2. REVIEW OF LITERATURE

Plants play an important role in our daily lives. From basic necessities to complex tools, plants and their products have been used since time immemorial. Since the beginning of human history, there has been a relationship between humans and the environment and this relationship extends to the use of plants as medicine. In the past, medicinal plants have traditionally been used to treat a wide range of diseases, and several researchers have investigated their potential to treat various ailments. Given that plants contain a variety of phytocompounds that actively act as medicines in the human body, the knowledge of their potential as medicinal agents is not surprising. In the world, there exists 300000 vascular plants and screening each one of them would not be practical due to time constraint. Thus, medicinal plants with traditional significance are screened in the laboratories. Traditional medicines have long been used to treat illness. Screening these plants would be one step ahead of screening the whole plants. Many researchers therefore, conduct exploratory research by surveying or investigating plants that have been utilized for particular disease for generations. These medicinal plants are brought to the laboratory for trial and error and to study their efficacy scientifically. A large number of medicinal plants have been screened for therapeutic purposes against many diseases. Diabetes mellitus is one such disease where the current allopathic medicine causes serious adverse side effects when taken for a longer period of time. So, a wide range of research is going on with the hopes of getting better alternative medicine with low cost, better efficacy and low side effects.

2.1. INTERNATIONAL

Analysing medicinal plants to cure diseases has become a new trend in the scientific world. With technological advancements, these medicinal plants are brought to laboratories where they are tested using various sophisticated techniques for further studies and drug processing. However, for easier screening, it is crucial to know the history of origin or context of use of medicinal plants. To explore the knowledge of older people or traditional healers about medicinal plants, Trojan Rodrigues et al. (2012) studied southern Brazil and reported a total of 81 species belonging to 42 families used specifically to treat diabetes. The most popular families mentioned in their work were Asteraceae and Myrtaceae. Similarly, Neamsuvan et al. (2015) studied Chana and Nathawee districts in Songkhla province, Thailand, and reported that 38 species belonging to 37 genera and 28 families were used as medicine by local healers in the area. Similarly, Barkouii et al. (2017) reported 48 ethno-medicinal plants belonging to 25 families from Chtouka Ait Baha and Tizit provinces of Morocco for the treatment of diabetes. Skhalli et al. (2019) interviewed 334 diabetic patients in Rabat, Morocco and found that 53.6% use herbal medicine to control the disease. They reported 30 plant species belonging to 18 families for the treatment of diabetes.

The ethnomedicinal plants reported or used by different healers were preceded to laboratory experiments. Arunachalam et al. (2012) studied the aqueous extract of *Merremia tridentata* (L.) Hellier f. root in streptozotocin (STZ) induced diabetic rats in three doses 50, 100 and 150 mg/kg bw. The three doses caused a significant reduction in blood glucose levels in the animal model in a dose-dependent manner. Dechandt et al. (2013) evaluated the antidiabetic activity of *Combretum lanceolatum* Pohl ex Eichler flower extract in STZ-induced diabetic rats. They divided the diabetic rats into four groups: diabetic control, diabetic treated with 500 mg/kg of Metformin and diabetic treated with 250 or 500 mg/kg of *C. lanceolatum* ethanolic extract for 21 days. The study observed a comparable anti-hyperglycemic effect of *C. lanceolatum* ethanolic extract to the reference drug metformin. The antidiabetic activity of the plant is due to the inhibition of gluconeogenesis. The data also indicated that the antidiabetic activity of the *C. lanceolatum* extract could be mediated, at least in part, through activation of AMP-activated protein kinase by quercetin. Yassa and Tohamy (2014) also studied the aqueous extracts of *Moringa oleifera* Lam. leaves in streptozotocin-induced diabetic rats and revealed the potent antidiabetic activity of the medicinal plant. In the same way, Zhang et al. (2016) investigated the antidiabetic potential of the aerial part of *Heracleum dissectum* Ledeb. They studied the methanolic extract and found that the plant extract can inhibit the elevation of plasma glucose. The petroleum ether fraction of the plant was found most potent inhibitory activities. Bourebaba et al. (2016) studied the antidiabetic property of methanolic extract of *Hyoscyamus albus* L. The study revealed that the nortropane alkaloids of plant reduced the blood glucose and lipid level in diabetic mice after 20 days of treatment at 10 and 20 mg/kg test concentrations. Riaz et al. (2020) has stated that active compounds in the stabilized formulation of *Holarrhena antidysentrica* Wall ex G. Don, *Prunus dulcis* (Mill) D.A Webb, *Cicer arietinum* L. and oleic acid have good antidiabetic activity inhibiting carbohydrate-digesting enzymes, *α*-amylase and *α*-glucosidase in comparison to standard drugs. Workers from Ethiopia have reported the crude extract and solvent fractions of *Terminalia brownii* Fresen. to have a significant antihyperglycemic activity in STZ induced diabetic mice, hypoglycemic activity and improvement of oral glucose tolerance in normal mice (Alema et al., 2020). The leaf latex of *Aloe pulcherrima* M.G. Gilbert & Sebsebe traditionally used in the treatment of diabetes mellitus showed a significant antidiabetic activity by improving diabetic dyslipidemia and body weight of diabetic mice (Amare et al., 2020).

