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A Systematic Review on the Pre-Clinical Study of *Cephalandra indica* and *Gymnema sylvestre* in Diabetes Mellitus Type 2

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Abstract:- Homoeopathy is one of the most widely used alternative therapies, utilized all over the world, and is important in the treatment of many different illnesses. The most frequently used homeopathic medications for diabetes include *Cephalandra indica, Syzygium jambolanum, phosphoric acid, Gymnema sylvestre, and Uranium nitricum*. The mother tincture form is utilized as a physiological active dose according to the patient's requirements and blood glucose level.

- ***Aim and objective –***

This study aimed to gather and analyze data from previous studies, in addition to examining and evaluating the anti-diabetic efficacy of *Cephalandra indica* and *Gymnema sylvestre.*

- ***Methodology-***

This review covers articles that appeared until 2023. The articles were gathered using databases like Google Scholar and PubMed (Medline). We used the terms "homoeopathy," "diabetes," "in vitro," "in vivo," "*Gymnema Sylvester*," and "*Cephalandra indica*."

- ***Result-***

The review contained both in vitro and in vivo research from earlier publications. This review paper presents scientific validation for the pharmacological efficacy of *Cephalandra indica* and *Gymnema sylvestre*, as well as the likely mechanism of action shown in preclinical research.

- ***Conclusion-***

Preclinical studies on homeopathic preparations of Gymnema sylvestre and Cephalandra indica have shown zero cytotoxicity, and they have a pharmacological and safety profile. The review contained both invitro and invivo research from earlier publications. In this review paper, the pharmacological activity of *Cephalandra indica* and *Gymnema sylvestre*, together with the likely mechanism of action revealed by preclinical studies, were validated scientifically. With proper research, the postulated dose conversion theory has to be verified. An overview of the existing studies on these two homoeopathic medicines is required. Despite adequate background data, human trials on diabetes mellitus using these drug candidates are lacking.

Keywords- *Cephalandra indica, Diabetes, Gymnema sylvestre, in Vivo, in Vitro, Preclinical Study.*

I. INTRODUCTION

Homoeopathy is one of the most widely used alternative therapies, utilized all over the world, and is important in the treatment of many different illnesses. Globally, the prevalence of diabetes mellitus is progressively increasing. Between the ages of 20 and 79, 537 million individuals worldwide are expected to have diabetes (10.5% of all adults in this age group). Globally, the number of people with diabetes is expected to increase from 643 million in 2030 to 783 million by 2045. [1]. The most often used homeopathic medications include *Cephalandra indica, Syzygium jambolanum, phosphoric acid, Gymnema sylvestre, and Uranium nitricum.* Depending on the patient's needs and blood sugar level, they are employed as physiological active doses. Many homoeopathic preparations are described in the literature, but their potential benefits in most cases have not been thoroughly reviewed.

Diabetes mellitus is a group of metabolic disorders characterized by an rise in blood glucose levels [2]. Diabetes mellitus is classified into two - Type 1 diabetes mellitus and Type 2 diabetes mellitus [2]. Diabetes mellitus is characterized by insulin deficiency and a propensity towards ketosis; it is most commonly caused by autoimmune destruction of the beta cells of pancreatic islet. Type 2 diabetes mellitus is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, decreased insulin secretion, and increased hepatic glucose synthesis are the hallmarks of type 2 diabetes mellitus [2]. Microvascular and macrovascular

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impairments, including retinal, nephropathy, neuropathy, and other conditions, are caused by long-term complications of diabetes. Oral hypoglycemic medications and insulin are two pharmacotherapies used to treat diabetes. However, they do have some adverse effects and require some reliance. [3]

Gymnema Sylvestre is used in the Ayurveda medical system to reduce blood sugar levels. Its leaves and gymnemic acids enhance insulin secretion, promote islet cell regeneration, and improve glucose consumption to produce its hypoglycemic effects [4]. *Cephalandra indica,* or ivy gourd, is a member of the Cucurbitaceous family. According to the science of Ayurveda, the herb has been utilized for treating diabetes mellitus from ancient times. *Cephalandra indica* has been reported to have an insulin-stimulating effect on β cells [5]. This study aimed to compile and assess the anti-diabetic effects of Gymnema sylvestre and Cephalandra indica from previous studies.

