RESEARCH PAPER

Pharmacognostic Characterization and Antidiabetic Mechanisms of Schima wallichii and Xylosma longifolia: A Comprehensive Review.

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ABSTRACT
Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia and its sequelae in micro- and macrovascular disease. Although various synthetic anti-diabetic drugs are available, long-term use of these causes serious side effects and cost more to the patient as well as patients' non compliance lead us to develop safer and antidiabetic drugs with multiple targets. Medicinal plants with traditional uses serve as the significant source of bioactive compounds from different classes that work on variety of modes to regulate glucose. India, a biodiversity hot spot region of world, is located in northeastern India and has valuable ethnomedicinal knowledge for treatment of diabetes. Among these, Schima wallichii (DC.) Korth. and Xylosma longifolia Clos. which receive much attention as an old remedy and increasing scientific evidence.
In this review, pharmacognostic, phytochemical, and biological studies on S. wallichii and X. longifolia were critically compiled and appraised with focus on their anti-diabetic potential. The macroscopic characters, microscopical characteristics, physico-chemical constants and chromatographic profiling were described as standard parameters to support the authenticity and quality control of these herbs. Phytochemicals reported studies appear to contain flavonoids, phenolics, tannins and other bioactive molecules having antidiabetic abilities. Sequential in vitro and in vivo studies showed pronounced antihyperglycemic effects associated with α-amylase and α-glucosidase inhibition, antioxidant-mediated protection of pancreatic β-cells, and increased peripheral glucose uptake reflecting an enhanced sensitivity towards insulin as well as a corrected lipid metabolism. Preliminary toxicological assessment indicate an overall positive safety profile, which is however based on few chronic toxicity and clinical investigations. In conclusion, this review emphasizes the therapeutic potential of S. walalichii and X. longifolia as multi-targeted antidiabetic agents and advocates for a systematic standardization, isolation of bioactive compounds along with clinical validation to enable them to be developed into evidence-based phytotherapeutic agents
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INTRODUCTION
Diabetes mellitus (DM) is a chronic metabolic disorder that has been recognized since ancient times and continues to pose one of the most formidable challenges to global healthcare systems. It is characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or a combination of both. Despite remarkable advances in biomedical research and pharmaceutical development, diabetes remains inadequately controlled in a large proportion of patients, leading to severe complications and increased mortality. The disease imposes an enormous burden not only on human health but also on socioeconomic development, particularly in low- and middle-income countries [1].

According to the most recent International Diabetes Federation (IDF) data (2025), diabetes continues to rise at an unprecedented rate, affecting a significant proportion of the adult population worldwide [2][3]. Currently, an estimated 589 million adults (20–79 years) are living with diabetes globally, representing approximately one in nine adults a figure that reflects the continuing upward trend in prevalence over recent years. Of considerable concern is that a large proportion of these individuals about 252 million adults remain undiagnosed, placing them at elevated risk for long-term complications and delayed interventions [4][5]. Projections indicate that by 2050 the number of adults with diabetes is expected to increase to approximately 853 million, or roughly one in eight adults, driven

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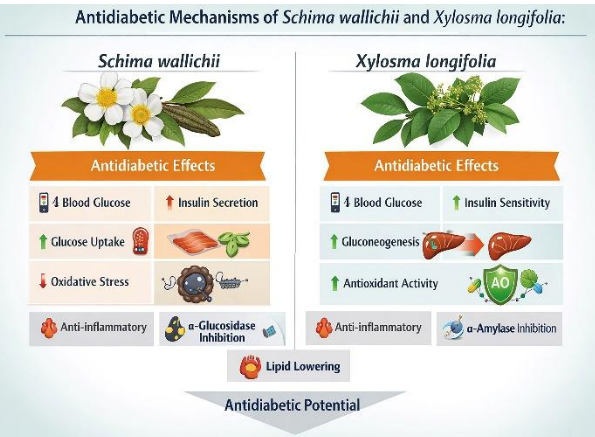
largely by population ageing, urbanisation, and lifestyle changes such as decreasing physical activity and rising obesity rates. Globally, over 80% of adults with diabetes reside in low- and middle-income countries, underscoring the disproportionate impact of the disease in resource-constrained settings where healthcare access and preventive services may be limited [6][7]. Diabetes is also a major cause of mortality, responsible for an estimated 3.4 million deaths annually, and contributes substantially to healthcare expenditure, with global diabetes-related costs surpassing USD 1 trillion in recent years.

