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**MEDICAL APPROACHES TOWARDS THE MANAGEMENT OF DIABETES  
MELLITUS/ PRAMEHA**

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**ABSTRACT**

Diabetes mellitus / *Prameha* is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. It is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein, metabolism resulting from defects in insulin secretion, insulin action, or both. Shows the symptoms of thirst, polyuria, weight loss etc. If left untreated, diabetes can cause many complications. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, damage to the eyes and cognitive impairment foot ulcers, damage to the nerves. There are mainly 2 types. They are type1 and type2 some other types are also there. Ayurveda has also described diabetes as *Prameha*. *Ayurvedic* system stated that when the human body and mind experience discomfort and pain that stage is called a disease. The root cause of a disease is an imbalance in *dosha* (bio- physiological bases), *dhatu* (tissue involved) and *mala* (excretory products) in terms of changes in their quantity and quality as well as their relative ratio to each other in an individual of the particular constitution.

**Keyword: Diabetes mellitus, Prameha, Ayurvedic, Insulin**

**INTRODUCTION**

*Ayurveda* is a holistic science deals with every aspect of life, right from birth up to old age. It supports adopting good dietary

habits and lifestyles to endure a healthy body and mind [1, 2]. It advocated the medication and other modalities to fight

the disease both at somatic and psychic levels. Millions of people are dying due to unhealthy conditions. Furthermore, we have acquainted with excellent techniques, astonishing advancement in medical science and technology but humanity still facing numerous health problems and hazards. Most of the developed diseases have a direct or indirect link with food habits and lifestyle [1, 3].

*Ayurvedic* system stated that when the human body and mind experience discomfort and pain that stage is called a disease. The root cause of a disease is an imbalance in *dosha* (bio- physiological bases), *dhatu* (tissue involved) and *mala* (excretory products) in terms of changes in their quantity and quality as well as their relative ratio to each other in an individual of the particular constitution [4-6].

Diabetes mellitus / *Prameha* is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin production, insulin action or both. *Prameha* (Diabetes Mellitus) is one of the lifestyle disorders whose pervasiveness is growing rapidly throughout the world [7, 8]. The conventional modern system of medicines has remedies to control and treat diabetes but is unable to provide complete relief. They are accompanied by other side

and adverse effects. So, *Ayurvedic* system of medicine can become a potential source of *Prameha rodhi* (antidiabetic) drugs that are relatively safe, significantly potent with negligible side effects and can able to improve the quality of human life [4, 9]. Moreover, the ayurvedic science also prefers and prescribes *Shodhana* (purification/ cleansing procedures), *Pathya-Apathya* (compatible diet and lifestyle) and *Yoga* in the effective management of diseases [10]. Nowadays *Prameha* (Diabetes Mellitus) is a common chronic metabolic disorder prevalent all over the world. The mortality rate due to *Prameha* (Diabetes Mellitus) is very high and it is ranked fifth amongst the ten major causes of death [11, 12].

*Prameha* is a *santarpanotha vyadhi*. That means, it is the resultant of over nutrition that leads to the *santarpanotha janita lakshana* like laziness, sedentary habits etc which make the body breeding ground for the *santarpanotha janita vyadhi* mentioned by *Acharya Charaka* [4]. In that series of *vyadhis*, *prameha* is the first disease. *Santarpana* (over nutrition) can be established due to both dietary and lifestyle factors. Along with that, mental factors such as anxiety, grief, and sorrow also cause impairment of *agni* leads to *amavastha* [10, 13]. This is well supported

by the finding of today's modern era where anxieties, depression like mental factors are one of the major contributing factors for the incident of type-2 diabetes mellitus [14].

Criteria for the diagnosis of diabetes mellitus

1. Symptoms of diabetes plus casual plasma glucose concentration 200 mg/dl (11.1mmol/l). Casual is defined as any time of day without regard to time since the last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss [15].

or

2. FPG 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h [16].

or

3. 2-hrs postload glucose 200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day. The third measure (OGTT) is not recommended for routine clinical use [17, 18].

## SYMPTOMS

- Increased thirst and increased appetite, Weight loss, Frequent urination, Blurring of vision, Headache, Fatigue, Slow healing of cuts etc. [7, 19-21].

If left untreated, diabetes can cause many complications. Serious long-term complications include:

- Cardiovascular disease, Stroke, Chronic kidney disease, Damage to the eyes and cognitive impairment, Foot ulcers, Damage to the nerves [7, 19-21].

## BURDEN OF DIABETES

The development of diabetes is projected to reach pandemic proportions over the next 10-20 years. International Diabetes Federation (IDF) data indicate that by the year 2025, the number of people affected will reach 333 million -90% of these people will have type 2 diabetes. In most western societies, the overall prevalence has reached 4-6%, and is as high as 10-12% among 60-70-year-old people. The annual health costs caused by diabetes and its complications account for around 6-12% of all health care expenditures [22, 23].

## TYPES ACCORDING TO THE MODERN ASPECT [16, 24, 25]:

- Type1 Diabetes, Type 2 Diabetes, Gestational Diabetes, Other types: LADA (Latent Autoimmune Diabetes in Adults), MODY (Maturity-Onset Diabetes of Youth), Secondary Diabetes Mellitus

### TYPE 1 DIABETES

It was previously called insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes [7]. It develops when the body's immune system destroys pancreatic beta cells, the only cell in the body that make the hormone insulin that regulates blood glucose [26]. This form of diabetes is usually striking in children and young adults, although disease onset can occur at any age. Type1 diabetes may account for 5% to 10% of all diagnosed. Risk factors for this type may include autoimmune, genetic, and environmental factors [27].

### TYPE2 DIABETES

It was previously called non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes [28, 29]. It may account for about 90% to 95% of all diagnosed cases of diabetes. It usually begins as insulin resistance a disorder in which the cells do not use insulin properly

[30]. As the need for insulin rises, the pancreas gradually loses its ability to produce insulin [31]. It is associated with older age, obesity [11], family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity and race/ethnicity. Indian, African Americans, Latino Americans, and some Asian, Americans or other pacific islanders are at particularly high risk for this type. Now it is increasingly being diagnosed in children and adolescents [31].

### GESTATIONAL DIABETES

Form of glucose intolerance that is diagnosed in some women during pregnancy. It may occur more frequently among African Americans and Indians. It is more common among obese women and women with a family history of diabetes [16, 25]. During pregnancy, gestational diabetes requires treatment to normalize maternal blood glucose levels to avoid complications in the infant. After pregnancy, 5% to 10% of women with gestational diabetes are found to have type2 diabetes [32]. Women who had gestational diabetes have a 20% to 50% chance of developing diabetes in the next 5-10 years. Other specific types of diabetes mellitus result from specific genetic conditions (such as maturity-onset diabetes

of youth), surgery, drugs, malnutrition, infections, and other illnesses [33]. Such types of diabetes may account for 1% to 5% of all diagnosed cases of diabetes [34].

### **LADA (LATENT AUTOIMMUNE DIABETES IN ADULTS)**

LADA is a form of autoimmune (type 1 diabetes) that is diagnosed in individuals who are older than the usual age of onset of type 1 diabetes. Alternate terms that have been used for “LADA” include Late-onset Autoimmune Diabetes of Adulthood, “slow onset type1” diabetes, and sometimes also called Type1.5. Often, patients with LADA are mistakenly thought to have type2 diabetes, based on their age at the time of diagnosis [35-38].

#### **Features of LADA**

- Patients usually aged  $\geq 25$  years.
- Clinical presentation “masquerading” as non-obese type2 diabetes
- Initial control achieved with diet alone or diet and oral hypoglycemic agents
- Insulin dependency occurs within months but can take 10 years or more [35-38].

About 80% of adults apparently with recently diagnosed Type2 diabetes but with GAD autoantibodies (i.e. LADA) progress to insulin requirement within 6 years. The potential value of identifying this group at high risk of progression to insulin

dependence includes the avoidance of using metformin treatment and the early introduction of insulin therapy [35-39].

### **MODY (MATURITY ONSET DIABETES OF THE YOUNG)**

It is a monogenic form of diabetes with an autosomal dominant mode of inheritance: Mutations in any one of several transcription factors or the enzyme glucokinase lead to sufficient insulin release from pancreatic  $\beta$  cells, causing MODY. Different subtypes of MODY are identified based on the mutated gene. Originally, the diagnosis of MODY was based on the presence of non-ketotic hyperglycemia in adolescents or young adults in conjunction with a family history of diabetes. However genetic testing has shown that MODY can occur at any age and that a family history of diabetes is not always obvious [40-42].

#### **Features suggestive of monogenic diabetes:**

- The majority have HNF-1 alpha or HNF-4 alpha mutation [43]. Generally,  $< 25$  years of age Strong family history of diabetes (typically 2-3 generations affected)
- Sulfonylurea sensitivity - Absence of insulin resistance phenotype: normal BP, TG, HDL-C
- PNDM (50% have 6.2 mutation) [44]

- Diabetes onset <6 month of age DEND syndrome [45]

Within MODY, the different subtypes can essentially be divided into 2 distinct groups: glucokinase MODY and transcription factor MODY, distinguished by characteristic phenotypic features and pattern on oral glucose tolerance testing. Glucokinase MODY requires on treatment, while transcription factor MODY (i.e. Hepatocyte nuclear factor-1 alpha) requires low dose sulfonylurea therapy and PNDM requires high- dose sulfonylurea therapy [41, 42].

#### SECONDARY DIABETES MELLITUS

Result from another medical condition or due to the treatment of a medical condition that causes abnormal blood glucose levels. The secondary occurrence of type 2 diabetes with various hormonal diseases (e.g. pituitary, adrenal and/or thyroid diseases) is a recurrent observation. Indeed, impaired glucose tolerance (IGT) and overt diabetes mellitus are frequently associated with acromegaly and Cushing syndrome [46, 47]. The increased cardiovascular morbidity and mortality associated with acromegaly and Cushing syndrome may partly be a consequence of increased insulin resistance that normally accompanies hormone excess.

Acromegalic patients are insulin resistant, both in the liver and in the periphery, displaying hyperinsulinemia and increased glucose turnover in the basal post-absorptive states. The prevalence of diabetes mellitus and that of IGT in acromegaly is reported to range 16–56%, whereas the degree of glucose tolerance seems correlated with circulating growth hormone (GH) levels, age, and disease duration. Moreover, a family history of diabetes and the concomitant presence of arterial hypertension has been found to predispose to diabetes as well. GH has physiological effects on glucose metabolism, stimulating gluconeogenesis and lipolysis, which results in increased blood glucose and free fatty acid levels. Conversely, insulin-like growth factor 1 (IGF-I) enhances insulin sensitivity primarily on skeletal muscles [48, 49].

#### HISTORICAL GLIMPSES:

- **Vedic Period:** Oldest authentic manuscripts are described about *Prameha (Diabetes Mellitus)* but in rudimentary form. *Atharvaveda* in *Kaushik Sutra* [K.Su.26/6-10] terms '*Aasrava*' & '*Prameha*' are used. Vedic commentators *Sayana* and *Kesava* mentioned the *Aasrava* as *mutratisara*..
- **Agni Purana:** *Kshaudrameha* and

*Akshaudrameha* are described [50].