II. MATERIAL AND METHODS

A. Search Strategy

The publications were gathered using electronic databases, which include PubMed- Medline, HomBrex, Google Scholar, and written literature such as library catalogs. We used the phrases 'homoeopathy' or 'homoeopathy', 'in vitro', 'in vivo', and *'Gymnema Sylvester'* and *'Cephalandra Indica'*. The condition 'diabetes' was used to search MeSH variants in PubMed and HomBerx. The search approach was intended to capture all preclinical trials along with descriptions until 2021.

B. Inclusion Criteria

The study includes in-vivo and in-vitro preclinical trials using homoeopathic medications, *Cephalandra indica* and *Gymnema sylvestre*, to establish anti-diabetic effectiveness in diabetic rat models.

C. Exclusion Criteria

All clinical studies were omitted. Animal experiments other than DMT2 were not taken into consideration, and surveys on diabetes mellitus without treatment were excluded from studies that included homeopathic remedies as a supplement.

D. Study Selection

Only preclinical trials Observational studies with some defined outcome measures published in research journals and literature available only in English were considered.

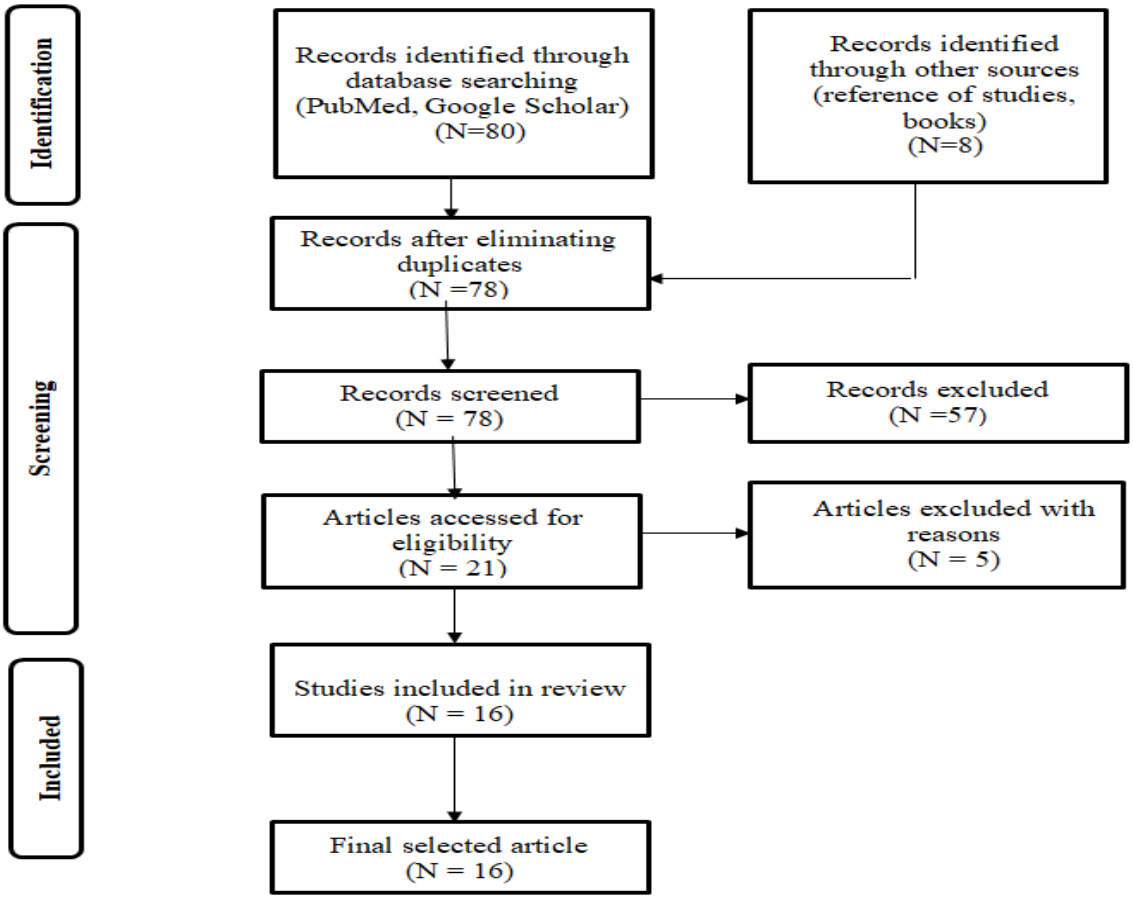

Fig 1 Study flow diagram

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- *Cephalandra Indica*

Cephalandra *indica* belongs to the Cucurbitaceae family and is commonly known as Kundru in Hindi and Ivy Gourd in English. The herb has been utilized since ancient times to treat diabetes mellitus, according to Ayurvedic medicine. [5]. According to D. P. Rastogi, When Cephalandra indica mother tincture was given to diabetic rats induced with alloxan, the rodents showed notable control over their blood sugar levels 14–20 days after the treatment was stopped. The hypothalamohypophysial-pancreatic axis, which indirectly releases inhibitory factors from hypothalamic neurons, inhibits growth hormone secretion and triggers insulin secretion from beta cells, lowers glucose levels. Histopathological studies verified pancreatic beta cell regeneration. [6]

Shibib studied Coccinia indica, also referred to as "tela kucha" in Bangladesh. Male streptozotocin-induced diabetic rats weighing 180–250 grams were given 200 mg/kg body weight of Coccinia indica (C. indica) leaves orally following an 18-hour fast. Blood glucose, hepatic glucose-6-phosphatase, fructose-1, 6-bisphosphatase, glucose-6-phosphate dehydrogenase (G6PDH), and red-cell G6PDH were measured after the rats were killed after 90 minutes. The findings demonstrate that the extracts of C. indica and Momordica charantia reduced blood glucose levels by inhibiting its synthesis. This was achieved by activating the primary enzyme of the shunt pathway, G6PDH, which enhanced glucose oxidation, and by decreasing the levels of the important gluconeogenic enzymes, fructose-1, 6-bisphosphatase and glucose-6-phosphatase. [7]