In the Indian context, the burden of diabetes has grown sharply in the past decade. Recent large-scale epidemiological data indicate that India is now home to one of the world's largest adult populations with diabetes, with approximately 90 million adults aged 20–79 years living with the condition in 2024, ranking second globally only to China [8][9]. This reflects a steep increase from earlier estimates and highlights a rapid rise in prevalence associated with urbanisation, dietary changes, sedentary lifestyles, and demographic transitions. Current projections suggest that by 2050, the number of adults with diabetes in India could increase substantially, emphasizing the need for improved prevention, early diagnosis, and comprehensive care strategies [10][11].



Graphical abstract showing the antidiabetic mechanism of *Schima wallichii* and *Xylosma longifolia*

Pathophysiology and Types of Diabetes Mellitus

Diabetes mellitus encompasses a group of metabolic disorders characterized by impaired carbohydrate, lipid, and protein metabolism. The condition primarily arises due to dysregulation of glucose homeostasis, which may result from insufficient insulin production, impaired insulin sensitivity, or both. Based on etiology and clinical presentation, diabetes is broadly classified into Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM). Type 1 diabetes mellitus, also known as insulin-dependent diabetes mellitus, is characterized by an absolute deficiency of insulin due to autoimmune destruction of pancreatic β-cells. The disease commonly manifests in childhood or adolescence, although adult onset has also been reported. The immune-mediated destruction involves autoreactive T-cells targeting β-cell antigens, including insulin, insulinoma-associated protein 2, zinc transporter 8, and 65 kDa glutamic acid decarboxylase. These autoantibodies often appear years before the onset of clinical symptoms such as polyuria, polydipsia, and unexplained weight loss. In addition to genetic susceptibility, environmental factors such as viral infections, particularly enteroviruses, and early exposure to dietary cow's milk proteins have been implicated in disease development. Patients with T1DM require lifelong insulin therapy, and although there is no definitive cure, emerging strategies such as immune modulation, β-cell replacement, and induction of immune tolerance are being explored [12].

In contrast, Type 2 diabetes mellitus accounts for more than 90% of all diabetes cases worldwide and is characterized by insulin resistance, impaired insulin secretion, or both. The etiology of T2DM is multifactorial, involving genetic predisposition combined with environmental and lifestyle factors such as physical inactivity, unhealthy dietary habits, obesity, and aging. The disease often develops gradually, beginning with a prediabetic state marked by impaired fasting glucose, impaired glucose tolerance, or elevated glycated hemoglobin (HbA1c) levels. Progressive β-cell dysfunction eventually leads to persistent hyperglycemia [13].

Type 2 diabetes is associated with a wide range of complications affecting multiple organ systems. Microvascular complications include neuropathy, nephropathy, and retinopathy, while macrovascular complications encompass cardiovascular diseases such as myocardial infarction and stroke. Additionally, T2DM is linked to chronic liver disease, accelerated arthritis, certain cancers, and increased susceptibility to infections. Chronic low-grade inflammation plays a pivotal role in disease progression, as evidenced by elevated levels of inflammatory biomarkers such as C-reactive protein, interleukin-6, and tumor necrosis factor-α. Current therapeutic options for T2DM include metformin, thiazolidinediones, insulin, α-glucosidase inhibitors, dipeptidyl peptidase-IV inhibitors, and glucokinase activators. However, these therapies are often associated with adverse effects, high cost, and limited long-term compliance.