- **Garuda Purana:** The term *Madhumeha* itself being used as “*madhuryacha tanorata*” [51].
- **Ramayana:** Description of the colour of urine like *madhu* [52].
- **Kautilya Arthashastra:** The word *Prameha* is found in *Kautilya Arthashastra* [53].
- **Charaka Samhita:** Acharya Charaka has described *prameha* in a very elaborative manner in *sutra sthana*, *nidanasthana* and *chikitsasthana*. At *nidanasthana* & *chikitsasthana* etiological factors, prodromal symptoms and complications related to *prameha* has been mentioned. At *sutrasthana* mentioned about *prameha pidika* and *avarana-janya madhumeha*. At *chikitsasthana* in *prameha chikitsa adhyaya* describes some more etiological factors of *prameha* emphasizing on certain abnormal dietary and physical activities. *Prameha* has been classified into two categories- *sthula* (over weight) and *krisha* (underweight) for treatment purpose. Further, *acharya* explains the hereditary aspect of the disease [4].
- **Sushruta Samhita:** Acharya Sushruta at *nidanasthana* describe the etiological factors of *prameha*, followed by etiopathogenesis and prodromal symptoms

of *prameha*. The complication of the *prameha* has been described according to the predominance of *dosha* along with the description of *prameha pidika*. Further, Acharya Sushruta concludes the chapter of *prameha nidana* with the statement that all *prameha* if not treated properly can lead to an incurable state of *madhumeha*. At *chikitsasthana* predisposing factors of *prameha* are mentioned along with the concept of *apathyanimittaja prameha* and *sahaja prameha*. The *apathyanimittaja prameha* has been stated as the resultant of sedentary life style and habit of over eating. The text has described various types of *kashaya kalpana* for different types of *prameha*. A separate chapter for treatment of *prameha pidika*/diabetic carbuncles and the treatment of *madhumeha* is dedicated in *chikitsasthana* [9].

- **Ashtanga Hridaya:** Acharya Vagbhatta at *nidanasthana* describes the etiological factors, pathogenesis of *vata*, *pitta* & *kaphaja prameha*. Vagbhatta described two most probable causes of *madhumeha*. i.e.: *dhatu kshaya* and *avarana*. At *chikitsasthana*, a detailed treatment regime for *prameha* has been mentioned [54].
- **Harita Samhita:** This text has mentioned *prameha* as *papajanya*

*vikara* and described 13 types of *prameha* with different nomenclature i.e. *Puya prameha*, *Takra prameha*, *Rasa prameha*, *Ghrita prameha* etc. which are differ from *brihtraiyee* [55].

• **Bhela Samhita:** This text has classified *prameha* in 2 types i.e. *svakrtameha* and *prakrtameha*.

• **Kashyapa Samhita:** *Acharya Kashyapa* has mentioned the symptoms of *prameha* child in *vedanadhyaya* and accepted the disease as *chirakari* [56].

• **Madhavanidana:** *Madhavakara* at 33<sup>rd</sup> chapter described the *prameha* similarly to *brihtraiyee* [10].

• **Dalhana:** In his commentary on *Sushruta Samhita*, '*Nibandha Samgraha*', he opines that females do not suffer from *prameha*.

• **Sharangadhara Samhita:** *Acharya Sharangdhara* mentioned 20 types of *prameha* in *poorvakhanda* chapter 7<sup>th</sup> / [59-62], [57].

#### ETIOLOGICAL FACTORS FOR PRAMEHA:

1. **Dietary factors** - Diet rich in sweet content, high fatty diet, milk and milk products, intake of freshly harvested crops, a diet of jaggery and its products are mentioned as the diets responsible for *Prameha* [58, 59].

2. **Lifestyle factors** - Sedentary lifestyle i.e. less physical activities in daily life as well as at workplace & certain mental factors like anger, grief, worry etc [60].

3. **Beeja doshaja** (Hereditary factors) – *Prameha* shows a strong hereditary connection in the people who have HLA (human leukocyte antigen) in their blood which is transmitted from the parents [61].

4. **Genetics** – It plays an important role in type-II diabetes with a complicated pattern. In its impairment of beta-cell functioning and an unusual response towards insulin is involved. i.e. defective fatty-acid binding protein2 (FABP2), defective lipoprotein lipase (LpL), Regulation of calpain-10 protein and peroxisome proliferator-activated receptor (PPAR) which may contribute to both type-2 diabetes and high blood pressure in some patients [62].

5. **Environmental factors** – Work-related exposures have been significantly linked with increased risk of diabetes. Recent data suggest that toxic substances in the environment, other than infectious agents or exposures that stimulate an immune response, are associated with the occurrence of these diseases. For type-1 diabetes, higher intake of

nitrites, and *N*-nitroso compounds, as well as higher serum levels of polychlorinated biphenyls have been associated with increased risk. In the case of a viral infection, a viral protein that enters the body resembles beta-cell protein. As a result, the immune system starts attacking both beta cells and viruses, being unable to distinguish one from the other [63].

**6. Obesity** – Lack of physical activities and a sedentary lifestyle lead to weight gain

and finally persons becoming obese which cause stress in the cellular membranes of the endoplasmic reticulum leads to inadvertently malfunction and suppressing insulin receptor signals causing diabetes [11].

**7. Poor diet** - Junk foods (unhealthy foods) usually high in calories and low in useful nutrients [64].

Table 1: - General *nidana* of *prameha*

<i>Nidana</i>	Ch. [4]	Su. [9]	A.S. [65]	A.H [54]
<i>Ahara</i>				
<i>Dadhi</i>	+	-	-	+
<i>Gramya, Anupa, Audaka Mamsa</i>	+	-	-	+
<i>Payaha</i>	+	-	-	+
<i>Navapana</i>	+	-	-	+
<i>Navanna</i>	+	-	-	+
<i>Guda Vikrita</i>	+	-	-	+
<i>Shleshmajanaka Ahara</i>	+	-	+	+
<i>Sheeta Dravya</i>	-	+	-	+
<i>Madhura Dravya</i>	-	+	-	+
<i>Amla, Lavana Rasa</i>	+	-	-	-
<i>Snigdha Dravya</i>	-	+	-	+
<i>Drava Anupana</i>	-	+	-	+
<i>Guru Dravya</i>	-	-	-	+
<i>Picchila Dravya</i>	-	-	-	+
<i>Mutranjanaka Dravya</i>	-	-	+	+
<i>Tikta, Katu, Kashaya Rasa</i>	-	-	-	+
<i>Vihara</i>				
<i>Asya Sukham</i>	+	-	-	+
<i>Swapna Sukham</i>	+	-	-	-
<i>Divaswapna</i>	-	+	-	-
<i>Avyayayama</i>	-	+	-	-
<i>Alasya</i>	-	+	-	-
<i>Manasa</i>				
<i>Vishada</i>	+	+	+	+
<i>Tyakta Chinta</i>	+	-	+	+
<i>Beeja Dosha</i>	+	+	+	+

Table 2: Specific nidana of Kaphaja, Pittaja, Vataja Prameha

<i>Kaphaja Prameha</i>	<i>Pittaja Prameha</i>	<i>Vataja Prameha</i>
<i>Ahara</i>		
<i>Hayanaka</i>	<i>Ushna</i>	<i>Kashaya</i>
<i>Yavaka</i>	<i>Amla</i>	<i>Katu</i>
<i>Chinaka</i>	<i>Lavana</i>	<i>Tikta</i>
<i>Koddalaka</i>	<i>Kashaya</i>	<i>Ruksha</i>
<i>Naishadha</i>	<i>Katu</i>	<i>Laghu</i>
<i>Itkata</i>	<i>Ajirna Bhojana</i>	<i>Sheeta</i>
<i>Mukundaka</i>	<i>Vishama Ahara</i>	
<i>Mahavrihi</i>		
<i>Pramodaka</i>		
<i>Navanna</i>		
<i>Sarpishmatam, Nava Harenu</i>		
<i>Masha Supya</i>		
<i>Gramya, Anupa, Audaka Mamsa</i>		
<i>Shaka, Tila, Palala</i>		
<i>Pishtanna</i>		
<i>Payaha</i>		
<i>Krishara</i>		
<i>Vilepi</i>		
<i>Ikshu Vikara</i>		
<i>Kshira</i>		
<i>Madhya</i>		
<i>Sleshma-meda-mutra-varadhaka</i>		
<i>Mandaka-Dadhi</i>		
<i>Drava Madhura, Taruna, Dravya</i>		
<i>Vihara</i>		
<i>Mrija Varjana</i>	<i>Atapa</i>	<i>Vyavaya</i>
<i>Vyayama Varjana</i>	<i>Agni</i>	<i>Vyayama, Vishama Sharira</i>
<i>Swapna, Shayya, Asana Prasanga</i>	<i>Santapa</i>	<i>Vamanan, Virechana atiyoga</i>
<i>Sleshma-meda-mutra-varadhaka Ahara</i>	<i>Shrama</i>	<i>Asthapana, Shirovirechana Atiyoga</i>
		<i>Vega sandharana, Annashana, Atopa, Shonita atiseka, Jagarana</i>
<i>Manasika</i>		
<i>Tyakta Chinta</i>	<i>Krodha</i>	<i>Abhighata, Udvega, Shoka</i>

## TYPES OF PRAMEHA

Prameha is classified as under [4, 7, 9, 10, 24, 25, 29, 54]

Sr. No.	Ayurvedic	Modern
1	<i>Doshika</i> <ul style="list-style-type: none"> <li><i>Kaphaja</i> (10)</li> <li><i>Pittaja</i> (6)</li> <li><i>Vataja</i> (4)</li> </ul>	Type-1 diabetes (beta cell destruction, usually leading to absolute insulin deficiency)
2	<i>Naidanika</i> <ul style="list-style-type: none"> <li><i>Sahaja</i></li> <li><i>Apathyanimittaja</i></li> </ul>	Type-2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)
3	<i>Samhanana</i> (body constitution - <i>sthoola pramehi, krisha pramehi</i> )	Genetic defects of the $\beta$ -cell
4	<i>Sadhyasadhyata</i> (prognostic)	Genetic defects in insulin action
5		Diseases of the exocrine pancreas
6		Endocrinopathies
7		Drug or chemical-induced diabetes
8		Infections
9		Gestational diabetes mellitus (GDM)
10		Idiopathic diabetes

## PRAMEHA & DIABETES MELLITUS- SIMILARITIES

1. **In terms of etiology** (predisposing factors and etiology) - The individuals who have less physical activity due to their sedentary lifestyle and the individual whose dietary intake in terms of calories is more and irregular may be a major predisposing factor indicated in both *ayurvedic* and modern literature [66].

2. **In terms of presentation of the disease** - The disease often manifests in the individuals who are overweight, with symptoms like increased urine frequency (*prabhuta mutrata*), passing of sweet urine (*madhumeho madhusamam*), symptoms like burning sensation (*paridaha*) & numbness (*suptata changeshu*) in the extremities which are also cardinal features of diabetes mellitus are very much alike, further supports that the syndrome of diabetes mellitus can be very much correlated to the disease of *prameha* [67].

3. **Family History** — It is one of the possible factors for the individual to get affected by *prameha*, as the same positive history for diabetes mellitus makes offspring of the diabetic couple 25% to 50% more prone for diabetes mellitus [37, 62, 68].

