Chapter 02

Review of literature
India has long tradition in the use of herbal remedies for the management and treatment of diabetes since the times of Charaka and Sushruta (Grover JK et al., 2002). Traditional medicines are based on the knowledge passed from generations and largely dependent on the use of plants.

Many commercial drugs originate from plant sources for example, aspirin (willow bark), digoxin (foxglove), quinine (cinchona), morphine (opium poppy), vincristine, vinblastine (catherunthes) and taxol (Yew).

The effective treatment of the disease and the confirmation of the efficacy of the traditional medicine is of utmost importance. We therefore designed a Neutraceutical formulation containing ten medicinal plants as a preventive remedy against Diabetic retinopathy and decided to determine the biological activity of these ten plants used in the formulation.

The study intended to examine the potential activity of the extracts of these plants and depending on activity, develop an alternate new therapeutic modality.

2.1 Justification of the study

The results of this study will contribute toward the growing database of knowledge on ethnobiology and help advocate the safe and effective use of traditional herbal remedies. It is believed that the screening of plant derived secondary metabolites, which are eventually going to the drugs, will add to the ever increasing scientific knowledge of medicinal plants, not only in India but also globally.

The plants showing substantial activity will be studied further for isolation, characterization and determining the mode of action of the drug. The ever increasing side effects of allopathic drugs necessitate the screening for and discovery of new compounds.
2.2 Objective of the study

To evaluate the efficacy of ten medicinal plants which are used in designing a Neutraceutical formulation as a preventive remedy against diabetic retinopathy.

2.3 Plants: A Therapeutic goldmine

Plants have always been a good source of drugs. The ethnobotanical information reports about 800 plants that may possess anti-diabetic potential (Jung M et. al 2006). The most useful plants are listed in table (Appendix II).

Therapeutic effectiveness of the Ayurvedic drug has been established and well documented by the great Acharyas in the form of classics attributed to them (DK Patel et al, 2012, Singh RH, 2004).

However a lot of changes have occurred in our living milieu since the time these classics were written and the impact of these changes on the therapeutic efficacy of the preparations formulated has not been ascertained.

Furthermore the art of preparing formulations requires a certain expertise and no information is available about the likely impact of changes in the manufacture techniques or improper preparation on the expression of biological activity. (Sarkar.PK et al, 2009).

(Sunil Kumar S et al, 2009) Ayurveda makes use of herbal preparations for their preventive and curative effects. Use of metallic preparations (bhasma), in which a process termed bhasmikarana used to prepare the drugs It is believed that the process converts the metal into its specifically desired chemical compound, which eliminates its toxicity and enhances medicinal benefit (Kumar. A et al, 2006; Wadekar MP et al, 2005).
2.4 Reported pharmacological and chemical evaluations

Li WL et al (2004) has demonstrated the hypoglycemic activity of myricetin, purified from Abelmoschus moschatus, in STZ – diabetic rats. The results indicate that myricetin has ability to enhance glucose utilization to lower plasma glucose in diabetic rats with deficient insulin levels.

![Myricetin](image1)

A new dibenzofuran (achyrofuran) isolated from Achyroline satureiodes has excellent hypoglycemic activity in experimental mice (Camey et al, 2002).

![Achyrophuran](image2)
Oyedemi SO et al (2011) have reported the aqueous extract of stem bark of *Afzelia africana* in diabetic rats at 100 or 200 mg/kg, p.o. dose level for 10 days.

The essential oil of *Allium cepa* in diabetic rats at 100 mg/kg, p.o. for 21 days treatment, significantly decreased the serum lipids, lipid peroxide (El – Soud NA et al, 2010)

Girija K et al (2011) and Sangamesswaran B et al (2010) have demonstrated The methanol extracts of leaves of *Amaranthus caudatus* in diabetic rats at a dose of 200 and 400 mg/kg p.o. for 21 d significantly decreased the blood glucose, total cholesterol (TC), triglyceride (TG), LDL and VLDL, but increased HDL, signifying its antidiabetic activity.

The ethanolic extract of *Annona squamosa* leaves in diabetic rats at 100 mg/kg, p.o. for 30 days treatment, significantly reduced the levels of blood glucose, glycosylated hemoglobin, urea and creatinine (Osmani OH et al 2009).