In a study by S. Venkateswaran and L. Pari, the level of hydroperoxides and reactive compounds with thiobarbituric acid dramatically decreased after 45 days of oral administration of 200 mg/kg of C. indica leaf extract on STZ-diabetic rats. By raising reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase, and glutathione-S transferase in the liver and kidney of streptozotocin-diabetic rats, this clearly supports the antioxidant ability of Coccinia indica leaf extract (CLEt). At 200 mg/kg body weight, CLEt outperformed glibenclamide in terms of efficacy. [8]

In the V. SHAKYA trial, 200 mg/kg of C. indica was given orally to STZ-induced diabetic rats. After 30 days, it showed a significant rise in liver glycogen, a reduction in blood glucose level, and a decrease in body weight. [9]

According to Balaraman, *C. indica* was studied for STZ-induced diabetes in Sprague-Dawley rats at 100 or 200 mg/kg b.w. orally for fourteen days. Body weight and alteration in fasting blood sugar levels were monitored every five days. Rats were cervically decapitated and sacrificed after a 14-day experimental period, at which point blood and liver samples were obtained. Biochemical measurements of plasma glucose, cholesterol, triglycerides, LDL, HDL, SGOT, SGPT, and ALP were performed from a blood sample. Liver glycogen content was determined using a homogenized liver sample. Significant antihyperglycemic and hypolipidemic effects were produced when an ethanol extract of the aerial parts of *Melothria maderaspatana* and *Coccinia indica* was given to rats with STZ diabetes (p 0.001). The results of the study indicate that the extracts had a substantial positive impact (p 0.001; p 0.05) on the recovery of altered biochemical markers and lowered body weight in treated mice. The standard medication used in the trial was glibenclamide (0.5 mg/kg b.w.). When 200 mg/kg of Kundru fruit extracts were given to the diabetic rats every day for 14 days, their blood glucose levels were lower than those of the diabetic control group. In the seventh and fourteenth days of the diabetes induction, there was a significant drop in blood sugar levels, indicating the antidiabetic effect. The result was similar to that of the common anti-diabetic drug Glibenclamide. Orally administered extracts of Coccinia indica's leaves and roots have been shown to have a hypoglycemic effect. [10]