## TREATMENT MODALITIES

Pharmacological and non-pharmacological management of disease have similarities in both the systems of medicine. Non-pharmacological regime includes increased physical activities, exercise supported by food intake to fulfill the required energy for the routine work in terms of less carbohydrate, with less fatty contents are advocated in both the systems of medicine [8]. Pharmacological intervention includes the regime to lower the rising levels of ama (hyperglycemia, hypercholesterolemia etc.) and nourishing the energy deprived tissues by correcting the state of hyperglycemia (*amavastha*) [69].

## PATHYA-APATHYA IN PRAMEHA:-

For the management of any disease, *ayurveda* gives equal importance to the drugs as well as to the *pathya* which are to be followed and to the *apathya* also, which are to be strictly omitted. *Pathya* mentioned in *ayurvedic* texts can be categorized mainly into the following two types-

1. **General pathya and General apathya** - To prevent the origin of the disease and to stay in the state of health these are to be followed regularly. These general

*pathya* include following rules of taking diet like *ashtavidhahara-visheshayatana*, taking *matra vata ahara*, *shada rasa ahara* other than dietary *pathya* there are some lifestyle related *pathya* i.e. regular exercises, abstinence from anger, sorrow, depression, and control of senses along with good code of conduct (*sadavritta*) are mentioned in general *pathya* for prevention of disease (both physical and mental illness) [13, 70].

The general *apathya* are *asaatmeyndriyarthra samyoga*, *pragya-paradha*, *parinama*, practice of faulty dietary habits like over eating (*atiashana*), untimely eating (*vishamashana*) etc, not following the *dinacharya* and *sadavritta* are the leading causes for anger, lust, grief, sorrow etc. which lead to disturbance in physical and mental *dosha* and ultimately causes disease [10].

2. ***Prameha specific pathya and Prameha specific apathya*** : *Prameha specific pathyas* are same as general *pathya* but *Prameha specific apathya* for the *prameha* are just the opposite of the *pathya* mentioned in the texts. As it is instructed the *apathya* like laziness (*utsahaheena*) in the form of a

sedentary lifestyle, not following the dietary recommendations mentioned for the *prameha* can lead to the fatal stage of the *prameha* [13, 70].

### **CHIKITSA (TREATMENT OPTIONS):-**

*Chikitsa* of *prameha* can be broadly divided into two ways:-

1. **For *sthula pramehi/ Apathyanimitajja prameha / Avaranajanya madhumeha:-***

Management of this condition starts with the avoidance of the dietary and lifestyle practices. As this condition is having the predominance of *ama* in the form of *vikrita kapha* (hyperglycemia, dyslipidemia), and *pitta* (decreased insulin sensitivity, insulin resistance), treatment goals should be *agni-deepaka* (improving insulin sensitivity) and *amapachana* (to reduce hyperglycemia and lipid profile etc). The above-said goals of *deepana*, *pachana* can be achieved by both diet and drugs, and lifestyle modifications (exercise etc) [10, 13, 71].

- **Dietary management** - Diet has taken must be less in *pichhila*, *snigdha* (unsaturated fats), less *madhur rasa* contents, more of

fibrous food, whole grains which improve the *agni* (insulin release & sensitivity) and also helps to reduce the burden on the *agni* (beta-cell response to oral intake of food & its sensitivity) by improving the *amavastha* (lipid profile & glycemic control) [13].

- **Drug management** - Drugs recommended for the management of *prameha* acts simultaneously as *deepana* (improves secretion of enzymes and hormones) *pachana* (Improves lipogenesis and glycogenesis), *medohara* (improves dyslipidemia), *pramehaghna* (improves glycemic control), *rasayana* (anti-oxidant). For the management of *apathyanimittaja prameha* (*avaranajanya madhumeha*

or *sthula prameha*) all these properties should be present in the drug or the drug combination [10].

- **Life style modifications for *prameha*:** - Physical exercise improves the *agni* and also enhances tolerability by reducing the stress both of physical and mental levels (*dukha sahisnuta*) [60].
2. **For *krisha pramehi*:** - Management for the *krisha pramehi* (malnourished/asthenic) is the nourishment of the individual through both diet and pharmacological regimens. The diet should be *laghu* and *santarpana*. Besides this, medicated oil preparations are also indicated which nourishes the under nourished tissues without aggravating the *amavastha* (hyperglycemia and dyslipidemia) [10, 13].

Table 3: Different targets for anti-diabetic agents with their mechanism with examples

Targets	Mechanism of action	Examples of inhibitor
Protein Tyrosine Phosphatase 1 B (PTP 1 B)	Inhibiting PTP 1 B increases insulin-sensitizing.	Norathyroil, MSI-1436, DPM-1001
Dipeptidyl peptidase-4 (DPP-4)	DPP-4 inhibitors control hyperglycemia by stimulating insulin secretion.	Sitagliptin, vildagliptin and Saxagliptin
Free fatty acid receptors 1 (FFAR 1) activation	Increases insulin secretion during increased glucose levels.	$\alpha$ -linolenic acid
G protein-coupled receptors (GPCR)	Inhibition decreases glucose-level.	Oleylethanolamide, lysophosphatidylcholine
Peroxisome Proliferator activated receptor- $\gamma$ (PPAR $\gamma$ )	Enhance insulin action by increasing uptake of glucose.	Thiazolidinediones.
$\alpha$ -glucosidase inhibitors (AGIs)	Inhibit carbohydrate absorption from the gut.	Acarbose, miglitol and voglibnse.
Aldose reductase inhibitors	Blocks glucose breakdown by polyol pathway.	Sorbinil , fidarestat and zopolrestat.

Glycogen phosphor ylase Inhibitors (GP)	Attenuate hyperglycemia	Benzazepinones and N-(3,5-Dimethyl-Benzoyl)-N-(β-D-Glucopyranosyl)urea.
Fructose-1,6-bisphosphatase inhibitor (FB Pase)	Control gluconeogenesis (overproduction)	Achyrofurin
Glucagon receptor inhibitor (GCGr)	Suppression of glucagon	Albiglutide and dulaglutide
Phosphoenol pyruvate carbox ykinase (PEPC K)	Control hepatic Gluconeogenesis	Glipizide
Sodium glucose co-Transporters	Inhibits secretion or utilization of insulin	Dapagliflozin, canagliflozin, Ernpagliflozin
α-amylase inhibitors	Regulates blood glucose and postprandial glucose levels	Acarbose

Table 4: List of Recently Filled Patent to Treat Diabetes

Publication no.	Published on Date	Title
WO20110D0823A1	06-01-2011	Insulin Derivative
AU2009257597B2	06-10-2011	PEFylated insulin
EP2256129B1	09-05-2012	Insulin derivative
US8556865B2	15-08-2013	Drug Delivery Pen
US8541368B2	24-09-2013	Glucagon Analogue
WO2016149222A3*	03-11-2013	Insulin analog containing a glucose-regulated conformational switch
US8071641B2	06-12-2013	Treating Diabetes from Cannabidiol
US5480891	26-06-2015	Treating Diabetes from
WO217070617A1*	27-04-2017	Diol modified insulin Analogue
US10335489B2	02-07-2019	Injectable solution at pH7

Table 5: Herbal drugs having anti-diabetic properties

Botanical name	Common name	Parts used	Extracts	Family	Result	References
<i>Aegle marmelos</i>	Golden apple	Leaf, Seed, Fruit	Ethanollic, Aqueous	Rutaceae	↓Glucose, ↓glycosylated Hemoglobin, ↑C peptide, ↑glucose Tolerance, ↑glycogen, ↑insulin	[72, 73]
<i>Allium sativum</i>	Garlic	Root	Ethanollic	Alliaceae	↓Glucose, ↓Lipid, ↑Insulin, ↓Oxidative stress	[74]
<i>Averrhoa bilimbi</i>	-	Leaf	Aqueous	Oxalidaceae	↓Glucose, ↓Lipid	[75]
<i>Aloe vera</i>	Barbados aloe	Leaf	Ethanollic	Liliaceae	↓Glycosylated hemoglobin	[75]
<i>Amaranthus esculentus</i>	-	Whole plant	Oil fraction	Amaranthaceae	↓Glucose, ↑Insulin	[76]
<i>Annona squamosa</i>	-	Leaf, Fruit-Pulp	Aqueous, Ethanollic	Annonaceae	↓Glucose, ↓Lipid, ↓Lipid peroxidation	[76], [77], [78], [79]
<i>Areca catechu</i>	Betelnut	Fruit	-	Arecaceae	↓Glucose	[80]
<i>Andrographis paniculata</i> Nees	Kalmeg, King of Bitters	Aerial parts	-	Acanthaceae	Prevents glucose absorption from gut, ↓Glucose	[81], [82], [83]
<i>Aerva lanata</i>	Sunny Khur	Aerial parts	Alcoholic	Amaranthaceae	↓Glucose	[84]
<i>Artemisia pallens</i>	Davana	Aerial parts	Methanollic	Compositae	↑ peripheral glucose utilization	[85]
<i>Beta vulgaris</i>	Beetroo	Whole	-	Chenopodiaceae	-	[86]

	t	plant		e		
<i>Baccharis trimera</i>	-	Leaf	Aqueous	Myrtaceae	↓Glucose	[87]
<i>Bryophyllum pinnatum</i>	-	Leaf	Alcoholic	Crassulaceae	↓Glucose	[88]
<i>Bombax ceiba</i>	cotton tree	Leaf	Isolated compound	Bombacaceae	↓Glucose	[89]
<i>Barleria lupulina</i>	-	Aerial parts	-	Acanthaceae	↓Glucose	[90]
<i>Boerhavia diffusa</i>	Tarvine	Leaf	Aqueous	Nyctaginaceae	↑plasma insulin and improves glucose tolerance	[91], [92]
<i>Canarium schweinfurthii</i>	-	Steam bark	Methanolic	Burseraceae	↓Glucose	[93]
<i>Chamaemelum nobile</i>	-	Leaf	Aqueous	Asteraceae	↓Glucose	[94]
<i>Coscinium fenestratum</i>	-	Stem bark	Alcoholic	Menispermaceae	↓Glucose, ↓Glycosylated hemoglobin, ↓Glycogen,	[95]
<i>Caesalpinia bonducella</i>	Cinnamon	Seed	Ethanolic	Cesalpiniaceae	↑Insulin from pancreatic cells	[96], [97]
<i>Capparis deciduas</i>	-	Fruit	Powdered	Capparidaceae	↑glucose-6-phosphate dehydrogenase	[98]
<i>Citrullus colocynthis</i>	Bitter apple	Seed	Aqueous,	Cucurbitaceae	↑Insulin	[99]
<i>Casearia esculenta</i>	Carilla Fruit	Root	Aqueous	Flacourtiaceae	↓Glucose, ↓Glycosylated hemoglobin	[100]
<i>Camellia sinensis</i>	Green tea	Leaf	Hot water extract	Theaceae	↓Glucose, ↑Insulin	[101]
<i>Egyptian Morus alba</i>	-	Stem bark	Alcoholic	Moraceae	↓Glucose, ↓Lipid peroxidation, ↑Insulin	[102]
<i>Enicostemma littorale</i>	chhota chirayata	Whole plant	Aqueous	Gentianeae	↓Glycosylated hemoglobin, ↓ glucose-6-phosphate activity in liver, ↑Insulin	[103], [104] [105]
<i>Eugenia jambolana</i>	black berry	Fruit pulp, seed	-	Myrtaaceae	↓Glucose ↓Lipid, ↑Glucose tolerance	[106], [107]
<i>Eugenia uniflora</i>	Pitanga	Leaf	Ethanolic	Myrtaaceae	Inhibit increase in plasma glucose level	[108]
<i>Glycyrrhiza glabra</i>	Licorice	Root	-	Fabaceae	↓Glucose ↓Abdominal fat	[109]
<i>Gymnema montanum</i>	-	Leaf	Alcoholic	Asclepiadaceae	↓Glucose, ↓Glycosylated hemoglobin, ↑Insulin	[110]
<i>Hintonia standleyana</i>	-	Stem bark	Methanolic	Rubiaceae	↓Glucose	[111]
<i>Hypoxis hemerocallidea</i>	-	Fruit	Aqueous	Hypoxidaceae	↓Glucose	[112]
<i>Hibiscus rosa sinensis</i>	China rose	Leaf, Flower	Ethanolic	Malvaceae	↑Insulin, ↑ utilization of glucose	[113]; [114]
<i>Ipomoea batatas</i>	Sweet potato	Storage Roots	Isolated compound	Convolvulaceae	↓Insulin resistance and acts by maltase inhibition	[115], [116]
<i>Lepidium sativum</i>	-	Leaf	Aqueous	Brassicaceae	↓Glucose	[117]
<i>Lycium barbarum</i>	Chirchita	Fruit	Polysaccharide extract	Solanaceae	↓Glucose, ↓Oxidative stress, ↑GLUT4, ↑Insulin	[118]
<i>Leonotis leonurus</i>	-	Leaf	Aqueous	Lamiaceae	↓Glucose	[78]
<i>Lantana camara</i>	-	Leaf	Leaf juice	Verbenaceae	↓Glucose	[119]
<i>Momordica charantia</i>	Bitter melon	Whole plant	Methanolic, Aqueous,	Cucurbitaceae	↓Glucose, ↓Glycosylated hemoglobin, ↓Oxidative stress, ↑Glycogen, ↓Lipid	[120], [121]

