Ayurveda has passed through several phases of evolution, metamorphosis and transformation before being a well-designed package for health care. In Ayurveda we find a vivid description of the drugs and disease solely attributed to their action in various manners. At present the quality of medicine required has increased alarmingly. Dravyaguna is mainly deals with the drugs their standardization, quality control, actions, metabolism, etc. The Ayurvedic material medica mainly depends on medicinal plants numbering 600 to 700 (based on Brihattratyee). Kakamachi is one of such a drug, which was utilized widely. There are many actions are quoted for Kakamachi but never studied on the modern experimental parameters. In Bhavaprakasha Nighantu one of its action is explained as Mehajit. This action in the present perspective related with diabetes. The need of the hour is to screen such unexplored knowledge in present trend of treatment. Diabetes mellitus is a major health problem for the world in the 21st century. Recent studies reveal that the prevalence rates are 10-18% in the urban Indian adult population and there is also evidence that the prevalence of type-2 diabetes is increasing in rural population too.

Though the use of many indigenous drugs has been described in classics and practiced for the treatment of Diabetes but still there is a need of standardization and uniformity about its identity and results. It is also necessary to find out more effective and safe drug, which not only controls the diseases but also tent to cure the complex disease like Diabetes. In the country like India where many peoples are below the poverty line and many cannot afford the expensive treatment for diabetes; in such condition there is serious need of such drug that should be effective, cheap, and easy available to a common person.

Kakamachi is explained right from Vedic Granthas to till date. It is also widely used in the Samhita period especially in the form of Shukdravya as well as Aushadha Dravya. Godanigrasha is the one who has given a special chapter in Rasayanadikara on Kakamachi. The drug has Tikta Katu Rasa, Ushna Veerya, and Katu Vipaka. It is indicated in Meha, Shotha, Kushtha, Shopha, Arsha, Jwara, Hikka, Shwash, Chhardi, etc. The drug is considered to be as antidiabetic as it explained as Mehajit in Bhavaprakash.
Nighantu. In Ayurvedic text so many drugs explained to possess Pramehaghna activity and were screened for the same like Amalaki, Haridra, Guduchi, etc. The symptoms of Diabetes can be co-related with Prameha. Kakamachi is easy available, cheap, common to approach. Many research works has been carried out in different aspects like isolation, extraction, activity screening, etc. The drug screened for its antimicrobial, anti fungal, hepato-protective, anticancer, antioxidant, etc. However, antidiabetic activity is yet to be screened. So for the present study it has been selected for antidiabetic activity in NIDDM (Type 2).

**Aims and Objectives:**

1) To assess clinical effect of Kakamachi in Diabetes Mellitus (NIDDM- Type-2)
2) To authenticate and standardize the herb by using modern techniques.
3) To specify the mode of action of Kakamachi in Prameha and Diabetes Mellitus (NIDDM- Type-2)
4) To assess the adverse effect of the drug if any in Kakamachi.

**Plan of Work:** The entire study was conducted as follows-

1. Thorough Review of literature right from Vedic period to till date
2. Collection and authentication to ensure identity, purity and quality standard by various traditional and analytical methods
3. Experimental study by acute and sub-acute toxicity to ensure safety in administration.
4. Clinical Study design to validate antidiabetic efficacy in NIDDM (Type 2).

It was controlled randomized parallel single blind clinical trial conducted at Tarachand Hospital, Pune and Indian Institute of Chemical Technology, Hyderabad.

**Methodology:**

**Review:** All Samhita, Nighantu, Rasagrantha and more than 15 published papers for their activities were studied.

**Collection of Drug:** Kakamachi was identified and assessed by following the API guidelines along with Ayurvedic identification method like Synonym and homonyms as Rudhi, Swabhava, Deshoktya, Lanchhana, Upama, Veeryena and Itharathva. It was collected from the peripheral part of Hyderabad in non-contaminated area at its full maturity in the month of November before 11 am. The drug was dried in shade and was subjected to powder by mesh no. 85 and fine powered was obtained.
Pharmacognostic Study-Macroscopy and Microscopic Study:

The external features were studied and co-related with the Ayurvedic Pharmacopoeia of India, which was found to be matching perfectly. The anatomical features were also been studied and compared with the standard Ayurvedic Pharmacopoeia of India and confirmed the observations.

