Summary
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The present study entitled "Study of Lagerstroemia speciosa (L.) Pers as a Hypoglycemic Agent" was undertaken with an aim to study the hypoglycemic action of Lagerstroemia speciosa leaves in Type 2 Diabetes mellitus.

For this study 100 patients of type 2 diabetes mellitus in the age group 30 – 70 years were taken from Govt. Ayurvedic College & Hospital, Guwahati and North Eastern India Ayurveda Research Institute, Bhetapara, Guwahati, Assam. The cases were selected regardless of their sex, socio-economic status, body weight etc, but after fulfilling the inclusion criteria i.e. increased fasting blood sugar (FBS) ≥ 126 mg/dl, increased post-prandial blood sugar (PPBS) ≥ 140 mg/dl and increased Glycosylated hemoglobin (HbA1c) ≥ 6.5 %. An informed consent for the study was obtained from each patient. The clinical Performa was filled up for all patients after doing proper interrogation and clinical data was filled up time to time during each follow-up. All selected cases were advised to take trial drugs (Lagerstroemia speciosa leaves powder) in the dose of 12 grams daily in two divided dose ½ hour before breakfast and dinner with warm along with dietary modification and regular physical exercise.

Chapter 1:
An introductory concept of Ayurveda with special reference to Prameha in every point of view i.e. definition, prevalence, types, etiology, pathogenesis, clinical features, complication etc. viz-a-viz Diabetes mellitus have been discussed.

Chapter 2:
In the Ayurvedic literature new approach to understanding the pramehaviz-a-viz diabetes have been discussed and seen that diabetes mellitus existed since the time immemorial with most ancient description of Ayurveda i.e. in Atharva Veda, Garuda Puran and in Valmiki Ramayana.

"Study of Lagerstroemia speciosa (L.) Pers as a Hypoglycemic Agent"
♦ In Ayurvedic literature like CharakSamhita, SushrutaSamhita, BhelSamhita, AstangaSamgraha, AstangaHridaya, Chakradutta, MadhavNidan, Bhavaprakash, Sarangadharsamhita and BhaisajyaRatnawali, described the disease Prameha vividly.

♦ The 3 dosik classifications are again subdivided into 20 type i.e. Kaphaja (10), Pittaja (6), and Vataja (4) as per urine character, most of which are found independently in various other systemic and metabolic disorders. Madhumeha is one of Vataja Prameha.

♦ Prameha is classified according to hetu in to two types i.e. Sahaja and Apathyanimittaja. According to the dehaprakriti i.e. Sthula and Krisha. According to prognosis i.e. Sadhya, Yapya and Asadhya.

♦ Sthulya is mentioned as nidanathakararoga of Prameha.

♦ Voracious eater, aversion to bath i.e. laziness and avoidance to physical activity i.e. sedentary lifestyle are the predisposing factor of Prameha.

♦ Those aharvihar which produces sleshma, meda, mutra causes Prameha.

♦ Dushya (10) involved in Prameha are specially abadhameda along with rasa, rakta, mamsa, vasa, majja, lasika, kleda, sukra and oja.

♦ The study of pathogenesis reveals that Kaphaja Prameha is comparable with insulin resistance due to obesity and over nutrition leading to DM, Pittaja Prameha is comparable with increase urination, muscle wasting due to increase adrenal secretion, glucagon, cortisol; and Vataja Prameha is comparable with absolute insulin deficiency.

♦ Regarding the etiological factor gives nice correlation about high carbohydrate and fatty diet and sedentary lifestyle with diabetes as a causative factor, is as like mentioned by the modern science obesity induced hyperinsulimemia and diabetes in type 2. Similarly directly vata aggravation precipitates Prameha (i.e. Vatik Prameha/ Madhumeha) which are life threatening due to faster deep seated dhatukshya is synonymous to type 1 diabetes in modern science.
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♦ The purvarupaas of Prameha are usually found as complication of diabetes mellitus.

