SYNOPSIS OF THE THESIS

"Effectiveness of Gymnema Sylvestre in Homoeopathic Management Of Type II Diabetes Mellitus – A Randomized Controlled Clinical Trial"

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TITLE AND SYNOPSIS

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Sr no.	Item	Guidelines
1)	**Title:**	Effectiveness of Gymnema Sylvestre in Homoeopathic Management Of Type II Diabetes Mellitus – A Randomized Controlled Clinical Trial
2)	**Introduction:**	Diabetes mellitus is taken from the Greek word diabetes, meaning siphon - to pass through and the Latin word mellitus meaning sweet. A review of the history shows that the term "diabetes" was first used by Apollonius of Memphis around 250 to 300 BC. Ancient Greek, Indian, and Egyptian civilizations discovered the sweet nature of urine in this condition, and hence the propagation of the word Diabetes Mellitus came into being. Mering and Minkowski, in 1889, discovered the role of the pancreas in the pathogenesis of diabetes. In 1922 Banting, Best, and Collin purified the hormone insulin from the pancreas of cows at the University of Toronto, leading to the availability of an effective treatment for diabetes in 1922. Over the years, exceptional work has taken place, and multiple discoveries, as well as management strategies, have been created to tackle this growing problem. Unfortunately, even today, diabetes is one of the most common chronic diseases in the country and worldwide. In the US, it remains as the seventh leading cause of death. [1] Diabetes mellitus is characterized by abnormally high levels of sugar (glucose) in the blood. Currently Diabetes Mellitus remains one of the most prevalent disease amongst all the countries over the world and also a leading cause of death due to multitude of complications associated with its progression. Currently Diabetes can be regarded as a “Treatable” disease, but not a “Curable” disease. Conventional line of treatment includes a variety of drugs with their actions focused on different mechanism to achieve glycemic control. In addition to negative health outcomes, T2DM can negatively impact the ability to participate in desired and meaningful daily activities. Studies suggest a significant link between diabetes and functional disability. Individuals with T2DM have reported problems with mobility, self-care, and domestic life. Additionally, complications of diabetes such as

vision impairment and neuropathy can negatively impact performance of home management tasks, driving, and community mobility. T2DM can also complicate common tasks like self-care by introducing a host of new activities like blood glucose monitoring, foot care, and medication management. Because of T2DM's nature as a lifelong chronic disease, individuals with T2DM are primarily responsible for T2DM management. In order to promote successful T2DM self-management, healthcare associations recommend attending DSM classes and participating in preventive care practices. Psychosocial factors have been implicated as one such group of significant and influential factors impacting DSM. Psychological factors like self-discipline, locus of control, coping and stress management skills, and self-efficacy may be barriers to successful and consistent performance of diabetes self- care activities. Social relationships have also been identified as a potential barrier to one's ability to fulfill complex self-management requirements.

Gymnema Sylvester

Gymnema sylvestre **is a woody climbing shrub that's native to the tropical forests of India, Africa and Australia.It has been a traditional remedy for various ailments, including diabetes, malaria and snakebites This herb is thought to inhibit sugar absorption and thus has become a popular study subject in Western medicine.**

Gymnema sylvestre **can help reduce sugar cravings.**

One of the primary active components in this plant is gymnemic acid, which helps suppress sweetness 1,2When consumed prior to a sugary food or beverage, gymnemic acid blocks the sugar receptors on your taste buds1.

Research shows that *Gymnema sylvestre* extracts can reduce the ability to taste sweetness and thus make sweet foods less appealing[1,2]

In a study in fasted individuals, half were given *Gymnema* extract. Those who received the extract had less appetite for sweet foods at a subsequent meal and were more likely to limit their food intake, compared to those not taking the extract[2]

Gymnemic acids in *Gymnema sylvestre* can block the sugar receptors on tongue, decreasing ability to taste sweetness. This can lead to reduced sugar cravings.

Gymnema sylvestre is considered to have anti-diabetic properties.

As a supplement, it has been used in combination with other diabetes medications to lower blood sugar. It's also called gurmar, which is Hindi for "destroyer of sugar"[4]

Similar to its effects on taste buds, *Gymnema sylvestre* can also block receptors in intestines and thus sugar absorption, lowering post-meal blood sugar levels.

Scientific proof of *Gymnema*'s ability to lower blood sugar is insufficient to recommend it as a stand-alone diabetes medication. However, research shows strong potential.

Studies suggest that consuming 200–400 mg of gymnemic acid reduces the intestinal absorption of the sugar glucose [4]

In one study, *Gymnema* appeared to improve blood sugar control in people with type 2 diabetes by lowering blood sugar levels 5

The study concluded that reducing blood sugar after a meal resulted in a decrease in average blood sugar levels over time. This could help decrease long-term complications of diabetes (5).

For people with high blood sugar or a high HbA1c, *Gymnema sylvestre* can help reduce fasting, post-meal and long-term blood sugar levels.

Gymnema's role in insulin secretion and cell regeneration may also contribute to its blood-sugar-lowering capabilities.

Gymnema sylvestre may stimulate insulin production in pancreas, promoting the regeneration of insulin-producing islet cells. This can help lower blood sugar levels 6,7

Gymnema sylvestre appears to contribute to favorable insulin levels by increasing insulin production and regenerating insulin-secreting islet cells. Both can help lower blood sugar levels.

Though Gymnema is known for lowering blood sugar levels and reducing sugar cravings, research shows that it may also influence fat absorption and lipid levels.

In one study in rats on a high-fat diet, *Gymnema* extract aided weight maintenance and suppressed the accumulation of liver fats. Also, animals fed the extract and a normal-fat diet experienced lower triglyceride levels 9

Another study found that *Gymnema* extract had an anti-obesity effect on animals fed a high-fat diet. It also decreased blood fat and "bad" LDL cholesterol levels (10

In addition, a study in moderately-obese people showed that *Gymnema* extract decreased triglycerides and bad "LDL" cholesterol by 20.2% and 19%, respectively. What's more, it increased "good" HDL cholesterol levels by 22%11

The positive effects of *Gymnema sylvestre* on LDL and triglycerides levels contribute to a lower risk of heart conditions 6&8).

***Gymnema sylvestre* extracts have been shown to aid weight loss in animals and humans.**

One three-week study showed reduced body weight in rats given a water extract of *Gymnema sylvestre*. In another study, rats on a high-fat diet that were fed a *Gymnema* extract gained less weight 12

Also a study in 60 moderately-obese people taking a *Gymnema* extract found a 5–6% decrease in body weight, as well as reduced food intake 11

By blocking sweet receptors on taste buds, *Gymnema sylvestre* may cause to eat fewer sweet foods and consume fewer calories. and a consistent calorie deficit can result in weight loss.