Kuppuswamy AK et al (2010) have reported that the ethanol extracts of Artocarpus heterophyllus in diabetic rats at a dose level of 400 mg/kg p. o. significantly reduced the blood glucose level, which revealed that the *Artocarpus heterophyllus* extract has significant anti-hyperglycaemic activity

The effect of ethanolic extract of *Asystasia gangetica* in diabetic rats at dose levels of 100 and 200 mg/kg, p.o. for 28 days treatment, significantly decreased blood glucose, glycosylated haemoglobin (HbA1C), TC, TG, LDL, VLDL, elevated haemoglobin and HDL levels.

Further it increases the levels of superoxide dismutase (SOD), catalase (CAT), reduces glutathione (GSH), glutathione reductase (GR), glutathione peroxidase (GPx) and glucose-6-phosphate dehydrogenase (G-6-PDH) and decreases lipid peroxidation (thiobarbituric acid reactive substances) indicating antidiabetic and antioxidant activity. (Chauhan SK et al, 2011)
Meliani N et al (2011) have showed the anti-diabetic activity of ethanolic root extract of *Boerhaavia diffusa* in diabetic rats at 100 and 200 mg/kg, p.o. dose level for 15 days treatment.

Alarcon – Aguilar et al (1997) have identified maturine, cacalol and cacalone (sesquiterpenes) having anti diabetic property in fasting mice. These were isolated from Psacalium decompositum, Psacalium peltatum and Acourtia thurberi.

Alloxan induced diabetic mice were used to evaluate Aegle marmelose leaf extracts. One group of mice was given injection and other oral, both exhibited hypoglycemic activity. The results were also indicative of regeneration of damaged pancreas. (Das et al, 2012)

The saponins and aqueous extract of *Berberis vulgaris* at 62.5 and 25.0 mg/kg, p.o. respectively in diabetic rats for 21 days significantly decreased the blood glucose level. (Thirumalai T et al, 2011)
2.5 Collective activity of plant constituents

Herbalists generally use unpurified plant extracts containing several different constituents. They claim that these can work together synergistically. They also claim that the toxicity is reduced when whole herb is used instead of isolated individual ingredient. ('Buffering')

According to Chen ZP et al, (1994) failure of a plant extract to exhibit invitro activity during screening may not mean that the plant has no inherent medicinal value. There exists a synergism between the plant constituent and plants do not contain a single active ingredient. When these compounds are isolated their activity may not reflect the true medicinal value of the plant. (Phillipson J D, 2001)

2.6 The herbal formulation

The herbal formulation included following plants (Plate – 1)

2.6 (a) Plant extracts rich in flavonoids to combat the oxidative stress
   {Acacia catechu [Khair], Emblica officinalis [Amla], Ficus benghalensis[Nyagrodha], Ficus glomerata [Udumbara], and Terminalia arjuna[Arjun]}

2.6 (b) Plant extracts exhibiting hypoglycemic activity
   {Momordica charantia [Karela], Syzgium cumini[Jambool bee], Tinospora cardifolia[Gulvel], Trigonella foenum[Methi]}