Gestational diabetes mellitus is another form of glucose intolerance that develops during pregnancy. Although generally asymptomatic and often resolving postpartum, GDM poses significant risks to both mother and fetus. Complications include fetal overgrowth, birth canal injuries, neonatal jaundice, perinatal mortality, and increased rates of cesarean delivery. Women with a history of gestational diabetes are at a substantially higher risk of developing Type 2 diabetes and associated cardiovascular, renal, hepatic, and retinal complications later in life. Early lifestyle interventions, including dietary modification and physical activity before the fifteenth week of gestation, have been shown to significantly reduce the risk of GDM. Insulin and metformin remain the primary pharmacological treatments, while postnatal follow-up and lifestyle management are essential for long-term risk reduction [14].

Role of Traditional Medicine in Diabetes Management

Due to numerous drawbacks of existing antidiabetic drugs, efforts have been shifted towards alternative approaches based on natural medicine and herbal health products. Conventional systems of medicine, developed based on ages of practical experience, are an extensive source of plant-derived antisweet active principles. The usefulness of TMS should be advocated for not only for the conservation of culture but also for global acceptance and mankind as a whole.

Scientific documentation and authentication of indigenous medicinal plants is essential to explore novel treatment options for safer and more effective antidiabetic drugs. Natural products tend to possess multitargeted functional aspects such as antioxidant, antiinflammatory, insulin-sensitizing and enzymatic inhibitory etc., which prove to be especially beneficial for complex metabolic disorders like diabetes. A global review reported 2004 medicinal plant species belonging to 197 families have been used traditionally for diabetes in 92 countries. The most commonly cited species were those that were experimentally validated antidiabetic activity and a variety of bioactive molecules. The research also offers the first complete anthology of ethnomedicinal plants that possess antidiabetic effect, demonstrating its significance for the discovery of new drugs [15].

A related work reports the antidiabetic activity of aqueous extracts of Tamarindus indica and Momordica charantia seeds in adipocytes through a decrease in glucose concentrations, the recovery of lipid profiles, modifications to oxidative stress and inflammatory markers, and normalization of activities exhibited by a metabolic enzyme. Saroglitazar also restores TET gene regulation and adds to the normalization of the metabolic pathway, emphasizing that plant-based therapeutics offer promising avenues for the management of T2DM [16]. Other studies reported that alcoholic leaf extract of Aegle marmelos also showed strong cytocompatibility with potent antioxidant activity, strong inhibition against α-amylase and AG (α-glucosidase), downregulation of glucose-induced stress, and upregulaltion of glucose uptake in HepG2 cells. Such effects of AM are mediated by bioactive phytoconstituents that further corroborate its therapeutic potential as antidiabetic and anti-metabolic disorder [17].

Northeastern region of India is known to be one of the biodiversity hotspots in the world with a large number of indigenous communities depended primarily on traditional medicine for their healthcare needs. As part of a broader investigation into possible antidiabetic medicinal plants, in-depth ethnobotanical surveys have been carried out with individual traditional practitioners known to be treating diabetes. Some of the commonly used medicinal plants for controlling blood glucose level and its complications have been reported by traditional practitioners known as Maiba and Maibi [18].

Diabetes mellitus is a condition caused by inadequate insulin or insulin resistance, in which chronic hyperglycemia develops. Drawbacks of traditional treatments have led to increased attention on plant-based phytochemicals, which exert antidiabetic effects via their antioxidant potential, enzyme inhibition and insulin-modifying properties. A number of other herbs are found to have positive experimental results but more clinical validations will be needed before being safely and effectively implemented for treatment. Several documented evidence has focused on antidiabetic role of polyherbal drugs, however, due to their combinatorial style effects diabetic complications mainly insulin secretion, sensitivity glucose homeostasis and oxidative stress and inflammatory pathways leading to its efficacy in managing diabetes. Experimental evidence demonstrates their effectiveness, which makes them promising adjuncts to standard diabetes care as they are also inexpensive, and holistic approaches in the management of diabetes that should be further studied [19]. Due to the increasing worldwide popularity of ethnomedicine, and also to progress in pharmacognosy, phytochemistry and molecular biology, there is now solid scientific background on the systematic verification of these traditional remedies [20]. Hence the present review advocates for pharmacognostic standardization and biological screening of a number of medicinal plants to narrow down the gap between our traditional wisdom and modern evidence based medicine in management of diabetes [21].

