Assessment of the Pharmacognostical, Phytochemicals and Antidiabetic properties of the flowers of *Acacia nilotica* Linn and *Acacia leucophloea* Willd

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in

Pharmacy
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By

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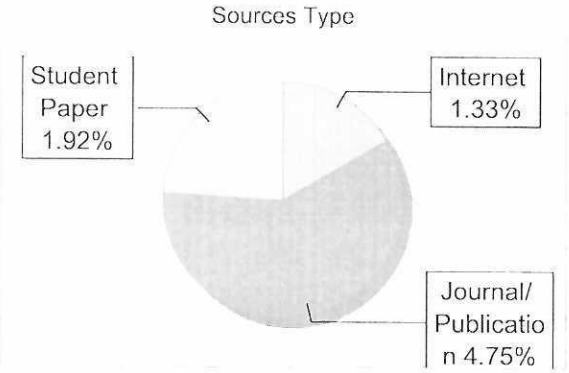
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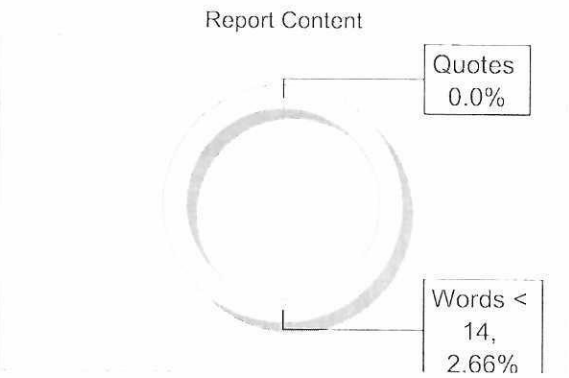
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LIST OF ABBREVIATIONS

Abbreviations	Indication
Acacia leucophloea	AL
Acacia nilotica	AN
Hydro Alchoholic Extact	HAE
g	Gram
mol	Molecular weight
w/v	Weight by volume
w/w	Weight by weight
mm	Millimeter
°C	Degree centigrade
M.p.	Melting point
h	Hour/s
ml	Mili litre
pH	Negative Logarithm of hydrogen ion concentration
min	Minute/s
%	Percentage
nm	Nanometer
ml	Mili litre
µg	Microgram
cm	Centimeter
mg	Milligram
w/v	Weight by volume
q.s	Quantity sufficient
rpm	Revolution per minute

TEM	Triethanolamine
MP	Methylparaben
PP	Propylparaben
PVP	Polyvinylpyrrolidone
$NaBH_4$	Sodium borohydride
$AgNO_3$	Silver nitrate
H_2SO_4	Sulfhuric acid
NaOH	Sodium hydoxide
HCl	Hydro chloric acid
DMSO	Dimethyl sulphoxide
MIC	Minimum inhibitory concentration
FT-IR	Fourier Transform Infrared
SEM	Scanning electron microscope
EDS	Energy dispersive spectrometer
XRD	X-ray Diffraction
Uv	Ultra-violet
SI. No.	Serial Number
ICH	International conference onharmonization
RH	Routh-Hurwitz
SD	Standard deviation
CDR	Cumulative percentage drug release

Abstract

The present study was designed to investigate the Pharmacognostical, phytochemical, pharmaceutical, and pharmacological potential of AN and AL for the development of a standardized herbal tablet formulation intended for the management of DM. Pharmacognostical evaluation of the flowers, including macroscopic, microscopic, and powder microscopic analyses, confirmed the identity, purity, and authenticity of the selected plant materials. Physicochemical parameters such as ash values, extractive values, and moisture content were found to be within acceptable limits, indicating good quality and suitability for further processing.

Preliminary phytochemical screening revealed the presence of bioactive constituents such as flavonoids, phenolic compounds, tannins, saponins, and triterpenoids. Quantitative estimation demonstrated significant levels of total phenolic and flavonoid contents, suggesting strong antioxidant potential. Chromatographic profiling using Thin Layer Chromatography (TLC), High Performance Thin Layer Chromatography (HPTLC), and High-Performance Liquid Chromatography (HPLC) established characteristic fingerprint profiles and confirmed the presence of marker compounds such as quercetin and lupeol.

The hydroalcoholic extracts were successfully formulated into herbal tablets using the direct compression method with suitable excipients. Pre-compression parameters indicated good flow properties, while post-compression evaluation showed that the tablets complied with pharmacopeial standards for weight variation, hardness, friability, and disintegration time. Among the formulations, batch F4 exhibited optimal performance.

Pharmacological evaluation demonstrated significant antidiabetic activity. In vitro studies showed concentration-dependent inhibition of α-amylase and α-glucosidase enzymes, while in vivo studies revealed a significant reduction in blood glucose levels and improved lipid profile in treated animals. Histopathological studies further confirmed the protective effects on pancreatic and other vital tissues.

In conclusion, the study establishes that standardized herbal tablets formulated from AN and AL possess promising antidiabetic activity and may serve as potential natural therapeutic agents for the management of DM.

INTRODUCTION

1. Introduction

1.1. Overview of Diabetes Mellitus

Persistent hyperglycaemia brought on by deficiencies in insulin production, action, or both characterizes DM , a chronic metabolic disease. It is a complex illness linked to abnormalities in the metabolism of proteins, fats, and carbohydrates. Diabetes is one of the main causes of morbidity and death in the world because chronic hyperglycemia in the disease causes long-term harm, malfunction, and failure of many organs, including the eyes, kidneys, nerves, heart, and blood vessels [1,2].

The body uses glucose as its primary energy source, and insulin, a peptide hormone released by pancreatic β-cells, controls its metabolism. Insulin inhibits the synthesis of glucose in the liver and promotes the absorption of glucose into peripheral tissues including skeletal muscle and adipose tissue. Elevated blood glucose levels in DM are caused by decreased insulin production, impaired insulin action, or both. Chronic diabetes problems are exacerbated by persistent hyperglycemia, which causes oxidative stress, inflammatory responses, and endothelial abnormalities [1,3].

The two most prevalent forms of DM are Type 1 DM [T1DM] and Type 2 DM [T2DM]. Absolute insulin insufficiency results from the autoimmune death of pancreatic β-cells in type 1 DM. It usually affects kids and teenagers and necessitate lifelong insulin treatment. On the other hand, insulin resistance with a score and relative insulin shortage are the hallmarks of Type 2 DM, which makes up 90–95% of all instances of the disease. Obesity, sedentary lifestyle, age, genetic susceptibility, and poor eating habits are major risk factors for Type 2 diabetes [4,5].

Other types of diabetes include secondary diabetes, which is brought on by endocrine abnormalities, pancreatic illnesses, infections, or the use of certain drugs, and gestational DM [GDM], which develops during pregnancy and raises the chance of developing Type 2 diabetes in the future. Laboratory tests including the oral glucose tolerance test [OGTT], fasting plasma glucose [FPG], and glycated hemoglobin

[HbA1c] values are used to diagnose diabetes. To avoid problems and enhance patient outcomes, early diagnosis and ongoing monitoring are crucial [6,7].

Polyuria, polydipsia, polyphagia, unexplained weight loss, exhaustion, hazy vision, and delayed wound healing are among the clinical signs of DM. Diabetes may cause immediate complications including hyperosmolar hyperglycemia and diabetic ketoacidosis if treatment is not received. Microvascular issues like diabetic retinopathy, nephropathy, and neuropathy, as well as macrovascular issues like peripheral vascular disease, coronary artery disease, and stroke, are examples of long-term consequences [8,9].

Lifestyle changes, medication treatment, and ongoing blood glucose monitoring are all part of managing DM. A good diet, consistent exercise, and weight control are all crucial aspects of managing diabetes. Insulin treatment and oral hypoglycemic medications are examples of pharmacological therapies. Conventional therapies, however, could have negative side effects, be expensive, and have low patient compliance. Because of their potential effectiveness and safety, studies on medicinal plants and herbal preparations have drawn more interest as alternative treatment methods [10–12].

The prevalence of diabetes is still rising alarmingly worldwide, especially in underdeveloped nations. The incidence of diabetes is predicted to rise dramatically over the next several decades, according to current epidemiological research, underscoring the need for efficient preventive and control techniques. Research on plant-based antidiabetic medicines has accelerated, offering significant prospects for developing new therapeutic agents with enhanced safety profiles [13–15].

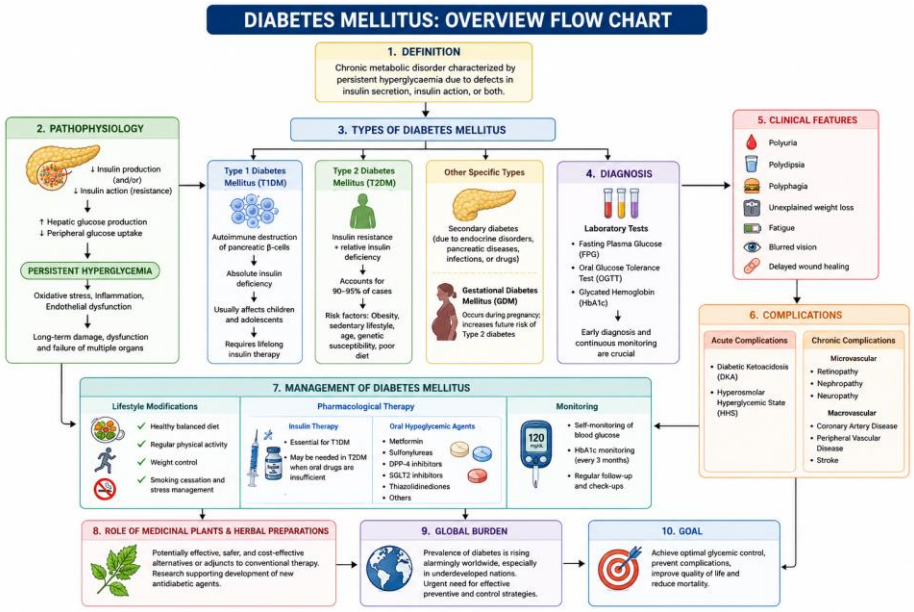


Figure 1 Flow chart overview of Diabetes

1.2. Global and Indian Scenario of Diabetes

One of the biggest worldwide public health issues of the twenty-first century is DM. Urbanization, sedentary lifestyles, aging populations, and poor eating habits have all contributed to the sharp rise in diabetes incidence in recent decades. Recent projections from throughout the globe indicate that 589 million persons between the ages of 20 and 79 had diabetes in 2024, accounting for about 11% of all adults globally. By 2050, this figure is expected to climb to over 853 million, suggesting a significant rise in the burden of illness worldwide [16,17].