			Chloroformic		peroxidation	
<i>Momordica cymbalaria</i>	Kaarali-kanda	Fruit	Aqueous	Cucurbitaceae	-	[122]
<i>Mangifera indica</i>	Mango tree	Fruit, Leaf, Stem Bark	Ethanollic	Anacardiaceae	↓Glucose	[77]
<i>Malmea depressa</i>	-	Root	Aqueous, Ethanolic	Annonaceae	↓Glucose	[123]
<i>Memecylon umbellatum</i>	-	Leaf	Alcoholic	Melastomataceae	↓Glucose	[124]
<i>Mucuna pruriens</i>	Velvet bean	Whole plant	alcoholic	Leguminosae	↑Insulin, ↓Glucose	[125]
<i>Psidium guajava</i>	Guava	Leaf, Fruit	Aqueous, Methanolic	Myrtaceae	↓Glucose	[126]
<i>Phyllanthus emblica;</i>	Gooseberry	Fruit	Aqueous	Euphorbiaceae	-	[127]
<i>Piper betle</i>	Pan	Leaf	Aqueous	Piperaceae	↓Glucose, ↓Glycosylated hemoglobin	[128]
<i>Picrorrhiza kurroa</i>	-	Leaf, Bark,	Alcoholic extract	Scrophulariaceae	↓Glucose levels in serum, ↓ serum lipid peroxides	[129]
<i>Phyllanthus amarus</i>	-	Leaf	Methanolic extract	Euphorbiaceae	↓Glucose, ↓Glycosylated hemoglobin	[130]
<i>Pterocarpus marsupium</i>	Vijaysar	Bark and wood	Isolated compounds	Fabaceae	↓Glucose	[131]
<i>Pterocarpus santalinus</i>	-	Bark	Aqueous	Leguminosae	↓Glucose	[132]
<i>Retama raetam</i>	-	Whole plant	Aqueous	Fabaceae	↓Glucose	[133]
<i>Raphanus sativus</i>	-	Whole plant	Aqueous	Brassicaceae	↓Glucose, ↓Lipid, ↓Insulin	[87]
<i>Syzygium cordatum</i>	-	Leaf	Aqueous	Myrtaceae	↓Glucose, ↑ Hepatic glycogen	[87]
<i>Salvia officinalis</i>	-	Leaf	Aqueous	Lamiaceae	↓Glucose ↓Gluconeogenesis	[87]
<i>Scoparia dulcis</i>	-	Whole plant	Aqueous	Scrophulariaceae	↓Glucose, ↓Lipid, ↓oxidative stress, ↑Insulin	[134]
<i>Strobilanthes crispus</i>	-	Leaf	Aqueous	Acanthaceae	↓Glucose	[87]
<i>Salacia reticulata</i>	Salacia	Leaf	Aqueous decoction	Celastaceae	↓Glucose, Inhibits alpha –glucosidase activity	[135]
<i>Salacia oblonga</i>	-	Root	Aqueous, methanolic	Celastaceae	↓Glucose, Inhibits alpha –glucosidase activity	[136]
<i>Swertia chiravita</i>	Indian gentian	fraction of plant	Isolated compound	Gentianaceae	↑ Insulin secretion from islets of Langerhans	[137]
<i>Scoparia dulcis</i>	Broom weed	Leaf	Aqueous	Scrophulariaceae	↓Glucose, ↓Glycosylated hemoglobin,	[138], [139]
<i>Syzygium alternifolium</i>	-	Seed	Aqueous, ethanolic	Myrtaceae	↓Glucose	[140]
<i>Sida cordifolia</i>	-	Root	Methanolic	Malvaceae	↓Glucose	[141]
<i>Terminalia chebula</i>	Chebule myrobalan	Fruit, seed	chloroform, Aqueous	Combretaceae	↓Glucose	[142]
<i>Terminalia superba</i>	-	Stem bark	methanolic,	Combretaceae	↓Glucose	[93]
<i>Terminalia pallid</i>	-	Fruit	Ethanollic	Combretaceae	↓Glucose	[143]
<i>Terminalia</i>	Arjuna	Stem	Ethanollic	Combretaceae	↓ Glucose-6-phosphatase, ↓aldolase	[144]

<i>arjuna</i>		bark				
<i>Tinospora cordifolia</i>	-	Leaf	Hexane	Menispermaceae	↓Glucose	[145]
<i>Trigonella foenum</i>	Fenugreek	Seed	proteins and saponins	Fabaceae	↓Glucose	[146]
<i>Ziziphus spinachristi</i>	Christ thorn	Leaf	n-butanol,	Rhamnaceae	↓Glucose	[146]

Table 6: List of important phytoconstituents used in the treatment of Diabetes mellitus

Phytoconstituents	Plant Name	Part used	References
<b>Alkaloids</b>			
Berberine	<i>Berberis</i> spp. <i>Tinospora cordifolia</i>	Roots, stem-bark	[147, 148]
Casuarine 6-o- -glucoside	<i>Syzygium malaccense</i>	Bark	[149]
Catharanthine, vindoline and vindolinine	<i>Catharanthus roseus</i>	Leaves, stems	[150]
Calystegine B2	<i>Nicandra physalodes</i>	Fruits	[151]
Cryptolepine	<i>Cryptolepis sanguinolenta</i>		[152]
Harmene, norharmene,	<i>Tribulus terrestris</i>		[153]
Jambosine	<i>Syzygium cumini</i>	Seeds, fruits, bark	[154]
Jatrorrhizine, magnoflorine, palmatine	<i>Tinospora cordifolia</i>		[155]
Javaberine A, javaberine A hexaacetate, javaberine B hexaacetate,	<i>Talinum paniculatum</i>	Roots	[156]
Lupanine	<i>Lupinus perennis</i>		[157]
Mahanimbine	<i>Murraya koenigii</i>	Leaves	[158]
Piperumbellactam A	<i>Piper umbellatum</i>	Branches	[159]
Radicamines A and B	<i>Lobelia chinensis</i>		[160]
Swerchirin	<i>Swertia chirayita</i>		[161]
Tecomine	<i>Tecoma stans</i>		[162]
Trigonelline	<i>Trigonella foenum-graecum</i>	Seeds	[146]
<b>Glycosides</b>			
Kalopanax	<i>Kalopanax pictus</i>	Stem bark	[163]
Jamboline or antimellin	<i>Syzygium cumini</i>	Seeds	[164]
Myrciacitrins I and II and myrciaphenones A and B	<i>Myrcia multiflora</i>	Leaves	[165]
Perlargonidin 3-o- -l rhamnoside	<i>Ficus benghalensis</i>	Bark	[166]
<b>Flavonoids</b>			
Bengalenoside	<i>Ficus benghalensis</i>	Stem bark	[167, 168]
Epigallocatechin gallate	<i>Camellia sinensis</i>	Leaves	[101]
Genistein	<i>Glycine</i> spp.	Soya beans	[169]
Prunin	<i>Amygdalus davidiana</i> var. <i>davidiana</i>	Stems	[170]

Mangiferin	<i>Anemarrhena asphodeloides</i>	Rhizomes	[171]
Marsupin, pterostilbene	<i>Pterocarpus marsupium</i>	Heartwood	[131]
Shamimin	<i>Bombax ceiba</i>	Leaves	[89]
Terpenoids and steroids			
Amyrin acetate	<i>Ficus racemose</i>	Fruits	[172]
Andrographolide	<i>Andrographis paniculate</i>	Leaves	[173]
Bassic acid	<i>Bumelia sartorum</i>	Root bark	[174]
Charantin	<i>Momordica charantia</i>	Seeds, fruits	[175]
Christinin A	<i>Zizyphus spina-christi</i>	Leaves	[176]
Ginsenosides	<i>Panax species</i>	Rhizomes	[177]
Gymnemic acid	<i>Gymnema sylvestre</i>	Leaves	[178]
Polysaccharides			
Aconitans A-D	<i>Aconitum carmichaeli</i>	Roots	[179]
Atractans A	<i>Atractylodes japonica</i>	Rhizomes	[180]
Ganoderans A and B.	<i>Ganoderma lucidum</i>	Fruit bodies	[181]
Galactomannan gum	<i>Cyamopsis tetragonolobus</i> <i>Amorphophallus konjac</i>	Seeds Tubers	[182]
Miscellaneous			
Allicin	<i>Allium sativum</i> <i>Allium cepa</i>	Bulbs	[183]
Bellidifolin	<i>Swertia japonica</i>		[184]
Bakuchiol	<i>Otholobium pubescens</i>	-	[185]
Curcuminoids	<i>Curcuma longa</i>	Rhizomes	[186]
Ellagitannins	<i>Terminalia chebula</i>	Fruits	[187]
Ferulic aci	<i>Curcuma longa</i>	Leaves seeds	[188]
Ginseng polypeptides	<i>Panax ginseng</i>	Roots	[189]
4-hydroxyisoleucine	<i>Trigonella foenum-graecum</i>	Seeds	[190]
Paeoniflorin, 8-debenzoylpaeoniflorin	<i>Paeonia lactiflora</i>	Root	[191]

**UPADRAVA:-**

*Upadrava* is the severe manifestation of the disease when not treated in a proper manner.