Table 1. Role of Traditional Medicine in Diabetes Management

Traditional Medicine/System	Observed Effects	Plants / Compounds	Evidence Citation
Ayurveda	Improves insulin sensitivity, enhances β-cell function, modulates glucose and lipid metabolism	*Gymnema sylvestre*, *Momordica charantia*, *Trigonella foenum-graecum*	[22]

Folk / Ethnomedicinal Practices (NE India)	Postprandial glucose reduction, antioxidant activity, anti-inflammatory effects	*Schima wallichii*, *Xylosma longifolia*, *Aegle marmelos*	[23]
Traditional Chinese Medicine (TCM)	Inhibits carbohydrate-metabolizing enzymes, enhances peripheral glucose uptake	*Coptis chinensis*, *Bauhinia variegata*	[24]
Herbal Polyherbal Formulations	Synergistic effect, improves insulin secretion, reduces oxidative stress	*Syzygium cumini*, *Allium sativum*, *Catharanthus roseus*	[25]
Complementary / Integrative Approaches	Combines diet, lifestyle, and herbal therapy to improve glycemic control	Various plant-based dietary interventions	[26]

Ethnomedicinal Importance of Medicinal Plants in Northeast India

North-East India is known to be the richest biodiversity hotspot of the world which witnesses an incomparable fusion of outstanding biological diversity and culturally rich ethnic background. The area has eight states: Assam, Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Tripura and Sikkim- with over 200 different indigenous ethnic communities residing in it. These societies have their own assigned traditional knowledge systems, mostly depending upon medicinal plants for primary health care, especially in rural and remote regions where the accessibility to modern medical centers is still restricted.

Ethnomedicine is an integral part of their routines of the tribal and rural people in Northeast India. Indigenous medicine is mostly practiced on the basis of knowledge tranfered through oral history from generation to generation. Indigenous healers known as Maiba, Maibi, Ojha and Vaidya are the mainstay in diagnosis and treatment of diseases. Medicinal plants are used as monoherapies or polypharmaceuticals for the treatment of various diseases such as metabolic disorders, infectious, inflammatory, gastrointestinal and reproductive system diseases. Diabetes mellitus is one of the major public health problems and use of plants that have traditional hypoglycaemic property has increased as it remains widely used in many rural areas.

In the area this extraordinary ethnobotanic diversity is evidenced by numerous studies in more than one state. [28] Ethnobotanical studies conducted in Assam have documented the use of 149 medicinal plant species for indigenous healthcare practice, which underscores the great dependence on this traditional mode of healing for primary health care management and treatment of metabolic disorders particularly. Likewise, in a wide survey carried out in Mizoram, more than 200 species of medicinal plants had been collected and used traditionally for diabetes and cancer treatment and revealing the unexploited phamacological benefit of these flora [29]. A more comprehensive regional assessment also listed several native plants used in antidiabetic treatment, and reflected the value and scientific interest of these traditional treatments.

Commonly prescribed medicinal plants used in Northeast India for controlling diabetes are Syzygium cumini, Momordica charantia, Gymnema sylvestre, Aegle marmelos, Tinospora cordifolia and Azadirachta indica. The plants are commonly used in the form of decoctions, infusions, powders or fresh extracts including leaves, bark, root, seed and fruit. Selection of the parts plant for use and methods for preparation was based on a long history of empirical knowledge regarding effectiveness, safety and dosages through generations in traditional practices.