Along with the crude extract study, various antidiabetic compounds were also seen to be isolated and studied. For instance, Ma et al. (2014) isolated new compounds, logmalicids 1 and 2 and 20 known compounds from traditionally used medicinal plant *Cornus officinalis* Siebold & Zucc. and studied anti-diabetic nephropathy activity. They revealed that loganins and logmalicids 1 and 2 were the active compounds of *C. officinalis* that reduced diabetic nephropathy. Ghhorbani et al. (2014) isolated curcumin, a hydrophobic low-molecular-weight flavonoid from *Curcuma longa* L. and when studied for its efficacy it has shown anti-hyperglycaemic and insulin sensitizer effects. Berberine extracted from *Berberis aristata* DC showed promising efficacy compared to rosiglitazone and metformin by reducing HbA1c, fasting blood glucose, and postprandial blood glucose despite having some adverse effects on liver.

Mohammad et al. (2017) isolated four compounds, namely 6-Paradol, 6-Shagaol, 6-Gingerol and Oleanolic acid from *Aframomum melegueta* K. Schum. and studied for its α-amylase and α-glucosidase inhibitory property. They revealed that, compound 6-gingerol and Oleanolic acid showed strong alpha-amylase and α-glucosidase inhibitory property. Two compounds, namely Plecthranthoic acid (and 3,4,5,7-Flavantetrol were isolated from *Ficus microcarpa* L.f and assayed for the inhibition of α-glucosidase, α-amylase, dipeptidyl peptidase (DPP) and also evaluated 5'-activated protein kinase activation potential of the two compounds. PA showed significant inhibition of α-glucosidase, α-amylase and DPP-4 activity. Along with that PA also showed a potent activator of AMPK (Aktar et al., 2018)

Berberine extracted from *Berberis aristata* showed promising efficacy compared to rosiglitazone and metformin by reducing HbA1c, fasting blood glucose, postprandial blood glucose despite having some adverse effects on liver (Liang et al., 2019). Nazir et al. (2021) isolated three compounds morin, phloroglucinol and 1-hexyl benzene from *Elaeagnus umbellata* (Thunb.) and studied for its antioxidant, antibacterial and antidiabetic activity. Among the isolated compound morin lowered fasting blood glucose, cholesterol level, triglycerides, low-density lipoprotein, HbA1c level and increased high-density lipoprotein in STZ-induced diabetic rats. Imitaz et al. (2023) isolated phenolic compounds, syringic acid, p-coumaric acid, morin and catechin from *Tradescantia pallid* (Rose) D.R.Hunt. In vitro antidiabetic potential of the compounds was analysed using α-amylase and non-enzymatic glycosylation of hemoglobin protein assays. They revealed that Morin and catechin had the potential of inhibiting against enzymatic as well as non-enzymatic assays.