Diabetes is becoming more and more common worldwide, especially in low- and middle-income nations where population expansion and fast lifestyle changes greatly increase the disease's incidence. According to reports, over 80% of people with diabetes live in low- and middle-income nations, where access to medical facilities and preventative programs may be restricted. Globally, diabetes-related comorbidities such neuropathy, blindness, renal failure, and cardiovascular disease greatly increase mortality and disability [17, 18].

India is one of the nations with the highest number of diabetics worldwide and one of the most seriously impacted by the disease. India has the second-highest number of individuals with diabetes in the world, with an estimated 89–90 million afflicted in 2024, according to latest epidemiological statistics. It is estimated that 10–11% of

individuals in India have diabetes, which has been steadily rising in recent years [19, 20].

Numerous causes, including urbanization, dietary changes, genetic vulnerability, obesity, and decreased physical activity, are responsible for the sharp increase in diabetes incidence in India. Due to sedentary lifestyles and greater intake of processed foods, prevalence rates are much higher in urban populations than in rural ones. But according to recent research, modernization and socioeconomic growth are also contributing to an increase in the incidence of diabetes in rural regions [21].

The high percentage of undetected diabetes patients in India is another serious issue. An estimated 40–45% of people with diabetes go untreated, which raises the risk of complications such diabetic nephropathy, neuropathy, retinopathy, and cardiovascular illnesses. A growing population at risk of developing diabetes in the future is also indicated by the rising incidence of prediabetes diseases including impaired glucose tolerance and impaired fasting glucose [20,22].

Diabetes has a significant financial cost both nationally and internationally. Expenses for medication, hospital stays, routine monitoring, and the treatment of complications are all included in the costs of managing diabetes. Growing diabetes-related healthcare costs present serious problems for healthcare systems, especially in emerging nations like India. As a result, creating affordable preventative and therapeutic methods continues to be a top goal [23].

The increasing prevalence of diabetes both nationally and internationally emphasizes the critical need for better treatment and prevention strategies. Due to their potential therapeutic advantages, cost, and safety, research on medicinal plants and herbal mixtures has drawn more interest in recent years. Promising solutions for long-term diabetes care may be offered by scientific confirmation of plant-based antidiabetic medicines [24].

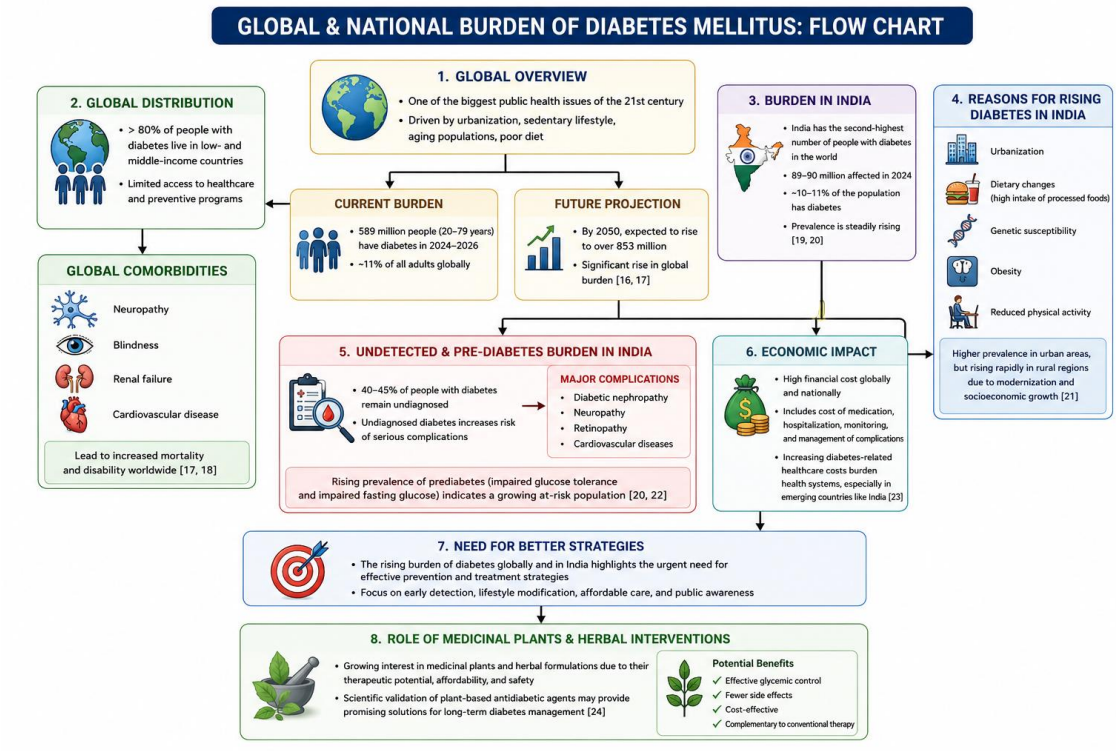


Figure 2 Global & National Burden of diabetes

1.3. Limitations of Current Antidiabetic Therapy

In order to keep blood glucose levels within normal physiological ranges, DM is mostly managed with pharmaceutical treatment and lifestyle changes. Insulin preparations and several classes of oral hypoglycemic medications, including sulfonylureas, biguanides, thiazolidinediones, dipeptidyl peptidase-4 [DPP-4] inhibitors, sodium-glucose cotransporter-2 [SGLT2] inhibitors, and glucagon-like peptide-1 [GLP-1] receptor agonists, are examples of conventional antidiabetic treatments. These treatments have greatly improved glycemic control and decreased complications connected to diabetes, but they have a number of drawbacks that restrict their long-term efficacy and patient compliance [25,26].

The incidence of side effects is one of the main drawbacks of traditional antidiabetic medications. For example, metformin, a common biguanide, may induce gastrointestinal problems such nausea, vomiting, diarrhea, and stomach pain, whereas sulfonylureas are linked to hypoglycemia and weight gain. Weight gain, fluid retention, and an elevated risk of cardiovascular problems have all been associated with

thiazolidinediones. Similarly, hypoglycemia episodes, lipodystrophy at injection sites, and patient discomfort from repetitive injections are also possible outcomes of long-term insulin treatment [26, 27].

The progressive nature of DM, especially Type 2 diabetes, is another major drawback of traditional treatment. Oral hypoglycemic medications become less effective when pancreatic β-cell activity deteriorates over time. This progressive decline often calls for the switch to insulin therapy or the inclusion of many medications, creating complicated treatment plans. Polypharmacy lowers patient adherence, raises the possibility of drug-drug interactions, and may result in prescription mistakes, particularly in older individuals [28].

Another significant issue is the high cost of contemporary antidiabetic drugs, especially in developing nations like India. Due to their high cost, more recent medication classes like SGLT2 inhibitors and GLP-1 receptor agonists are not as accessible to those with low incomes. Many patients find it challenging to control their diabetes because of the financial burden of long-term medication, monitoring, and complication management, which raises total healthcare costs [29].

Conventional antidiabetic treatments often fail to address the underlying causes of diabetes, such as insulin resistance, oxidative stress, inflammation, and metabolic dysfunction, in addition to being expensive and having negative side effects. Many synthetic medications don't considerably improve pancreatic β-cell regeneration or stop the course of illness; instead, they mainly target blood glucose reduction. Therefore, even with pharmaceutical therapy, individuals may continue to have deteriorating metabolic imbalances [30].

Lifestyle issues and patient compliance are further limitations. Strict adherence to food guidelines, exercise regimens, and medication schedules is necessary for effective diabetic treatment. However, inadequate glycemic control is often the consequence of poor drug adherence brought on by side effects, complicated treatment plans, and ignorance. Furthermore, regular blood glucose checks and repeated insulin injections may make patients less inclined to stick with therapy [31].

Furthermore, despite the availability of treatments, the possibility of long-term consequences is still a serious worry. Many individuals have microvascular and macrovascular consequences, including diabetic neuropathy, nephropathy, retinopathy, and cardiovascular illnesses, even with appropriate glucose control. Among people with

diabetes, these problems dramatically lower quality of life and raise death rates [32].

In light of these constraints, there is increasing interest in investigating alternative medicinal modalities, especially herbal and plant-based medications. Traditional medical systems have made extensive use of medicinal plants because of their accessibility, affordability, and relatively low frequency of adverse effects. Through processes including increasing insulin secretion, boosting insulin sensitivity, blocking enzymes that break down carbohydrates, and lowering oxidative stress, a number of medicines derived from plants have shown promise in treating diabetes. Thus, the development of herbal antidiabetic medicines and their scientific confirmation may provide viable alternatives for efficient diabetes treatment [33].

1.4. Role of Medicinal Plants in Diabetes Management

For generations, people have employed medicinal plants to treat a variety of illnesses, including DM. Plant-based treatments have long been used by traditional medical systems like Ayurveda, Unani, and Traditional Chinese Medicine to regulate blood sugar levels and enhance general metabolic health. Due to their therapeutic potential, affordability, and comparatively lower side effects than synthetic medications, medicinal plants have garnered increasing scientific attention in recent years for the treatment of diabetes [34, 35].

Through a variety of processes, bioactive substances originating from plants, including alkaloids, flavonoids, glycosides, tannins, terpenoids, and phenolic compounds, have shown notable antidiabetic effect. By increasing insulin secretion, increasing insulin sensitivity, promoting peripheral tissue glucose uptake, preventing intestinal glucose absorption, and lowering hepatic glucose synthesis, these substances aid in controlling blood glucose levels. Furthermore, a variety of plant components have antioxidant qualities that shield pancreatic β-cells from oxidative damage and maintain their functional integrity [36, 37].

The antidiabetic potential of a number of medicinal plants has been scientifically assessed in both experimental and clinical investigations. Promising hypoglycemic and antihyperglycemic properties have been shown by plants such Gymnema sylvestre, Momordica charantia, Trigonella foenum-graecum, Azadirachta indica, and Syzygium cumini. These plants work in a variety of ways, such as by inhibiting enzymes that break

down carbohydrates, such α-amylase and α-glucosidase, which slow down the absorption of glucose and lower postprandial hyperglycemia [38, 39].