2.6 (c) Plant extract that strengthens the pericytes
   {Withania somnifera [Ashwagandha]}
<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Common Name</th>
<th>Family</th>
<th>Conc. Parts</th>
<th>Photograph</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Bark.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td><em>A. catechu</em></td>
<td>Khair</td>
<td>Mimosoidae</td>
<td>0.75</td>
<td><img src="bark1.png" alt="Image" /></td>
</tr>
<tr>
<td>2</td>
<td><em>E. officinales</em></td>
<td>Amla</td>
<td>Euphorbiaceae</td>
<td>2.3</td>
<td><img src="bark2.png" alt="Image" /></td>
</tr>
<tr>
<td>3</td>
<td><em>F. benghalensis</em></td>
<td>Nyagrodha</td>
<td>Moraceae</td>
<td>2.3</td>
<td><img src="bark3.png" alt="Image" /></td>
</tr>
<tr>
<td>4</td>
<td><em>F. glomerata</em></td>
<td>Udumbara</td>
<td>Moraceae</td>
<td>1.6</td>
<td><img src="bark4.png" alt="Image" /></td>
</tr>
<tr>
<td>5</td>
<td><em>T. arjuna</em></td>
<td>Arjun</td>
<td>Combretaceae</td>
<td>0.50</td>
<td><img src="bark5.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td><strong>Seeds</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><em>M. charantia</em></td>
<td>Karela</td>
<td>Cucurbitaceae</td>
<td>0.25</td>
<td><img src="seeds6.png" alt="Image" /></td>
</tr>
<tr>
<td>7</td>
<td><em>T. foenum</em></td>
<td>Methi</td>
<td>Fabaceae</td>
<td>2.3</td>
<td><img src="seeds7.png" alt="Image" /></td>
</tr>
<tr>
<td>8</td>
<td><em>S. cumini</em></td>
<td>Jambool</td>
<td>Myrataceae</td>
<td>1.5</td>
<td><img src="seeds8.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td><strong>Leaves</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td><em>Tinospora cordifolia</em></td>
<td>Gulvel</td>
<td>Combretaceae</td>
<td>0.45</td>
<td><img src="leaves9.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td><strong>Roots</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td><em>Withania somnifera</em></td>
<td>Ashwagandha</td>
<td>Solanaceae</td>
<td>0.12</td>
<td><img src="roots10.png" alt="Image" /></td>
</tr>
</tbody>
</table>
2.6 (a) Plants rich in flavonoids to combat the oxidative stress

The main goal of the current research was to study the plants namely Acacia catechu [Khair], Emblica officinalis [Amla], Ficus benghalensis [Nyagrodha], Ficus glomerata [Udumbara], and Terminalia arjuna [Arjun] reportedly containing good quantity of Polyphenolic compounds, Proanthocyanidins and flavonoids.

Acacia catechu (L.f) Willd

Acacia catechu is official in Ayurvedic Pharmacopoeia of India, Indian Pharmacopoeia, British Pharmacopoeia and United States Pharmacopoeia. It is also listed in Australian Register of Therapeutic Goods (ARTG), British Herbal Pharmacopoeia, and Herbs of Commerce–American Herbal Products Association (AHPA).

The key ingredient is Catechin. It has significant antioxidant and antimicrobial effects (Naik GH, 2003), hepatoprotective, antipyretic and digestive properties (Kirtikar KR et al, 1985, Wallis TE, 1967). It is reported that Acacia catechu has hypoglycemic activity (Sing KN, 1976). The plant has been in the treatment of diarrhoea and throat infection because the catechin present in it imparts astringent activity (Jayasekhar P, 1997).

Acacia catechu extract is considered safe by US FDA and is included in GRAS [Generally Recognized as Safe] list.

Kingdom: Plantae.
Order: Fabales.
Family: Fabaceae.
Subfamily: Mimosoidae.
Genus: Acacia Spp: catechu

Habitat: Occurring throughout India in dry types of mixed forests. Commonly found in Punjab through Assam to an altitude of 1200m.
Parts used: Heartwood [concentrated extract]

Dose: Powder 3-6g, decoction

50 – 100ml.

Classical use: Charaka advocated *Acacia catechu* heartwood decoction as the best medicine for all skin diseases, internally as well as externally. He prescribed the flowers or the fermented wine from the resinous exudates in prescriptions for internal use in haemothermia, urinary disorders and blood poisoning. Sushruta prescribed the drug internally in obesity, urethral discharges and jaundice.

By 16th century, Acacia catechu was established as a potent drug for obstinate skin diseases including leprosy, erysipelas, obstinate urinary disorders, polyurea, diabetes, disease of mouth, cough, and hoarseness of voice.

Active principles and pharmacology: The constituents of heartwood extract are catechin and catechutannic acid, makes it a potent remedy for skin diseases, cough, relaxed condition of throat, mouth and gums; also for diaahoea.25 – 60% tannins, 20 -30% mucilage, Flavonoids [9 investigated in this research], and resins make it a strong astringent and clotting agent. The greater concentration it causes cancer but at mild concentration it exhibits excellent antioxidant property.

*Emblica officinalis* [Gaetrn]

Commonly referred to as: *Phyllantus emblica* L.

Adaptogens are a class of pharmacologically active substances that, in a nonspecific manner, enhance the resistance of an organism to adapt to various stressors.