In the study by Manish Gunjan, in diabetes-induced animals, blood glucose levels decreased after receiving Kundru fruit extracts (200 mg/kg) for 14 days as compared to the diabetic control group. Blood glucose levels significantly decreased on days seven and fourteen of the diabetes induction, indicating the fruit's anti-diabetic properties. [11]

According to Hossain, the study sought to determine whether the different fractions of the ethanolic extract of Stevia rebaudiana leaves—Petroleum ether, ethyl acetate, and chloroform—had any antihyperglycemic, oral glucose tolerance test (OGTT), and antihyperlipidemic (total cholesterol and triglycerides) effects. The different fractions of the extract were found to significantly lower blood glucose levels (p 0.05) when given orally to hyperglycemic rats induced by alloxan at a single dose of 150 mg/kg body weight. The lipid content, which increased in hyperglycemic rats, was significantly reduced by the various fractions. In addition, the plant fractions increase the rats' ability to tolerate high glucose levels. As a result, this research provides the way for plant-based antihyperglycemic and antihyperlipidemic therapies. It also demonstrates that various fractions of the Stevia rebaudiana leaf ethanolic extract—Petroleum ether, ethyl acetate, and chloroform—have favorable effects on reducing elevated glucose levels severity, increasing antihyperlipidemic activity, and enhancing glucose tolerance activity. [12]

According to Mohammed, the study aimed to investigate, in vivo interactions between the anti-diabetic and anti-oxidative properties of *Coccinia grandis* leaf extract in experimentally-induced diabetic rats. Streptozotocin-induced albino Wistar diabetic rats received ethanol extract, prepared in saline, orally for 21 days. Biochemical parameters, histological analysis, liver and muscle glycogen, and in vivo antioxidant activity were measured and compared in normal, diabetic control, standard (metformin), and treated animals. The administration of ethanolic leaf extract (500 mg/kg) to experimental rats with streptozotocin-induced diabetes resulted in a significant (P 0.001) decrease in blood sugar

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(312–169 mg/100 mL), an increase in body weight (181-210 g), and increase in serum insulin (1.28–3.10 IU/dL). When compared to diabetic control rats, it also kept the lipid profile, hepatic and renal functions within the normal range and was nearly as effective as metformin, a common anti-diabetic medication. According to the findings, *Coccinia grandis* ethanolic leaf extract has potent anti-diabetic properties and can be effectively used in the treatment of diabetes. [13]

In a study, Subasri Muthuviveganandavel examined the biological effects of oral administration of Cephalandra indica mother tincture (MT) on the blood serum of male albino rats' immunological and physiological activity of the proteins, glucose, cholesterol, and triglycerides. The findings of this study are fundamental information gathered through experimentation. It is quite astounding to see how *Cephalandra indica* (MT) affects blood serum biochemical markers in male albino rats. Male albino rats' blood serum total protein, glucose, and cholesterol responses to *Cephalandra indica* (MT) for low-dose acute effects were studied [14].

- *Gymnema Sylvestre: an in-vivo study*

Gymnema Sylvestre is also known as ‘gurmar’ (family Asclepiadaceae), which translates to "sugar destroyer." Sathya S. conducted a study on *Gymnema sylvestre* R.Br. leaf water extract, which was tested for its ability to lower blood sugar levels in both healthy and diabetic rats induced with alloxan. Both healthy and diabetic rats induced with alloxan were administered a grated dose (2 ml/kg) of the water extract of *Gymnema sylvestre* leaf. Normal rats demonstrated a significant fall in blood sugar levels, whereas diabetic rats showed a significant increase. In diabetic rats, the protein level is also reduced. Patients with diabetes had higher levels of creatinine, urea, and uric acid. Following the herbal remedy, the levels were almost back to normal. [15]