Targeting many metabolic pathways at once is one of the main benefits of medicinal herbs. Herbal medications include a variety of phytochemicals that have synergistic effects, in contrast to synthetic treatments that often function via a single mechanism. When it comes to treating complicated metabolic diseases like DM, which includes many pathological processes including insulin resistance, inflammation, oxidative stress, and poor glucose metabolism, this multi-targeted strategy is very helpful [40].

Many medicinal plants have preventive benefits against diabetes complications in addition to glycemic control. Antioxidants obtained from plants, for instance, lower oxidative stress and lipid peroxidation, which are important factors in the development of diabetes sequelae such neuropathy, nephropathy, and retinopathy. Herbal extracts' anti-inflammatory and lipid-lowering qualities also help diabetes patients' cardiovascular health [41].

The accessibility and affordability of herbal medications, especially in developing nations like India, is another significant reason in their appeal. Due to restricted access to modern medical facilities, a significant segment of the population receives primary healthcare via traditional medicine. Because herbal formulations have fewer side effects than synthetic medications, they not only save healthcare expenses but also increase patient compliance [42].

The discovery and isolation of bioactive substances with antidiabetic properties have been made possible by recent developments in phytochemical and pharmacological research. The standardization and quality control of herbal medications have been made easier by contemporary analytical techniques such spectroscopic approaches, high-performance liquid chromatography [HPLC], and high-performance thin-layer chromatography [HPTLC]. Additionally, the stability, bioavailability, and therapeutic effectiveness of plant-based medications have been enhanced via formulation development, including tablets, capsules, and nanoparticles [43].

Acacia species are among the many therapeutic plants that have garnered significant interest because of their varied pharmacological characteristics, which include antidiabetic, antioxidant, anti-inflammatory, and antibacterial effects. Acacia species have the potential to be used as natural antidiabetic medicines since they contain flavonoids, tannins, and phenolic chemicals. Therefore, creating standardized herbal

formulations for the treatment of diabetes requires a thorough pharmacognostical, phytochemical, and pharmacological examination of Acacia species [44].

1.5. Overview of Genus Acacia

The genus Acacia is a broad group of shrubs and trees that are extensively dispersed across tropical and subtropical parts of the globe. It is a member of the Fabaceae [Leguminosae] family. There are around 1300 species in the genus, many of which are important economically, ecologically, and medicinally. Acacia species are widely distributed across Africa, Australia, Asia, and the Americas, where they are vital to regional healthcare systems and traditional medicine [45,46].

In terms of taxonomy, the genus Acacia belongs to the Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida, Order Fabales, Family Fabaceae, and Genus Acacia. AN, AL, Acacia catechu, and Acacia arabica are among the many species of Acacia that are extensively spread in India. These species are well-suited to challenging climatic circumstances including dryness and low soil fertility, and they are often found in dry and semi-arid locations [47].

In terms of morphology, Acacia species are usually medium-sized trees or shrubs with little yellow or cream-colored flowers clustered in globular or spike-like inflorescences, bipinnate leaves, and prickly branches. Typically, the fruits are pods or legumes with many seeds. Many Acacia species have therapeutic qualities due to the abundance of tannins and other phenolic chemicals in their bark. In traditional medical practices, Acacia species' flowers, leaves, bark, and pods are often used medicinally [48].

Acacia species are found in many areas of India, especially in arid states like Madhya Pradesh, Gujarat, Rajasthan, and sections of southern India. These plants are renowned for their capacity to adapt to a wide range of environmental circumstances, such as high temperatures and limited water supplies. They are essential parts of agroforestry systems because of their ecological significance, which includes soil stability, nitrogen fixation, and increased soil fertility [49].

Acacia species' varied components have historically been used to cure a variety of illnesses. The leaves and bark are often used to treat inflammatory diseases, wounds, ulcers, diarrhea, and dysentery. Certain species, including Acacia senegal, provide gum that is utilized in medicinal formulations and as a demulcent. Furthermore, because of their hypoglycemic qualities, extracts from Acacia species have long been utilized to

treat metabolic conditions like DM [50].

Acacia species include a variety of bioactive components, such as flavonoids, tannins, alkaloids, glycosides, saponins, terpenoids, and phenolic compounds, according to phytochemical studies. Flavonoids and tannins are especially prevalent among these components and are recognized for their antidiabetic and antioxidant qualities. The ability of Acacia species to treat a variety of illnesses is greatly enhanced by the presence of these phytochemicals [51].

Pharmacological research has shown that extracts from several Acacia species sections contain a variety of biological actions, including hepatoprotective, antidiabetic, antioxidant, anti-inflammatory, antibacterial, and wound-healing properties. Acacia extracts have been shown in experimental investigations to significantly lower blood glucose levels in diabetic animal models. The traditional use of Acacia species in the treatment of diabetes and associated metabolic problems is supported by these results [52,53].

Because of their rich phytochemical profile and documented pharmacological actions, AN and AL have garnered significant study attention among the numerous species of Acacia. These species may have hypoglycemic effects since they are known to contain high concentrations of flavonoids, tannins, and phenolic substances. Thus, the creation of standardized herbal formulations and tablet dosage forms for antidiabetic treatment requires a thorough pharmacognostical, phytochemical, and pharmacological study of these species [54].



A **B**

Figure 3 ***Figure Show*** **A:** ***AN*****, B:** ***Acacia leucopholea***

1.6. Ethnomedicinal Uses of Acacia Species

For ages, traditional medical systems have made substantial use of plants of the genus Acacia. The bark, leaves, flowers, pods, seeds, and gum of Acacia species have been used by several indigenous groups in Asia, Africa, and Australia to cure a variety of illnesses. Because Acacia species are available in a variety of climatic zones and have a rich phytochemical makeup, they are widely used in ethnomedicine [55,56].

AN has been used extensively in traditional Indian medicine, especially Ayurveda and folk medicine, to treat inflammatory, skin, and gastrointestinal ailments. AN bark is often used as an astringent to treat bleeding problems, dysentery, and diarrhea. Because of its antibacterial and wound-healing qualities, decoctions made from the bark and leaves have long been used to treat wounds, ulcers, and infections. The tree's gum is also used to treat respiratory disorders and throat infections [57].

AN's blooms and pods have also long been used to treat metabolic diseases. Preparations produced from powdered flowers or pods are used to manage high blood sugar levels in a number of rural areas. According to these customs, AN may have hypoglycemic effects, which has prompted researchers to look at the plant's potential for treating diabetes [58].

In a same vein, traditional medicine has acknowledged the many medicinal uses of AL. AL bark is often used in decoction form to treat inflammatory disorders, fever, and cough. In some areas, leaf extracts are utilized topically to heal wounds, edema, and skin infections. Preparations derived from this species' roots and bark have also been utilized by traditional healers to treat digestive issues and enhance overall health [59].

AL has long been used to treat diabetes and other metabolic disorders in many regions of India, especially in rural and tribal communities. People with symptoms including increased thirst, frequent urination, and fatigue—all of which are often linked to DM—are given herbal formulations made from the bark or flowers. The potential use of AL as a natural source of antidiabetic compounds is suggested by these ethnomedical practices [60].

Acacia species are often used to treat inflammatory conditions, dental issues, and liver ailments in addition to their significance in managing diabetes. Because of its astringent qualities, bark extracts have long been used as mouthwashes to strengthen teeth and cure gum disease. Powdered bark is applied to wounds in certain traditional systems to encourage healing and stave against infection. These uses demonstrate the wide range

of medicinal potential of Acacia species [61].

Gum exudates from several Acacia species, especially Acacia senegal, have been widely employed in medicinal formulations as stabilizers and demulcents. Gum arabic is used in traditional medicine to alleviate inflammation, enhance digestion, and ease sore throats. Because of its calming qualities, it may be used to treat gastrointestinal distress and respiratory conditions [62].

Modern pharmacological research is based on ethnomedical knowledge of Acacia species, which offers important insights into their therapeutic potential. Experimental studies showing antioxidant, anti-inflammatory, antibacterial, and antidiabetic properties have validated many of the traditional applications of these plants. To confirm their traditional usage and create standardized herbal formulations appropriate for therapeutic applications, thorough pharmacognostical and phytochemical research of Acacia species are crucial [63,64].

1.7. Phytochemical Constituents of Acacia

Acacia plants are known for having a rich and varied phytochemical makeup, which greatly enhances the variety of pharmacological activity they exhibit. Numerous bioactive substances, including flavonoids, tannins, alkaloids, glycosides, terpenoids, phenolic compounds, and saponins, have been found in the bark, leaves, flowers, pods, and seeds of Acacia species. The medicinal potential of Acacia species in the treatment of several disorders, including DM, is attributed to these phytochemicals [65,66].

Phenolic compounds are thought to be the most prevalent phytochemicals found in Acacia species. Numerous Acacia species have been shown to contain phenolic chemicals, including gallic acid, catechin, epicatechin, and ellagic acid. By scavenging free radicals and lowering oxidative stress, these substances have potent antioxidant activity, which is important in the pathophysiology of diabetes and its consequences. Phenolic chemicals' antioxidant capacity protects pancreatic β-cells and increases insulin production [67,68].

Another significant class of phytochemicals that are often present in Acacia species are flavonoids. Various plant parts, including flowers and leaves, have been shown to contain flavonoids such quercetin, kaempferol, rutin, and luteolin. These substances have a variety of pharmacological actions, such as hepatoprotective, anti-inflammatory, and antidiabetic properties. By increasing peripheral tissues' absorption of glucose and

boosting insulin sensitivity, flavonoids help control blood glucose levels. Their function in regulating postprandial hyperglycemia is further supported by their capacity to block enzymes that break down carbohydrates, such as α-amylase and α-glucosidase [69,70]. Acacia species' bark and pods are rich in tannins, which give them their distinctive astringent qualities. Several species, especially AN and AL, have been shown to contain both hydrolyzable and condensed tannins. Tannins contribute to the hypoglycemic effects of plant extracts and have antibacterial, antioxidant, and anti-inflammatory properties. Additionally, the presence of tannins promotes wound healing and offers defense against microbial infections [71].

Certain Acacia species have also been shown to contain alkaloids in addition to phenolics, flavonoids, and tannins. Alkaloids are nitrogen-containing substances with a variety of biological functions, such as antidiabetic, analgesic, and antibacterial properties. Alkaloids contribute to the overall therapeutic effectiveness of Acacia extracts, although being present in comparatively lesser amounts than other phytochemicals [72].