The amazing ecological gradient of Northeast India that includes tropical rainforests to subtropical and alpine, is home to a unique diversity level of medicinal plants. The environmental diversity, together with strict ethnocultural systems, makes the region an important pool of bioactive phytodiversity. It has recognized that some of the plants used by indigenous people have shown pharmacological activities in experimental and preclinical studies such as anti-oxidant, anti-inflammatory, insulin sensitizer, and carbohydrate-metabolizing enzyme inhibition which are also relevant to diabetes treatment [27]. Such results provide scientific evidence for folkloric systems of medicine and showed the potential application in modern drug discovery. However, ethnomedicine of Northeast India is at risk due to rapid urbanization, habitat destruction, and cultural disintegration besides loss of interest among next generation. There is thus an urgent need for the systematic archiving, conservation and validation (for natural products with therapeutic potential) of this traditional knowledge in order to ensure its sustainable exploitation. Pharmacognostic standardization, phytochemical, and biological evaluation of ethnomedicines are necessary for their conversion into evidence-based phytomedicines. Recent-years rising attention and interest across the globe to natural and plant medicines evoke scientific renaissance on traditional ethnomedical practices of Northeast India. Combining traditional indigenous knowledge with modern scientific methods holds great promise to produce safe, efficacious and culturally appropriate treatments for chronic conditions such as diabetes. Thus, medicinal plants of Northeast India have valuable ethnomedicinal significance in not only the traditional healthcare systems but also their prospects are significant for future-trend pharmaceutical and nutraceutical [28][29].

Botanical Description and Distribution

Schima wallichii (DC.) Korth. (Family: Theaceae)

Schima wallichii (DC.) Korth., commonly called as needlewood is a big evergreen tree of family Theaceae. It is native to subtropical and tropical regions ranging from Northeast India to the Eastern Himalaya and as far spread as Bhutan, South China (*Agelifer caprai*), upland Southeast Asia, including Myanmar. It is most often found in mixed evergreen forest and grows to an elevation of 2500 m. Ethnomedicinal significance of Schima wallichii Hook.f & Thoms A review *Schima wallichii* has tremendous ethnomedicinal value among the local and rural inhabitants of Northeast India. In traditional medicine, the plant (especially the bark and leaves) is used for its medicinal properties. Ethnomedicine data indicate that they use it to treat-diabetes, inflammation & infection, thus reflecting its potential therapeutic value in local health-care [3,30]. As *S. wallichii* is still in use of folk medicine, there is a potential for natural products to be used as medicine in industry and thus the demand for systematic pharmacological studies about this plant is increasing although more researches are needed on their phytochemical activity.

Xylosma longifolia (Family: Salicaceae)

Xylosma longifolia Clos. is a medium-sized evergreen shrub or small tree in the family Salicaceae. The leaves are simple and arranged alternately along the stem with toothed margins. It is widespread throughout bump and moist tropical lowland forests, occurring naturally as an understory shrub. The plant is widely distributed throughout South and Southeast Asia, ranging from the East Himalayan region to Nepal, Myanmar, Thailand, Vietnam, Laos and Southern China. X. longifolia is distributed all over Northeast India, especially in Assam, Arunachal Pradesh, Manipur, Meghalaya and Tripura. This species has many common names in different areas, indicating its nomenclatural recognition and ancient relationship with native populations [31]. Ethnomedicinal significance of *Xylosma longifolia Roxb.* among the ethnic communities of North East India. Different parts of the plant, especially leaves and bark, have been used by traditional healers for treatment of various diseases. Its use is recorded in ethnomedicine for the treatment of diabetes, dysentery and febrile conditions evidently indicating its potentiality to control metabolic disorders and such disorders [32]. The ongoing exploitation of this plant in traditional medicine highlights the medicinal value and paves the way for scientific investigations to substantiate its pharmacological properties.

Pharmacognostic Standardization

Macroscopic and Microscopic Evaluation

Herbs can be considered one of the earliest legacy systems from which ethnobotanical and archaeological data evidence herbal medicine use for nearly 60,000 years. Regular use of herbal medicines has persisted in the global practice and is still considered as important part of traditional medicine in some developing countries where modern pharmacological industry is not developed [33]. It was estimated that traditional medicine is the main source of health care for as much as 80% of the continuous population in many developing countries around the world. Among traditional systems of medicine in India, Ayurveda, Siddha and Unani have a long tradition and play key roles in providing health care to the masses apart from socio-cultural and the economic importance.

