EXECUTIVE SUMMARY

Food is the most frequently consumed “Drug” without prescription. Global modernization and rapid expansion of human activities across the earth, excessive usage of pesticides and inorganic manures in agriculture have made the fruits, vegetables and other eatables toxic and a significant disease causing factor. The WHO also has voiced their concern about the scarcity for drugs in the future and as a remedial measure promote alternative healing techniques. This has led many to adopt herbal medicine as an alternative which provides safe and secure form of treatment. Hence, there is an urgent need to study the plants with medicinal efficiencies.

Efforts are made to describe the herb with such uses and convert into the modern form of drug by taking active molecules and researching into its efficacy as a nutraceuticals. With this background, an effort is made to cull the therapeutic effects of a consumable herb “Pisonia grandis R.Br.” (Nachukottai keerai). The leaves, stems and roots of this herb are extensively used by tribals in India especially in Tamil Nadu and Puducherry as a remedy to treat rheumatism, arthritis and diabetes. As only few studies were done pharmacologically for its various medicinal properties, the author chooses this study to throw more light on the anti-diabetic activity of Pisonia grandis R.Br.

The alarming statistics regarding new number of diabetic cases in younger age group around the globe become a daunting public health concern in developing countries. India has the second largest number of diabetic population in the world. Nearly 90 percent of the population in India reported to be having type 2 diabetes. This increases the economic burden of individual as well the nation. Due to change in the life style of people of Puducherry, a majority of the population is falling prey to diabetic and other complications.
The World Health Organization (WHO) estimated that 80% of the population of developing countries rely on traditional medicine mostly plant drugs, for their primary health care needs. Demands for medicinal plants are increasing both in developing and developed countries. The present study is utilization of *Pisonia grandis* (Pg henceforth) which is mostly used as an ornamental shrub and less used for its therapeutic value. *Pisonia grandis* (R.Br.) is rich in phyto-constituents such as alkaloids, flavonoids, steroids, triterpenoids, tannins and glycosides. The main objective of the study is to highlight the prevalence of Diabetes Mellitus (DM) in Puducherry district and also to analyze the nutritional and anti-diabetic properties of *Pisonia grandis* leaves.

The study was conducted by adopting multi-methodological procedure. It consist of four phases, in Phase I, the Survey method - A cross sectional study was conducted among the 4870 individuals both male and female between the age group of 30 and 80 years attending the rural and urban Primary Health Centres of the Puducherry district. Out of 4870 individuals, 1112 were found to be diabetic. Statistical methods like chi-square test and Binary logistic regression analysis (odds ratio) were applied to meet the study objectives. In Phase II - the Experimental study, the leaves were first authenticated by the Botanical Survey of India, Coimbatore Branch. The leaves of Pg were collected from the plants grown in soil with normal Ph, EC and other nutrients like Zinc, Copper, Manganese and Iron. The leaves were tested for the presence of nutrients like carotenoids, vitamin C, Carbohydrates, Iron and the anti oxidant activity adopting to appropriate standard procedures. The nutrients were also tested for retention under different cooking methods like blanching, steaming, sautéing and drying and the values compared with the fresh leaves. The leaves were also studied for bioactive compounds which are extra-nutritional constituents that typically occur in small quantities in foods. The sequential soxhlet apparatus
was used for the study, in which the dried powder of *Pisonia grandis* was done with Chloroform (S), Ethanol (S), Methanol (S) & Petroleum ether. The extracts were concentrated, residues designated as PGSX1, PGSX2, PGSX3, PGSX4 and PGSX5 respectively. In Phase III, the experimental study on the acute toxicity and anti-diabetic activity of *Pisonia grandis R. Br.* leaves against streptozotcin induced diabetic male wistar rats was analysed. For analysing the efficacy in human subjects ten newly diagnosed male & female diabetic samples were randomly selected from Puducherry region between the age group of 30 and 50 years. The samples were included based on their age, blood glucose level >200mg/dl and free from major illness. The samples, not satisfying the inclusion criteria were excluded from the study. In phase IV, the standardisation of recipes was carried out. The outcome of the prepared items was evaluated for taste, consistency, flavour, mouth feel, colour and appearance. In Phase V, the insulin secretion levels after administering 200ml Pg leaves soup with 35gms of Pg leaves in the normal subjects are documented as case report.