Table 1 Major Phytochemical Constituents Reported in Acacia Species

S. No.	**Phytochemical Class**	**Major Compounds Reported**	**Plant Part**	**Pharmacological Significance**
1	Phenolic Compounds	Gallic acid, Ellagic acid, Catechin	Bark, Flowers, Pods	Antioxidant, Antidiabetic
2	Flavonoids	Quercetin, Kaempferol, Rutin	Leaves, Flowers	Antidiabetic, Anti-inflammatory

3	Tannins	Condensed tannins, Hydrolysable tannins	Bark, Pods	Astringent, Antimicrobial
4	Alkaloids	Simple nitrogenous compounds	Leaves, Bark	Antimicrobial, Hypoglycemic
5	Saponins	Triterpenoid saponins	Leaves, Seeds	Hypolipidemic, Antidiabetic
6	Glycosides	Flavonoid glycosides	Leaves, Flowers	Antioxidant
7	Terpenoids	Lupeol, β-amyrin	Bark, Leaves	Anti-inflammatory
8	Sterols	β-sitosterol	Seeds, Bark	Cholesterol-lowering
9	Carbohydrates	Gum polysaccharides	Gum exudates	Demulcent, Stabilizer
10	Proteins & Amino acids	Various amino acids	Seeds	Nutritional value

Other significant components found in a number of Acacia species include saponins and glycosides. By lowering glucose absorption and enhancing lipid metabolism, these substances are known to have hypoglycemic and hypolipidemic effects. Additionally, saponins increase the permeability of cell membranes, which makes it easier for active

ingredients to be absorbed and increases their bioavailability. Because of these characteristics, saponins are useful ingredients in herbal remedies for metabolic conditions [73].

Table 2 Phytochemicals Identified in Selected Acacia Species

S. No.	Species	Major Phytochemicals Reported	Plant Part Studied
1	*AN*	Tannins, Flavonoids, Phenolics, Saponins	Bark, Leaves, Flowers
2	*AL*	Flavonoids, Alkaloids, Terpenoids	Bark, Flowers
3	*Acacia catechu*	Catechin, Epicatechin	Heartwood
4	*Acacia arabica*	Tannins, Glycosides	Bark
5	*Acacia senegal*	Gum arabic polysaccharides	Gum

Additionally, various parts of Acacia plants have been found to contain terpenoids and sterols like lupeol and β-sitosterol. These substances help the treatment of chronic illnesses and are linked to anti-inflammatory and antioxidant qualities. In tissues impacted by persistent hyperglycemia, terpenoids also help to stabilize cellular membranes and lessen oxidative damage [74].

Table 3 Analytical Techniques Used for Phytochemical Identification

S. No.	Technique	Purpose	Information Obtained
1	TLC	Preliminary screening	Presence of phytochemicals
2	HPTLC	Fingerprinting	Identification of marker compounds
3	HPLC	Quantitative estimation	Concentration of bioactive compounds
4	GC–MS	Compound identification	Molecular structure analysis
5	UV–Visible Spectroscopy	Compound characterization	Absorption maxima
6	FTIR	Functional group identification	Structural information

The precise identification and quantification of bioactive components found in Acacia species has been made possible by contemporary phytochemical investigations using sophisticated analytical techniques like High-Performance Thin-Layer Chromatography [HPTLC], High-Performance Liquid Chromatography [HPLC], and Gas Chromatography–Mass Spectrometry [GC–MS]. These methods are crucial for

setting quality control standards and ensuring herbal compositions are consistent from batch to batch. When creating dependable and repeatable herbal dosage forms, such tablets, standardization of plant extracts based on phytochemical markers is especially crucial [75,76].

Table 4 Bioactive Compounds Responsible for Antidiabetic Activity

S. No.	**Compound**	**Phytochemical Class**	**Reported Activity**
1	Quercetin	Flavonoid	Improves insulin sensitivity
2	Catechin	Phenolic	Antioxidant activity
3	Gallic acid	Phenolic acid	Glucose-lowering
4	Lupeol	Terpenoid	Anti-inflammatory
5	β-sitosterol	Sterol	Hypolipidemic

Overall, Acacia species' historic usage in the treatment of diabetes and other metabolic diseases is supported by the presence of a variety of phytochemical ingredients. Finding the active ingredients causing antidiabetic action requires a thorough phytochemical investigation hydroalcoholic extracts, especially from the flowers of certain Acacia species as AN and AL. These studies provide a solid foundation for the development and assessment of standardized herbal pills meant to effectively control diabetes [77].

1.8. Pharmacological Activities of Acacia Species

The many pharmacological characteristics of species of the genus Acacia have been extensively studied. Because they include bioactive phytochemicals including flavonoids, tannins, phenolic compounds, alkaloids, and terpenoids, a variety of plant parts, including bark, leaves, flowers, pods, and seeds, have shown notable biological activity. The historic usage of Acacia species in the treatment of various ailments is supported by these chemicals, which have a variety of therapeutic benefits [78,79].

Antidiabetic activity has drawn a lot of interest among the several pharmacological actions that have been described. Both in-vitro and in-vivo experimental methods have been used to assess extracts from several Acacia species. AN and AL hydroalcoholic and aqueous extracts have been shown to dramatically lower blood glucose levels in animal models of diabetes. Insulin secretion is thought to be stimulated, peripheral glucose absorption is improved, and enzymes that break down carbohydrates, such α-amylase and α-glucosidase, are inhibited [80,81].

Table 5 Antidiabetic Activity of Selected Acacia Species

S. No.	Species	Plant Part	Extract Type	Experimental Model	Reported Activity
1	*AN*	Bark	Hydroalcoholic	STZ-induced diabetic rats	Significant reduction in blood glucose
2	*AL*	Bark	Aqueous	Alloxan-induced diabetic rats	Improved glucose tolerance

Another significant pharmacological characteristic of Acacia species is antioxidant action, in addition to antidiabetic effect. Diabetes and its consequences are mostly caused by oxidative stress. In tests including DPPH, ABTS, and FRAP, Acacia species extracts have shown potent free radical scavenging activity. The presence of phenolic and flavonoid molecules, which aid in neutralizing reactive oxygen species and

shielding cellular structures from oxidative damage, is primarily responsible for the antioxidant capacity [84].

Table 6 Antioxidant Activity of Acacia Species

S. No.	Species	Extract	Method Used	Result
1	*AN*	Methanolic	DPPH assay	Strong radical scavenging activity
2	*AL*	Aqueous	FRAP assay	High antioxidant capacity

The anti-inflammatory properties of Acacia species are another significant pharmacological action. Metabolic diseases like DM are often linked to inflammation. According to experimental research, Acacia species extracts lessen inflammatory reactions by preventing the synthesis of inflammatory mediators including prostaglandins and cytokines. This anti-inflammatory characteristic helps to avoid tissue damage linked to long-term illnesses [85].

Acacia species have also shown strong antibacterial action against a variety of bacterial and fungal diseases. Bark and leaf extracts have been shown to prevent the development of pathogens such Candida albicans, Escherichia coli, and Staphylococcus aureus. Tannins, flavonoids, and alkaloids, which damage microbial cell membranes and prevent enzyme function, are primarily responsible for the antibacterial action [86].

Table 7 Other Pharmacological Activities of Acacia Species

S. No.	Activity	Species	Key Findings
1	Anti-inflammatory	*AN*	Reduced inflammation in animal models
2	Antimicrobial	*AL*	Inhibited bacterial growth

Apart from the aforementioned functions, hepatoprotective and wound-healing qualities have been identified for some Acacia species. Because individuals with diabetes are more likely to have liver malfunction and delayed wound healing, these exercises are very crucial for them. Research has shown that giving Acacia extracts to experimental animals improves tissue regeneration and lessens cellular damage [87].

All things considered, the variety of pharmacological activity shown by Acacia species emphasizes their potential as therapeutic agents in the treatment of diabetes and its consequences. Their usage in herbal formulations, such as tablet dosage forms made from hydroalcoholic extracts of flowers of certain species like AN and AL, is supported by the presence of many bioactive chemicals. In order to create standardized herbal formulations for successful medicinal applications, further pharmacognostical, phytochemical, and pharmacological research is necessary [88].

1.9. Need for Standardisation of Herbal Drugs

Because of their medicinal effectiveness, cultural acceptability, and relatively low side effects, the use of herbal medicines has grown dramatically around the globe. Herbal medications are still extensively utilized in both developed and developing nations, and they are a crucial part of traditional healthcare systems like Ayurveda, Unani, and Siddha. However, correct plant material identification, processing, and formulation are critical to the safety, effectiveness, and quality of herbal medicines. As a result, standardizing herbal medications is thought to be essential to guaranteeing their dependability and therapeutic efficacy [89,90].

The process of achieving uniform quality, purity, and potency of herbal medicines by

using scientific standards and verified analytical methods is known as standardization. Herbal preparations, in contrast to manufactured medications, include complex combinations of phytochemicals, and their medicinal effects might differ according on storage conditions, drying techniques, harvesting time, and geographic region. Standardization is required to preserve homogeneity in herbal products since such changes may result in inconsistent pharmacological action [91,92].

The potential for adulteration and replacement is one of the main issues with herbal medications. The use of the wrong plant species, contamination with foreign components, or faulty processing techniques may all result in adulteration, whether on purpose or accidentally. In addition to potentially endangering consumer safety, such activities may diminish the medicinal effectiveness of herbal medications. In order to identify adulteration and guarantee the authenticity of plant materials, pharmacognostical evaluation—which includes both macroscopic and microscopic identification—is essential [93].

Ash levels, extractive values, moisture content, and drying loss are examples of physicochemical characteristics that are crucial to the standardization of herbal drugs. By detecting the presence of inorganic contaminants, leftover solvents, and moisture levels, these characteristics aid in determining the purity and quality of plant materials. Controlling physicochemical properties during processing and storage is crucial because too much moisture in herbal products might encourage microbial development and shorten shelf life [94,95].

Another crucial component in the development of herbal drugs is phytochemical standardization. The bioactive components found in plant extracts are analyzed both qualitatively and quantitatively. To detect marker molecules and guarantee batch-to-batch consistency, techniques including thin-layer chromatography [TLC], high-performance thin-layer chromatography [HPTLC], high-performance liquid chromatography [HPLC], and spectroscopic approaches are often used. For the purpose of keeping an eye on the quality and therapeutic efficacy of herbal formulations, the selection of suitable marker chemicals is especially crucial [96,97].