According to *Charaka*,  
*upadrava* of the *prameha* are:

-

Thirst, diarrhea, fever, burning sensation, debility, anorexia, indigestion,

purification of the muscles. These symptoms show an advanced stage of the disease as a result of improper management. As *prameha* is a metabolic disorder symptom related to GI upset like anorexia, abdominal bloating, diarrhea, debility (severe weakness) shows the involvement of

autonomic systems in the chronic stages of type- 2 diabetes mellitus. As involvement of autonomic neuropathy is one of the advanced complications of diabetes mellitus leading to GI upsets, cardiovascular impairment leading to hypotension can lead to debility like conditions [4].

**According to Sushruta, upadrava of the prameha are:-** Acharya Sushruta classifies the complications according to the advancement of the diseased state.

- **Kaphaja prameha (primary stage)** - It may be due to excessive sweetness of blood which may appear through sweat on the skin, indigestion, anorexia, vomiting, sleepiness, cough, common cold, asthma, excessive growth of the muscles and Lethargy [9].
- **Pittaja prameha (intermediate stage)** - The rashes on the scrotum, burning pain in the *basti* (below naval region), pricking pain on the penis, cardiac pain, fever, acid secretion, vomiting, anorexia, *murcha* (Unconsciousness), thirst, sleepiness, anaemia, the yellow color of skin, eyes, feces and urine [9].

- **Vataja prameha (final stage)** - Heart diseases, greediness for eating, sleeplessness, tremors, stiffness of the body, passage of hard stool [9].

### DIAGNOSTIC CRITERIA FOR DIABETES MELLITUS

The following tests are used for diagnosis:

- A. **Fasting plasma glucose (FPG) test:** It measures blood glucose in a person who has not eaten anything for at least 8 hours. This test is used to detect diabetes and pre-diabetes [192, 193].
- B. **An oral glucose tolerance test (OGTT):** It measures blood glucose after person fasts at least 8 hours and 2 hours after the person drinks a glucose-containing beverage. This test can be used to diagnose diabetes and pre-diabetes [192, 194].
- C. **A random plasma glucose test:** It is also called a casual plasma glucose test, measures blood glucose without regard to when the person being tested last ate. This test, along with an assessment of symptoms, is used to diagnose diabetes but not pre-diabetes. Test results indicating that a person has diabetes should be confirmed with a second test on a different day [195].

## CONCLUSION

After a literature review of *prameha* and Type-2 diabetes, it can be said that both the disease entities have similarities in terms of their etiology, etiopathogenesis, presentation of the disease. the treatment prescribed in the *ayurvedic* texts can be used to manage the condition of type-2 diabetes mellitus. *Ayurvedic* medication supported by practicing *pathya* is worth useful. Secondly, in the chronic cases of type-2 diabetes where the desirable blood glucose levels are yet to be attained, *Ayurvedic* drugs can be a good adjuvant to conventional medicines.

*Ayurvedic* drugs with multiple actions both at the GI levels (incretin effect, insulin secretagogue action, improving first phase insulin response etc) tissue levels (improving the peripheral glucose uptake etc) along with potent anti-hyperlipidemic action are a good answer to the complex metabolic derangement of diabetes mellitus. Healthy lifestyle measures both in the form of dietary and other lifestyle modifications such as regular exercise, sufficient sleep, avoidance and proper management of stress and anxiety supported by the *Ayurvedic* medicine can improve the quality of life of diabetics in a significant manner. *Ashayasukham*

(Inactivity, idle sitting), *Svapnasukham* (an excessive amount of sleep, sleep even at day time) avoidance of physical exercise, *Snanadvishi* (avoidance of cleaning), avoidance of *Sodhana Karma*, and all regimens which increase *Kapha*, *Meda* and *Mutra* are the etiological factors of *Prameha*. Excessive sleeping even at daytime vitiates *Kapha Dosh* and *Medodhatu*. The etiological factors that are responsible for the particular type of *Prameha* should be avoided to prevent that type of *Prameha Nidana Parivarjana* plays a first step in the fight against diabetes. The study of *Nidana* (etiological factors) reveals the rich knowledge of the *Ayurveda* in the prevention of Diabetes by following *Nidana Parivarjana*.

## REFERENCES

1. Sharma, S. and D.S. Baghel, *Ayurceuticals: A progressive opportunity in wellness and medical tourism*. Journal of Pharmacy Research, 2017. **11**(7): p. 903-911.
2. Krishna, S., K. Dinesh, and P. Nazeema, *Globalizing Ayurveda- Opportunities and Challenges*. International Journal of Health Sciences and Research, 2020. **10**(3): p. 55-68.
3. Baghel, D., et al., *Amalgamation of*

- Ayurvedic concept with modern medical practice to manage kidney stone (Urolithiasis): An abbreviated review.* Indian Drugs, 2018. **55** (11): p. 7-18.
4. Sastri, K., *Charak Samhita by Agnivesa.* Chaukhambha Bharti Academy, Varansi, 2013.
  5. Samal, J., *The concept of public health in Ayurveda.* International Ayurvedic Medical Journal, 2013. **1**(2): p. 1-5.
  6. Sivananda, S., *Practice of Ayurveda . Divine Life Society . Rishikesh.* 2006.
  7. Mellitus, D., *Diagnosis and classification of diabetes mellitus.* Diabetes care, 2005. **28**(S37): p. S5-S10.
  8. Taylor, E.N., M.J. Stampfer, and G.C. Curhan, *Diabetes mellitus and the risk of nephrolithiasis.* Kidney international, 2005. **68**(3): p. 1230-1235.
  9. Yadavji, A.T., *Sushruta Samhita by Sushruta.* Krishnada Academy, Varanasi, 1980.
  10. Tripathi, B., *Madhava nidana by madhavakara.* Chaukhambha Surbharati Prakashan, Varanasi, 1996.
  11. Sagar, A.M., et al., *An survey on obesity stigma and its assessment with update: a review.* Plant Archives, 2019. **19**(2): p. 2153-2161.
  12. Faruk Yusuf, Y.S.A.S.A.D., Manish Kumar, Indu Melkani, Dileep Singh Baghel, Bimlesh Kumar, Linu Dash, Anupriya, Varimadugu Bhanukirankumar Reddy, Amrik Singh, Amarish Kumar Sharma, *Diabetic nephropathy and its therapeutic options: A Review.* International Journal of Healthcare Sciences, 2020. **8**(2): p. 277-290.
  13. Chuneekar, K.C. and G. Pandey, *Bhavprakash nighantu.* Chukhamba bharti academy, Varanasi, 2004.
  14. Hackett, R.A. and A. Steptoe, *Type 2 diabetes mellitus and psychological stress—a modifiable risk factor.* Nature Reviews Endocrinology, 2017. **13**(9): p. 547.
  15. Melchionda, N., et al., *WHO and ADA criteria for the diagnosis of diabetes mellitus in relation to body mass index. Insulin sensitivity and secretion in resulting subcategories of glucose tolerance.* International journal of obesity, 2002. **26**(1): p. 90-96.
  16. Association, A.D., *Gestational diabetes mellitus.* Diabetes care,

2004. **27**: p. S88.
17. Davidson, M.B., et al., *Relationship between fasting plasma glucose and glycosylated hemoglobin: potential for false-positive diagnoses of type 2 diabetes using new diagnostic criteria*. *Jama*, 1999. **281**(13): p. 1203-1210.
18. Bartoli, E., G. Fra, and G.C. Schianca, *The oral glucose tolerance test (OGTT) revisited*. *European journal of internal medicine*, 2011. **22**(1): p. 8-12.
19. McAulay, V., I. Deary, and B. Frier, *Symptoms of hypoglycaemia in people with diabetes*. *Diabetic Medicine*, 2001. **18**(9): p. 690-705.
20. Nathan, D.M., *Long-term complications of diabetes mellitus*. *New England Journal of Medicine*, 1993. **328**(23): p. 1676-1685.
21. Artasensi, A., et al., *Type 2 diabetes mellitus: A review of multi-target drugs*. *Molecules*, 2020. **25**(8): p. 1987.
22. Lin, X., et al., *Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025*. *Scientific reports*, 2020. **10**(1): p. 1-11.
23. Hussain, S., et al., *Burden of diabetes mellitus and its impact on COVID-19 patients: a meta-analysis of real-world evidence*. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 2020. **14**(6): p. 1595-1602.
24. Association, A.D., *Diagnosis and classification of diabetes mellitus*. *Diabetes care*, 2010. **33**(Supplement 1): p. S62-S69.
25. Association, A.D., *Diagnosis and classification of diabetes mellitus*. *Diabetes care*, 2014. **37**(Supplement 1): p. S81-S90.
26. Rewers, M., et al., *Newborn screening for HLA markers associated with IDDM: diabetes autoimmunity study in the young (DAISY)*. *Diabetologia*, 1996. **39**(7): p. 807-812.
27. Orchard, T.J., et al., *Prevalence of complications in IDDM by sex and duration: Pittsburgh Epidemiology of Diabetes Complications Study II*. *Diabetes*, 1990. **39**(9): p. 1116-1124.
28. Bailey, C.J., *Biguanides and NIDDM*. *Diabetes care*, 1992. **15**(6): p. 755-772.
29. Olokoba, A.B., O.A. Obateru, and L.B. Olokoba, *Type 2 diabetes mellitus: a review of current trends*.

- Oman medical journal, 2012. **27**(4): p. 269.
30. Ranabhat, K., et al., *Type 2 diabetes and its correlates: a cross sectional study in a tertiary hospital of Nepal*. Journal of community health, 2017. **42**(2): p. 228-234.
31. DeFronzo, R.A., et al., *Type 2 diabetes mellitus*. Nature reviews Disease primers, 2015. **1**(1): p. 1-22.
32. Yogev, Y. and G.H. Visser. *Obesity, gestational diabetes and pregnancy outcome*. in *Seminars in Fetal and Neonatal Medicine*. 2009. Elsevier.
33. Buchanan, T.A. and A.H. Xiang, *Gestational diabetes mellitus*. The Journal of clinical investigation, 2005. **115**(3): p. 485-491.
34. Hartling, L., et al., *Screening and diagnosing gestational diabetes mellitus*. Evidence report/technology assessment, 2012(210): p. 1.
35. Naik, R.G., B.M. Brooks-Worrell, and J.P. Palmer, *Latent autoimmune diabetes in adults*. The Journal of Clinical Endocrinology & Metabolism, 2009. **94**(12): p. 4635-4644.
36. Furlanos, S., et al., *Latent autoimmune diabetes in adults (LADA) should be less latent*. Diabetologia, 2005. **48**(11): p. 2206-2212.
37. Andersen, M.K., *New insights into the genetics of latent autoimmune diabetes in adults*. Current Diabetes Reports, 2020. **20**(9): p. 1-10.
38. Hernandez, M. and D. Mauricio, *Latent Autoimmune Diabetes in Adults: A Review of Clinically Relevant Issues*. Diabetes: from Research to Clinical Practice: Volume 4, 2021: p. 29-41.
39. Ludvigsson, J., *Therapy with GAD in diabetes*. Diabetes/metabolism research and reviews, 2009. **25**(4): p. 307-315.
40. Fajans, S.S., G.I. Bell, and K.S. Polonsky, *Molecular mechanisms and clinical pathophysiology of maturity-onset diabetes of the young*. New England Journal of Medicine, 2001. **345**(13): p. 971-980.
41. Gardner, D.S. and E.S. Tai, *Clinical features and treatment of maturity onset diabetes of the young (MODY)*. Diabetes, metabolic syndrome and obesity: targets and therapy, 2012. **5**: p. 101.
42. Thanabalasingham, G. and K.R. Owen, *Diagnosis and management of maturity onset diabetes of the young*