The result obtained from the study in Chapter III, related to Phase I on the prevalence of diabetics and pre-diabetics was between 40 and 50 years. More than half of them were unaware of their diabetic condition. The p-value <0.05 reflects that there is a statistical association between the gender, physical exercise, diabetes and HbA1c with respect to RBS group category. The odds ratio reveals that the subjects having HbA1c>7 are highly susceptible to have above 200 RBS, which means that the subjects who has HbA1c>7 (Glycosylated Hemoglobin) are prone to have 11 times risk when compared to their HbA1c<7. The study reveals that the age, gender, physical activity, body composition and biochemical analysis of the individuals were significant predictors of diabetes. It was clearly observed that the BMI was high in Pre-diabetic subjects but it was low among diabetics.
In Chapter IV many bioactive compounds were noticed. The ethanolic extract of *Pisonia grandis R.Br.* (Nachikottai keerai) was subjected to reversed phase HPLC analysis (model: NEXERA make: Shimadzu) using PDA detector to identify the polar compounds. The designated extracts were validated by adopting HPLC and GC-MS chromatogram. Interpretation was made by using NIST library, Pub Chem, Chem Spider and Chemical Book and molecular formula, molecular weight and molecular structure were ascertained.

The nutritive value of the *Pisonia grandis R.Br.* leaves shows that the iron and Vitamin C content of leaves increased while steaming. In HPLC method, various active constituents were discovered at different retention time, percentage area and peak levels. And in the preliminary phytochemical screening the presence of flavonoids and other phyto-constituents were found. After the preliminary screening, the ethanolic extract was subjected to GC-MS chromatogram, in which various phyto-constituents were discovered which having the active principles against various disease. Further, the study was narrowed to prove the anti-diabetic effect of the Pg leaves in animals & human subjects. In Chapter V - 500 mg/kg of ethanolic extract reduced the blood glucose level from 279 mg% to 233 & 220 mg% at 7th and 14th days respectively which was significant when compared to control (p>0.05). The results of the extract was comparable to that of 10 mg/kg of Glibenclimide (p>0.05). From the observed results in T2D patients, the PGCA powder steadily decreases the FBS and PPBS in day 15 and day 30 when compared to first day (i.e. before administration of powder in type II diabetes). In Chapter VI, the Phase IV, the results obtained from organo-leptic evaluation of foods using *Pisonia grandis R.Br.* leaves reported by the panel members are discussed and were excellent. Sambar and soup scored 4 and 3 for consistency, taste, appearance, and flavour. The other recipes also scored 3 but the dumplings scored 1 due to hardness of the recipe.
In Chapter VII, the Phase V of the study focused on analyzing the insulin levels of Pg leaves soup in the normal healthy subjects. This showed initial insulin values were very low because of overnight fasting. After consuming the Pg leaves soup the serum insulin values increased steadily till the 75th minute. After the 75th minute there was a gradual decline in insulin level. The values started to normalize i.e. 0 -17 µU/mL at the 165th minute.

Hence, it is appropriate to highlight the research findings of *Pisonia grandis* R.Br. leaves that is easily available at low cost and is rich in iron and calcium enabling eradication of malnutrition like Iron deficiency & Osteoporosis and significantly control diabetes. Further, the present study recommends the prospect of more aggressive introduction and utilization of *Pisonia grandis* R.Br. leaves by the food sector. It also implies that it may be worthwhile for food industry to take up the production of *Pisonia grandis* R.Br leaf powder as food as well as medicine in managing diabetes that has very high prevalence and eating away considerable portion of national and individual's income. It is for time that promotion of *Pisonia grandis* R.Br. leaf incorporation into the diet will go a long way in not only alleviating micronutrient deficiencies but also towards the development of functional foods for several chronic degenerative disorders like diabetes, rheumatoid arthritis and also as diuretic.