Another essential element in standardizing herbal drugs is microbiological assessment. During harvesting, processing, and storage, bacteria, fungus, and other microbes may contaminate herbal materials. Degradation of active ingredients and the creation of hazardous metabolites may result from microbial infection. To guarantee the safety of herbal products, it is thus essential to assess the microbial load and use appropriate

sterilizing and preservation methods [98].

Standardization promotes regulatory compliance and the acceptability of herbal medicines in international markets in addition to quality control. Guidelines for quality control and standardization of herbal medications have been created by international organizations like the World Health Organization [WHO]. Procedures for herbal product identification, authenticity, extraction, formulation, and stability testing are all included in these recommendations. Following these guidelines enhances the legitimacy of herbal remedies and makes it easier for them to be included into contemporary healthcare systems [99].

To guarantee constant treatment performance, thorough pharmacognostical and phytochemical standardization is especially crucial for medicinal plants like AN and AL. When developing formulations and conducting pharmacological assessments, standardized herbal extracts provide dependable results. Standardization guarantees consistent distribution of active ingredients and enhances formulation stability and efficacy when creating tablet dosage forms from hydroalcoholic extracts of Acacia flowers [100].

All things considered, standardizing herbal medications is crucial to guaranteeing their quality, safety, and therapeutic consistency. It facilitates the acceptability of plant-based medications in contemporary pharmacy practice and offers a scientific foundation for the creation of trustworthy herbal formulations. Thus, the development of successful herbal medication delivery systems depends on the implementation of established procedures in the assessment of medicinal plants [101].

1.10. Importance of Herbal Tablet Formulation

Because of their broad acceptability, safety, and therapeutic promise, herbal formulations have drawn a lot of interest in contemporary pharmaceutical research. Because of their simplicity, stability, precise dose, and ease of administration, tablets are among the most popular pharmaceutical preparations among different dosage forms. Herbal extracts are formulated into tablet dosage forms that guarantee accurate administration of bioactive ingredients and improve patient compliance. As a result, creating standardized herbal tablets has emerged as a key tactic for enhancing the medicinal plants' therapeutic efficacy [102,103].

The enhancement of dosing accuracy and uniformity is one of the main benefits of

herbal tablet formulation. The quantity of active ingredients in crude plant materials and traditional decoctions often varies, which may have an impact on therapeutic results. Standardizing the amount of active chemicals and guaranteeing constant pharmacological action are made feasible by turning plant extracts into tablet dosage forms. This is especially crucial for herbal medications used to treat long-term conditions like DM [104].

Additionally, the stability and shelf life of herbal remedies are improved by tablet format. Solid dosage forms, like tablets, provide superior protection against environmental elements including moisture, temperature, and light, whereas liquid herbal medicines are often more vulnerable to microbial contamination and chemical deterioration. The mechanical strength and disintegration characteristics of tablets are enhanced by the addition of appropriate excipients, such as binders, disintegrants, lubricants, and diluents, which guarantees effective drug release and absorption [103,105].

Enhancing patient acceptance and convenience is a key component of herbal tablet composition. Tablets are ideal for widespread distribution and usage in community healthcare settings since they are simple to carry, store, and administer. Furthermore, pills make it possible to cover up the disagreeable taste and smell that are often connected to herbal extracts, which improves patient compliance even further. This benefit is especially useful for creating plant extracts that may have strong natural tastes, such hydroalcoholic extracts of AN and AL [104].

The effectiveness and purity of herbal pills have been significantly enhanced by contemporary pharmaceutical technology. To create tablets with consistent weight, hardness, and dissolve properties, methods including wet granulation, direct compression, and dry granulation are often used. The effective creation of herbal tablets depends heavily on preformulation studies, which include assessments of flow characteristics, compressibility, and excipient compatibility. These investigations guarantee that the final formulation satisfies pharmacopeial requirements for performance and quality [105,106].

Additionally, the creation of tablets containing herbal extracts facilitates the incorporation of traditional medicine into contemporary healthcare systems. Standardized herbal pills promote commercialization and regulatory clearance while offering dependable medicinal results. Tablet dosage forms provide an efficient way to

distribute bioactive components in a regulated and repeatable way for creating antidiabetic formulations from hydroalcoholic extracts of certain Acacia species. Therefore, a crucial stage in converting traditional medical knowledge into pharmaceutical medicines with scientific validation is the formulation of herbal tablets [106,107].

1.11. Rationale of the Study

Both conventional and contemporary healthcare systems continue to rely heavily on medicinal plants as a source of therapeutic substances. Due to their varied pharmacological characteristics and comparatively safer therapeutic profiles when compared to synthetic medications, plant-derived bioactive chemicals have attracted more scientific attention in recent years. Because of their widespread range and therapeutic potential, members of the genus Acacia have garnered significant interest among medicinal plants. AN and AL, in particular, have been utilized extensively in traditional medical systems to treat infections, gastrointestinal diseases, inflammatory illnesses, and metabolic abnormalities [108,109].

AN and AL contain a variety of bioactive components, including flavonoids, tannins, phenolic compounds, saponins, and glycosides, according to recent phytochemical studies. Antioxidant, antibacterial, anti-inflammatory, and wound-healing properties are only a few of the biological activities that these phytoconstituents support [108,109]. However, environmental variables including regional variance, seasonal variations, harvesting circumstances, and post-harvest processing techniques often impact the medicinal efficacy of crude plant materials. Phytochemical composition and therapeutic efficacy may be inconsistent as a consequence of this diversity. Thus, to guarantee consistent quality, safety, and repeatability of herbal medications, standardization of herbal raw materials and formulations is crucial [110].

The poor physicomechanical characteristics of crude herbal powders, such as their uneven particle size distribution, limited flowability, and poor compressibility, are another significant drawback. These features make it difficult to directly formulate herbal ingredients into tablets or other solid dosage forms. The mechanical characteristics, stability, and homogeneity of herbal formulations are greatly enhanced by the use of pharmaceutical formulation methods, such as granulation and the addition

of appropriate excipients [111]. Accurate dosing, increased stability, ease of transportation, and greater patient compliance are just a few benefits of tablet dosage forms. Consequently, a logical and scientifically supported strategy for enhancing therapeutic administration and patient acceptance is the creation of standardized herbal tablets employing extracts of AN and AL [111].

The safety and shelf-life of herbal products are still significantly impacted by microbiological contamination and phytoconstituent degradation during storage, in addition to formulation-related issues. Microbial growth and pharmaceutical activity loss might result from improper storage conditions and excessive moisture content. To guarantee the efficacy and safety of herbal formulations, contemporary pharmaceutical research highlights the significance of performing stability testing, microbiological quality evaluation, and physicochemical characterisation [112]. In order to preserve product integrity throughout distribution and storage, these assessments are crucial.

Additionally, the growing demand for herbal remedies throughout the world calls for the creation of standardized, scientifically proven dosage forms that adhere to legal criteria. When developing herbal therapeutic products, international health organizations have emphasized the need of stability testing, formulation standardization, and quality assurance [113]. Therefore, it makes sense to formulate herbal tablets with standardized extracts of AN and AL in order to increase stability, boost therapeutic consistency, and make large-scale production easier.

The current study aims to standardize raw plant materials, assess their physicochemical and phytochemical properties, and create stable herbal tablet formulations using suitable pharmaceutical techniques in light of the pharmacological significance of AN and AL as well as the drawbacks of traditional herbal preparations. The results of this research should facilitate the incorporation of traditional herbal knowledge into contemporary pharmaceutical practice by helping to design dependable herbal dosage forms with consistent quality, increased stability, and greater therapeutic effectiveness.

AIM AND OBJECTIVES

2. Aim and Objectives

2.1. Aim

The current research uses specific medicinal plant components from AN and AL to create and assess standardized herbal tablet formulations. The rigorous standardisation of raw plant materials, the extraction of bioactive components, and the creation of stable tablet dosage forms with desired physicochemical and pharmaceutical properties are the main objectives of the research. By using contemporary pharmaceutical methodologies and standardized processing processes, the ultimate goal is to improve the therapeutic reliability, stability, and patient acceptance of herbal formulations [114,115].

2.2. Objectives

The current study's goals are to produce and assess herbal tablet formulations made from AN and AL methodically. The particular goals consist of:

Collection and Authentication of Plant Materials: To collect plant materials of AN and AL from suitable geographical sources and authenticate them using standard botanical identification procedures [114].

Preparation of Plant Extracts: To prepare suitable extracts from selected plant parts using appropriate extraction techniques to obtain maximum yield of phytoconstituents [115].

Phytochemical Screening: To perform qualitative phytochemical screening of plant extracts for the identification of major classes of phytoconstituents such as alkaloids, flavonoids, tannins, glycosides, and phenolic compounds [116].

Pre-formulation Studies: To conduct pre-formulation studies, including evaluation of flow properties, particle size distribution, moisture content, and compressibility characteristics of herbal powders [117].

Formulation of Herbal Tablets: To formulate herbal tablets using suitable excipients and pharmaceutical techniques such as wet granulation or direct compression [118].

Evaluation of Tablet Parameters: To evaluate formulated tablets for physicochemical parameters including hardness, friability, weight variation, disintegration time, thickness, and uniformity of content [118].

Stability Studies: To conduct stability studies under controlled environmental conditions to assess the stability and shelf life of the formulated herbal tablets [119].

Quality Standardisation: To establish quality control parameters for the developed herbal tablets in accordance with pharmacopoeial and regulatory guidelines [120].

REVIEW OF LITERATURE

3. Review Of Literature

3.1. Review on DM

Persistent hyperglycaemia brought on by decreased insulin production, insulin resistance, or both is a hallmark of DM [DM], a chronic metabolic disease. Because of its fast-rising prevalence and related problems, it is one of the biggest worldwide public health issues. According to recent epidemiological studies, changes in lifestyle habits, increasing consumption of energy-dense meals, urbanization, and aging populations are the main causes of the significant increase in the worldwide burden of diabetes over the last ten years [121,122]. Diabetes is becoming more common, which is linked to higher healthcare costs and worse quality of life, especially in developing nations where access to sufficient medical resources is still restricted [123].

Type 1 DM [T1DM], type 2 DM [T2DM], gestational DM [GDM], and other particular variants brought on by hereditary or secondary causes are the broad classifications for DM. Absolute insulin insufficiency is the hallmark of type 1 DM, an autoimmune disease marked by immune-mediated death of pancreatic β-cells. Recent investigations have documented its frequency in adults, despite the fact that it typically occurs in infancy and adolescence [124]. On the other hand, 90–95% of cases of diabetes globally are type 2 DM, which is characterized by increasing pancreatic β-cell dysfunction and insulin resistance [125,126].