As a part of standardization analytical study was carried out with the help of HPLC, HPTLC. Florescence study, Preliminary phyto-chemical study and other Pharmacopoeial methods like-determination of foreign matter, ash, acid insoluble ash, alcohol soluble extractive, water soluble extractive, etc. A detailed data generated was compared with the available standards in API. For non-available earlier data like fluorescence study which serve as fingerprint. An analytical study by ICP was conducted for the detection of heavy metals like As, Cd, Pb, Hg etc in the drug for the safety assessment of the medicine.

Toxicity Study: A toxicity study was carried out to assess the LD$_{50}$ values and dose finalization in Swiss Albino rats. The results indicate that the LD$_{50}$ of Kakamachi was 1525 mg/kg and there was no general gross behavioral change in the animal during the course of the study. In sub-acute toxicity it is found that during the course of treatment the animals did not showed any mortality. Estimation of Biochemical values in the animals exhibits no significant change or the organ weight.

CLINICAL STUDY:

Procedure: Permission and NOC of the Institutional Ethical Committee of TAMV, Pune and IICT, Hyderabad was taken prior to the trials. The patient had given the full idea about the clinical trial and after giving information consent form (ICF), the patients were enrolled for the study.

Base line Screening: An elaborate proforma was prepared containing clinical history as well as biochemical examination to follow-up the patient. A complete general and physical examination was carried out of the patients under trial.

Criteria For diagnosis: Symptoms of diabetes plus casual i.e. any time plasma glucose concentration $\geq$200 mg/dl. OR Fasting i.e. no caloric intake for at least 8 hours plasma glucose (FPG) $\geq$ 126 mg/dl OR 2-hour post-load glucose $\geq$200 mg/dL was considered as
provisional diagnosis of diabetes. Patient were selected who fulfilled the criteria as below-

**Inclusion Criteria:**
- Patients willingly participating in the trial and giving consent form (ICF).
- Age group of 25-60 years, irrespective of sex and religion.
- Each patient screened and investigated by SGOT, SGPT, BUN, S. Creatinine, Glycosylated Hb, Lipid Profile, GTT and BSL along with subjective parameter. A confirm diagnosed patient of NIDDM had formed the subject of present study.

**Exclusion criteria:**
- Patients un-willingly participating in the trail and not giving consent form (ICF)
- Patients with IDDM, Juvenile diabetes, and other associated complication
- Patients who are already under the treatment of other than Sulphonylurea group.
All the patient were enrolled by random sampling method in three group as-

- **Group A**- Kakamachi whole plant powder.
- **Group B**- Sulphonylurea group medicine.
- **Group C**- Kakamachi whole plant Powder and Sulphonylurea group medicine.

**Diets and Restriction:** Same dietary and daily regime had been advised in all the groups.

**Drug Regime:**
**Dose, Duration and Mode of Administration:** The patients in each group undergone for three months clinical trial period and followed up for another one month. The drug was administered orally at 3 gms two times a day with water before meals, where as in the Sulphonylurea group dose were maintained fixed as decided by the experts. In combination group the dose was half of both the medications.

**Criteria for Assessment of the Treatment:**

**Objective:** To assess the disease and monitor hazardous condition. Blood Glucose level along with Liver function and Renal Function Test, Lipid profile etc were performed.

**Subjective:** Assessment of signs and symptoms by to Ayurvedic parameters by Grading Analog Scale (GAS) and were performed before, in-between and after the treatment.

**Acceptance, Rejection Criteria and Rescue Medicine:** Blood Glucose level was considered as the acceptance, rejection and withdrawal parameters for continuation and discontinuation of the therapy. The Fasting blood glucose level >130 mg/dl and post load
glucose level >224 mg/dl with successive investigation were considered as non-responding. The patient who doesn’t followed the advice of the investigators and unable to perform the investigations for assessment were considered as dropped out by giving proper consultation. All the possible therapy including insulin therapy was considered as a rescue medicine to tackle any emergency if necessary.

Follow up study: Patients were followed up for every 15 days or less if necessary to access the variations in symptoms during and after completion of the therapy.

Adverse Drug Reaction Monitoring: Every patient was carefully observed for Adverse Drug Reaction.