Most of the pharmacological properties assigned to *E.officinalis* are attributed to its strong antioxidant action. Both, in vitro and in vivo experiments confirm it to posses'
potent antioxidant activity (Chopra RN, 1956). It not only acts as antioxidant by itself but it also activates the antioxidant enzyme systems like superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) present in the body (Chaudhuri RK, 2002; Suresh KG, 2006; Scartezzini P, 2006; Bhattacharya SK, 2002). It has shown adaptogenic activity in various stress induced models like physical stressor (cold immobilization) and chemical stressor (ethanol induced gastric mucosal damage). It also exhibited immunomodulatory activity both in vitro and in vivo studies (Sai Ram M, 2002).

Kingdom: Plantae.

Order: Malpighales.

Family: Euphorbiaceae.


**Habitat:** South Indian hills up to 1500m.

**Parts used:** Fruit.

**Dose:** Powder 3-6g, juice 10 – 20ml.

**Classical use:** In order to promote intellect and prevent senility and for longevity, the powder of amla is mixed with honey was prescribed by (Charaka Samhitaa, Sushruta Samhitaa, Astaanga Hridayaa, Vrindamaadhava). Sesamum seeds, Eclipta alba, Embelia ribes, Pterocarpus marsupium, calcined gold, calcined iron were used as adjuvants.

The most popular supporting drugs were Sesamum seeds, Eclipta alba for making Amla a potent age sustainer. Among over the counter drugs, Chyavanprasha and Brahma Rasaayana are prescribed extensively during winter.

Dhaatryaarishtha (Bhaishaajya Ratnaavali), a fermented alchoholic compound containg amla juice, Piper longum, honey and sugar, is an appetizer, digestive, carminative, haemantic and mildly laxative, prescribed
in anemia, jaundice, diabetes, hiccups; and also in intermittent fever. Triphala churna, Dhaatri Lauha, Itirfal- e – Ustukhudus are other popular Unani preparations.

**Active principles and pharmacology:** The plant gave the tannins, glucogallin, cheoulagic and 3,6- digalloylgucose. The fruit contains vitamin C, L – (+)- thioascorbic acid, cytokinin substances, nucleosides and phyllembin.

The fruit pulp contains moisture 81.2, protein 0.5, fat 0.1, mineral matter 0.7, fiber 3.4, carbohydrates 14.1, Ca 0.05, P 0.02%; Fe 1.2mg, nicotinic acid 0.2mg, vitamin C 600mg/100g. It also contains pactin, tannin containing gallic acid, ellagic acid and glucose retarding oxidation of the vitamin.

**Ficus benghalensis Linn**

*Ficus bengalensis* is commonly known as a Banyan tree. This tree is considered to be sacred tree in India (Jander EA, 2008; Trevedi PS et al, 1969). The bark leaves and fruits are used as astringent, haemostatic, anti-septic, anti-inflammatory, antioxidant and anticancer agent (CP Khare, 2004)

Kingdom: Plantae.

Order: Urticales.

Family: Moraceae.

Genus:*Ficus* Spp:benghalensis.

**Habitat:** Found throughout India, is planted around temples and in
gardens.

**Parts used:** Bark, latex, leaf and fruit.

**Dose:** Powder 3-5g, decoction 50 – 100ml, latex 5-10 drops.

**Classical use:** Charaka prescribed aqueous extract of leaf buds Nygrodha, Udumbra (*F.glomerata*) and Ashvattha (*F.religiosa*) mixed with sugar and honey for checking diarrhea. It also exhibits anti oxidative and anti diabetic properties.

**Active principles and pharmacology:** The bark yielded 3 types of Flavonoids A, B and C. [all three exhibit effective hypoglycemic property]

In a study, alcoholic extract prepared from stem bark of *Ficus benghalensis* was studied for its long team feeding effects on blood sugar of albino rats, which were made diabetic through i.v. injection of alloxan monohydrate.

Different doses (25, 50 and 75mg/day/100g body weight of the rat) over different duration showed significant hypoglycemic potential.

The blood sugar once lowered, remained unaltered when treatment was discontinued. The extract was also able to bring down the levels of cholesterol and blood urea. Total protein remained unaffected.