2.2. NATIONAL

India has an ancient heritage of traditional medicine, which provides plenty of information on ancient practices and traditional uses of medicinal plants. Documentation of such vital information was done by many researchers to prevent the loss of the data or information. Ayyanar and Ignacimuthu (2011) gathered a huge ethnomedicinal information from Kani tribals of Tirunelvelhi hills Western Ghats of India and reported 90 species belonging to 83 genera that are used for curing about 65 ailments. Similarly, Thirumalai et al. (2012) carried out a survey work at Javadhu hills, Tamil Nadu, and their investigations revealed 40 medicinal plants used for the treatment of Diabetes. In the year 2013-2014, a survey was carried out a survey in Jodhpur, Rajasthan to explore the indigenous plants used for the treatment of Diabetes mellitus and reported 21 ethnomedicinal plants (Goyal, 2015). Likewise, a survey work was carried out by Adhan and Anand (2017) in Sadhuragiri hills, Tamil Nadu, India, and reported huge ethnomedicinal knowledge from Paliyar tribals of that area. They documented 65 plant species for the treatment of diabetes. The most dominant family was Asteraceae.

Various works have been carried out to study the antidiabetic property of the plants in laboratory. Kumar et al. (2010) studied the antidiabetic effects of *Cassia* *siamea* Lam. methanolic leaves extract in streptozotocin-induced diabetic rats and found significant improvement in the blood glucose level and body weight. In the same way, Sunil et al. (2011) investigated the efficacy of hexane extract of *Sympolocos cochinchinensis* (Lour) S. Moore in STZ-induced type 2 diabetic rats. The study found that the treatment with hexane extract with 250 and 500 mg/kg body weight showed a substantial reduction in the blood glucose level. While in the oral glucose tolerance test, the treatment showed a highly significant reduction of 12.07% and 23.58% in plasma glucose levels. Likewise, Kumar et al. (2011) investigated the antidiabetic potential of alcoholic leaves extract of *Alangium lamarckii* Thwaites on STZ-nicotinamide induced type 2 diabetic rats. Administration of alcoholic extract of *A. lamarckii* at two dosages 250 and 500 mg/kg did not show any significant change in blood glucose level of normoglycemic rats. In contrast, the oral glucose tolerance test depicted a reduction in blood glucose levels. Similarly, Rajkumar et al. (2011) studied the effect of alcoholic stem extract of *Gymnema montanum* (Roxb.) Hook.f on blood glucose, plasma insulin, and carbohydrate metabolic enzymes STZ-induced diabetic rats. On being treated with *G. montanum* orally at the doses 25, 50, 100 and 200 mg/kg daily for three weeks, there was a significant reduction in blood glucose levels and improved plasma insulin levels and had a more pronounced effect in 100 mg and 200 mg/kg. However, Verma et al. (2012) investigated the anti-hyperglycemic and antihyperlipidemic properties of hydro-alcoholic extract of fruits of *Sapindus mukorossi* Gaertn and its beneficial effect on hematological parameters with histopathological analysis in STZ-induced diabetic rats. They found that daily oral administration of the extract (250 and 500 mg/kg bw) and glibenclamide for 20 days showed beneficial effects on blood glucose level and lipid level and had a favourable effect on the histopathological changes in the pancreas in STZ-induced diabetes.

Moreover, Krishnan et al. (2014) evaluated the antidiabetic effects of *Musa paradisiaca* L. tepal extracts (MPTE) in STZ-induced diabetic rats. They have isolated and characterized the phytocompound, syringin, a phenyl propanoid glucoside from the plant and evaluated their antidiabetic efficacy in STZ-induced diabetic rats. Syringin was isolated from MPTE and characterized using spectral studies. Diabetic rats were administered 50 mg/kg per day orally for 30 days. After the experimental period, rats were sacrificed, and blood was collected for important biochemical parameters such as blood glucose, insulin, haemoglobin, HbA1c, total protein, urea, uric acid and creatinine. Serum aminotransferases and alkaline phosphatases were assayed. The data revealed the presence of phenyl propanoid glycoside, syringin in MPTE. Elevated blood glucose and HbA1clevels, the reduced plasma insulin and haemoglobin levels in diabetic rats were significantly reversed to near normal after oral administration of syringin. Balamurgan et al. (2014) also evaluated the ethanol extract of *Melastoma malabathricum* L. in alloxan-induced diabetic rats and administered the dose 150 and 300 mg/kg of body weight and found that *M. malabathricium* extract altered lipid profiles and was reversed to near normal than diabetic control rats. Similarly, Kaur et al. (2016) isolated the chemical constituents of *Dillenia indica* L. to evaluate their antioxidant and antidiabetic activity. Alcoholic extract of *D. indica* was subjected to column chromatography for compound isolation, and chromane was yielded. The chromane was administered to STZ-induced (50 mg/kg) induced diabetic rats. Their effect administration of chromane and *D. indica* significantly attenuated the elevated fasting blood glucose, indicating that *D. indica* possessed antidiabetic activity. Ahmed et al. (2017) also evaluated the *Pistacia atlantica* Desf. leaves for antidiabetic efficacy and found that the leaves extracts provide a rational basis for the isolation and development of antidiabetic and anti-hypertensive agents.