Research Gap:

Although Diabetes Mellitus is a fairly common lifestyle associated disease treated by many Homoeopaths on daily basis, properly formulated research studies seem to be lacking in our literature. The number of research studies including Homoeopathy in the management of

		T2 DM are insufficient in quantity as well as quality. There is a drastic need of studies to be carried out for evaluating the benefit of homoeopathic drugs in cases of T2 DM so as to provide a better and safer alternative treatment. We need to carry out studies involving common and rare homoeopathic medicines in their various strengths like Mother Tinctures, decimal scale, centesimal scale, millesimal and higher potencies. Keeping in mind this gap, an attempt is made hereby to evaluate one such drug in mother tincture strength for management of diabetic patients. Gymnema Sylvester is one of the rare and less commonly used homoeopathic remedy known for its antidiabetic properties. It is known to control the blood sugar levels through the action of its various active principles mainly alkaloids. Not much is known about this remedy except for a few provings carried out by our pioneers. Recently some studies have been carried out by various researchers to study the anti-diabetic potential of Gymnema Sylvester with varying degrees of success. Hence, the current study makes an attempt to evaluate the effactiveness of "Gymnema Sylvester" in management of T2 DM.
3.1)	**Primary Research Question:**	Is Gymnema Sylvester effective in the management of Type II Diabettes Mellitus
3.2)	**Secondary Research Question 1 : (if any)**	Not Applicable
3.3)	**Secondary Research Question 2 : (if any)**	Not Applicable
4.1)	**Primary Hypothesis :-**	Gymnema Sylvester is effective in the management of Type II Diabettes Mellitus
4.2)	**Other Hypothesis 1:-**	Gymnema Sylvester is not effective in the management of Type II Diabettes Mellitus.
4.3)	**Other s 2**	Not Applicable

05)	**Review of Literature :-**	**Definition:** Diabetes mellitus (DM) is a metabolic disease of multiple etiologies characterized by chronic hyperglycemia with defects in carbohydrate, protein and fat metabolism due to defect in insulin secretion, insulin action or a combination of both.2 Thus it is a disease involving inappropriately elevated blood glucose levels. DM has several categories, including type 1, type 2, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes due to endocrinopathies, steroid use, etc. The main subtypes of DM are Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM), which classically result from defective insulin secretion (T1DM) and/or action (T2DM). T1DM presents in children or adolescents, while T2DM is thought to affect middle-aged and older adults who have prolonged hyperglycemia due to poor lifestyle and dietary choices. The pathogenesis for T1DM and T2DM is drastically different, and therefore each type has various etiologies, presentations, and treatments. [1] **Aetio-Pathogenesis of Type 2 DM:** In the islets of Langerhans in the pancreas, there are two main subclasses of endocrine cells: insulin-producing beta cells and glucagon secreting alpha cells. Without the balance between insulin and glucagon, the glucose levels become inappropriately skewed. In the case of DM, insulin is either absent and/or has impaired action (insulin resistance), and thus leads to hyperglycemia. [1] T1DM is characterized by the destruction of beta cells in the pancreas, typically secondary to an autoimmune process. The result is the absolute destruction of beta cells, and consequentially, insulin is absent or extremely low. T2DM involves a more insidious onset where an imbalance between insulin levels and insulin sensitivity causes a functional deficit of insulin. Insulin resistance is multifactorial but commonly develops from obesity and aging. The genetic background for both types is critical as a risk factor. T2DM involves a more complex interplay between genetics and lifestyle. There is clear evidence suggesting that T2DM is has a stronger hereditary profile as compared to T1DM. The majority of patients with the disease have at least one parent with T2DM. [1]

Monozygotic twins with one affected twin have a 90% likelihood of the other twin developing T2DM in his/her lifetime. Approximately 50 polymorphisms to date have been described to contribute to the risk or protection for T2DM. A genome-wide association study (GWAS) found genetic loci for transcription factor 7-like 2 gene (TCF7L2), which increases the risk for T2DM. Other loci that have implications in the development of T2DM include NOTCH2, JAZF1, KCNQ1, and WFS1. [1]

MODY is a heterogeneous disorder identified by non-insulin-dependent diabetes diagnosed at a young age (usually under 25 years). It carries an autosomal dominant transmission and does not involve autoantibodies as in T1DM. Several genes have implications in this disease, including mutations to hepatocyte nuclear factor-1-alpha (HNF1A) and the glucokinase (GCK) gene, which occurs in 52 to 65 and 15 to 32 percent of MODY cases, respectively. [1]

Gestational diabetes is essentially diabetes that manifests during pregnancy. It is still unknown why it develops; however, some speculate that HLA antigens may play a role, specifically HLA DR2, 3, and 4. Excessive proinsulin is also thought to play a role in gestational diabetes, and some suggest that proinsulin may induce beta-cell stress. Others believe that high concentrations of hormones such as progesterone, cortisol, prolactin, human placental lactogen, and estrogen may affect beta-cell function and peripheral insulin sensitivity. [1]

Several endocrinopathies, including acromegaly, Cushing syndrome, glucagonoma, hyperthyroidism, hyperaldosteronism, and somatostatinomas, and others have been associated with glucose intolerance and diabetes mellitus, due to the inherent glucogenic action of the endogenous hormones excessively secreted in these conditions. Conditions like idiopathic hemochromatosis are associated with diabetes mellitus due to excessive iron deposition in the pancreas and the destruction of the beta cells. [1]

Epidemiology: Globally, 1 in 11 adults has DM (90% having T2DM). The onset of T1DM gradually increases from birth and peaks at ages 4-6 years and then again from 10-14 years. Approximately 45% of children present at an age <10 years. The prevalence in people under

age 20 is about 2.3/1000. There are no apparent gender differences in the incidence of childhood T1DM. In some populations, such as in older males of European origin (over 13 years), they may be more likely to develop T1DM compared to females (3:2 male to female ratio). The incidence of T1DM has been increasing worldwide. In Europe, Australia, and the Middle East, rates are rising by 2% to 5% annually. In the United States, T1DM rates rose in most age and ethnic groups by about 2% yearly, and rates are higher in Hispanic youth. The exact reason for this pattern remains unknown. However, some metrics, such as the United States Military Health System data repository, found plateauing over 2007 to 2012 with a prevalence of 1.5 per 1000 and incidence of 20.7 to 21.3 per 1000. [1]

The onset of T2DM is usually later in life, though obesity in adolescents has led to an increase in T2DM in younger populations. T2DM has a prevalence of about 9% in the total population of the United States, but approximately 25% in those over 65 years. The International Diabetes Federation estimates that 1 in 11 adults between 20 and 79 years had DM globally in 2015. Experts expect the prevalence of DM to increase from 415 to 642 million by 2040, with the most significant increase in populations transitioning from low to middle-income levels. T2DM varies among ethnic groups and is 2 to 6 times more prevalent in Blacks, Native Americans, Pima Indians, and Hispanic Americans compared to Whites in the United States. While ethnicity alone plays a vital role in T2DM, environmental factors also greatly confer risk for the disease. For example, Pima Indians in Mexico are less likely to develop T2DM compared to Pima Indians in the United States (6.9% vs. 38%). [1]