Beside Flavonoids other compounds like friedelin, β sitosterol, rutin, quercetin, dimethoxy ethers of Leucoperlargonidin-3-O –alpha rhamnoside has been observed.

*Ficus glomerata* Roxb:

![Ficus glomerata](image)

Kingdom: Plantae.

Order: Urticales.

Family: Moraceae.

Genus: *Ficus* Spp: glomerata.
Habitat: Found throughout India, grows wild in many forests and hills. Often found around subterranean water streams.

Parts used: Bark, and fruit.

Dose: Powder 3-5g, decoction 50 – 100ml,

Classical use: Charaka prescribed tender leaves of Udumbara as astringent and styptic in diarrhea and haemorrhages, for treating vaginal laxity. In Unani medicine, fruits, also root water, are recommended as a tonic to diabetes.

Active principles and pharmacology: Stem bark gave glunol acetate, β sitosterol, leucocynidin-3–O–β-glucopyranoside, leucocynidin-3-O–β-rhamnopyranoside, lupeol, ceryl behenate, lupeol acetate and alpha amyrin acetate, tannins are also present. The alcoholic extract has antiprotozoal activity against Entamoeba histolytica. The bark also exhibits significant hypoglycemic activity.

Terminalia arjuna(Roxb.ex DC.) W &A

Kingdom: Plantae.

Order: Myratales.

Family: Combretaceae.


Habitat: Commonly found in Madya Pradesh, Bihar, and Peninsular India grows as an avenue tree.

Parts used: Bark.

Dose: Powder 3-6g, decoction 50 – 100ml, decoction with milk 50 – 100ml,

Classical use: Charaka used bark and leaves in internal
prescriptions for cardiac disorders, diarrhea, intrinsic haemorrhages, piles, ulcers. Sushruta used it in vaginal discharges migraine, obesity, and chronic skin disease.

According to Vrindamaadhava, those who take the powdered bark, processed with milk, purified butter or jaggery water, are relieved of cardiac disorders, chronic fevers, and attain longevity. It has anti cancer and anti diabetic activity.

**Active principles and pharmacology:** Stem bark contains atriterpene, arjungenine, triterpene glycosides I, II, III. Flavones, baicalein and arjunolone characterized as 6,4-dihydrooxy – 7-methoxyflavone. Dry bark contains 20-24% tannins.

Intra ventricular and intra arterial administration of alcoholic extract produced long lasting hypotension and bradycardia, suggesting thereby its activity through CNS – neurons.

2.6 (b) Plant extracts exhibiting hypoglycemic activity

In diabetic retinopathy major damage is done by high blood glucose levels, compounds that reduce blood glucose maintain healthy conditions of pericytes, smooth muscle cells in retinal blood vessels and over proper metabolism. Researchers have found that diabetic patients who are able to maintain appropriate blood sugar levels have fewer eye problems than those with poor control. Diet and exercise play important roles in the overall health of those with diabetes.

Current concepts of the pathogenesis of retinal microangiopathy strongly suggest that it is dependent on the metabolic abnormalities of diabetes mellitus.

This has led to speculation that retinal microangiopathy might be prevented or its progression halted by controlling the blood glucose concentration to lower levels than has been possible in the past with conventional insulin therapy and conventional monitoring.
Intensive regulation of the blood glucose level in insulin-dependent diabetes mellitus is a therapeutic choice made available by technologic advances: the introduction of devices for insulin delivery and for the patient’s self-monitoring of the blood glucose level, as well as of methods for measuring the level of glycosylated hemoglobin.

For an individual patient, selection of the optimal insulin regimen and the optimal target for the blood glucose levels should take into account the susceptibility to microvascular complications inherent in the classification of that patient’s diabetes, the patient’s retinopathy status and the potential risks, such as severe hypoglycemia and, perhaps, acceleration of retinopathy.

With normal or nearly normal blood glucose levels many of the metabolic and endocrine abnormalities of diabetes are corrected, but the biologic significance and the impact on diabetic retinopathy of this improvement remain to be clarified.

**Momordica charantia L**

Kingdom: Plantae.

Order: Violes.

Family: Cucurbitaceae.