♦ Prameha and Madhumeha are synonymous because Prameha in its due course converted to Madhumeha which is incurable. Prameha present with the features of excessive urination and lastly sweetish urination.

♦ Vagabhatta clearly mentioned that sweetness in the Prameha remains at any stage in the body which directly denoting hyperglycemia, whatever describes in modern science. When blood sugar exceeds the renal threshold then sugar passes through the urine named glycosuria synonymous to Madhumeha.

♦ Prameha is diagnosed if the person has purvarupa of Prameha along with some increase of urine volume. Or the person has all or half of the purvarupa along with excessive urination.

♦ Ayurveda advise treatment of Prameha on the basis of body constitution; Sthula (obese) with samsodhan and krisha (lean) with santarpan followed by medication. Followed by various pathyaahar and vihar along with medicines.

Chapter 3:

In this chapter modern review, definition, historical perspective and background, prevalence, classification, etiology, pathogenesis, clinical features, methods of diagnosis and management discussed.

♦ Definition implies that diabetes is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs (WHO).

♦ Natural historical development described under the heading of "Historical perspective" and "Background". These two paragraphs strongly clears
that Ayurveda is the ancient science which recognized first diabetes as Prameha and Madhumeha along with its complication and management.

- Prevalence has been mentioned to alarm the increased incidence in the present and future.

- Diabetes is one of the most common non-communicable diseases (NCDs). It is the fourth or fifth leading cause of death.

- According to the International Diabetic Federation (IDF) as on 2013, about **382 million** people worldwide, or **8.3%** adults, are estimated to have Diabetes. About **80%** live in low-and middle-income countries. If these trends continue, by 2035, some **592 million** people, or one adult in 10, will have Diabetes. This equates to approximately three new cases every 10 seconds or almost 10 million per year.

- Diabetes is among the top 10 causes of disability, resulting in life-threatening complications such heart disease, stroke, lower limb amputation and blindness. Diabetes causes one death in every six seconds.

- **50%** of people with diabetes are undiagnosed. **80%** of people with diabetes live in low-and-middle income countries.

- Diabetes impacts negatively on many aspects of global development, including economic and environmental sustainability, human development and other infectious and non-communicable diseases.

- With the spread of fast-food outlets and more sedentary lifestyles, the prevalence of diabetes in India is rising alarmingly.

- According to the Indian Council of Medical Research-Indian Diabetes study (ICMR-INDIAB) - 2013, India has 62.4 million people with diabetes. This is set to increase to over 100 million by 2030.

- Diabetes is increasingly afflicting young and affluent urban people in India, a survey reveals almost one in every eight person living in a metro is diabetic. The prevalence of diabetes is the highest in the urban...
(12.4%) areas, followed by the midland (8.1%), highland (5.8%) and coastal division (2.5%).

♦ As insulin is the main pathological hall marks, so that details about the insulin secretion, complication produced due to lack of insulin have been described in a flow chart.

♦ Recent classifications of diabetes mellitus along with its pathogenesis have been described and summary is that type 1 diabetes occur due to autoimmune destruction of beta cell as well as idiopathic cause. Type 2 diabetes occurs mostly due to overweight resulting hyperinsulinemia and insulin resistance. On the other hand 3rd classification reflects the carbohydrate intolerance during pregnancy as Gestational DM. And other classification indicates endocrine, genetic, drugs induced causes of diabetes.

♦ Type 1 diabetes mellitus usually develops in childhood and adolescence and patients require lifelong insulin injection for survival.

♦ Type 2 diabetes mellitus (T2DM) usually develops in adulthood and is related to obesity, lack of physical activity and unhealthy diets. T2DM is thought to occur in genetically predisposed persons who are exposed to series of environmental influences that precipitate the onset of clinical symptoms.

♦ T2DM is the more common type of diabetes (90% worldwide) and treatment may involve lifestyle changes and weight loss alone, or oral medications or even insulin.