Diabetes in India: The burden of diabetes is high and increasing globally, and in developing economies like India, mainly fueled by the increasing prevalence of overweight/obesity and unhealthy lifestyles. The estimates in 2019 showed that 77 million individuals had diabetes in India, which is expected to rise to over 134 million by 2045. According to the IDF in 2019, the top three countries with the highest number of individuals with diabetes are China (116.4 million), India (77.0 million), and the United States of America (31.0 million). This trend is expected to continue in 2030 and 2045, with China

(140.5 and 147.2 million) and India (101.0 and 134.2 million) continuing to have the highest burden of diabetes. [3]

In India, the burden of diabetes has been increasing steadily since 1990 and leaps and at a faster pace from the year 2000. Fig 1 shows the increasing trend in diabetes prevalence in India during the past decade in India as per IDF. The prevalence of diabetes in India has risen from 7.1% in 2009 to 8.9% in 2019. Currently, 25.2 million adults are estimated to have IGT, which is estimated to increase to 35.7 million in the year 2045. India ranks second after China in the global diabetes epidemic with 77 million people with diabetes. Of these, 12.1 million are aged >65 years, which is estimated to increase to 27.5 million in the year 2045. It is also estimated that nearly 57% of adults with diabetes are undiagnosed in India, which is approximately 43.9 million. (3)

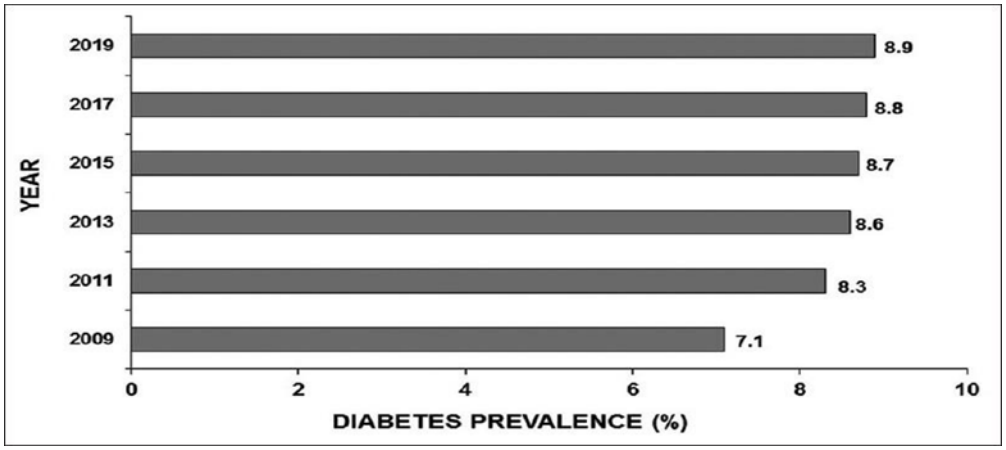


Fig 1. Trends in diabetes prevalence during the past decade in India. (3)

Recent researches in India regarding T2DM:

1. The India State-Level Disease Burden Initiative Diabetes study collaborators reported that the prevalence and number of people with diabetes in India increased from 5.5% and

26.0 million in 1990 to 7.7% and 65.0 million in the year 2016. According to this report, Tamil Nadu had the highest prevalence in 2016, followed by Kerala, Delhi, Punjab, Goa, and Karnataka. The report on the state-level disease burden in India stated that the percent change in diabetes prevalence among all ages in India from 1990 to 2016 was 64.3%, while the age-standardized prevalence was 29.3 %. (3) The first study was conducted in Mumbai in 1963 among 18,243 individuals, and the prevalence of diabetes was found to be 1.5% based on urine analysis. The national prevalence of diabetes was reported to be 2.1% in the multicenter ICMR survey conducted between 1972 and 1975 in Ahmedabad, Calcutta, Cuttack, Delhi, Poona, and Trivandrum, as well as neighboring rural areas. (3)

2. In the Indian Council of Medical Research–India DIABetes study, the largest nationally representative epidemiological survey conducted in India on diabetes and prediabetes, the data from 15 states/UT of the country showed that the prevalence of diabetes ranged from

3.5 to 8.7% in rural to 5.8 to 15.5% in urban areas and the prevalence varied from 4.3% in Bihar to 13.6% in Chandigarh. The prevalence of diabetes was higher in urban areas (11.2%) compared to rural areas (5.2%). (3)

3. The recent Secular Trends in Diabetes in India study which assessed the change in diabetes prevalence between 2006 and 2016 in urban and rural areas of Tamil Nadu reported that the prevalence of diabetes increased from 18.6% in 2006 to 21.9 in 2016 in the city, while in the smaller towns, it increased from 16.4 to 20.3, and in the periurban villages, from 9.2 to 13.4, respectively. (3)

These findings highlight the fact that India's current rapid economic and nutritional transitions increase the risk of type 2 diabetes, and that the "diabetogenic" environment in India is now as bad, if not worse, as in the United States.(3)

Pathophysiology: The pathology of DM can be unclear since several factors can often contribute to the disease. Hyperglycemia alone can impair pancreatic beta-cell function and contributes to impaired insulin secretion. Consequentially, there is a vicious cycle of hyperglycemia leading to an impaired metabolic state. Blood glucose levels above 180 mg/dL are often considered hyperglycemic in this context, though because of the variety of mechanisms, there is no clear cutoff point. Patients experience osmotic diuresis due to saturation of the glucose transporters in the nephron at higher blood glucose levels. Although the effect is variable, serum glucose levels above 250 mg/dL are likely to cause symptoms of polyuria and polydipsia.

Insulin resistance is attributable to excess fatty acids and pro-inflammatory cytokines, which leads to impaired glucose transport and increases fat breakdown. Since there is an inadequate response or production of insulin, the body responds by inappropriately increasing glucagon, thus further contributing to hyperglycemia. While insulin resistance is a component of T2DM, the full extent of the disease results when the patient has inadequate production of insulin to compensate for their insulin resistance.

Chronic hyperglycemia also causes non-enzymatic glycation of proteins and lipids. The extent of this is measurable via the glycation hemoglobin (HbA1c) test. Glycation leads to damage in small blood vessels in the retina, kidney, and peripheral nerves. Higher glucose levels hasten the process. This damage leads to the classic diabetic complications of diabetic retinopathy, nephropathy, and neuropathy and the preventable outcomes of blindness, dialysis, and amputation, respectively. (1)

Evaluation: Fasting glucose levels and HbA1c testing are useful for the early identification of T2DM. If borderline, a glucose tolerance test is an option to evaluate both fasting glucose levels and serum response to an oral glucose tolerance test (OGTT). Prediabetes, which often precedes T2DM, presents with a fasting blood glucose level of 100 to 125 mg/dL or a 2-hour post-oral glucose tolerance test (post-OGTT) glucose level of 140 to 200 mg/dL.(4)

According to the American Diabetes Association (ADA), a diagnosis of diabetes is through any of the following:

1. An HbA1c level of 6.5% or higher.

2. A fasting plasma glucose level of 126 mg/dL (7.0 mmol/L) or higher (no caloric intake for at least 8 hours).

3. A two-hour plasma glucose level of 11.1 mmol/L or 200 mg/dL or higher during a 75-g OGTT.

4. A random plasma glucose of 11.1 mmol/L or 200 mg/dL or higher in a patient with symptoms of hyperglycemia (polyuria, polydipsia, polyphagia, weight loss) or hyperglycemic crisis.