**Habitat:** Found throughout India, up to 1500m.

**Parts used:** Fruit and leaves.

**Dose:** Juice 10 – 20ml.

**Classical use:** Charaka prescribed
decoction of fruits and leaves, internally in haemothermia and cough. Sushruta prescribed it for toxicity, as an antiseptic and purgative; fruits as a potherb in the form of a diet in fevers, hiccup, urinary discharges, skin diseases, and gout. As a popular household remedy, the juice of the raw fruit is given in diabetes; the juice has blood purification properties.

**Active principles and pharmacology:** Seed powder contains triterpene glycoside named momordicosides A, B, C, D and E, bitter principles Momordicines I, II, III, it also contains a insulin like polypeptide containing 17 types of amino acids.

Fruits also have 5 – hydroxytryptamine and a neutrl compound characantin, diosgenin, Cholesterol, lansosterol and beta sitosterol. Seed powder exhibits hypoglycemic activity due to charantin (momordicin) its shows extra pancreatic activity.

Hypoglycemic activity was tested against the steptozotocin- induced diabetes mellitus in rabbits(1-3g/day) and was found comparable to to that of glybenclamide and positively associated with lipogenesis.

**Syzgium cumini L. Skeels**

Kingdom: Plantae.

Order: Myratales.

Family: Myrataeae.

Genus: *Syzgium* Spp: cumini

**Habitat:** Found throughout India, Up to 1800m.

**Parts used:** Bark, seed, leaf and fruit.
Dose: Powder 3-6g, decoction of bark 50 – 100ml,

Classical use: Charaka prescribed the seeds, leaves and the stones of the fruits for diarrhea, nausea, vomiting, consumption and bark is astringent. Sushruta used the fruit internally in obesity, menstrual disorders, cold infusion in intrinsic haemorrhages. The juice with amra and amla leaves mixed with goat's milk and honey are effective in diarrhea with blood and sluggish digestion. In classical Unani compounds, Quars-e-Ziabetes Khaas, the seeds of jambu are prescribed for diabetes mellitus.

Active principles and pharmacology: Stems, leaves and fruits contain essential oil having alpha and beta-pinene. Limonine, cis-ocimene, trans-ocimene, alpha-humulene and bornyl acetate as major constituents.

Fruits contain the anthocyanins, delphinidin-3-gentiobioside, malvidin-3-laminarabinoside and petunidin-3-gentibioside, mallic acid and gallic acid.

In clinical trials, 6 non-diabetic and 5 diabetics were administered 150g of jambu fruits (pulp 115g) after overnight fasting. Average of fasting blood sugar in non diabetics was 75.3 (± 2.63 SE) in diabetics 240 (± 44.3 SE). After 1 hour, 2 hour, 3 hour the blood sugar level was 68.1 (± 3.7 SE), 67.1 (± 4.6 SE) and 68.3 (± 2.11 SE); in second group 240 (± 44.3 SE), 254 (± 12.6 SE), and 276.6 (± 49.67 SE).

**Tinospora cordifolia (Wild.) Miers.ex Hk. f. Thoms**

Kingdom: Plantae.

Order: Ranunculales.

Family: Combretaceae.


Habitat: Found throughout tropical India, ascending to 300m.
**Parts used:** Stem, root and flowers.

**Dose:** Juice 5 – 10 ml, decoction 5 – 10ml.

**Classical use:** A cooled decoction of guduuchi mixed with honey, or a paste of guduuchi leaves mixed with butter milk is use for jaundice. [Charaka Samhitaa, Astaanga Hridaya, Bangasena, Bhaavaprakash] Among over the counter drugs, guduuchi satva [Bhaavaprakash] is prescribed for chronic fevers, diabetes and wasting disease. In classical Unani compounds, Sat-e -Gilo is incorporated with Haab-e –Tabaasheer and Quars-e–Ziabetus Khaas, are prescribed for diabetes mellitus.

Seenthil Sarkarai is the principal ingredient of Siddha compound Sandana podi, prescribed for Diabetes.

**Active principles and pharmacology:** The creeper contains tinosporon, tinosporic acid, tinosporol, alpha sitosterol, and cordifolide; a furanoid bitter principal, tinosporine and quartenary alkaloids magnoflorine and tembetarine. The hepatoprotective activity has been studied in carbon tetra chloride-induced liver damage in rats, it prevented fibrosis and stimulated regeneration of hepatic tissue. The drug has been found to non toxic in acute toxicity studies.