In a similar study conducted by Subba et al. (2019), Pressure boiling extract of *Fraxinus floribunda* Wall. showed a reduction in plasma glucose concentration when treated in STZ-induced diabetic rats. Administration of *Swietenia macropphylla* King, *Litsea glutinosa* (Lour.) C.B.Rob. and *Phlogacanthus thyrsiformis* (Roxb. Ex Hardw.) Mabb. in STZ-induced diabetic rats showed a significant decrease in the blood glucose level (Sharma et al., 2020). Ethanolic extracts of leaves and flowers of *Phlogacanthus thyrsiflorus* Nees lowered the blood glucose level in STZ-induced albino rats compared to standard drug metformin-treated rats, and the negative control group (Koushik et al., 2020). Studies on selected natural anti-diabetic plants such as *Anogeissus latifolia* (DC.) Wallish ex Guill & Perr. *Aegle marmelos* (L.) Correa, *Trigonell foenum-graecum* L. and *Mangifera indica* L. improve glucose homeostasis inhibits DPP-IV, thereby showing a potential therapeutic approach against Type II diabetes mellitus treatment (Ansari et al., 2021).

2.3. REGIONAL

Northeastern India is well known for its homely abode for various endemic floras and faunas. Located at the confluence of Indo-Chinese, Indo-Myanmar, and Indian biogeographical realms, the area is exceptional in that, it provides an abundance of habitats and diverse biota with high degree of endemism. The area also provides diversity in indigenous tribes, of about 225 tribes out of 450 tribes in India (Chatterjee et al., 2006). It is believed that the tribals residing in the area have profound knowledge about the medicinal plants and their uses. Many researchers started their diabetic research on plants by survey work and by documenting the knowledge. Syiem and Khup (2007) evaluated *Flemingia macrophylla* (Willd.) Prain ex Merr., a traditionally used plant of the north eastern India for hypoglycaemic and anti-hyperglycaemic effect on mice and found glucose reducing potential of the plant.