The ADA recommends screening adults aged 45 years and older regardless of risk, while the United States Preventative Service Task Force suggests screening individuals between 40 to 70 years who are overweight.(5)

To test for gestational diabetes, all pregnant patients have screening between 24 to 28 weeks of gestation with a 1-hour fasting glucose challenge test. If blood glucose levels are over 140 mg/dL, patients have a 3-hour fasting glucose challenge test to confirm a diagnosis. A positive 3-hours OGTT test is when there is at least one abnormal value (greater than or equal to 180, 155, and 140 mg/dL for fasting one-hour, two-hour, and 3-hour plasma glucose concentration, respectively).(6)

Conventional management of Type 2 DM: The physiology and treatment of diabetes are complex and require a multitude of interventions for successful disease management. Diabetic education and patient engagement are critical in management. Patients have better outcomes if they can manage their diet (carbohydrate and overall caloric restriction), exercise regularly (more than 150 minutes weekly), and independently monitor glucose. Lifelong treatment is often necessary to prevent unwanted complications. Ideally, glucose levels should be maintained at 90 to 130 mg/dL and HbA1c at less than 7%. While glucose

control is critical, excessively aggressive management may lead to hypoglycemia, which can have adverse or fatal outcomes. (1)

In T2DM, diet and exercise may be adequate treatments, especially initially. Other therapies may target insulin sensitivity or increase insulin secretion by the pancreas. The specific subclasses for drugs include

1. **Insulin secretion enhancers:**

A) Sulphonylureas (KATP blockers).

1st generation (Tolbutamide) & 2nd generation (Glibenclamide, Glimepiride, Gliclazide, Glipizide).

B) Meglitinide/Phenylalanine analogues: Repaglinide, Nateglinide.

C) Glucagon like peptide-1 (GLP-1) receptor agonists: Exetanide, Liraglutide.

D) Dipeptidyl Peptidase-4 (DPP-4) inhibitors: Sitagliptin, Vildagliptin, Saxagliptin, Alogliptin, Linagliptin.

2. **Overcome insulin resistance:**

A) Biguanide (AMPK Activators) : Metformin

B) Thiazolidinediones (PPARÝ activator): Pioglitazone

3. **Miscellaneous Antidiabetic drugs:**

A) α-Glucosidase Inhibitors : Acarbose, Voglibose, Migilitol.

B) Amylin analogue: Pramlintide.

C) Dopamine-D2 receptor agonist: Bromocriptin.

D) Sodium-glucose cotransport-2 (SGLT-2) inhibitor: Dapagliflozin. (7)

Metformin is the first line of the prescribed diabetic medications and works by lowering basal and postprandial plasma glucose. Insulin administration may also be necessary for T2DM patients,especially those with inadequate glucose management in the advanced stages of the disease. In morbidly obese patients, bariatric surgery is a possible means to normalize glucose levels. It is recommended for individuals who have been unresponsive to other treatments and who have significant comorbidities. (8) The GLP-1 agonists' liraglutide and semaglutide correlate with improved cardiovascular outcomes. The SGLT-2 inhibitors empagliflozin and canagliflozin have also shown to improve cardiovascular outcomes along with potential renoprotection as well as prevention for the development of heart failure.

Regular screenings are necessary since microvascular complications are a feared complication of diabetes. Regular diabetic retinal exams should be performed by qualified medical personnel to assess for diabetic retinopathy. Clinicians can also recommend patients perform daily foot inspections to identify foot lesions that may go unnoticed due to neuropathy. Low-dose tricyclic antidepressants, duloxetine, anticonvulsants, topical capsaicin, and pain medications may be necessary to manage neuropathic pain in diabetes. The antiproteinuric effect of the angiotensin- converting enzyme (ACE) inhibitors and the angiotensin receptor blockers (ARBs) makes them the preferred agents to delay the progression from microalbuminuria to macroalbuminuria in patients with both Type 1 and Type 2 diabetes mellitus.

The FDA has approved pregabalin and duloxetine for the treatment of diabetic peripheral neuropathy. Tricyclic antidepressants and anticonvulsants have also seen use in the management of the pain of diabetic neuropathy with variable success.

The ADA also recommends regular blood pressure screening for diabetics, with the goal being 130 mmHg systolic blood pressure and 85 mmHg diastolic blood pressure. (9) Pharmacologic therapy for hypertensive diabetics typically involves angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, beta-blockers, and/or calcium

channel blockers. The ADA recommends lipid monitoring for diabetics with a goal of low-density lipoprotein cholesterol (LDL-C) being less than 100 mg/dL if no cardiovascular disease (CVD) and less than 70 mg/dl if atherosclerotic cardiovascular disease (ASCVD) is present. Statins are the first-line treatment for the management of dyslipidemia in diabetics. (10)

Differential Diagnosis for T2 DM:

In addition to T1DM, T2DM, and MODY, any disorder that damages the pancreas can result in DM. There are several diseases of the exocrine pancreas, including:

- Cystic fibrosis
- Hereditary hemochromatosis
- Pancreatic cancer
- Chronic pancreatitis

Hormonal syndromes that can lead to impaired insulin secretion include:

- Pheochromocytoma
- Acromegaly
- Cushing syndrome

Drug-induced insulin resistance is also in the differential of classical diabetes. These drugs include:

- Phenytoin
- Glucocorticoids

- Estrogen

Other diseases in the differential of diabetes mellitus include:

- Gestational diabetes
- Thyroid disorders.(1)

Complications of T2 DM:

Regardless of the specific type of diabetes, complications involve microvascular, macrovascular, and neuropathic issues.

1. Microvascular and macrovascular include nephropathy, retinopathy, neuropathy, and ASCVD events, especially if it is associated with other comorbidities like dyslipidemia and hypertension. In T2DM, fasting glucose of more than 100 mg/dL significantly contributes to the risk of ASCVD, and cardiovascular risk can develop before frank hyperglycemia.(11)

2. DM is also a common cause of blindness in adults aged 20 to 74 years in the United States.(12)

3. Diabetic Renal disease is the leading contributor to end-stage renal disease (ESRD) in the United States, and many patients with ESRD will need to start dialysis or receive a kidney transplant. If the albuminuria persists in the range of 30 to 300 mg/day (microalbuminuria), it seems to be a predictable earliest marker for the onset of diabetic neuropathy. (12)

4. DM is also the leading cause of limb amputations in the United States; this is primarily due to vasculopathy and neuropathy associated with DM. (12)

5. In people with type 1 diabetes, diabetic retinopathy typically sets in about 5 years after disease onset. Approximately 10% at ten years, 40% at 15 years, and 60% at 20 years will have nonproliferative retinal disease. Uncontrolled blood pressure is an added risk factor for macular edema. Sudden loss of vision can occur for several reasons e.g. vitreous hemorrhage, vascular occlusion (central retinal vein or branch vein occlusion involving the macula), retinal detachment, end-stage glaucoma, and ischemic optic neuropathy.