Complex metabolic abnormalities that affect insulin signaling pathways are part of the pathophysiology of type 2 DM. Reduced glucose absorption and increased hepatic glucose production result from insulin resistance in peripheral tissues such skeletal muscle, adipose tissue, and the liver. These changes lead to metabolic imbalance and persistent hyperglycemia [127]. Numerous metabolic processes, including as oxidative stress mechanisms, inflammatory reactions, and the production of advanced glycation end products, are triggered by chronic hyperglycemia. These mechanisms are thought to have a significant role in the development of long-term diabetes problems and cellular damage [128].

DM is linked to a number of risk factors, both modifiable and non-modifiable. One of the most modifiable risk factors, especially for type 2 diabetes, is still obesity. Insulin sensitivity is eventually compromised by excess adipose tissue, which also leads to systemic inflammation and metabolic hormone dysregulation [129]. Genetic susceptibility, sedentary lifestyles, poor eating habits, hypertension, and dyslipidemia are additional risk factors. Together, these variables raise the risk of metabolic dysfunction and disease development [130].

Depending on the severity and length of the condition, DM may have a variety of clinical symptoms. Polyuria, polydipsia, polyphagia, exhaustion, inexplicable weight loss, and hazy eyesight are typical symptoms. Diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome are two severe consequences that may result from untreated or poorly controlled diabetes. Microvascular conditions like diabetic neuropathy, nephropathy, and retinopathy, as well as macrovascular conditions like cardiovascular disease and stroke, are examples of chronic consequences [131,132].

For early management and the avoidance of complications, an accurate diagnosis of DM is crucial. Glycated hemoglobin [HbA1c] estimate, oral glucose tolerance testing, and fasting plasma glucose measurement are currently used diagnostic criteria. Among them, HbA1c testing is a commonly used biomarker of long-term glycaemic management and has emerged as a crucial diagnostic and monitoring tool for DM [133].

Comprehensive therapy approaches, including as medication intervention, lifestyle modification, and patient education, are used in the management of DM. Dietary control, consistent exercise, and weight control are examples of lifestyle changes that are regarded as important preventative interventions. Oral hypoglycemic medications, insulin therapy, and more recent drug classes that target certain metabolic processes involved in glucose control are examples of pharmacological treatment [134]. However, long-term medication is often linked to negative side effects and decreased patient compliance, highlighting the need of alternate treatment modalities [135].

The use of natural goods and medicinal plants as supplemental therapy for managing diabetes has garnered recent scientific attention. Plant-derived chemicals are interesting candidates for the creation of innovative medicinal formulations since they have shown notable hypoglycemic, antioxidant, and anti-inflammatory qualities. Due to its potential to enhance glycaemic management and reduce side effects, the integration of herbal medications with contemporary pharmaceutical technology has drawn more attention in recent years [136].

The ongoing increase in the incidence of diabetes emphasizes how crucial it is to provide safe, efficient, and reasonably priced treatment plans. New pharmaceutical targets, better disease management, and improved patient outcomes are the goals of ongoing research. Therefore, it is crucial to comprehend the epidemiology, pathophysiology, and clinical characteristics of DM in order to create novel drug delivery methods and efficient treatment strategies, especially those employing herbal medicinal items [137].

3.2. DM Pathophysiology

Persistent hyperglycemia brought on by deficiencies in insulin production, action, or both is the hallmark of DM, a multifactorial metabolic disease. Genetic predisposition, environmental factors, and metabolic dysfunction interact intricately in the pathophysiology of diabetes. Insulin resistance and increasing β-cell malfunction are the main characteristics of type 2 DM, whereas autoimmune death of pancreatic β-cells causes absolute insulin insufficiency in type 1 DM [138,139].

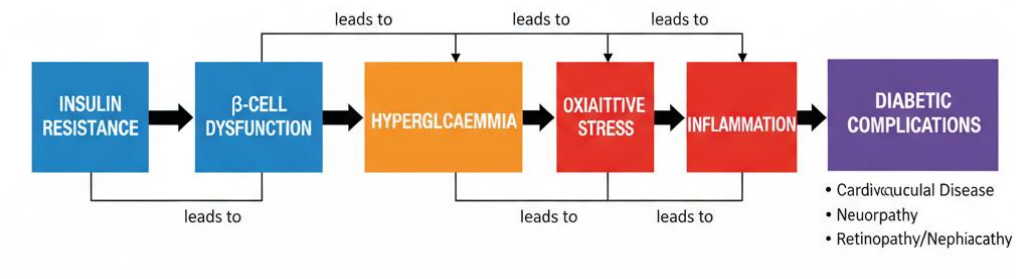


Figure 4 Pathophysiological Mechanisms in DM

3.2.1. Resistance to Insulin

One of the main characteristics of type 2 DM is insulin resistance, which happens when peripheral tissues, including adipose tissue, skeletal muscle, and the liver, do not react well to insulin. Increased hepatic glucose synthesis and decreased muscle tissue glucose absorption are the outcomes of this compromised response, which eventually raises blood glucose levels. The liver is crucial for maintaining glucose homeostasis, and hepatic insulin resistance exacerbates hyperglycemia by increasing gluconeogenesis and glycogenolysis [140,141].

Insulin resistance is also greatly influenced by adipose tissue malfunction. Increased quantities of free fatty acids and pro-inflammatory cytokines, such as interleukin-6 [IL-6] and tumor necrosis factor-α [TNF-α], are released by enlarged adipocytes and disrupt insulin signaling pathways. These inflammatory mediators increase metabolic abnormalities linked to diabetes and reduce insulin receptor function [142].

3.2.2. Dysfunction of β-Cells

When blood glucose levels rise, pancreatic β-cells produce and secrete insulin. Prolonged insulin resistance in type 2 DM increases the strain on β-cells, leading to compensatory hyperinsulinemia in the early stages of the illness. Continuous metabolic stress eventually causes β-cell depletion, decreased insulin production, and β-cell death [143].

The two main causes of β-cell dysfunction are glucotoxicity and lipotoxicity. Insulin production and secretion are hampered by oxidative stress and mitochondrial dysfunction brought on by prolonged exposure to high glucose and fat concentrations. One of the hallmarks of severe DM is this increasing loss of β-cell activity [144].

3.2.3. Oxidative Stress's Function

The pathophysiology of DM and its consequences is significantly influenced by oxidative stress. Reactive oxygen species [ROS] are

produced in excess as a result of hyperglycemia, which damages cells and interferes with insulin signalling. Additionally, ROS buildup causes endothelial dysfunction and activates inflammatory pathways, which exacerbates the vascular problems linked to diabetes [145].

Diabetes often impairs antioxidant defense systems, resulting in an imbalance between antioxidant capacity and oxidant generation. Tissue damage and the development of diabetes consequences such neuropathy, nephropathy, and retinopathy, are accelerated by this imbalance [146].

3.2.4. Mechanisms of Inflammation

It is becoming more well acknowledged that chronic low-grade inflammation plays a significant role in the onset and advancement of DM. Adipose tissue, macrophages, and other immune cells generate inflammatory mediators that disrupt insulin signaling pathways and increase insulin resistance. Cytokine production and metabolic dysfunction are caused by the activation of nuclear factor-kappa B [NF-κB] and other inflammatory transcription factors [147].

By encouraging endothelial dysfunction and vascular damage, inflammation also contributes significantly to the development of diabetes complications. Both microvascular and macrovascular problems linked to diabetes are accelerated by persistent inflammatory responses [148].

3.2.5. Hormonal Imbalance's Function

In DM, abnormal glucose metabolism is mostly caused by hormonal imbalance. Hormones that counteract the effects of insulin and raise blood glucose levels include glucagon, cortisol, growth hormone, and catecholamines. Hyperglycemia is a result of increased hepatic glucose synthesis caused by elevated glucagon release from pancreatic α-cells [149].

Additionally, by increasing insulin secretion and preventing glucagon release, incretin hormones like glucagon-like peptide-1 [GLP-1] are

essential for controlling blood sugar levels. Patients with type 2 DM have been shown to have impaired incretin response, which exacerbates metabolic dysregulation [150].

3.3. DM Complications

Prolonged hyperglycemia and metabolic imbalance are the main causes of the extensive range of problems linked to DM. Both microvascular and macrovascular problems arise from long-term elevated blood glucose levels, which cause structural and functional changes in a variety of tissues and organs. Diabetic patients' morbidity, mortality, and worse quality of life are all greatly impacted by these problems. Complex biochemical processes, such as oxidative stress, inflammation, and the buildup of advanced glycation end products, are involved in the pathophysiology of diabetes problems. These pathways cumulatively result in tissue damage and organ failure [151,152].

Acute and chronic diabetic problems are the two main categories. While chronic consequences develop gradually over time and are sometimes permanent if improperly handled, acute complications occur quickly and need prompt medical attention. Microvascular problems, which impact tiny blood arteries, and macrovascular complications, which affect major blood vessels, are further classifications for chronic complications [153].

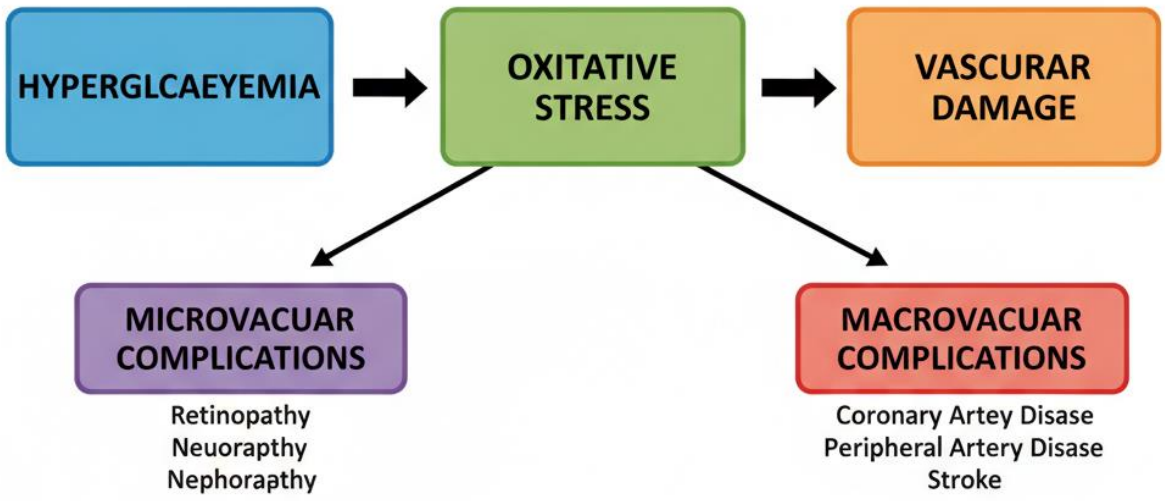


Figure 5 Flow Diagram of Diabetic Complications

3.3.1. DM Acute Complications

Sudden metabolic disruptions cause acute complications of DM, which may be fatal if left untreated. Diabetic ketoacidosis [DKA], hyperosmolar hyperglycemic state [HHS], and hypoglycemia are the most frequent acute consequences. Hyperglycemia, ketosis, and metabolic acidosis are the hallmarks of diabetic ketoacidosis, which is mostly seen in people with type 1 DM. It is caused by a lack of insulin and an excess of ketone bodies produced by enhanced lipolysis [154].