According to Pitchai Daisy, dihydroxy gymnemic triacetate, an active substance, has reportedly been isolated from *Gymnema Sylvestre* acetone extract, and its ideal dose has been determined and patented. In order to measure plasma glucose, insulin, glycated hemoglobin (HbA1c), tissue glycogen, lipid parameters including triglycerides, total cholesterol, LDL cholesterol, and HDL cholesterol, and the activities of hepatic marker enzymes that include aspartate aminotransferase (AST) and alanine amino transfer, streptozotocin-induced diabetes rats were given this active substance (20 mg/kg body weight) orally for 45 days. Dihydroxy gymnemic triacetate, a chemical found in Gymnema sylvestre, has been shown in studies to have hypoglycemic and hypolipidemic effects with long-term usage, indicating that it may find application as a drug to treat diabetes. [16]

According to a study conducted by Shravan Kumar Dholi, gymnemic acid was studied for its pharmacological hypoglycaemic action in diabetic rats and its effects on streptozotocin-induced diabetes in rats. After treatment for 24 hours at doses of 100 mg and 500 mg/kg, gymnemic acid lowered glucose, cholesterol, triglycerides, urea, creatinine, and lipids in a single-dose study. Gymnemic acid decreased creatinine, urea, lipids, triglycerides, and glucose after 15 days in a chronic study (multiple dose study), and it significantly decreased glucose levels at day 15 in diabetic rats. When diabetic rats were given dosages of 100 mg/kg and 500 mg/kg of gymnemic acid during a glucose tolerance test, their glucose levels were found to be considerably lower than those of the control group. Based on histological studies, gymnemic acid affects the pancreatic tissue's capacity to regenerate. [17]

Bo Liu 1 conducted a study to evaluate the effects of a novel GS extract (called OSA-Om Santal Adivasi) on insulin secretion from isolated human islets of Langerhans and the MIN6 beta-cell line, as demonstrated in the study. Low concentrations (0.06-0.25 mg/ml) of OSA had no adverse effects on MIN6 cell viability, whereas higher concentrations (> or = 0.5 mg/ml) led to an increase in Trypan blue uptake. Insulin secretion from MIN6 cells was stimulated by OSA in a concentration-dependent manner. The effect of OSA, which was mediated by Ca2+ influx through voltage-operated calcium channels, was an increase in beta-cell Ca2+ levels. The insulin secretagogue effects of OSA in MIN6 cells and isolated human islets were partially reliant on the presence of extracellular Ca2+. OSA also reversibly increased insulin secretion from isolated human islets. These results show that GS-isolated OSA at low concentrations produces insulin secretion. [18]

Sadish K. Shanmugam conducted study, *Gymnema sylvestre*, the phytoconstituents of the leaf extracts were evaluated using ethyl acetate, chloroform, and water. To test for comparative antidiabetic action, 1.5 kg of *Gymnema sylvestre* plant material was macerated with 3.75 liters of ethyl acetate, water, and chloroform. By injecting 60 mg/kg of STZ intraperitoneally, 36 male wistar rats were administered to develop diabetes. For a duration of 21 days, the animals were given a variety of therapies. Using a one-touch glucometer, glucose levels were taken on day 1, the first day of any medication, and on days 7, 14, and 21. The pancreas was examined histopathologically using the staining of hematoxylin and eosin. SPSS software was utilized for the statistical analysis, which involved one-way ANOVA and Dunnet's multiple comparisons. The study found that when diabetic rats were given various GS extracts, their blood glucose levels dropped to normal in streptozotocin-induced diabetic rats. The aqueous extract demonstrated the greatest (59%) decrease in blood sugar levels when the lowered percentage of blood glucose levels was compared with glibenclamide (62%), indicating the potential of *Gymnema sylvestre* as the most significant antidiabetic drug [28]

- *Gymnema Sylvestre: an in-vitro study*

A Al-Romaiyan study reports the effects of a novel high-molecular-weight GS extract titled Om Santal Adivasi (OSA®) on plasma levels of insulin, C-peptide, and glucose in a small group of T2DM patients. Significant increases in circulating insulin and C-peptide were brought on by the oral administration of Om Santal Adivasi OSA® (1 g/day, 60 days), and these changes were connected to substantial reductions in blood glucose levels after meals and during fasting. In in vitro experiments with isolated human islets of Langerhans, OSA® directly enhanced insulin production from human cells, which is consistent with an in vivo method of action that involves boosting insulin secretion. According to these in vitro and in vivo results, OSA® may be a viable alternative treatment for the hyperglycemia associated with type 2 diabetes. 19]