6. T2DM may also contribute to cancer development, specifically bladder cancer, in those using pioglitazone.(13)

7. Those with gestational diabetes are at a higher risk for cesarean delivery and chronic hypertension. Pregnant patients with T2DM generally have a better prognosis in terms of neonatal and pregnancy complications compared to those with T1DM.(14)

8. In T2DM, hyperosmolar hyperglycemic syndrome (HHS) is an emergent concern. It presents similarly to DKA with excessive thirst, elevated blood glucose, dry mouth, polyuria, tachypnea, and tachycardia. However, unlike DKA, HHS typically does not present with excessive urinary ketones since insulin still gets produced by pancreatic beta cells. Treatment for DKA or HHS involves insulin administration and aggressive intravenous hydration, careful management of electrolytes, particularly potassium.(15)

Homoeopathy in the management of T2 DM: The homoeopathic approach to the study of disease is from its clinical standpoint. It regards clinical symptoms totality as the nearest approach to the factual reality. Homoeopathy regards clinical symptoms as those that render themselves perceptible to our senses as a resultant of forces – chemico-physical, vital, psychological – that are acting and reacting in and through the human organism in disease conditions. The clinical symptoms are, thus, dynamic and co-extensive with diseases; whereas pathological changes are static changes brought about as ultimate end results of the disease processes.

This holistic conception of Man led Hahnemann to distinguish between the notions of a mechanical and a creative cause or evolutionary cause. Hahnemann did not approach the

subject of medicine from the angle of causalism; but tackled the problem of disease through pure observation of phenomena. (16)

In §5, Hahnemann writes 'Useful to the physician in assisting him to cure are the particulars of the most probable exciting cause of the Acute Disease, as also the most significant points in the whole history of the Chronic Disease, to enable him to discover its Fundamental Cause, which is generally due to a chronic MIASM.(17)

In § 80, Hahnemann says – Incalculably greater and more important than the two chronic miasms just named, however, is the chronic miasm of psora, which, while those two reveal their specific internal dyscrasia, the one by the venereal chancre, the other by the cauliflower-like growths, does also, after the completion of the internal infection of the whole organism, announce by a peculiar cutaneous eruption, sometimes consisting only of a few vesicles accompanied by intolerable voluptuous tickling itching (and a peculiar odor), the monstrous internal chronic miasm – the psora, the only real fundamental cause and producer of all the other numerous, I may say innumerable, forms of disease, which, under the names of nervous debility, hysteria, hypochondriasis, mania, melancholia, imbecility, madness, epilepsy and convulsions of all sorts, softening of the bones (rachitis), scoliosis and kyphosis, caries, cancer, fungus nematodes, neoplasms, gout, hemorrhoids, jaundice, cyanosis, dropsy, amenorrhoea, hemorrhage from the stomach, nose, lungs, bladder and womb, of asthma and ulceration of the lungs, of impotence and barrenness, of megrim, deafness, cataract, amaurosis, urinary calculus, paralysis, defects of the senses and pains of thousands of kinds, etc., figure in systematic works on pathology as peculiar, independent diseases.(17)

Homoeopathic Materia Medical literature is blessed with many remedies which can be used for the treatment of T2DM. a number of remedies are available which can be used as a near specific medicine for the threatment of DM these remedies can be used in variable potencies according to the requirement of the case ranging from Mother tincture to LM potency. Some remedies can be used in the form of Mother tincture in daily doses with a fixed frequency similar to allopathic medicines and they can be very helpful in glycemic control. This study

attempts to evaluate the effectivness of Gymnema Sylvester Mother Tincture in the management of T2 DM.

The following are glimpses of research regarding Homoeopathy in the management of T2DM.

1. In a non-randomized retrospective study in 2017, the addition of individualized homeopathic treatment to conventional treatment was associated with better glycaemic control in T2DM patients compared with standard conventional treatment alone. The decrease in fasting glucose and HbA1c was larger in patients with poorer glycaemic control at baseline. (18)

2. A 2013 study shows Homeopathic drug S jambolanum has protective effects on Streptozotocin induced diabetic rats.(19)

3. In an observational study 2008, complementary homeopathic therapy of diabetic neuropathy was feasible and promising effects in symptom scores and cost savings were observed.(20)

4. A study in April 2021 including homeopathic medicines Insulinum, Pancreatinum and Uranium nitricum in '6C' potency showed that they exhibit antihyperglycemic effects in streptozotocin induced diabetic rats.(21)

5. A study in March 2020 showed that there was significant reduction in fasting blood sugar, post prandial blood sugar levels both groups (gymnema sylvestre 6 CH and gymnema sylvestre homoeopathic mother tincture) in type 2 diabetes mellitus cases. The results suggested that gymnema sylvestre 6 CH and gymnema sylvestre mother tincture has beneficial anti diabetic effective and warrants future investigation.(22)

6. A 2020 comparative study showed that that both the drug Gymnema Sylvester Q and Syzygium Jambolanum Q have same blood suger lowering capacity. (23)

7. A 2021 research study findings showed that Gymnema S mother tincture and 200C have the ability to lower blood glucose levels in diabetic rats, suggesting its efficacy in vivo.(24)

8. A research study by Parveen Kumar sharma et al shows that Gymnema Sylvester MT showed a significant response in lowering the blood glucose levels in diabetic patients. (25)

Gymnema sylvestre (G. sylvestre)

The plant is native to central and western India, tropical Africa and Australia. Some the other names are as follows [26]

Sanskrit: Meshashringi, madhunashini,

Hindi: Gur-mar, merasingi,

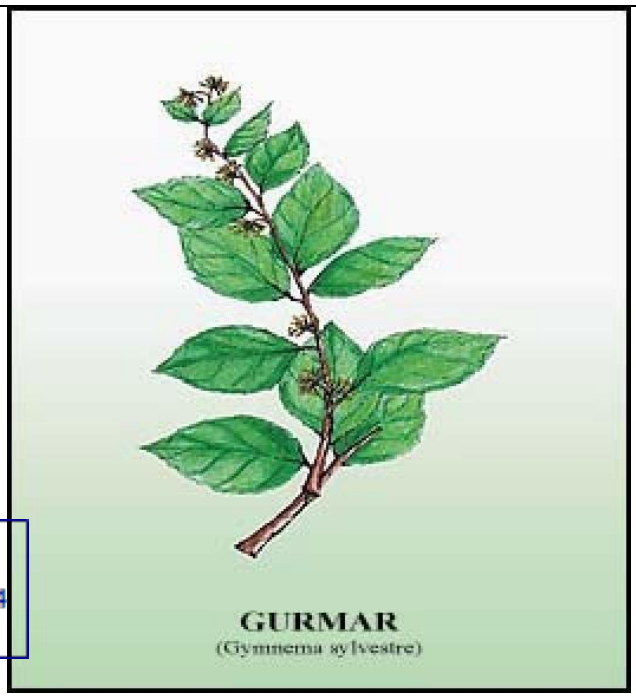
Marathi: Kavali, kalikardori, vakundi,

Gujrathi: Dhuleti, mardashingi,

Telugu: Podapatri,

Tamil: Adigam, cherukurinja,

Kannada: Sannagerasehambu.