♦ Sex, age and ethnic background are important factors in determining the risk of developing T2DM.
Criteria for diagnosis of diabetes mellitus:

<table>
<thead>
<tr>
<th>Test</th>
<th>Normoglycemia</th>
<th>Increased Risk</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Impaired Fasting Glucose</td>
<td>Impaired Glucose Tolerance</td>
</tr>
<tr>
<td>PG, fasting (mg/dl)</td>
<td>&lt;100</td>
<td>100 – 125</td>
<td>≥126</td>
</tr>
<tr>
<td>PG, 2-hour (mg/dl)</td>
<td>&lt;140</td>
<td>140 – 199</td>
<td>≥200</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td>5.7 - 6.4</td>
<td>≥6.5</td>
</tr>
<tr>
<td>PG, Random (mg/dl)</td>
<td></td>
<td>&gt;200 mg/dL plus symptoms of diabetes</td>
<td></td>
</tr>
</tbody>
</table>

♦ The common clinical features of diabetes are osmotic symptoms-polyuria, polydipsia and polyphagia; and non-osmotic symptoms-weakness, fatigue, weight loss etc.

♦ From pathophysiologic point of view, person with T2DM consistently demonstrate three cardinal abnormalities:
  > Resistance to the action of insulin in peripheral tissues, particularly muscle and fat but also liver.
  > Defective insulin secretion, particularly in response to a glucose stimulus.
  > Increased glucose production by the liver.

♦ The untreated cases of diabetes have a lot of complications like diabetic ketoacidosis, hyperglycemic hyperosmolar non-ketotic coma, lactic acidosis etc. as acute complications and retinopathy, neuropathy, nephropathy, cardiovascular diseases etc. as chronic complications.

♦ Complication of diabetes mellitus and its prevention is more important as there is no treatment available to reverse these complications. So that details about the pathogenesis of diabetic complications, types of complications etc. have been shown in different well arrange flow chart.

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♦ Management approach for both type 1 and type 2 with the help of diet, exercise and drugs have been shown in different algorithmic chart and it shows that instead of high energy diet low energy diet with low fats and high fiber diet is beneficial.

♦ Lifestyle intervention: The components of lifestyle intervention include medical nutrition counseling, exercise recommendations and comprehensive diabetes education with purpose of changing the paradigm of care in diabetes from provider focused to patients focused.

♦ The oral hypoglycemic agents (OHA) are used in type 2 DM in case of failures of diet and exercise management. Commonly used OHA are Sulfonylureas, Biguanides, Thiazolidinediones etc.

♦ The available oral hypoglycemic agent can be divided by mechanism of action into several groups: insulin sensitizer with primary action in the liver, insulin sensitizer with primary action in peripheral tissues, insulin secretagogues, agents that’s slow the absorption of carbohydrates.

♦ Insulin plays important role in the management of longstanding Type 2 DM. Insulin can be used in combination with any of OHA in patients who fails to reach the glycemic target.

♦ Similarly anaerobic exercise and weight loss are more helpful to increase the insulin sensitivity and if these two measures failed than advised for combining of diet, exercise and drugs.

Chapter 4:

For the study Lagerstroemia speciosa (L.) Pers leaves have been selected. Their identification, constituents, properties and research work done on them are discussed in this part.

♦ Lagerstroemia speciosa (Jarul/ Tinish/ Ajhar) leaves powder whose taste (rasa) is Kasaya and Katu. This drug has Laghu and Rukshaguna which helps in suppression of kaphadosa. This drug has been also mentioned
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in BhavaprakashNighantu (Ayurvedic classic of 16 century) in Vatadivarga and which have hypoglycemic action.

♦ The active principles of the plant which act as insulin like action is Corosolic Acid and others active principles are lagerostromin and Lagertannins. Corosolic acid activates the transport of glucose across the cell membrane, resulting blood sugar reduction. It has inhibitory effects on post prandial hyperglycemia by inhibiting alpha-amylase and alpha-glycosidase. Lagerstroemin is an ellagitannin works as insulin receptor activator by increasing tyrosine- phosphorylation of the sub-unit of insulin receptor. Lagertannins stimulates glucose transport and adipocyte differentiation inhibitory activity in 3T3 - L1 cells as adipogenesis, the differentiation and proliferation of adipocytes is a major mechanism leading to weight gain and obesity.