According to a study conducted by T. Fushiki, *Gymnema sylvestre* leaf extract were used in the study. The release of gastric inhibitory peptides into the portal vein in response to a duodenal infusion of D-glucose was investigated using pure gymnemic acid and inhibitors of many potential glucose sensors and carriers in the intestinal lumen. By infusing D-glucose intraduodenally, the concentration of the portal immunoreactive gastric inhibitory peptide was significantly and dose-dependently increased. Phlorizin, pure gymnemic acid, and Gymnema sylvestre leaf extract were all simultaneously infused, but not cytochalasin B. This resulted in a considerable reduction in the rise in the portal immunoreactive stomach inhibitory peptide caused by glucose. The vagal glucoreceptor in the lumen of the glycolysis inhibitors mannoheptulose, procaine, and lidocaine did not alter the amounts of portal immunoreactive gastric inhibitory peptide. These findings demonstrate the presence of a glucose receptor for the release of an immunoreactive gastric inhibitory peptide that interacts with purified gymnemic acid, phlorizin, and leaf extract of Gymnema sylvestre. It is also likely that this glucose receptor differs from both a vagal glucoreceptor and a glucose transporter in the lumen. [20]

Rashmi S. Shenoy conducted the study. In order to evaluate the potential of the ethanolic extract of Gymnema sylvestre (EEGS) for blood glucose management, the triterpene glycoside (TG) fraction was separated and purified using in vitro procedures. The HPLC-purified active fraction, TG, was characterized using FTIR, LC-MS, and NMR. With IC50 values of 3.16 0.05 g/mL, 74.07 0.51, 5.69 0.02, and 1.17 0.24 g/mL, respectively, in comparison to the control, the purified fraction (TG) significantly inhibited the activities of yeast glucosidase, sucrase, maltase, and pancreatic amylase. To examine TG, triterpene glycosides such as gymnemagenin and gymnemic acids I, IV, and VII were employed. In vitro studies employing mouse pancreatic β-cell lines (MIN6) revealed that TG exhibited defense against H2O2-induced ROS production and did not have any deleterious impact on cell survival. The current study suggests that TG is now a safe nutraceutical option and functional food ingredient for the treatment of diabetes due to its successful isolation and therapeutic potential. [21]

III. DISCUSSION

The current review illustrates that numerous drugs which are used in the homeopathic system of medicine to manage hyperglycemia, but only a few have had their therapeutic effects confirmed by scientific studies. *Cephalandra indica* and *Gymnema sylvestre* have demonstrated efficacy in minimizing blood sugar levels, stimulating pancreatic beta-cell regeneration [6], increasing insulin secretion [18], and minimizing the formation of AGEs, and their probable molecular mechanism of action has also been recognized. The rationale for selecting the dosage level of the drugs at which their efficacy was examined was not mentioned in the research discussed above. Furthermore, some of the researchers diluted mother tinctures and potencies in water before administration, while others used undiluted drugs, with no explanation specified in any of the reviewed studies. Considering all of the above, additional studies should be conducted to rectify the previous discrepancies in animal models, and the results should be made available to biomedical researchers in order to achieve uniformity in preclinical homoeopathic research.

More pharmacological research (in vivo or in vitro) is necessary to confirm the anti-diabetic effect, underlying mechanisms of action, long-term safety, and potential toxicological effects of these drugs before they can be used appropriately in humans, as there have only been a limited number of studies conducted. These drugs are therapeutically used in potentized forms, and the scientific community is divided over their usefulness. As a result, scientifically controlled studies on potentized versions are encouraged in order to investigate their mechanism and efficacy. In addition, these studies must consider long-term safety as well as potential drawbacks in addition to estimating the benefits.

The above-mentioned investigations on *Cephalandra indica* and *Gymnema sylvestre* confirm no toxicity or potency when compared to standard and vehicle controls. Further research using the parenteral method of administration could provide a new perspective for administering homoeopathic medicines and comparing their efficacy with oral intake in *C. indica* animal model tests.