G. sylvestre (Asclepiadaceae), a vulnerable species is a slow growing, perennial, medicinal woody climber found in central and peninsular India. Fig. 2 shows a 5-year old parent plant. It is a potent antidiabetic plant and used in folk, ayurvedic and homeopathic systems of medicine. It is also used in the treatment of asthma, eye complaints, inflammations, family planning and snakebite. In addition, it possesses antimicrobial, antihypercholesterolemic, hepatoprotective and sweet suppressing activities. It also acts as feeding deterrents to caterpillar, Prodenia eridania; prevent dental caries caused by Streptococcus mutans and in skin cosmetics. G. sylvestre leaves contain triterpene saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene saponins are gymnemasides. Besides this, other plant constituents are flavones, anthraquinones, hentri-acontane, pentatriacontane, α and β-chlorophylls, phytin, resins, d-quercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin related glycosides and stigmasterol. The plant extract also tests positive for alkaloids. Leaves of this species yield acidic glycosides and anthroquinones and their derivatives. (27)

Anti-diabetic action of Gymnema Sylvester: Gymnemic acid molecules fill the receptor location in the absorptive external layers of the intestine thereby preventing the sugar molecules absorption by the intestine, which results in low blood sugar level. G. sylvestre

leaves have been found to cause hypoglycemia in laboratory animals and have found a use in herbal medicine to help treat adult onset diabetes mellitus (NIDDM). When Gymnema leaf extract is administered to a diabetic patient, there is stimulation of the pancreas by virtue of which there is an increase in insulin release.(28)There are some possible mechanisms by which the leaves and especially Gymnemic acids from G. sylvestre exert its hypoglycemic effects are:

1) It increases secretion of insulin.

2) It promotes regeneration of islet cells.

3) It increases utilization of glucose: it is shown to increase the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase.

4) It causes inhibition of glucose absorption from intestine. (29)

Materia Medica of Gymnema Sylvester:

1. **Materia medica by Dr. John Henry Clarke:**

Gymnema sylvestre. N. O. Asclepiadaceae. Tincture of leaves. Clinical.-Snake-bite. Taste, altered.

Characteristics.-This plant, which grows in the Deccan peninsula, Assam, and some parts of Africa, is a woody climber with long, slender branches. The powdered root has a reputation among the natives as a remedy for snake-bite. It is mentioned here an account of a single symptom observed from chewing one or two leaves, which had a bitterish, astringent, and slightly acid taste. Immediately after chewing them the sense of taste for sugar was lost, and also the taste for bitters, the effect lasting some hours. Everything else could be tasted, as the ginger in gingerbread but not the sweet. Quinine tasted like chalk. (29)

		Gymnema sylvestre will abolish the taste of bitter things, sense of taste altered, powdered root for snake-bite. Sore throat, dark livid redness of fauces and erysipelatous swelling of face are most marked. Headache, throbbing in forehead and temples and over eyes with bluish-white coating of Tongue. Burning in eyes. Desire for heat and quiet. (30) **2. Boericke' Materia Medica :** Merasingi or Gur-mar. An excellent remedy for diabetes and also poison of snake bite. Patient feels tired after passing large quantities of urine which is loaded with sugar, high specific graviy, burning all over the body, diabetic carbuncle may appear anywhere over the body, great thirst, weakness all around. Dose – Q, 3x. (31)
o6. 1)	**Primary Objectives :-**	To evaluate effectiveness of Gymnema Sylvester in the management of Type II Diabettes Mellitus at the end of 3months.
6.2)	**Other Objectives 1:-**	To find clinical indications of Gymnema Sylvestre in Type II Diabettes Mellitus
6.3)	**Other Objectives 2:-**	To find clinical course of patient taking Gymnema Sylvestre in cases of Type II Diabettes Mellitus.
	Other Objectives 3:-	NA
07)	**Methodology :-**	**I) Study Design:** A randomized controlled clinical trial **II) Study Setting:** Cases will be collected from OPD and IPD of the Institute **III) Study population:** Diagnosed cases of type II diabettes mellitus **IV) Sample Size: 160** Sample size was determined using the estimates of mean and standard deviation values from literature using the formula $n = \frac{2\,(Z_\alpha + Z_\beta)^2\ [s]^2}{}$

d^2

where Z_α is the z variate of alpha error i.e. a constant with value 1.96, Z_β is the z variate of beta error i.e. a constant with value 0.84
(Reference: Allen JC. Sample Size Calculation for Two Independent Groups: A Useful Rule of Thumb. Proceedings of Singapore Healthcare 2011:20(2);138-40)
Approximate estimates:
80% power

Type I error to be 5%

Type II error to be 20%

True difference of atleast10 units between the groups

Pooled standard deviation of 22

Substituting the values,

$$n = \frac{2\,(2.8)^2\,[22]^2}{(10)^2}$$

n = 75.89
Approximately 76 to 80 subjects / patients per group should complete the trialat the endpoint follow up

V) Sampling technique: Simple random sampling technique
Subjects will be divided in to two groups using computer generated sequences.Trial group (T group) and Control group (C Group)

VI) Methods of selection of study subject:
Inclusion Criteria:
All cases of Above 30years will be taken.
All sexes will be included.
Cases on oral hypoglycaemic treatmen
Cases having HbA1Cbetween 5.6% to 9% with or without clinical sypmtoms
Only those patients who require Gymnema Sylvestre shall be included in Group A since the effectiveness and utility of Gymnemasylvester is to be studied.

Exclusion Criteria:
Cases with complications of diabetes mellitus
Immuno-compromised patient
Pregnant women & lactating mothers
Cases on exogenous Insulin therapy

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Subject withdrawal criteria:

Patient not willing to continue

Patient not regular with follow-ups

Patient needing emergency medical or surgical intervention.

VII) Operational Definition:. Diabetes mellitus (DM) is a metabolic disease of multiple etiologies characterized by chronic hyperglycemia with defects in carbohydrate, protein and fat metabolism due to defect in insulin secretion, insulin action or a combination of both.2

VIII. Methods of Measurement:

Blood sugar fasting and postprandial will be taken in the beginning , after 6 weeks and 12weeks.