*Trigonella foenum-graecum* Linn

Kingdom: Plantae.

Order: Fabales.
Family: Fabaceae.


**Habitat:** Commonly found in Kashmir, Punjab and upper Ganges plains. Wildly cultivated in many parts of India.

**Parts used:** Seeds.

**Dose:** Powder 3-5g.

**Classical use:** Methikaa was not used during the period of Charaka and Sushruta. During Vedic period, Methi was the pole with which sacrificial horses were tied. It entered into Indian medicine during the period of Bhaavamisra.

According to Maadhava Dravyaguna, it harmonizes all body functions, alleviates rheumatic affections and possesses digestive and laxative properties. Methi is included in number of Ayurvedic compound preparations for its carminative, galactogogue and anti-diabetic activity.

**Active principles and pharmacology:** The plant contains a number of steroidal sapogenins, especially diosgenin found in oily embryo. The alkaloid trigonelline, trigocoumarin, trimethyl coumarin and nicotinic acid are also present. Mucilage [25-40%] is a prominent constituent of seeds, contains mannogalactans.

Seeds contain 45-60% carbohydrate, 20-30% protein high in lysine and tryptophan, 5 - 10% fixed oils [lipid], pyridine like alkaloids mainly trigonelline, choline, gentianine, carpine, the Flavonoids apigenin, luteolin,
orientin, quercetin, vitexin, and isovitexin; free amino acids, calcium and iron; saponins (0.6-1.7%).

Chronic administration of seed extracts enhances food consumption and motivation to eat in rats and also induced hyperinsulinemia and hypocholesterolaemia. In two diabetic insulin dependent subjects, daily administration of 25g of Fenugreekseed powder reduced plasma glucose profile, glucosurea and daily insulin requirement (56-20 units) after 8 weeks.

2.6(c) Plant extract that strengthens the pericytes

**Withania somnifera (Linn) Dunal**

Kingdom: Plantae.

Order: Tubiflorie.

Family: Solanaceae.


**Habitat:** Found throughout drier parts of India in waste places and on bunds. Extensively cultivated in Manaasaa and Ganj Basodaa of Madyparadesh. Indian plants differ from the known chemotypes of Israel in composition of withanolides.

**Parts used:** Roots and ash.

**Dose:** Root powder 3-6g, ash 2-3g,

**Classical use:** Charaka divided the plant substances into fifty groups according to physiological actions of their decoctions. Ashwagandha of his period was included in Vaajikarana (asphoridic) but was not mentioned in (jivaniya–prometer of longevity). It is
also grouped as sex drug for promoting virility. During 7th century, Withania somnifera was included as Ashwagandha among twenty age sustaining compounds.

In Bhaavprakaash (is one of the structuring dynamics of Rk Veda. It highlights the ENLIGHTENING quality involved in structuring Rk Veda) the drug is included in formulations which promote intellect, life span and virility (247). Paste of root is applied to penis for toning up erectile tissue; mixed with mother’s milk a paste of the root is applied to sagging breast. It is also prescribed for stress, fatigue, and run down conditions (248).

**Active principles and pharmacology:** Roots contain alkaloids nicotine, somnine, somniferine, somniferinine, withanine, withaninine, pseudowithanine, tropane, pseudotropane, choline, anaferine.

A double blind clinical trial, to study the effect of Ashwagandha on the prevention of the process of ageing in 101 healthy individuals in age group of 50-59 years, indicated increase in haemoglobin, RBC, hair melanin, and seated stature.

Research on drug acting on CNS, established it as anti anxiety, and adoptogenic. In combination with with Cyperus rotundus 1g thrice daily was administered to patients of rheumatoid arthritis for a period of 1 year. Results were better in maiden cases (excellent 28%, good 12%, fair 45%, poor 17% and no response 2%). The response was poorer in long term cortisone-treated cases (excellent 23%, good 19%, fair 21%, poor 26% and no response 13%).the efficacy of the herb was lower in case of osteoarthritis (excellent 12%, good 23%, fair 34%, poor 15% and no response 16%). Sub acute toxicity studies with repeated injections at a dose of 100mg/kg body weight for 30 days in wistar rat of either sex did not result in any mortality or changes in peripheral blood constituents.