Sen et al. (2011) documented 113 antidiabetic plants belonging to 56 families from tribals of Tripura, India. In Nalbari district of Assam, Chakravorty and Kalita (2012a; 2012b), also documented 35 ethnobotanicals belonging to 28 families, used by the local people of that area and later revealed that one of the reported medicinal plants, *Phlogacanthus thyrsiflorus* Nees. was effective against STZ -induced mice, when studied for in-vivo efficacy. Tarafdar et al. (2015) studied 39 medicinal plant species belonging to 37 genera and 28 families were presented used by traditional healers of Unakoti area of the state of Tripura, India for diabetes and found that out of 39 collected plants, *Ananas comosus* (L.) Merr., *Holarrhena antidysenterica* Wall., and *Phlogacanthus thyrsiflorus* Nees. showed considerable use value relative frequency of citation. Verma et al. (2013) evaluated the antidiabetic and antihyperlipidemic potential of ethanolic extract of *Clitoria ternatea* L. (Fabaceae) along with pancreatic β-cells regeneration activity. They have found that the most significant pancreatic regeneration activity, antidiabetic and antihyperlipidemic activity. Singh et al. (2020) reported 201 plant species belonging to 72 families, 140 genera in a survey conducted in Mizoram, India. They also claimed that 103 plants had not been reported previously by any other workers for the treatment of diabetes. Kalita et al. (2016) studied the antioxidant and antidiabetic effect of *Musa balbisiana* Colla root, shoot and inflorescence extract on STZ-induced diabetic rats. The root extract treated rats showed potent fasting blood glucose reduction, total cholesterol, triglycerides level and low-density lipoprotein. The prolonged hyperglycemia in the diabetic patients comes with several complications such as low wound healing, or microbial infections. Kandimalla et al. (2016) studied the wound healing property of *Cymbopogon nardus* L. oil extract, in diabetic wounds of mice and reported the wound healing potential of essential oil in diabetic condition. The essential oil also showed invitro growth inhibition on three fungal species *Candida albicans* and *C. glabrata* and *C. tropicalis* in dose dependent manner, indicating *Cymbopogon nardus* L. to be potent antifungal agents. Another complication of diabetes is neurophathy. Kandimalla et al. (2017), studied the bioactive fraction of *Annona reticula* L. bark and *Ziziphus jujuba* Mill. root bark extracts, were tested in STZ induced neuropathy male Wistar rats. The methanolic and water fraction of the two plants along with insulin reduce the thermal and mechanical hyperalgesia and alloydinia. However, the treatments with insulin alone failed do so confirming the efficacy of the plants in diabetic neuropathy. Tamuk et al. (2020) studied the ethanolic extract of *Solanum spirale* Roxb. in STZ rats and revealed hypoglycemic property of the plant extract. Kaushik et al. (2020) studied the ethanolic extract of *Phlogacanthus thyrsiflorus* Nees. leaves and flower extract and revealed a potent glucose reducing potential along with restoration of lipid profile, of the STZ induced diabetic rats. Kashyap et al. (2021) evaluated *Premna herbacea* Roxb. methanolic extract against TIIDM both on free fatty acid treatment L6 muscle cells and high fructose fed rats. They revealed that the plant extract enhanced the glucose uptake in L6 insulin-resistant muscle cells and recover the elevated glucose level in the rats. Dutta et al. (2022) collected 10 ethnomedicinal plants and studied there in vitro α-amylase and α-glucosidase activity and showed that the traditional medicine used by different tribes has the potential to inhibit α-amylase and α-glucosidase activity along with good antioxidant property. Kashyap et al. (2023) isolated Kaemferol-3-O-rutinoside from *Antidesma acidum* Retz. and observed a stimulation of glucose uptake through induction of Sirutinin 1 and translocation of GLUT4 in L6 insulin resistant muscle cells. Gurumayun et al. (2023) isolated compounds Taxifolin-3-O-glucoside and Quercetin 3-O-rhamnoside from *Osbeckia nepalensis* Hook. and studied its antidiabetic property. They revealed that the methanolic extract and its compound ameliorates gluconeogenesis in liver cells showing the former compound to have better binding energy with Glucose 6 Phosphatase 1 Protein. Another medicinal plant *Allium hookeri* Thwaites is shown to prevent impaired glucose metabolism in TIIDM by stimulating glutathione biosynthesis in Sprague-Dawley rats. The extract has also been seen to reduce plasma glucose level along with increase in glucose uptake in sodium palmitate treated muscle cells (Deka et al., 2021). Basumatary et al. (2024) studied the fruit pulp of *Hodgsonia heteroclita* (Roxb.) Hook.f. & Thomson ethanolic extract in STZ -induced mice and revealed glucose lowering potential of the fruit extract.

In Kokrajhar district many preliminary studies on the plant has been conducted on medicinal plants by many researches (Narzary et al., 2015; Swargiary et al., 2016; Swargiary and Brahma, 2017). Boro et al. (2018) studied the ethanolic extract of *Morus indica* L. roots on rats and revealed hepatoprotective property of the extract. Sarma et al. (2021) conducted a survey on the ethnobotanicals used against diabetes in Kokrajhar district Assam and revealed a total of 23 plant species for the treatment of diabetes. Brahma et al. (2022) studied traditionally used antidiabetic medicinal plants viz., *Bambusa balcooa* Roxb., *Phyllanthus emblica* L., *Punica granatum* L., *Hodgsonia heteroclita* (Roxb.) Hook.f. & Thomson for preliminary phytochemical screening and revealed the therapeutic properties of the plants. Medicinal plants have the ability to reduce plasma glucose concentration, mediate signal cascades in organism's body, and reduce diabetic complications and many more. So, medicinal plant-based research could be beneficial for the search of new or effective antidiabetic medicine.