The majority of the homoeopathic medications mentioned in this study are derived from plants, and it is important to highlight that the hypoglycemic impact of plant-derived medications might interfere with allopathic hypoglycemic pharmaceuticals and insulin, both of which are routine therapies for diabetic patients [22]. Although some diabetic people use herbal medicine without alerting their doctors, most doctors encourage their patients to avoid it. This kind of treatment could lead to medication interactions or erratic and imprecise blood glucose monitoring [23]. Therefore, studies assessing the effects of homoeopathic therapies in

combination with allopathic medications in diabetic rats are encouraging and could yield important details regarding possible toxicity, herb-drug interactions, or significant hazards.

Numerous in vitro techniques that rely on chemicals, isolated organs, cells, and membranes are available to examine the effectiveness and safety of drugs for diabetes. These assays offer a rapid drug screening platform and could help clarify the cellular and molecular effects of drugs, supporting their effectiveness in animal studies. Since there limited number of homeopathic medications to control diabetes, testing these medications quickly will be made easier by employing in vitro models.

IV. CONCLUSION

The current review presents researchers with current information on the state of pre-clinical studies on homeopathic preparations from *Cephalandra indica* and *Gymnema sylvestre*, that have the potential to manage hyperglycemia and can serve as a roadmap for future investigations. Future anti-diabetic studies may be designed as multi-institutional, controlled, blinded trials to ensure quality and reproducibility in the evaluations should be carried out because replication of effects in essential preclinical research is of the utmost importance.

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REFERENCES

[1]. Arvind Kumar 1, R. G. (2023). Prevalence of diabetes in India: A review of IDF Diabetes Atlas 10th edition. *Current Diabetes Reviews*.

[2]. Loscalzo, J. (2022). Harrisons principle of internal medicine. In J. Loscalzo, S. Anthony , K. Dennis L. , H. Stephen , & L. Dan, *Harrisons principle of internal medicine 21st edition vol 2* (p. chapter 176). McGraw Hill Publishes.

[3]. Bandawane D, J. A. (2011). Antidiabetic and antihyperlipidemic effect of. *Indian J Pharm Educ Res*, 45:114-20.

[4]. Parijat Kanetkar, R. S. (2007). Gymnema sylvestre: A Memoir. *J Clin Biochem Nutr.*, ; 41(2): 77–81.

[5]. Chopra R.N., C. I. (1958). Indigenous drugs of India. 2nd ed. U.N. Dhar & Sons Ltd. In C. I. Chopra R.N., *CHOPRAS INDIGENOUS DRUGS OF INDIA* (pp. 314-316). Kolkata: Bimal kumar dhur academic pubisher.

[6]. D.P. Rastogi, A. S. (1988). A novel anti-diabetic action of Cephalandra indica mother tincture. *Br Homeopath J*, 77(03): 147-151.

[7]. B A Shibib, L. A. (1993). Hypoglycaemic activity of Coccinia indica and Momordica charantia in diabetic rats: depression of the hepatic gluconeogenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and elevation of both liver and red-cell shunt enzyme glucose-6-phosp. *Biochem J.*, 292(Pt 1): 267–270.

[8]. S. Venkateswaran, L. Pari. (2002). Effect of Coccinia indica leaves on antioxidant status in streptozotocin-induced diabetic rats. *Journal of Ethnopharmacology*, Volume 84, Issues 2–3, Pages 163-168.

[9]. SHAKYA, V. (2008). Antidiabetic activity of Coccinia indica in streptozotocin induced diabetic rats. *Asian Journal of Chemistry*, 6479-6482.

[10]. Balaraman, A. K. (2010). Antihyperglycemic and hypolipidemic effects of Melothria maderaspatana and Coccinia indica in Streptozotocin induced diabetes in rats. *Saudi Pharmaceutical Journal*, 18(3):173-178.

[11]. Gunjan, M. (2010). Pharmacognostic and antihyperglycemic study of Coccinia indica. *International Journal of Phytomedicine* , 36-40.