Quality, safety and efficacy are of the essence in assuring herbal medicines, although these products have been widely employed; they rely heavily on identification and standardization of raw plant materials. Absence of systematic quality assurance results in contamination, adulteration, substitution and variation in therapeutic outcomes which seriously complicate the global utilization and commercialization sustainability of herbal products. That is why pharmacognostic standardization has taken a new dimension with the evolution of herbal drugs. Preliminary screening of organic extracts of aerial parts were found to be possessed antimicrobial activity against all tested human pathogens. This examination is based on macroscopic characters: morphological aspects that include leaf shape, size, venation pattern, bark texture and its surface characters, as well as organoleptic properties such as color, odor, taste and touch. These characters are the chief parameters at the time of the crude drug evaluation. Microscopic examination also reinforces plant authentication because internal structures are often specific to species. Developed features distinguishing taxa, such as the arrangement of epidermal cells, stomatal type and index, trichome type and distribution, number of vein islets and vein termination numbers, all combined with vascular tissue organization (among others), are constantly used for creation of specific diagnostic markers [34]. Cross sections of plant organs supply further information of distinctive features which distinguish actual plant materials from allied species or substitutes. Recent pharmacognostic investigations preferentially combine macroscopic, microscopic, anatomical and organoleptic examinations in order to develop an extensive set of baseline standards for medicinal plant materials. These systematic evaluations are important to guarantee the identity, quality, purity and consistency of herbal drugs and provide a basis for further phytochemical, pharmacological and clinical studies [35].

Physicochemical Parameters

Physicochemical characters are the basic quality control parameters used for standardization and testing of medicinal plant materials. Normal values including ash, extractive and moisture content and pH are important in quality, purity and standardization of crude drugs. Ash values are important to establish the purity of these drugs and monitoring the adultration as well as substitution. The extractive values are based on the amount of active phytoconstituents that are soluble in different solvents, which indicates type and abundance of bioactive components present. Moisture determination is essential to avoid any microbial proliferation, enzymatic action, and phytoconstituents degradation during storage leading to stability and shelf-life of herbal materials [36]. The pH is a measure related to the assessment of chemical stability and compatibility of plant extracts, especially for formulation preparation. Act together, these parameters will guarantee a batch-to-batch consistency of medicinal plant materials, which was a key component for quality assurance and safety of the medicinal Nectar obtained from them working in traditional medicine systems as well as employing modern herbal formulations.

Phytochemical Screening and Chromatographic Profiling

Phytochemical screening and chromatographic fingerprinting are used as a scientific tool for the biopotential assessment and qualification of medicinal herbs. The preliminary phyto chemical screening tests of Schima wallichii and Xylosma longifolia revealed the presence of bioactive compounds like flavonoids, phenolics, tannins, saponins and alkaloids which are responsible for antidiabetic and antioxidant effects. Chromatographic methods mainly HPTLC and HPLC helps to form a characteristic chemical fingerprint for authentication, to check the cases of adulteration as well as in maintaining batch-to-batch consistency [37]. They further provide comparative correlation of phytochemical formulation and biological response, reinforcing the reproducibility, safety and scientific substantiation of herbal formulations [38].

Antidiabetic Potential and Biological Evaluation

In-Vitro Antidiabetic Studies

In vitro assessment of antidiabetic activity of plant extracts is an initial step for studying their mode of action especially for the postprandial hyperglycemia. One of the main targets in those studies are carbohydrate-digestive enzymes α-amylase and α-glucosidase which impact directly on the glucose release and absorbance from dietary starches. Inhibition of these enzymes results in the slowing-down of carbohydrate digestion, decreasing glucose absorption and thus promoting control of postprandial hyperglycaemia, an important therapeutic target for managing diabetes [39]. Systematic studies in multiple species of plants have further supported the legitimacy of this approach, showing that bioactive plant extracts could inhibit these enzymes significantly and dose-dependently. A comprehensive review has indicated that flavonoids and other phytoconstituents are frequently acting as dual inhibitor (α-glucosidase and α-amylase), rendering them promising candidate for the natural antidiabetic drug development. In addition, the traditional use of some other ethnomedicinal plants has been affirmed through the research, indicating that phenolics- and flavonoids-rich extracts manifesting significant α-amylase and α-glucosidase inhibitions also possess antioxidant activity which is relevant to maintain antidiabetic effect. These in vitro findings strongly support the need for further in vivo testing and exploration of mechanism, thereby linking traditional use with scientific evidence and suggesting natural therapeutic approaches to diabetes regulation [40].