Chapter 5:

Details of clinical study including aim and objective, plan of the study and assessment of result are discussed in this part.

♦ An open non-comparative clinical trial was done on 100 patients of type 2 diabetes mellitus for 3 months. Patients were selected from Govt. Ayurvedic College & Hospital, Guwahati and North Eastern India Ayurveda Research Institute, Bhetapara, Guwahati, Assam, which have fulfilled the inclusion criteria.

In demographic profile age, sex, socioeconomic status, habitats, education, occupation, dietary habit, addiction, physical activates, BMI of 100 registered patients has been focused for the incidence –

♦ The present clinical study of Age and Sex incidence in patients of Type 2 Diabetes mellitus revealed maximum number of patients reported in between 41 – 50 years (41%) and 51 – 60 years (40%) followed by 61 – 70 years (13%). The study of sex incidence revealed that the maximum number of patients are female (52%) followed by male
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(48%). Incidence of Type 2 Diabetes mellitus in India is higher in female than male.
♦ Study of socioeconomic status showed that incidence of maximum number of Type 2 Diabetes mellitus cases from the higher income group (44%).
♦ Among the 100 cases of Type 2 Diabetes mellitus more patients are from urban (72%) area followed by rural area (28%).
♦ Out of 100 patients of Type 2 Diabetes mellitus, maximum numbers of patients were graduate/post graduate (62%).
♦ In present study in 100 cases of Type 2 Diabetes mellitus shows servicemen (38%), housewife (30%) are highly affected due to their low physical activity similarly of businessman (29%), so that excess fat deposition may triggered to the development of diabetes.
♦ In this area more patients are non-vegetarian, so our study also shows that incidence is more among non-vegetarian (94%).
♦ Regarding the addiction in Type 2 Diabetes mellitus 30% patient having no addiction, where maximum number betel/ tobacco (33%) followed by smoker patient (25%) and alcohol (12%). Alcohol and smoking both of these factors are the most risk factors to develop Type 2 DM.
♦ Regarding incidence in physical activities more patients are mild active (60%) followed by moderate active (32%) and severe active (8%). Similarly BMI of the 100 patient more are in over weight group (52%) followed by non-obese (40%) and obese (8%).
♦ Among 100 patients in our study (38%) patient have positive family history and rest (62%) were negative family history.

Assessment of the therapeutic response of each patient was subjected to series of laboratory test i.e. FBS, PPBS and Glycosylated hemoglobin (HbA1c) before and after completion of treatment.
Laboratory investigations shown significant result (P< 0.01) in FBS, PPBS and HbA1c after treating with trial drugs for 3 months.

In case of FBS before treatment i.e. Mean ± SD is 168 ± 36 and values after treatment are: Mean ± SD is 135 ± 19.5, SE value is 4.09 and Z value is 7.33 which is highly significant (P< 0.01).

Similarly effect of treatment on PPBS, before treatment i.e. Mean ± SD is 202 ± 44.4 and values after treatment are: Mean ± SD is 166 ± 26.4, SE value is 5.16 and Z value is 6.97 which is highly significant (P< 0.01).

Effect of treatment on HbA1c is as follows, before treatment: Mean ± SD is 7.3 ± 0.76, and after treatment: Mean ± SD is 6.5 ± 0.41, SE value is 0.086 and Z value is 9.3 which is also very highly significant (P< 0.01).

In all cases blood sugar falls in sequential manner and not showed any unwanted hypoglycemic effect even the blood sugar may be slightly in a high range before treatment. This study directly support that the trial drugs has no any unwanted hypoglycemic affect.

In study it has been observed that our trial drug acts as a mild purgative.