Severe hyperglycemia, dehydration, and elevated plasma osmolarity without substantial ketosis are the hallmarks of the hyperosmolar hyperglycemic condition, which is more often linked to type 2 DM. Hypoglycaemia, on the other hand, occurs due to excessive insulin administration, inadequate food intake, or increased physical activity, leading to dangerously low blood glucose levels [155].

Table 8 Classification of Acute Complications of DM

S. No.	Complication	Characteristics	Major Causes	Clinical Features
1	Diabetic Ketoacidosis [DKA]	High glucose with ketone formation	Insulin deficiency	Acidosis, dehydration, ketonuria
2	Hyperosmolar Hyperglycaemic State [HHS]	Severe hyperglycaemia without ketosis	Dehydration	Altered consciousness
3	Hypoglycaemia	Low blood glucose	Excess insulin	Sweating, dizziness

3.3.2. Long-Term DM Complications

Long-term exposure to hyperglycemia causes chronic complications of DM to develop gradually. Damage to blood arteries, nerves, kidneys, and other essential organs is the main cause of these issues. The length of diabetes and poor glycaemic management are directly linked to the development of chronic problems [156].

- **Microvascular Issues:** Diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy are examples of microvascular problems, which entail damage to tiny blood vessels. One of the most common causes of blindness in the world, diabetic retinopathy is defined by damage to the blood vessels in the retina, which leads to microaneurysms, hemorrhages, and neovascularization [157].

  One of the main causes of end-stage renal failure and chronic kidney disease is diabetic nephropathy. Glomerular hypertrophy, elevated albumin excretion, and a gradual deterioration in renal function are its hallmarks. Kidney function is eventually compromised by persistent hyperglycemia, which thickens the glomerular basement membrane and causes mesangial enlargement [158].

  Peripheral nerve injury is a typical sign of diabetic neuropathy, which may include numbness, tingling, discomfort, and loss of feeling. In diabetic individuals, it dramatically raises the risk of lower limb amputation and foot ulcers [159].

  - **Macrovascular Issues:** Cardiovascular disease, cerebrovascular disease, and peripheral arterial disease are examples of macrovascular problems, which entail damage to big blood arteries. Cardiovascular disease is the leading cause of mortality among diabetic individuals and includes conditions such as coronary artery disease, myocardial infarction, and heart failure [160].

Stroke and brief ischemic episodes brought on by a decreased blood flow to the brain are examples of cerebrovascular illness. Blood flow to the lower limbs is impacted by peripheral artery disease, which may result in gangrene, ulceration, and tissue ischemia [161].

Table 9 Classification of Chronic Complications of DM

S. No.	Type	Complication	Target Organ	Major Effects
1	Microvascular	Retinopathy	Eyes	Vision impairment
2	Microvascular	Nephropathy	Kidneys	Renal failure
3	Microvascular	Neuropathy	Nerves	Loss of sensation
4	Macrovascular	Cardiovascular Disease	Heart	Myocardial infarction
5	Macrovascular	Cerebrovascular Disease	Brain	Stroke
6	Macrovascular	Peripheral Arterial Disease	Limbs	Ulceration

3.4. Role of Oxidative Stress in DM

The development and course of DM and its related problems are significantly influenced by oxidative stress. It results from an imbalance between the body's antioxidant defense system and the generation of reactive oxygen species [ROS]. Chronic hyperglycemia in diabetes causes an overabundance of reactive oxygen species, which interfere with regular cellular processes and cause tissue

damage. One of the main causes of insulin resistance, β-cell dysfunction, and vascular problems seen in diabetes patients is the buildup of ROS [162,163].

Numerous metabolic mechanisms, such as glucose auto-oxidation, activation of the polyol pathway, increased production of advanced glycation end products [AGEs], and activation of protein kinase C [PKC], mediate oxidative stress caused by hyperglycemia. Proteins, lipids, and nucleic acids are oxidatively damaged as a consequence of these pathways combined increased generation of free radicals. Cellular integrity is altered by such molecular damage, which also speeds up the development of diabetes problems [164].

Pancreatic β-cell dysfunction is one of the major effects of oxidative stress in DM. Because pancreatic β-cells have comparatively low quantities of antioxidant enzymes like catalase and superoxide dismutase, they are especially vulnerable to oxidative damage. Constant exposure to high glucose concentrations causes β-cells to produce more ROS, which impairs insulin production and ultimately causes β-cell death [165]. This gradual reduction in the ability to produce insulin is a major factor in the deterioration of glycaemic control.

By disrupting insulin signaling pathways, oxidative stress also plays a role in insulin resistance. Insulin receptor activity is hampered by stress-sensitive signaling pathways activated by excessive free fatty acids and inflammatory mediators produced during diabetes circumstances. These changes promote prolonged hyperglycemia by reducing the absorption of glucose by peripheral tissues such skeletal muscle and adipose tissue [166].

Oxidative stress is a key factor in the development of diabetes complications affecting several organs in addition to metabolic disorders. Oxidative stress destroys neuronal cells and interferes with nerve transmission in diabetic neuropathy, resulting in neuropathic pain and sensory impairment. Oxidative stress causes glomerular damage, mesangial enlargement, and renal fibrosis in diabetic nephropathy, which eventually impairs kidney function. Similarly, diabetic retinopathy and cardiovascular problems are mostly caused by oxidative stress-induced endothelial dysfunction [167,168].

To counteract reactive oxygen species, the body has built-in antioxidant defense systems. Superoxide dismutase [SOD], catalase [CAT], and glutathione peroxidase [GPx] are examples of enzymatic antioxidants; glutathione, vitamin C, and vitamin E are examples of non-enzymatic antioxidants. However, increased ROS generation in diabetes situations overwhelms the antioxidant defense mechanism, resulting in oxidative damage and the advancement of the illness [169].

Antioxidants have been shown to have therapeutic promise in reducing problems associated with oxidative stress in DM. Promising outcomes in lowering oxidative damage, enhancing insulin sensitivity, and safeguarding pancreatic β-cells have been shown by natural antioxidants produced from medicinal plants. It has been shown that plant-derived polyphenols and flavonoids improve glycaemic management and prevent diabetes complications by increasing antioxidant enzyme activity and decreasing lipid peroxidation [170,171].

It is crucial to comprehend how oxidative stress affects DM in order to create treatment approaches that effectively slow the disease's course and avoid complications. The discovery of medicinal plants that are high in antioxidants serves as a crucial foundation for the creation of innovative herbal compositions that may have antidiabetic properties. As a result, the study of antioxidant processes continues to be a major focus of diabetes research and medication development [172].

Table 10 Source of Oxidative Stress

S. No.	Source of Oxidative Stress	Mechanism	Resulting Effects	Associated Complications
1	Glucose Auto-oxidation	Direct oxidation of glucose	Free radical generation	Cellular damage

2	Polyol Pathway Activation	Increased sorbitol accumulation	Osmotic stress	Neuropathy
3	Advanced Glycation End Products [AGEs]	Protein glycation	Tissue stiffening	Nephropathy
4	Protein Kinase C Activation	Altered cell signalling	Vascular dysfunction	Retinopathy
5	Lipid Peroxidation	Oxidation of membrane lipids	Membrane damage	Cardiovascular disease

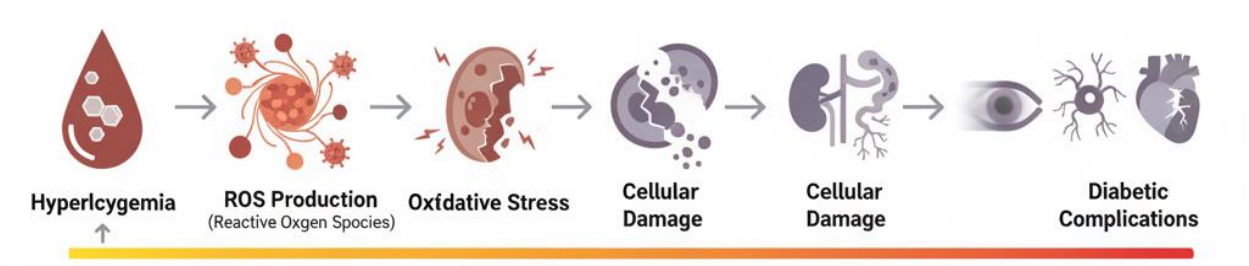


Figure 6 Role of Oxidative Stress in DM

3.5. DM Experimental Models

Understanding the pathophysiology of the illness and assessing the therapeutic effectiveness of antidiabetic medications depend heavily on experimental models of DM. These models provide important insights into insulin resistance, metabolic changes, pancreatic β-cell malfunction, and problems related to DM. Choosing the right experimental model is crucial to getting accurate and repeatable findings, especially when researching natural products and herbal mixtures [173,174].

To replicate the clinical characteristics of DM in lab animals, a number of experimental models have been created. Chemically induced models, genetically induced models, diet-induced models, and surgically induced models are the general categories into which these models fall. Depending on the kind of diabetes being studied and the desired study goal, each model has certain benefits and drawbacks [175].

3.5.1. Models Induced by Chemicals

Because they are easy to use, repeatable, and affordable, chemically induced diabetes models are among the most used experimental techniques. In these models, diabetogenic drugs that specifically harm pancreatic β-cells are administered, causing insulin insufficiency and hyperglycemia. Alloxan and streptozotocin [STZ] are two diabetogenic drugs that are often utilized.