$HbbA_1C$ before treatment and after 12weeks.

Detailed Homoeopathic case will be taken of trial group to find clinical homoeopathic symptoms of Gymnema Sylvestre

IX.STUDY INSTRUMENT/ DATA COLLECTION TOOLS:

Complete Homoeopathic case taking format to understand any clinical homoeopathic symptoms .

Appropriate reference books like Homoeopathic Materia Medica,Medicine books, repertories if required, different Homoeopathic journals,research papers will be considered.

OUTCOME ASSESSMENT TOOL:

Blood sugar Fasting & Post prandial.

HbA1C

X. METHODS OF DATA COLLECTION RELEVANT TO OBJECTIVE:

After receiving ethical approval from Institutional ethical committee patients will be informed about the research via patient information sheet and Informed consent will be taken in each and every case before the study from the patient, after the consent being approved by the ethical committee(EC). Random sampling will be applied.The clinical

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presentation of each patient in terms of location, sensation, modalities, and concomitants with emphasis on the intensity of symptoms will be studied.

Group T will be prescribed gymnema Sylvester along with oral hypoglycemic drug and group C will be on oral hypoglycemic drugs only

Blood sugar fasting and postprandial will we taken. HBA^1C will be done.

Patients of both groups will be advised to continue the same diet and lifestyle.

No patient was advised to use any vitamins or natural supplements.

Cases will be withdrawn from the study on the basis of subject withdrawal criteria.

Gymnema will begiven 15 drops thrice a day

DATA MANAGEMENT AND ANALYSIS PROCEDURE:

Data receiving:

160 cases from the study setting will be considered. Case will be divided into two groups. Group T will be prescribed Gymnema Sylvester and group C will be asked to continue the same treatment

Case Processing and Analysis:

Data will be analyzed by using Microsoft Word and excel. Appropriate reference from textbook of Organon of medicine, various homoeopathic Materia medica, repertories, research papers and various websites.

Blood sugar fasting & post prandial will be done inn the beginning after 6wk and at 12wk HBA1C wil be Don before trial and after 12 weeks of both the group.

Selection of Potency:

Since Gymnema Sylvestre is clinically indicated in lower attenuations and also depending on the availability of the drug, it shall be employed in Mother tincture (Q)only.

Repetation of medicine

The doses of the Medicine will be repeated on the basis of principles laid down by Dr Hahnemann.

Duration of study:

Duration of study – 3years

Duration of each case – Each case will be studied for up to 7 days or till remission occurs whichever is earlier.

Duration of follow of each case – each case will be followed up everyday

XI. DATA ANALYSIS PLAN AND METHODS:

Statistical methodology:

Data collected will be compiled on MS Office Excel sheet and will be subjected to statistical analysis using an appropriate package like SPSS software.

Normality of numerical data will be checked using Shapiro-wilk test or Kolmogorov-smirnov test. Depending on the normality of data, statistical tstes will be determined. Descriptive statistics like frequency (n) & percentage (%) of categorical data, mean & Standard deviation of numerical data in each group will be depicted.

(a) for a numerical continuous data following a normal distribution, inter group comparison (2 groups) will be done using t test, else a non parametric substitute like Man Whitney U test will be used.

(b) comparison of frequencies of categorical variables between 2 groups/ association of variables(2 categorical) will be done using chi square test / Fisher's exact test / McNemar test / Mc Nemar Bowker test of symmetry / Cochran's Q.

(c) intra group comparisons for a numerical continuous data following a normal distribution will be done using repeated measures ANOVA for >2 observations or Friedman's test will be used.

Keeping Alpha error at 5% and Beta error at 20%, power at 80%, p<0.0g will be considered statistically significant.

XII. Additional points for Research in AYUSH- Not applicable

XIII. Additional points for RCT-

Patients fulfilling the eligibility criteria were enrolled and randomised into two groups – Group T will be prescribed Gymnema Sylvester and group C will be prescribed placebo

		both in medicated pills form. The allocation in the respective groups was as per computer generated sequences **XIV. Additional points for all Experimental Studies-** None
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1	**Timeline/Gantt Chart :-**	**Time line or Gantt Chart: Provided and attached in Annexure III**
10	**Annexures :-**	**I) Case record form/Questionnaire/Performa or any other study instrument to be used in study**

Annexure I

Case taking Proforma

Preliminary data:

Case no: Date:

Age: Religion:

Sex: Marital Status:

Occupation:

Chief Complaint: (origin, duration, progress &concomitten)

- Blood sugar fasting & post prandial
- HBA^1C

Patients complaints with details of its Location ,sensation and modalities.

Other associated symptoms both mental and physical.

Personal history:

Appetite: Thirst:

Craving: Aversion:

Food/Drink/agg/amel: Stool:

Urine: Perspiration:

Sleep: Dreams:

Thermal Reaction:

Past History:

Family History:

H/o Drug allergy/ Interaction:

General Physical Examination:

Temperature-

Pulse-

Blood Pressure-

Respiratory Rate-

Systemic Examination:

Cardio-Vascular System-

Central Nervous System-

Respiratory System-

Per Abdomen

Case Processing:

Analysis & Evaluation:

Clinical Diagnosis.

Prescription:

Date	Prescription

General Management:

Follow ups:

Date	Symptoms	Prescriptions

HBA^{1}C

Before	**12 Week**

Blood Sugar

Duration	**O Week**	**6 Week**	**12 Week**
Fasting			
Post prandial			

B.Questionnaire : Not Applicable

C. Any other Study Instrument to be used in study

Annexure II

Informed consent form:

Topic:**. Effectiveness of Gymnema Sylvestre in Homoeopathic Management Of Type II Diabetes Mellitus – A Randomized Controlled Clinical Trial**

Date:

Name of the Patient: Age:

Sex:

Registration number:

Address:

Contact Number:

Name of the Researcher:

Name of the Institute:

Address:

1. I, the undersigned,_____hereby give my consent for research and homoeopathic treatment under the guidance and supervision of Dr._____.
2. I give my consent for the administration of homoeopathic medicines for the same purpose.
3. I have been well informed regarding the treatment and the research completely and I have understood it.
4. I have been informed about the necessary investigations to be done during the course of the treatment.
5. I have read the patient information sheet completely and understood it.
6. I give my consent for the photography if required for the purpose of diagnosis and treatment.
7. I give my consent to use information regarding my disease and the treatment for the purpose of research and in doing so I assume that my identity shall not be revealed.
8. I have been informed that I have full rights to participate/refuse above research work. Also I have been informed that I can withdraw myself. from the research and treatment before the schedule completion without giving any explanation.
9. I also certify that no guarantee/assurance has been given about the results that may be obtained.
10. All the above information has been given to me in my own language and I have understood it.