- (*MODY*). *Bmj*, 2011. **343**.
43. Ellard, S., *Hepatocyte nuclear factor 1 alpha (HNF-1 $\alpha$ ) mutations in maturity-onset diabetes of the young. Human mutation*, 2000. **16**(5): p. 377-385.
  44. Rubio-Cabezas, O., et al., *Permanent neonatal diabetes mellitus—the importance of diabetes differential diagnosis in neonates and infants. European journal of clinical investigation*, 2011. **41**(3): p. 323-333.
  45. Singh, P., S.C. Rao, and R. Parikh, *Neonatal diabetes with intractable epilepsy: DEND syndrome. The Indian Journal of Pediatrics*, 2014. **81**(12): p. 1387-1388.
  46. Ewald, N., et al., *Prevalence of diabetes mellitus secondary to pancreatic diseases (type 3c). Diabetes/metabolism research and reviews*, 2012. **28**(4): p. 338-342.
  47. Greene, S., et al., *Management of secondary diabetes mellitus after total pancreatectomy in infancy. Archives of disease in childhood*, 1984. **59**(4): p. 356-359.
  48. Zhuang, H.-X., et al., *Insulin-like growth factor (IGF) gene expression is reduced in neural tissues and liver from rats with non-insulin-dependent diabetes mellitus, and IGF treatment ameliorates diabetic neuropathy. Journal of Pharmacology and Experimental Therapeutics*, 1997. **283**(1): p. 366-374.
  49. Abhishek Chatterjee, et al., *In-Vitro Anti-inflammatory and Anti-oxidant Activities of Hinguleswara Rasa-Based Herbomineral Formulations. Asian J Pharm Clin Res*, 2018. **11** (Special issue 2): p. 24-27.
  50. Chaturvedi, B., *Agni Purana*. 2002: Diamond Pocket Books (P) Ltd.
  51. Chaturvedi, B., *Garuda Purana*. 2002: Diamond Pocket Books (P) Ltd.
  52. Buck, W., *Ramayana*. 1981: Univ of California Press.
  53. Waldauer, C., W.J. Zahka, and S. Pal, *Kautilya's Arthashastra: A neglected precursor to classical economics. Indian Economic Review*, 1996: p. 101-108.
  54. Hridaya, A., *of Vagbhatta*. Edited with the Vidyotini Hindi commentary, by Kaviraja Atrideva Gupta, Chaukambha Sanskrit Sansthan, Varanasi, 2000.
  55. Acharya, Y., *Sushruta Samhita of Sushruta, Sutra Sthana*. Ch, 2008. **45**:

- p. 207.
56. Teewari, P., *Kashyapa samhita*. Chaukhamba Sanskrit samsthan, Varanasi, 2007.
57. Tripathi, B., *Sharangadhara samhita*. Chaukhamba Surabharati Prakashan, Varanasi, 1994.
58. Kumari, J., et al., *A comparative clinical study of Nyagrodhadi Ghanavati and Virechana Karma in the management of Madhumeha*. Ayu, 2010. **31**(3): p. 300.
59. Kapur, K., A. Kapur, and M. Hod, *Nutrition management of gestational diabetes mellitus*. Annals of Nutrition and Metabolism, 2021: p. 1-13.
60. Yuan, S., et al., *Obesity, Type 2 Diabetes, Lifestyle Factors and Risk of Gallstone Disease: A Mendelian Randomization Investigation*. Clinical Gastroenterology and Hepatology, 2021.
61. Strojek, K., et al., *Nephropathy of type II diabetes: Evidence for hereditary factors?* Kidney international, 1997. **51**(5): p. 1602-1607.
62. Ali, O., *Genetics of type 2 diabetes*. World journal of diabetes, 2013. **4**(4): p. 114.
63. Longnecker, M.P. and J.L. Daniels, *Environmental contaminants as etiologic factors for diabetes*. Environmental health perspectives, 2001. **109**(suppl 6): p. 871-876.
64. Peet, M., *Diet, diabetes and schizophrenia: review and hypothesis*. The British journal of psychiatry, 2004. **184**(S47): p. s102-s105.
65. Vidyanath, R., *A Hand Book of Astanga Sangraha*. Chaukhamba Surbharati Prahshan, Varanasi, India, 2006.
66. Sharma, H. and H. Chandola, *Prameha in ayurveda: correlation with obesity, metabolic syndrome, and diabetes mellitus. Part I—etiology, classification, and pathogenesis*. The journal of alternative and complementary medicine, 2011. **17**(6): p. 491-496.
67. Rastogi, S., N. Pandey, and K. Sachdev, *Linking Prameha etiology with diabetes mellitus: Inferences from a matched case-control study*. Ayu, 2018. **39**(3): p. 139.
68. Cervin, C., et al., *Genetic similarities between latent autoimmune diabetes in adults, type 1 diabetes, and type 2 diabetes*. Diabetes, 2008. **57**(5): p. 1433-1437.

69. Bhusal, N., G. Mangal, and G. Gunjan, *Etiological factors of prameha (prediabetes) and madhumeha (diabetes): An Ayurvedic review* Int. J. Res. Ayurveda Pharm, 2017. **8**(5): p. 146-149.
70. Bapalal, V., *Nighantu Adarsh Chaukhambha Bharati Academy, Varanasi*, 1999.
71. Simranjeet Kaur, S.S., Nitika Anand, Sakshi Sabharwal, Dileep Singh Baghel, *Hyperlipidemia: Impact of phytotherapy*. International Journal of Research and Analytical Reviews, 2019. **6**(1): p. 525-531.
72. Narender, T., et al., *Antihyperglycemic and antidyslipidemic agent from Aegle marmelos*. Bioorganic & medicinal chemistry letters, 2007. **17**(6): p. 1808-1811.
73. Sharma, R. and V. Arya, *A review on fruits having anti-diabetic potential*. Journal of Chemical and Pharmaceutical Research, 2011. **3**(2): p. 204-212.
74. Hattori, A., et al., *Antidiabetic effects of Ajoene in genetically diabetic KK-Ay Mice*. Journal of nutritional science and vitaminology, 2005. **51**(5): p. 382-384.
75. Fetrow, C.W. and J.R. Avila, *Professional's handbook of complementary & alternative medicines*. 2001: Springhouse Publishing Company.
76. Nojima, H., et al., *Antihyperglycemic effects of N-containing sugars from Xanthocercis zambesiaca, Morus bombycis, Aglaonema treubii, and Castanospermum australe in streptozotocin-diabetic mice*. Journal of natural products, 1998. **61**(3): p. 397-400.
77. Ojewole, J., *Antiinflammatory, analgesic and hypoglycemic effects of Mangifera indica Linn.(Anacardiaceae) stem-bark aqueous extract*. Methods and findings in experimental and clinical pharmacology, 2005. **27**(8): p. 547-554.
78. Ojewole, J., *Antinociceptive, antiinflammatory and antidiabetic effects of Leonotis leonurus (L.) R. BR.(Lamiaceae) leaf aqueous extract in mice and rats*. Methods and findings in experimental and clinical pharmacology, 2005. **27**(4): p. 257-264.
79. Prakash, P. and N. Gupta, *Therapeutic uses of Ocimum sanctum*

- Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review.* Indian journal of physiology and pharmacology, 2005. **49(2)**: p. 125.
80. Chempakam, B., *Hypoglycaemic activity of arecoline in betel nut Areca catechu L.* Indian journal of experimental biology, 1993. **31(5)**: p. 474-475.
81. Borhanuddin, M., M. Shamsuzzoha, and A. Hussain, *Hypoglycaemic effects of Andrographis paniculata Nees on non-diabetic rabbits.* Bangladesh Medical Research Council Bulletin, 1994. **20(1)**: p. 24-26.
82. Reyes, B., et al., *Anti-diabetic potentials of Momordica charantia and Andrographis paniculata and their effects on estrous cyclicity of alloxan-induced diabetic rats.* Journal of ethnopharmacology, 2006. **105(1)**: p. 196-200.
83. Zhang, X.-F. and B.-h. Tan, *Anti-diabetic property of ethanolic extract of Andrographis paniculata in streptozotocin-diabetic rats.* Acta Pharmacologica Sinica, 2000. **21(12)**: p. 1157-1164.
84. Agrawal, R., N.K. Sethiya, and S. Mishra, *Antidiabetic activity of alkaloids of Aerva lanata roots on streptozotocin-nicotinamide induced type-II diabetes in rats.* Pharmaceutical biology, 2013. **51(5)**: p. 635-642.
85. Subramoniam, A., et al., *Effects of Artemisia pallens Wall. on blood glucose levels in normal and alloxan-induced diabetic rats.* Journal of Ethnopharmacology, 1996. **50(1)**: p. 13-17.
86. Best, C., *Recent work on insulin.* Endocrinology, 1924. **8(5)**: p. 617-629.
87. Makheswari, M.U. and D. Sudarsanam, *Database on antidiabetic indigenous plants of Tamil Nadhu, India.* Int J Pharma Sci Res, 2012. **3(2)**: p. 287-293.
88. Ojewole, J.A., *Antinociceptive, anti-inflammatory and antidiabetic effects of Bryophyllum pinnatum (Crassulaceae) leaf aqueous extract.* Journal of Ethnopharmacology, 2005. **99(1)**: p. 13-19.
89. Saleem, R., et al., *Hypotensive, hypoglycaemic and toxicological studies on the flavonol C-glycoside shamimin from Bombax ceiba.* Planta medica, 1999. **65(04)**: p. 331-334.

90. Suba, V., et al., *Anti-diabetic potential of Barleria lupulina extract in rats*. *Phytomedicine*, 2004. **11**(2-3): p. 202-205.
91. Pari, L. and M.A. Satheesh, *Antidiabetic activity of Boerhaavia diffusa L.: effect on hepatic key enzymes in experimental diabetes*. *Journal of Ethnopharmacology*, 2004. **91**(1): p. 109-113.
92. Satheesh, M.A. and L. Pari, *Antioxidant effect of Boerhavia diffusa L. in tissues of alloxan induced diabetic rats*. 2004.
93. Kamtchouing, P., et al., *Anti-diabetic activity of methanol/methylene chloride stem bark extracts of Terminalia superba and Canarium schweinfurthii on streptozotocin-induced diabetic rats*. *Journal of ethnopharmacology*, 2006. **104**(3): p. 306-309.
94. Eddouks, M., et al., *Potent hypoglycaemic activity of the aqueous extract of Chamaemelum nobile in normal and streptozotocin-induced diabetic rats*. *Diabetes research and clinical practice*, 2005. **67**(3): p. 189-195.
95. Shirwaikar, A., K. Rajendran, and I. Punitha, *Antidiabetic activity of alcoholic stem extract of Coscinium fenestratum in streptozotocin-nicotinamide induced type 2 diabetic rats*. *Journal of ethnopharmacology*, 2005. **97**(2): p. 369-374.
96. Chakrabarti, S., et al., *Advanced studies on the hypoglycemic effect of Caesalpinia bonducella F. in type 1 and 2 diabetes in Long Evans rats*. *Journal of Ethnopharmacology*, 2003. **84**(1): p. 41-46.
97. Sharma, S., S. Dwivedi, and D. Swarup, *Hypoglycaemic, antihyperglycaemic and hypolipidemic activities of Caesalpinia bonducella seeds in rats*. *Journal of Ethnopharmacology*, 1997. **58**(1): p. 39-44.
98. Yadav, P., S. Sarkar, and D. Bhatnagar, *ACTION OF CAPPARIS DECIDUA AGAINST ALLOXAN-INDUCED OXIDATIVE STRESS AND DIABETES IN RAT TISSUES*. *Pharmacological Research*, 1997. **36**(3): p. 221-228.
99. Al-Ghaithi, F., et al., *Biochemical effects of Citrullus colocynthis in normal and diabetic rats*. *Molecular and cellular biochemistry*, 2004. **261**(1): p. 143-149.
100. Prakasam, A., S. Sethupathy, and K.