In-Vivo Antidiabetic Studies

In-vivo -evaluation in streptozotocin and alloxan induced diabetic rats is now considered as a golden standard for the preclinical assignment of anti diabetic potential of plant extracts. These models recapitulate critical pathophysiologic aspects of human diabetes, such as β-cell destruction, glucose intolerance and dyslipidemia, with practical applicability to drug screening [41]. Several investigations indicated that fasting blood glucose significantly decreased in diabetic rats after oral administration of herbal extracts. For instance, ethanolic and water extracts of different medicinal plants exhibited significant antihyperglycemic activity in the STZ-mouse model of diabetes that was similar to standard hypoglycemic drugs. These extracts also appear to alleviate hyperlipidemia by reducing total cholesterol, triglycerides, LDL and VLDL with increasing HDL showing improved metabolic homeostasis. In addition, plant treatments often improve antioxidant defence by elevating activities of enzymes including superoxide dismutase and catalase and reducing oxidative stress markers the levels of which are importantly involved in diabetes development and its complications [42]. Histological studies in both of these research show regeneration or preservation of β-cell architecture after treatment, indicating the restorative potential of phytoconstituents. These in vivo results support the ethnobotanical use of medicinal plants and mechanism-based evidence for glucose regulation, insulin sensitization and lipid metabolism. Altogether, the findings highlight the pharmacological activities of plant extracts in diabetes treatment as well as the need for additional dose optimization, safety profiling and translation research [43].

Antidiabetic Mechanism of Action

The hypoglycaemic actions of medicinal plants are attributed to a combination of related biochemical and molecular pathways, which work together to enhance glucose homeostasis. One of these key mechanisms is the protection of pancreatic β-cell mediated by antioxidants which are obtained through scavenging of reactive oxygen species (ROS), the reduction of oxidative stress as well as maintaining structural and functional integrity of β-cells, where flavonoids, phenolic compounds in plants phytochemicals acts. High oxidative stress is one of the mechanisms involved in β-cell dysfunction and apoptotic destruction; however phytochemical antioxidants potentiate the body's endogenous antioxidant systems like SOD and CAT to protect against such damage and facilitating insulin production [44]. Furthermore, a number of plant extracts increase peripheral glucose utilization by increasing the expression of glucose transporter (e.g., GLUT-4). The several mechanisms whereby some plant extracts induce enhanced peripheral glucose uptake probably via increased peripheral uptake include up-regulating the gene or protein expression of glucose transporters and activating signal pathways through AMPK to PPARγ, thereby improving insulin sensitivity in skeletal muscle. Also, one of the significant approach is regulation of carbohydrate-metabolizing enzymes, where bioactive compounds inhibit hydrolytic digestive enzymes such as α-amylase and α-glucosidase that leads to retardation in assimilation of carbohydrates and thereby, reduction in postprandial hyperglycemia. These phytochemicals may also modulate hepatic gluconeogenesis and lipolysis, to exert a systemic metabolic control. Overall, these mechanisms demonstrate a multi-targeting mode of action that considers the beneficial effects of medicinal plants in traditional diabetes treatment and emphasizes their potential use as new antidiabetic drugs [45].