[12]. Hossain, M. S. (2011). ANTIHYPERGLYCEMIC AND ANTIHYPERLIPIDEMIC EFFECTS OF DIFFERENT FRACTIONS OF STEVIA REBAUDIANA LEAVES IN ALLOXAN INDUCED DIABETIC RATS. *International Journal of Pharmaceutical Sciences and Research* , 2 7):1722-1729

[13]. Mohammed, S. I. (2016). In vivo antidiabetic and antioxidant activities of Coccinia grandis leaf extract against streptozotocin induced diabetes in experimental rats. *Asian Pacific Journal of Tropical Disease*, 6(4):298-304.

[14]. Subasri Muthuviveganandavel, M. V. (2014). EFFICACY OF CEPHALANDRA INDICA MOTHER TINCTURE ON THE BIOCHEMICAL PARAMETER OF MALE ALBINO RAT. *WORLD JOURNAL OF PHARMACY AND*, ISSN- 2278-4375.

[15]. Pitchai Daisy 1, J. E. (2009). A novel dihydroxy gymnemic triacetate isolated from Gymnema sylvestre possessing normoglycemic and hypolipidemic activity on STZ-induced diabetic rats. *Journal of Ethnopharmacology*, Volume 126, Issue 2, Pages 339-344.

[16]. Shravan Kumar Dholi, R. R. (2014). In vivo anti diabetic evaluation of gymnemic acid in streptozotocin induced rats. *The Pharma Innovation Journal* , 3(7): 82-86.

[17]. Bo Liu 1, H. A.-A.-R. (2009). Characterisation of the insulinotropic activity of an aqueous extract of Gymnema sylvestre in mouse beta-cells and human islets of Langerhans. *Cell Physiol Biochem*, ;23(1-3):125-32.

[18]. A Al-Romaiyan 1, B. L.-A.-C. (2010). A novel Gymnema sylvestre extract stimulates insulin secretion from human islets in vivo and in vitro. *Phytotherapy research*, Volume24, Issue9 Pages 1370-1376.
[19]. T Fushiki 1, A. K. (1992). An extract of Gymnema sylvestre leaves and purified gymnemic acid inhibits glucose-stimulated gastric inhibitory peptide secretion in rats. *The Journal of Nutrition*, 122(12):2367-73.
[20]. Rashmi S. Shenoy, 1. ,. (2018). In Vitro Antidiabetic Effects of Isolated Triterpene Glycoside Fraction from Gymnema sylvestre. *Evid Based Complement Alternat Med.*, 7154702.
[21]. Ramesh C. Gupta, 1. D. (2017). Interactions between antidiabetic drugs and herbs: an overview of mechanisms of action and clinical implications. *Diabetology Metabolic Syndrome*, 9: 59.
[22]. Fallah-Hoseini, H. F. (2006). Review of Anti-Diabetic Medicinal Plant Used in Traditional Medicine. *Journal of Medicinal Plants*, , 5, 1-8.
[23]. Anoja Priyadarshani Attanayake, 1. K. (2013). Efficacy and toxicological evaluation of Coccinia grandis (Cucurbitaceae) extract in male Wistar rats. *Asian Pac J Trop Dis.*, 3 (6): 460–466.
[24]. Manish Gunjan, G. K. (2010). Pharmacognostic and antihyperglycemic study of Coccinia indica. *International Journal of Phytomedicine*, 36-40.
[25]. Rashmi Santosh Tupe, A. K. (2015). SYZYGIUM JAMBOLANUM AND CEPHALANDRA INDICA HOMOEOPATHIC PREPARATIONS INHIBIT ALBUMIN GLYCATION AND PROTECT ERYTHROCYTES: AN IN VITRO STUDY. *Homoeopathy*, 104(3):197-204.
[26]. Sathish Sampath 1, A. N. (2013). Effect of homeopathic preparations of Syzygium jambolanum and Cephalandra indica on gastrocnemius muscle of high fat and high fructose-induced type-2 diabetic rats. *Homeopathy*, 102(3):160-71.
[27]. Sathya S., K. R. (2008). Hypoglycemic effect of Gymnema sylvestre (retz.,) R.Br leaf in normal and alloxan induced diabetic rats. *Anc. Sci. Life 28 (2)*, 12-14.
[28]. Sadish K. Shanmugam1*, D. K. (2023). Exploring Antidiabetic Potential of Gymnema sylvestre. *Journal of Applied Pharmaceutical Sciences and Research*, 6(2).