Signature of the participant/left hand thumb impression:

Date:

Signature of the researcher:

Date:

Name of the witness: Signature:

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- **Informed consent in vernacular language**:-

सर्व तलूंखू अनमतू पा

Effectiveness of Gymnema Sylvestre in Homoeopathic Management Of Type II Diabetes Mellitus – A Randomized Controlled Clinical Trial

दिूनाक:

रग्णपत्रक्

र. रग्णाचूंनाव:

वय: द ग:

पत्ता:

सशू धकाचूंनाव :

पत्ता :

1. मू खा ू सह करणार, _____
   यासश धनवउपचारासाठू -
   _____याच्याि
   ूंखरूं खू खा ू भाग घू्ण्यासमाझू अनमतू िूंशवतू .
2. उपचारासाठू आवश्यकहू दमओपदिूकऔषधाच्यासूंवनासाठू मू अनमतू िूंतआहूं.
3. म ामाझ्यावरकू ूजाणारूं उपचारवसश धनयासि भातसपणमादहतू िूंण्यातआ ू असनतू म ासमज
   ू आहं.
4. म ायासशू धनाि रम्यानकराव्या ागणारू्याआवश्यकत्याचाचण्याबद्दमादहतू िूंण्यातआ
   ू आहूं.
5. मू रुग्णमादहतू पत्रकसपणवाच ूंअसनम ातूं समज ूंआहूं.
6. याउपचाराि रम्यानरू गदनि ानवउपचारयासाठू
   जरछायादचत्रणकरावूं ाग ूंतरत्या ामाझू अनमतू आ ह.
7. माझ्यारू गाबद्दू
   चू वउपचाराचू मादहतू सश धनासाठू वापरण्याबाबतमाझू समतू
   आहूंआदणअसूंकर तानामाझू ओळखदि ू जाणारनाहू हूंमू गहू
   तधरत .
8. सश धनातभागघू्ण्याचाि अवानघू्ण्याचाम ापणअदधकारआहूं.
   तसूंचकाह कारणनि ूंताका ावधू पणह ण्याआधू सद्धासश धनातगतहू णारूं
   उपचारनाकारू शकतू हूं म ामादहतू आहूं.
9. मू हूंप्रमादणतकरतू दकउपचारवत्याचूंदनष्कष/
   परणामयासि भातम ाकू ठ ाह ग्वाहू िूंण्यातआ ू
   ू नाहू .
10. ~~वरू सवमादहतू म ामाझ्याभाषूं तयू ग्याप्रकारू समजवण्यातआ ू~~ असनम

तूं न टसमज ू आहूं. रुग्णाचूंनाव स्वाक्षरू / डाव्याअगठ्याचाठसा/

दि ूनाक साक्षू ि ूंराचूंनाव स्वाक्षरू दि ूनाक

सश धकचूंनाव स्वाक्षरू दि ूनाक

PATIENT INFORMATION SHEET

Dear patient I am glad to inform you that I, PhD student has undertaken a PhD research project. In the research project the subject will be**“”**

During this project, a minimum of 100 cases of Hypertension will be included out of which 50 cases will be treated by giving Homoeopathic Medicine SpartiumScoparium, while the remaining 50 shall be asked to continue with previous medications along with placebo.

Through this information sheet you are informed about the following important features of this research project: -

1. The sole aim of the researcher is to restore the sick to health and cure.
2. Your consent about voluntary participation in the project is the most important prerequisite. Hence you are requested to fill the “Informed consent form”. It is attached with this sheet. You have the right to opt out of the project at any time without having to give any reason for doing so.
3. One of the main objectives of this study is to treat patients and observe the effects and to find out the success rate.
4. Cases fitting into case definition will be included in this study.
5. You are requested to give detail, true information about your complaints and other required information. Your name and address will be kept confidential.
6. The Medicine used in this study are prepared by standard Pharmacy viz. Dr. Willmar Schwabe;manufactured by following the norms of standard Homoeopathic Pharmacopoeia.
7. The Project will be started after being sanctioned by the properly formed “Ethical Committee”.
8. Drug used in this study viz. SpartiumScopariumis not harmful to human beings.
9. You are requested to come regularly or as asked by the physician for the follow-up.
10. Required and appropriate investigations will be done from time to time. You are requested to cooperate.
11. The study duration will be of 03 years.
12. You will be informed about alternative treatments available and their risks and benefits.
13. No major life-threatening complications will occur with this medication.

I thank you very much for your consent and participation in this research project.

Dated:_____ Yours sincerely,

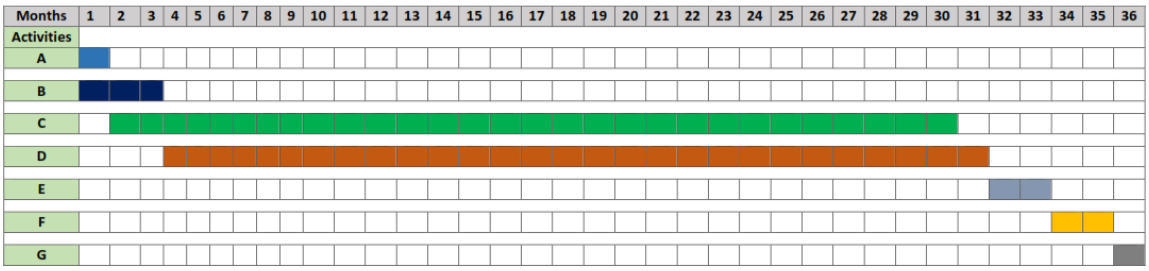
उन्नत श्री पंडित

PhD Student.

Annexure III

Time line or Gantt Chart:

GANTT CHART



SR. NO.	ACTIVITIES	MONTHS DURATION
A	Introduction	1 month
B	Review of Literature	3 months
C	Data Collection	29 months
D	Data Management & Analysis	28 months
E	Observations & Results	2 months
F	Summary & conclusion	2 months
G	Presentation	1 month

Gantt chart or Timeline of Research:

PROJECTED TIMELINE CHART FOR DISSERTATION

Time Frame	Apr-Jul 2021	Aug-Nov 2021	Dec 2021-Mar 2022	Apr-Jul 2022	Aug-Nov 2022	Dec 2022-Mar 2023	Apr-Jul 2023	Aug-Nov 2023	Dec 2023-Mar 2024
A									
B									
C									
D									
E									
F									
G									
H									

		I

Key	Title
A	Registration and Introduction
B	Aims and Objectives
C	Review of Literature
D	Materials and Methods
E	Observation and Discussion Results
F	Discussion, Summary and Conclusion
G	Bibliography
H	Departmental Dissertation Examination, Correction andSubmission
I	Final Submission of Dissertation and PPT Preparation

11	**Knowledge Gap**	Literatures have mentioned about gymnema sylvestre action on diabetes mellitus but control studies are not done in homoeopathy.
12	**Generation of new knowledge**	Effectiveness of Gymnema Sylvester in diabetes may be found. New homoeopathic clinical symptoms of gymnema may be found.