Table 2. Antidiabetic Mechanisms and Evidence for *Schima wallichii* and *Xylosma longifolia*

Mechanism	Observed Effects	Evidence
Antioxidant-mediated β-cell Protection	Protection against oxidative stress; preservation of β-cell integrity; enhancement of endogenous antioxidant enzyme activity	Natural flavonoids and phenolics improve oxidative balance and protect β-cells, aiding insulin secretion *in vitro/in vivo* [41][46].
α-Amylase and α-Glucosidase Inhibition	Slows carbohydrate digestion; reduces postprandial glucose spikes	Phytochemical extracts show significant enzyme inhibition linked to antidiabetic activity [42][46].
Enhanced Peripheral Glucose Uptake	Upregulates GLUT transporters; increases insulin sensitivity in muscle/adipose tissue	Bioactive plant compounds modulate AMPK and insulin signaling, improving glucose uptake [43][46].
Lipid Metabolism Regulation	Improves serum lipid profiles; reduces LDL and triglycerides; increases HDL	Herb extracts improve lipid parameters in STZ/alloxan diabetic models (*in vivo*) [44][46].
Safety/Toxicological Indicators	Favorable acute safety profile; need for subchronic/chronic studies	Preliminary toxicity data support low acute toxicity; detailed chronic profiling needed [41][45][46].

Safety and Toxicological Considerations

A detailed knowledge of safety and toxicological profiles is necessary to design medicinal plant extracts for their use in the clinic. Conventional poisonous species such as *Schima wallichii* and *Xylosma longifolia* have ethomedicinal safety but systematic scientific process are required to validate that statement [47]. Some novel preclinical studies demonstrate new evidence of safety of *S. wallichii*. In a 28 days sub-acute toxicity study in Wistar rats, the methanolic leaf extract showed no mortality and any major adverse clinical signs at an oral dose of 800 mg/kg body weight as such indicating high safety (No observed adverse effect level: NOAEL). These results indicate a good safety profile at doses applicable for therapeutic investigation but few long-term and chronic exposure studies are available [48]. In spite of this, a more general toxicological literature suggests that not all medicinal plants are safe per se, because many botanicals contain bioactive compounds with adverse effects at high or chronic consumptions. An important recent review on preclinical safety of herbal medicines emphasized the significance of thorough toxicological evaluation comprising acute, sub-acute, and chronic toxicity studies, and toxicokinetic profiling for a better understanding of safety and translational implication for human application. Such studies are crucial, as differences in plant species, extraction process and bioactive compound concentrations may greatly affect toxicity profiles. Thus, although available data suggest that S. wallichii is relatively safe, additional subchronic toxicity/genotoxicity/long-term safety testing must be characterized for both *Schima wallichii* and *Xylosma longifolia* to safely integrate them into evidence-based therapeutics [49].

Conclusion

Schima wallichii and *Xylosma longifolia* are ethnomedicinally important medicinal plants of the indigenous communities of Northeast India, having huge potential in diabetes treatment. Pharmacognostical studies such as macroscopy, microscopy, physicochemical standards and TLC profiling are established for the standardization that is playing a major role in verity of plant materials which will ensure same quality, purity and assure good efficacy. In vitro, it shows a pronounced inhibition of blood glucose regulating enzymes like α-amylase and α-glucosidase indicating its role in controlling postprandial hyperglycemia. Their therapeutic potential has been confirmed in different in vivo models, with fasting blood glucose lowering, lipid profile improvement, increased insulin sensitivity and β cell function recovery. Insights into the mechanisms involved suggest that anti-diabetic effects are mediated by antioxidant-direct β cell protection, facilitation of glucose transporters, increased peripheral glucose uptake and regulation of liver and gut carbohydrate metabolism. Acute toxicity assays indicate a good safety profile, but complete sub-chronic and chronic toxicity assessments are needed. Cumulatively, the findings provide support for therapeutic potential of S. wallichii and X. longifolia as multi-targeted antidiabetic agents. It should have the aim to focus on isolation of bioactive compounds, standardizing doses, evaluating long-term safety and efficacy, with clinical trials translating these findings into evidence-based plant-derived phytopharmaceuticals for diabetes management as a safe effective culturally relevant alternative or adjunct to current therapies

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