**Hypoglycemic compounds:** Reduce blood glucose levels [lower is the blood glucose levels lesser vascular damage.] Researchers have found that diabetic patients who are able to maintain appropriate blood sugar levels have fewer eye problems than those with poor control. Diet and exercise play important roles in the overall health of those with diabetes.
Current concepts of the pathogenesis of retinal microangiopathy strongly suggest that it is dependent on the metabolic abnormalities of diabetes mellitus. This has led to speculation that retinal microangiopathy might be prevented or its progression halted by controlling the blood glucose concentration to lower levels than has been possible in the past with conventional insulin therapy and conventional monitoring.

Intensive regulation of the blood glucose level in insulin-dependent diabetes mellitus is a therapeutic choice made available by technologic advances: the introduction of devices for insulin delivery and for the patient's self-monitoring of the blood glucose level, as well as of methods for measuring the level of glycosylated hemoglobin.

For an individual patient, selection of the optimal insulin regimen and the optimal target for the blood glucose levels should take into account the susceptibility to microvascular complications inherent in the classification of that patient's diabetes, the patient's retinopathy status and the potential risks, such as severe hypoglycemia and, perhaps, acceleration of retinopathy. With normal or nearly normal blood glucose levels many of the metabolic and endocrine abnormalities of diabetes are corrected, but the biologic significance and the impact on diabetic retinopathy of this improvement remain to be clarified.

Ashwagandha [Withania somnifera] Not only strengthens the pericytes but also allows them to proliferate in presence of elevated concentration [25mM glucose.] Pericytes thus keeps away vascular damage and prevents Diabetic retinopathy.

2.7 Conclusion

Plants are important components in our therapeutic arsenal in the fight against the disease. They have and will most likely continue to serve as an important source of new therapeutic molecules. It is hoped that
documented ethanobiological plant archives would be an asset from which further discoveries are made.

**Overview of chapter 2:**

A person having type I diabetes for more than 5 years and if blood glucose is not maintained at normal levels, 100% of the patients are prone to have diabetic retinopathy, 60% of the type 2 patients are equally susceptible to disease.

The onset of retinopathy is because of four reasons- Oxidative stress, hyperglycemia, improper angiogenesis and weakening of pericytes the smooth muscle cells lining the vascular endothelium in retina. So the aim of the current research was to formulate an herbal formulation that will act as preventive remedy against Diabetic retinopathy.

And the objectives were to develop and test the innovative formulation for its ability to overcome the four problems associated with diabetic retinopathy.

1. The formulation contains, secondary metabolites (Polyphenolics, Proanthocynidins and Flavonoids) [to overcome oxidative stress], their antioxidant potential was evaluated by FRAP assay, Radical scavenging ability was determined by DPPH and ABTS assay, Lipid peroxidation by TBARS assay. They have good antioxidant property and radical scavenging ability to combat oxidative stress;

2. The insulin like polypeptides of *Momordica charantia*[Karela], Bitter compounds of *Syzgium cuminii*[Jambool beeze], *Tinospora cardifolia*[Gulvel], and Saponins of *Trigonella foenum*[Methi], help in maintaining blood glucose [For their hypoglycemic properties],

3. Flavonoids apigenin, luteolin, orientin, quercetin, vitexin, and isovitexin; free amino acids, calcium and iron; saponins of *Trigonella foenum* helps in proper blood vessel formation [angiogenic nature of formulation ] and
4. The alkaloids nicotine, somnine, somniferine, somniferinine, withanine, withaninine, pseudowithanine, tropane, pseudotropane, choline, anaferine of *Withania somnifera*, not only imparts strength to pericytes but also allows them to proliferate and divide at alleviated blood glucose levels [25mM] which is the case in diabetes.

Since the study is recommending edible formulation, the cytotoxicity [MTT assay] was performed. The drug was evaluated for its absorption via intestine [using goat intestine model]. Safety of the drug can be guaranteed for it is reducing lipid peroxidation [TBARS assay], No DNA damage [Comet assay], and Imparts strength to vascular pericytes [Pericyte culture and CAM assay]. The results of the entire assays are promising and the drug can be safely consumed. For evaluating long term safety and health benefits the drug is undergoing clinical trials.

* * * * * * *