- Pugalendi, *Antihyperglycaemic effect of Casearia esculenta root extracts in streptozotocin-induced diabetic rats*. Die Pharmazie, 2002. **57**(11): p. 758-760.
101. Gomes, A., et al., *Anti-hyperglycemic effect of black tea (Camellia sinensis) in rat*. Journal of Ethnopharmacology, 1995. **45**(3): p. 223-226.
102. Singab, A.N.B., et al., *Hypoglycemic effect of Egyptian Morus alba root bark extract: effect on diabetes and lipid peroxidation of streptozotocin-induced diabetic rats*. Journal of ethnopharmacology, 2005. **100**(3): p. 333-338.
103. Maroo, J., et al., *Glucose lowering effect of aqueous extract of Enicostemma littorale Blume in diabetes: a possible mechanism of action*. Journal of ethnopharmacology, 2002. **81**(3): p. 317-320.
104. Murali, B., U. Upadhyaya, and R. Goyal, *Effect of chronic treatment with Enicostemma littorale in non-insulin-dependent diabetic (NIDDM) rats*. Journal of ethnopharmacology, 2002. **81**(2): p. 199-204.
105. Vijayvargia, R., M. Kumar, and S. Gupta, *Hypoglycemic effect of aqueous extract of Enicostemma littorale Blume (chhota chirayata) on alloxan induced diabetes mellitus in rats*. 2000.
106. Achrekar, S., et al., *Hypoglycemic activity of Eugenia jambolana and Ficus bengalensis: mechanism of action*. In vivo (Athens, Greece), 1991. **5**(2): p. 143-147.
107. Grover, J., V. Vats, and S. Rathi, *Anti-hyperglycemic effect of Eugenia jambolana and Tinospora cordifolia in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism*. Journal of Ethnopharmacology, 2000. **73**(3): p. 461-470.
108. Guzman, F., et al., *Identification of microRNAs from Eugenia uniflora by high-throughput sequencing and bioinformatics analysis*. PLoS One, 2012. **7**(11): p. e49811.
109. Saxena, S., *Glycyrrhiza glabra: medicine over the millennium*. 2005.
110. Ananthan, R., et al., *Antidiabetic effect of Gymnema montanum leaves: effect on lipid peroxidation induced oxidative stress in experimental diabetes*. Pharmacological research, 2003. **48**(6): p. 551-556.

111. Guerrero-Analco, J.A., et al., *Antihyperglycemic effect of constituents from Hintonia standleyana in streptozotocin-induced diabetic rats*. *Planta medica*, 2005. **71**(12): p. 1099-1105.
112. Ojewole, J.A., *Antinociceptive, anti-inflammatory and antidiabetic properties of Hypoxis hemerocallidea Fisch. & CA Mey.(Hypoxidaceae) corm ['African Potato'] aqueous extract in mice and rats*. *Journal of ethnopharmacology*, 2006. **103**(1): p. 126-134.
113. Sachdewa, A. and L. Khemani, *Effect of Hibiscus rosa sinensis Linn. ethanol flower extract on blood glucose and lipid profile in streptozotocin induced diabetes in rats*. *Journal of ethnopharmacology*, 2003. **89**(1): p. 61-66.
114. Sachdewa, A., R. Nigam, and L. Khemani, *Hypoglycemic effect of Hibiscus rosa sinensis L. leaf extract in glucose and streptozotocin induced hyperglycemic rats*. 2001.
115. Kusano, S. and H. Abe, *Antidiabetic activity of white skinned sweet potato (Ipomoea batatas L.) in obese Zucker fatty rats*. *Biological and pharmaceutical bulletin*, 2000. **23**(1): p. 23-26.
116. Matsui, T., et al., *Anti-hyperglycemic effect of diacylated anthocyanin derived from Ipomoea batatas cultivar Ayamurasaki can be achieved through the  $\alpha$ -glucosidase inhibitory action*. *Journal of agricultural and food chemistry*, 2002. **50**(25): p. 7244-7248.
117. Mishra, S.B., et al., *An analytical review of plants for anti diabetic activity with their phytoconstituent and mechanism of action*. *Int J Pharm Sci Res*, 2010. **1**(1): p. 1647-52.
118. Wu, H., H. Guo, and R. Zhao, *Effect of Lycium barbarum polysaccharide on the improvement of antioxidant ability and DNA damage in NIDDM rats*. *Yakugaku Zasshi*, 2006. **126**(5): p. 365-371.
119. Garg, S., et al., *Antilymphocytic and immunosuppressive effects of Lantana camara leaves in rats*. *Indian journal of experimental biology*, 1997. **35**(12): p. 1315-1318.
120. Shetty, A., et al., *Effect of bitter gourd (Momordica charantia) on glycaemic status in streptozotocin induced diabetic rats*. *Plant Foods for Human Nutrition*, 2005. **60**(3): p. 109-112.

121. Sathishsekar, D. and S. Subramanian, *Beneficial effects of Momordica charantia seeds in the treatment of STZ-induced diabetes in experimental rats*. Biological and Pharmaceutical Bulletin, 2005. **28**(6): p. 978-983.
122. Rao, B.K., M. Kesavulu, and C. Apparao, *Antihyperglycemic activity of Momordica cymbalaria in alloxan diabetic rats*. Journal of Ethnopharmacology, 2001. **78**(1): p. 67-71.
123. Andrade-Cetto, A., E. Martínez-Zurita, and H. Wiedenfeld, *Hypoglycemic effect of Malmea depressa root on streptozotocin diabetic rats*. Journal of ethnopharmacology, 2005. **100**(3): p. 319-322.
124. Amalraj, T. and S. Ignacimuthu, *Evaluation of the hypoglycaemic effect of Memecylon umbellatum in normal and alloxan diabetic mice*. Journal of ethnopharmacology, 1998. **62**(3): p. 247-250.
125. Akhtar, M.S., A.Q. Qureshi, and J. Iqbal, *Antidiabetic evaluation of Mucuna pruriens, Linn seeds*. JPMA. The Journal of the Pakistan Medical Association, 1990. **40**(7): p. 147-150.
126. Ojewole, J., *Hypoglycemic and hypotensive effects of Psidium guajava Linn.(Myrtaceae) leaf aqueous extract*. Methods and findings in experimental and clinical pharmacology, 2005. **27**(10): p. 689-696.
127. Qureshi, S.A., W. Asad, and V. Sultana, *The effect of Phyllanthus emblica Linn on type-II diabetes, triglycerides and liver-specific enzyme*. Pakistan Journal of Nutrition, 2009. **8**(2): p. 125-128.
128. Arambewela, L., L. Arawwawala, and W. Ratnasooriya, *Antidiabetic activities of aqueous and ethanolic extracts of Piper betle leaves in rats*. Journal of Ethnopharmacology, 2005. **102**(2): p. 239-245.
129. Husain, G.M., P.N. Singh, and V. Kumar, *Antidiabetic activity of standardized extract of Picrorhiza kurroa in rat model of NIDDM*. Drug discoveries & therapeutics, 2009. **3**(3).
130. Raphael, K.R., M. Sabu, and R. Kuttan, *Hypoglycemic effect of methanol extract of Phyllanthus amarus Schum & Thonn on alloxan induced diabetes mellitus in rats and its relation with antioxidant potential*. 2002.

131. Manickam, M., et al., *Antihyperglycemic activity of phenolics from Pterocarpus marsupium*. Journal of natural products, 1997. **60**(6): p. 609-610.
132. Kondeti, V.K., et al., *Effect of Pterocarpus santalinus bark, on blood glucose, serum lipids, plasma insulin and hepatic carbohydrate metabolic enzymes in streptozotocin-induced diabetic rats*. Food and Chemical Toxicology, 2010. **48**(5): p. 1281-1287.
133. Maghrani, M., J.B. Michel, and M. Eddouks, *Hypoglycaemic activity of Retama raetam in rats*. Phytotherapy Research, 2005. **19**(2): p. 125-128.
134. Latha, M. and L. Pari, *Effect of an aqueous extract of Scoparia dulcis on plasma and tissue glycoproteins in streptozotocin induced diabetic rats*. Die Pharmazie-An International Journal of Pharmaceutical Sciences, 2005. **60**(2): p. 151-154.
135. Yoshikawa, M., et al., *Kotalanol, a potent  $\alpha$ -glucosidase inhibitor with thiosugar sulfonium sulfate structure, from antidiabetic Ayurvedic medicine Salacia reticulata*. Chemical & pharmaceutical bulletin, 1998. **46**(8): p. 1339-1340.
136. Li, Y., T.H.-W. Huang, and J. Yamahara, *Salacia root, a unique Ayurvedic medicine, meets multiple targets in diabetes and obesity*. Life sciences, 2008. **82**(21): p. 1045-1049.
137. Saxena, A.M., et al., *Mechanism of blood sugar lowering by a swerchirin-containing hexane fraction (SWI) of Swertia chirayita*. Indian journal of experimental biology, 1993. **31**(2): p. 178-181.
138. Pari, L. and S. Venkateswaran, *Hypoglycaemic activity of Scopariadulcis L. extract in alloxan induced hyperglycaemic rats*. Phytotherapy Research, 2002. **16**(7): p. 662-664.
139. Latha, M., et al., *Insulin-secretagogue activity and cytoprotective role of the traditional antidiabetic plant Scoparia dulcis (Sweet Broomweed)*. Life sciences, 2004. **75**(16): p. 2003-2014.
140. Rao, B.K. and C.A. Rao, *Hypoglycemic and antihyperglycemic activity of Syzygium alternifolium (Wt.) Walp. seed extracts in normal and diabetic rats*. Phytomedicine, 2001. **8**(2): p. 88-93.
141. Kanth, V.R. and P. Diwan, *Analgesic, antiinflammatory and hypoglycaemic*

