and biochemical parameter study).

Multiple dose of *Erythrina variegata* ethanolic extract (EVEE) 100 mg/kg for 15 days not produced much difference in glucose level at different intervals. Treatment with *Erythrina variegata* ethanolic extract (EVEE) 300 mg/kg to diabetic rats for 15 days produced a significant (P<0.005, P<0.01) reduction in SG levels on the day 1st, 7th and 15th day of administration. Whereas, treatment with *Erythrina variegata* aqueous extract (EVAE)100 and 300 mg/kg to diabetic rats produced significant reduction in glucose levels on all the intervals.
when compared to basal values (0 day). The % reduction in glycemia was found to be 17.31%, 18.68% & 26.82% in EVAE 100 mg/kg, 50.24%, 43.86 & 57.26% in EVAE300 mg/kg and 59.59%, 57.78% & 72.76% in GLB treated animals respectively on 1st, 7th & 15th day. The reduction in glycemia was significant (P<0.001) form 7th day in the *Erythrina variegata* aqueous extract (at both dose level) treated animals when compared to diabetic control.

**Madhuca indica** ethanolic extract (MIEE) at both the doses not produced any significant reduction in SG levels when compared to basal values (0 day). Whereas, *Madhuca indica* aqueous extract (MIAE) at the doses of 100 and 300 mg/kg for 15 days showed significant (P<0.01) reduction in SG levels on 1st, 7th 15th days of administration. The % reduction in glycemia was found to be 20.30%, 25.80% after administration of 7th and 15th days of MIEE 100 mg/kg and 22.12%, 44.60% and 49.78% 1st, 7th and 15th days of MIAE 300 mg/kg treatment when compared to diabetic control and the effect was comparable with GLB.

**Pondanus odoratus** ethanolic extract (POEE) at a dose of 100 mg/kg for 15 days not produced much difference in glucose level at different intervals. Treatment with POEE 300 mg/kg to diabetic rats for 15 days produced a significant (P<0.05, P<0.01) reduction in SG levels on the day 7th and 15th day of administration. Whereas, treatment with *Pondanus odoratus* aqueous extract (POAE) 100 mg/kg for 15 days not produced much difference in glucose level at different intervals. Administration of POAE at the dose of 300 mg/kg to diabetic rats produced significant (P<0.05) reduction in glucose levels on day 7th and 15th when compared to basal values (0 day). Treatment with POEE 300 mg/kg showed 19.44 and
30.54% reduction in glycemia on the day 7th and 15th respectively. Whereas % reduction in glycemia in case of POAE 300 mg/kg was found to be 19.85%, 20.62% on the day 7th and 15th respectively.

Ichnocarpus frutescens ethanolic extract (IFEE) at a dose of 100 mg/kg for 15 days not produced much difference in glucose level at different intervals. Treatment with IFEE 300 mg/kg to diabetic rats for 15 days produced a significant (P<0.01, P<0.001) reduction in SG levels on the day 1st, 7th and 15th day of administration. Whereas, treatment with Ichnocarpus frutescens aqueous extract (IFAE) 100 mg/kg produced significant (P<0.01) reduction in blood glucose on 15th day and treatment with IFAE 300 mg/kg to diabetic rats produced significant reduction in glucose levels on all the intervals when compared to basal values (0 day). Whereas the % reduction in glycemia in case of IFAE 300 mg/kg was found to be 30.08%, 5.052% & 67.25% on the day 7th, 10th and 15th respectively.

Among the four plants, Ichnocarpus frutescens, Madhuca indica, and Pondanus odoratus aqueous extracts showed better anti-diabetic activity when compared with its ethanolic extract of the same plants. Whereas, Erythryna variegate both hydroalcoholic and ethanolic extracts have exhibited ant-diabetic activity.

Chapter 7

This chapter describes the preliminary phytochemical studies of Erythryna variegate, Ichnocarpus frutescens and Madhuca indica, along with HPTLC finger print profiling. Further, estimation of β-sitosterol and lupeol in Ichnocarpus frutescens and Erythryna variegate, were carried out using TLC densitometric methods.
The amount of Lupeol found in *Ichnocarpus frutescens* (IFAE) was 0.216 % w/w. Moreover, the amount of β-sitosterol was found be 0.062 w/w in *Erythrina variegata* ethanolic extract (EVEE) quantified by TLC densitometric method.

An exhaustive bibliography was appended at the end of the thesis.
The work incorporated in the thesis has been presented in conferences/communication

Presented in conferences


Communicated

1. Antidiabetic activity of *Madhuca indica* against alloxan induced diabetic model in rats
   S. Ganapaty and R. Nandeesh. Communicated to IJAPBC.

2. Estimation of β-sitosterol and Lupeol in *Erythrina variegata* and *Ichnocarpus frutescens* by HPTLC.
   S. Ganapaty and R. Nandeesh. Communicated to Ethnobotanical leaflets.

3. Antidiabetic activity of *Erythrina variegate* against alloxan induced diabetic model in rats
   S. Ganapaty and R. Nandeesh. Communicated to Pharmacognosy magazine.

4. Alpha amylase and alpha glucosidase inhibitory action of *Madhuca indica*.