Assessment of over-all effect of therapies: Each patient was assessed on the basis of fasting and Post-prandial blood sugar levels and Grading analog scale. The patients were classified by the scoring pattern as well as percentage reduction in improved, marked improved, moderate improved, mild improved and no improved category.

Statistical Analysis: The data obtained was analyzed statistically by Mean Score, Standard Deviation (S.D.), Standard Error (S.E.), % of relief, Student’s ‘t’ Test, ‘p’ Value, Chi Square test and ANOVA and the results were interpreted accordingly.

Observations and results:

All the recruited patients were categorized on the basis of Age, sex, religion, etc. Total 109 patients were recruited in the study, which are randomly divided in Group A, Group B and Group C. In all groups the drug, doesn’t have any adverse effect on LFT. The data shows p value of >0.10 in group A and B where as in group C it was <0.10, and there was no significant difference in the means of groups among themselves. In all groups the drug, doesn’t have any adverse effect on RFT. The data shows p value >0.10 in group A where as in B and C the values are increased with special reference to BUN but are under normal limit. In S. Creatinine the p values are of <0.05 for Group A and C where as in Group B it was of <0.01 and there was no significant difference in the means of groups among themselves.

In all the three groups, the lipid profile was found to be having no significant difference in the means of groups among themselves. Total cholesterol levels increased in Group B and C, where as Group A has mild relief exhibiting p value of >0.10. S. Triglycerides increased in all Group A, B and C. Serum HDL decreased in Group A, where as in Group B and C it was increased with p value >0.10. Serum LDL increased in
Group B and C, where as Group A has relief showing p value >0.10. S. VLDL levels increased in all Group A, B and C. Glycosylated Hb improved in Group C indicating p value <0.10, where as in Group A and B shows mild increase and there was significant improvement in Group C as compare to other two groups. GTT was improved in all stages of time bound analysis in all Groups except at 180 Mins. It was found that there is not significant difference of mean between the groups.

The fasting BSL was found to be improved in all Group, A, B and C exhibiting p value <0.01, <0.001, <0.02 respectively. The Post-Meal BSL is also found to be improved in all Group, A, B and C respectively, presenting p value <0.001 in each group. In the BSL there was no significant difference in the means of groups among themselves. The corresponding Urine sugar was improved in both fasting and post-meal analysis in all groups. In follow-up after stopping medicine for 15 days Group A shows remarkable improvement as the BSL, even though it expresses p value which was not significant at >0.10. In Group B and C has exhibited rise in the BSL both in Fasting and Post Lunch, exhibiting non-response after the withdrawal of medicine. In follow-up after continuing the medicine for 30 days there was relief in fasting BSL expressing p value of <0.10, <0.01 and <0.01 in Group A, B and C respectively. In Post-Lunch BSL there was relief expressing p value of <0.01, <0.001 and <0.001 in Group A, B and C respectively.

The GAS for subjective parameters found to be improved in Group A and C, showing p value <0.001, where as Group B doesn’t have significant improvement in it. The ANOVA exhibits significant difference in the means of the groups among themselves. The overall effect of therapy exhibits that Group A has only 44 % relief where as Group B shows 78.25% % and Group C has 68.17% relief.

Conclusion:

Kakamachi is found to elucidate roughly in all the Ayurvedic Grantha starting from Vedic period to till date. There is time-to-time explanation mentioned in the text for the handling of Kakamachi. The drug performs all standard parameters as per API and WHO. The drug also screened for the acute, sub-acute toxicity and heavy metal contains and found to be safe for administration. The drug doesn’t have any side effect or adverse on vital organs like Liver and Kidney functions. The drug was unable to exhibit significant relief in Lipid profile on the contrary it was enhancing Serum triglycerides.
LDL, VLDL and decreasing HDL. The drug as a single doesn’t have shown relief in Glycosylated Hb but in combination with Sulphonylurea group it has a significant relief. Kakamachi shown 44% relief in BSL but it is interesting to observe that the drug has improved the subjective parameters as compare to other two groups. It is concluded that Kakamachi can be used in early diagnosed, less complicated and less severe Diabetes Mellitus.

The entire work was presented in the thesis as preamble, Chapter -I as Drug Profile, Chapter –II as Disease Profile, Chapter –III as Standardization and safety study, Chapter –IV as Clinical Study, Chapter -V as Discussion and Conclusion and Chapter -VI as Summery followed by Bibliography and Annexure.