- activities of *Sida cordifolia*. Phytotherapy Research, 1999. **13**(1): p. 75-77.
142. Rao, N.K. and S. Nammi, *Antidiabetic and renoprotective effects of the chloroform extract of Terminalia chebula Retz. seeds in streptozotocin-induced diabetic rats*. BMC complementary and alternative medicine, 2006. **6**(1): p. 17.
143. Rao, B.K., et al., *Antidiabetic activity of Terminaliapallida fruit in alloxan induced diabetic rats*. Journal of Ethnopharmacology, 2003. **85**(1): p. 169-172.
144. Ragavan, B. and S. Krishnakumari, *Antidiabetic effect of T. arjuna bark extract in alloxan induced diabetic rats*. Indian Journal of Clinical Biochemistry, 2006. **21**(2): p. 123.
145. Singh, S.K., *Polypeptide-k" as phytoinsulin: How much and how far*. International Journal of Green Pharmacy (IJGP), 2017. **11**(02).
146. Mishkinsky, J., et al., *Hypoglycaemic effect of Trigonella foenum graecum and Lupinus termis (leguminosae) seeds and their major alkaloids in alloxan-diabetic and normal rats*. Archives Internationales de Pharmacodynamie et de thérapie, 1974. **210**(1): p. 27-37.
147. Pan, G.-Y., et al., *The antihyperglycaemic activity of berberine arises from a decrease of glucose absorption*. Planta Medica, 2003. **69**(07): p. 632-636.
148. Singh, S., et al., *Chemistry and medicinal properties of Tinospora cordifolia (Guduchi)*. Indian Journal of Pharmacology, 2003. **35**: p. 83-91.
149. Xin, Y., et al., *Glycosylated Iminosugars: Isolation, Synthesis and Biological Activities*. Progress in Chemistry, 2019. **31**(11): p. 1472.
150. Chattopadhyay, R., *A comparative evaluation of some blood sugar lowering agents of plant origin*. Journal of ethnopharmacology, 1999. **67**(3): p. 367-372.
151. Griffiths, R.C., et al., *The isolation from Nicandra physalodes and identification of the 3-O-β-D-glucopyranoside of 1α, 2β, 3α, 6α-tetrahydroxy-nor-tropane (Calystegine B1)*. Tetrahedron letters, 1996. **37**(18): p. 3207-3208.
152. Luo, J., et al., *Cryptolepis sanguinolenta: an ethnobotanical approach to drug discovery and the isolation of a potentially useful new antihyperglycaemic agent*. Diabetic

- medicine, 1998. **15**(5): p. 367-374.
153. Cooper, E.J., et al., *Effects of the  $\beta$ -carbolines, harmine and pinoline, on insulin secretion from isolated human islets of Langerhans*. European journal of pharmacology, 2003. **482**(1-3): p. 189-196.
154. Ayyanar, M. and P. Subash-Babu, *Syzygium cumini (L.) Skeels: A review of its phytochemical constituents and traditional uses*. Asian Pacific journal of tropical biomedicine, 2012. **2**(3): p. 240-246.
155. Patel, M.B. and S. Mishra, *Hypoglycemic activity of alkaloidal fraction of Tinospora cordifolia*. Phytomedicine, 2011. **18**(12): p. 1045-1052.
156. Thanamool, C., et al., *Talinum paniculatum (Jacq.) Gertn: a medicinal plant with potential estrogenic activity in ovariectomized rats*. Int. J. Pharm. Pharm. Sci, 2013. **5**: p. 478-485.
157. Lopez, P.M.G., et al., *Quinolizidine alkaloids isolated from Lupinus species enhance insulin secretion*. European journal of pharmacology, 2004. **504**(1-2): p. 139-142.
158. Mitra, A. and M. Mahadevappa, *Antidiabetic and hypolipidemic effects of mahanimbine (carbazole alkaloid) from Murraya koenigii (rutaceae) leaves*. International Journal of Phytomedicine, 2010. **2**: p. 22-30.
159. Tabopda, T.K., et al., *Bioactive aristolactams from Piper umbellatum*. Phytochemistry, 2008. **69**(8): p. 1726-1731.
160. Shibano, M., et al., *Two new pyrrolidine alkaloids, radicamines A and B, as inhibitors of  $\alpha$ -glucosidase from Lobelia chinensis LOUR*. Chemical and pharmaceutical bulletin, 2001. **49**(10): p. 1362-1365.
161. Bajpai, M.B., et al., *Hypoglycemic effect of swerchirin from the hexane fraction of Swertia chirayita*. Planta medica, 1991. **57**(02): p. 102-104.
162. Hammouda, Y. and M.S. Amer, *Antidiabetic effect of tecomine and tecostanine*. Journal of Pharmaceutical Sciences, 1966. **55**(12): p. 1452-1454.
163. Park, H.-J., et al., *A potent anti-diabetic agent from Kalopanax pictus*. Archives of pharmacal research, 1998. **21**(1): p. 24-29.
164. Shrikant Baslingappa, S., et al., *Jamun (Syzygium cumini (L.)): a review of its food and medicinal uses*.

- Food and Nutrition Sciences, 2012. **2012**.
165. Matsuda, H., N. Nishida, and M. Yoshikawa, *Antidiabetic principles of natural medicines. V. Aldose reductase inhibitors from Myrcia multiflora DC.(2): Structures of myrciacitrins III, IV, and V*. Chemical and pharmaceutical bulletin, 2002. **50(3)**: p. 429-431.
166. Cherian, S. and K. Augusti, *Antidiabetic effects of a glycoside of leucopelargonidin isolated from Ficus bengalensis Linn*. Indian journal of experimental biology, 1993. **31(1)**: p. 26-29.
167. Brahmachari, G., *Bioactive natural products: opportunities and challenges in medicinal chemistry*. 2012: World Scientific Publishing Co. Pte. Ltd., London
168. Ahmad, S., et al., *Phytochemical composition and pharmacological prospectus of Ficus bengalensis Linn.(Moraceae)-A review*. Journal of medicinal plants research, 2011. **5(28)**: p. 6393-6400.
169. Mezei, O., et al., *Soy isoflavones exert antidiabetic and hypolipidemic effects through the PPAR pathways in obese Zucker rats and murine RAW 264.7 cells*. The Journal of nutrition, 2003. **133(5)**: p. 1238-1243.
170. Choi, J.S., et al., *Hypolipemic and hypoglycemic activities of Prunus davidiana in high fat-fed rats*. Archives of pharmacal research, 1991. **14(1)**: p. 44-47.
171. Miura, T., et al., *The suppressive effect of mangiferin with exercise on blood lipids in type 2 diabetes*. Biological and Pharmaceutical Bulletin, 2001. **24(9)**: p. 1091-1092.
172. Narender, T., et al., *Synthesis of  $\alpha$ -amyrin derivatives and their in vivo antihyperglycemic activity*. European journal of medicinal chemistry, 2009. **44(3)**: p. 1215-1222.
173. Yu, B.-C., W.-C. Chen, and J.-T. Cheng, *Antihyperglycemic effect of andrographolide in streptozotocin-induced diabetic rats*. Planta medica, 2003. **69(12)**: p. 1075-1079.
174. Naik, S.R., et al., *Probable mechanism of hypoglycemic activity of bassic acid, a natural product isolated from Bumelia sartorum*. Journal of ethnopharmacology, 1991. **33(1-2)**: p. 37-44.
175. Ng, T., et al., *Insulin-like molecules in Momordica charantia seeds*. Journal of ethnopharmacology, 1986.

- 15(1): p. 107-117.
176. Glombitza, K.-W., et al., *Hypoglycemic and antihyperglycemic effects of Zizyphus spina-christi in rats*. *Planta medica*, 1994. **60**(03): p. 244-247.
177. Konno, C., et al., *Isolation and hypoglycaemic activity of Panaxans A, B, C, D and E, Glycans of Panax ginseng Roots I*. *Planta medica*, 1984. **50**(05): p. 434-436.
178. Patel, K., M. Gadewar, and R. Tripathi, *Pharmacological and analytical aspects of gymnemic acid: a concise report*. *Asian Pacific Journal of Tropical Disease*, 2012. **2**(5): p. 414-416.
179. Konno, C., et al., *Isolation and hypoglycemic activity of aconitans A, B, C and D, glycans of Aconitum carmichaeli Roots I*. *Planta medica*, 1985. **51**(02): p. 160-161.
180. Konno, C., et al., *Isolation and hypoglycemic activity of atractans A, B and C, glycans of Atractylodes japonica Rhizomes I*. *Planta medica*, 1985. **51**(02): p. 102-103.
181. Hikino, H., et al., *Isolation and hypoglycemic activity of ganoderans A and B, glycans of Ganoderma lucidum fruit bodies*. *Planta medica*, 1985. **51**(04): p. 339-340.
182. Doi, K., et al., *Treatment of diabetes with glucomannan (konjac mannan)*. *The Lancet*, 1979. **313**(8123): p. 987-988.
183. Kumari, K., B. Mathew, and K. Augusti, *Antidiabetic and hypolipidemic effects of S-methyl cysteine sulfoxide isolated from Allium cepa Linn*. *Indian journal of biochemistry & biophysics*, 1995. **32**(1): p. 49-54.
184. Basnet, P., et al., *Bellidifolin stimulates glucose uptake in rat I fibroblasts and ameliorates hyperglycemia in streptozotocin (STZ)-induced diabetic rats*. *Planta medica*, 1995. **61**(05): p. 402-405.
185. Krenisky, J.M., et al., *Isolation and antihyperglycemic activity of bakuchiol from Otholobium pubescens (Fabaceae), a Peruvian medicinal plant used for the treatment of diabetes*. *Biological and Pharmaceutical Bulletin*, 1999. **22**(10): p. 1137-1140.
186. Du, Z.-y., et al.,  *$\alpha$ -Glucosidase inhibition of natural curcuminoids and curcumin analogs*. *European journal of medicinal chemistry*, 2006. **41**(2): p. 213-218.

187. Gao, H., et al., *Inhibitory effect on  $\alpha$ -glucosidase by the fruits of Terminalia chebula Retz.* Food Chemistry, 2007. **105**(2): p. 628-634.
188. Nomura, E., et al., *Synthesis of amide compounds of ferulic acid, and their stimulatory effects on insulin secretion in vitro.* Bioorganic & medicinal chemistry, 2003. **11**(17): p. 3807-3813.
189. Attele, A.S., J.A. Wu, and C.-S. Yuan, *Ginseng pharmacology: multiple constituents and multiple actions.* Biochemical pharmacology, 1999. **58**(11): p. 1685-1693.
190. Narender, T., et al., *4-Hydroxyisoleucine an unusual amino acid as antidyslipidemic and antihyperglycemic agent.* Bioorganic & medicinal chemistry letters, 2006. **16**(2): p. 293-296.
191. Hsu, F.-L., C.-W. Lai, and J.-T. Cheng, *Antihyperglycemic effects of paeoniflorin and 8-debenzoyl-paeoniflorin, glucosides from the root of Paeonia lactiflora.* Planta medica, 1997. **63**(04): p. 323-325.
192. Nachtergaele, C., et al., *COVID-19 pandemic: Can fasting plasma glucose and HbA1c replace the oral glucose tolerance test to screen for hyperglycaemia in pregnancy?* diabetes research and clinical practice, 2021. **172**: p. 108640.
193. Reichelt, A.J., et al., *Fasting plasma glucose is a useful test for the detection of gestational diabetes.* Diabetes care, 1998. **21**(8): p. 1246-1249.
194. Mari, A., et al., *A model-based method for assessing insulin sensitivity from the oral glucose tolerance test.* Diabetes care, 2001. **24**(3): p. 539-548.
195. Rhee, M.K., et al., *Random plasma glucose predicts the diagnosis of diabetes.* PloS one, 2019. **14**(7): p. e0219964.