- **Diabetes Induced by Streptozotocin:** One of the most used methods for causing diabetes in lab animals is streptozotocin [STZ]. By producing reactive oxygen species and causing DNA alkylation, this nitrosourea chemical specifically kills pancreatic β-cells. Persistent hyperglycemia and decreased insulin output ensue from the β-cell necrosis that follows. Depending on the dose and delivery method, STZ-induced animals are often employed to research type 1 and type 2 DM [176,177].

  Because low-dose STZ causes insulin resistance and partial β-cell malfunction, it is often used in conjunction with a high-fat diet to mimic type 2 DM. This model is very helpful for assessing the effectiveness of antidiabetic medications and herbal formulations because it closely mimics the pathophysiology characteristics of type 2 diabetes in humans [178].

- Diabetes Induced by Alloxan: Another common diabetogenic substance that specifically targets pancreatic β-cells by

producing reactive oxygen species is alloxan. Through oxidative damage and disturbance of calcium homeostasis inside β-cells, it causes diabetes. Due to animal response heterogeneity, alloxan-induced diabetes is less stable than streptozotocin models, while being very simple to create [179].

3.5.2. Models of Diet-Induced Diabetes

Insulin resistance and metabolic abnormalities linked to type 2 DM are often studied using diet-induced models. In these models, animals are fed a high-fat diet [HFD] or a high-sucrose diet to cause insulin resistance and obesity. Long-term high-fat food intake causes metabolic changes as elevated body weight, hyperlipidemia, and poor glucose tolerance [180].

For researching how obesity and lifestyle variables contribute to the development of diabetes, diet-induced diabetes models are very useful. These animals are often utilized in pharmacological and nutritional studies because they closely mimic the metabolic alterations seen in real type 2 DM [181].

3.5.3. Models of Genetically Induced Diabetes

Animals having hereditary mutations that predispose them to DM are used in genetically induced models. Leptin signaling pathway abnormalities cause obesity, insulin resistance, and hyperglycemia in db/db and ob/ob mice, which are common instances. These models are especially helpful for researching the genetic processes that underlie metabolic diseases like diabetes [182].

The use of genetically induced models is often restricted by their expensive cost and specific breeding requirements, despite the fact that these models provide important insights into disease processes. However, they continue to be crucial instruments for examining molecular elements of the pathophysiology of diabetes [183].

3.5.4. Models Induced by Surgery

Another technique for causing diabetes in test animals is the surgical excision of pancreatic tissue. Reduced insulin production and the emergence of hyperglycemia are the outcomes of partial or complete pancreatectomy. These models provide useful information on insulin insufficiency and pancreatic function, but they are less often utilized because of their technical complexity and greater death rates [184].

3.6. Review on herbal remedies as Antidiabetic Activity

The possible use of herbal remedies in the treatment of DM has drawn a lot of interest in recent years. The investigation of plant-based medicinal agents has been prompted by the rising incidence of diabetes and the drawbacks of traditional pharmacotherapy. Numerous phytoconstituents found in medicinal plants, including flavonoids, alkaloids, terpenoids, glycosides, and phenolic compounds, have antihyperglycemic effects via a variety of pathways. These strategies include reducing oxidative stress, inhibiting the enzymes that break down carbohydrates, increasing peripheral glucose absorption, and stimulating insulin production [185,186].

In both experimental and clinical research, a number of medicinal plants have shown strong antidiabetic effect. Compounds originating from plants provide benefits include fewer adverse effects, better patient compliance, and the capacity to target many metabolic pathways at once. In order to create standardized herbal formulations with increased therapeutic effectiveness, recent studies have emphasized the significance of fusing traditional herbal knowledge with contemporary pharmacological research [187].

Momordica charantia is one of the medicinal herbs that has been researched a lot because of its hypoglycemic qualities. Charantin, vicine, and polypeptide-p are among the plant's bioactive components that enhance glucose tolerance and have insulin-mimetic properties. Momordica charantia extracts have been shown in experiments to dramatically lower blood glucose levels and enhance lipid metabolism in diabetic mice [188].

Another significant therapeutic plant is Gymnema sylvestre, sometimes known as "gurmar." The plant includes gymnemic acids, which are known to increase insulin release from pancreatic β-cells and inhibit intestinal glucose absorption. In experimental settings, regular treatment of Gymnema sylvestre extracts has improved glycaemic control and decreased fasting blood glucose levels [189].

Another well-researched plant with antidiabetic properties is Trigonella foenum-graecum. This plant's seeds include saponins and soluble fibers that increase insulin sensitivity and postpone the gastrointestinal tract's absorption of glucose. Following the ingestion of fenugreek seed extracts, blood glucose and serum cholesterol levels have been shown to significantly decrease in both clinical and experimental trials [190].

Significant antihyperglycemic and antioxidant properties have also been demonstrated for Azadirachta indica. Limonoids, flavonoids, and tannins found in the plant improve insulin sensitivity and lessen oxidative stress linked to diabetes. Neem leaf extracts have been proven in experiments to enhance glucose metabolism and lessen problems related to persistent hyperglycemia [191].

Syzygium cumini, which is often used in traditional medicine to treat DM, is another potential medicinal plant. Alkaloids and flavonoids found in Syzygium cumini seeds improve pancreatic β-cell activity and lower blood glucose levels. Research has shown that it improves glycaemic control and lowers oxidative damage in diabetic situations [192].

The strong antidiabetic properties of Pterocarpus marsupium are well-known. The plant includes pterostilbene and epicatechin, which increase insulin release and encourage the regeneration of pancreatic β-cells. Studies have shown that administering Pterocarpus marsupium extracts significantly lowers blood glucose levels [193].

The significance of polyherbal formulations in the therapy of diabetes has also been highlighted by recent research. Multiple medicinal plants are combined in polyherbal formulations to provide better glycemic control and synergistic therapeutic benefits. Because of their improved therapeutic effectiveness and

fewer side effects, these formulations are being investigated more and more as possible substitutes for synthetic medications [194].

Finding plants with strong hypoglycemic and antioxidant properties is crucial, as seen by the rising interest in herbal antidiabetic treatment. The creation of safe and efficient herbal compositions depends heavily on the scientific confirmation of traditional medicinal herbs via experimental research. The ongoing study of medicinal plants offers a solid basis for the progress of herbal medication development for the treatment of diabetes and the identification of new therapeutic agents [195].

Table 11 Herbal herbal remedies for Diabetes

S. No.	**Plant Name**	**Family**	**Active Constituents**	**Mechanism of Action**
1	*Momordica charantia*	Cucurbitaceae	Charantin, Vicine	Insulin-mimetic action
2	*Gymnema sylvestre*	Apocynaceae	Gymnemic acids	Stimulates insulin secretion
3	*Trigonella foenum-graecum*	Fabaceae	Saponins, Fibre	Delays glucose absorption
4	*Azadirachta indica*	Meliaceae	Limonoids	Enhances insulin sensitivity

5	*Syzygium cumini*	Myrtaceae	Alkaloids	Improves β-cell function
6	*Pterocarpus marsupium*	Fabaceae	Epicatechin	β-cell regeneration
7	*Ocimum sanctum*	Lamiaceae	Eugenol	Antioxidant activity
8	*Allium sativum*	Amaryllidaceae	Allicin	Improves glucose metabolism

3.7. Review on Acacia Species

One of the most extensively dispersed genera of flowering plants in tropical and subtropical areas is the genus Acacia, which is a member of the Fabaceae family. There are about 1,000 species of trees and shrubs in the genus, many of which have significant therapeutic benefit. These species are found in many parts of Australia, Africa, and India, and they have long been used in traditional medicine to treat a variety of illnesses, including as DM, infections, inflammation, and metabolic abnormalities [196, 197].

A number of species, including AN and AL, have become especially significant because of their rich phytochemical composition and variety of pharmacological actions. Their medicinal potential and ongoing usage in contemporary herbal medicine studies are supported by the presence of bioactive ingredients such tannins, flavonoids, alkaloids, glycosides, and phenolic compounds [198].

3.7.1. Description of Botany

Plants belonging to the genus Acacia are typically small to medium-sized trees or shrubs characterized by bipinnate leaves and the presence of prickles or thorns on their branches. The bark is generally rough in

texture, rich in tannins, and varies in color from dark brown to grey. The leaves are compound and finely divided, giving them a feathery or delicate appearance. A key distinguishing feature of Acacia species lies in their floral morphology. The flowers are usually small, numerous, and arranged in characteristic inflorescences such as globular heads or cylindrical spikes. They are predominantly yellow or cream in color and possess numerous stamens, which impart a soft, fluffy appearance to the inflorescence. The fruits are typically elongated pods containing multiple seeds embedded within a fibrous pulp. These morphological features, particularly the structure and arrangement of flowers, serve as important diagnostic characters for identification and differentiation of Acacia species[199].

AN is a medium-sized tree characterized by feathery bipinnate leaves and dark, fissured bark. The flowers are arranged in bright yellow, globular inflorescences, which are compact and spherical in appearance due to the presence of numerous stamens. The pods are relatively short and constricted between the seeds, giving them a beaded appearance. In contrast, AL is a moderately sized tree with spreading branches, bipinnate leaves, and pale, rough bark. Its flowers are arranged in elongated, cylindrical spike-type inflorescences, typically cream to pale yellow in color. The pods are flat, elongated, and contain multiple seeds without constrictions, which serves as a distinguishing feature from closely related species. These morphological differences, particularly in floral arrangement and pod structure, provide reliable criteria for identification and differentiation between the two species[200].

Acacia species may thrive in arid and dry conditions because of their ecological flexibility. They are useful for agricultural uses and ecological restoration because of their vast root systems, which stabilize soil and fix nitrogen [201].

3.7.2. Conventional Applications

Acacia species are widely utilized to cure a variety of illnesses in traditional medical systems including Ayurveda, Unani, and folk medicine. Bark, leaves, pods, and seeds are just a few of the plant components that have been utilized medicinally. Decoctions made from Acacia species' bark have historically been used to treat inflammatory conditions, dysentery, and diarrhea [202].

Infections, wound healing, and DM have all historically been treated using AN. The leaves have been administered topically to cure ulcers and skin infections, while the bark and pods have been used as astringents and antibacterial agents [203].

In a same vein, fever, cough, gastrointestinal issues, and inflammatory illnesses have all historically been treated using AL. In addition to being used as a tonic, the bark extract has been utilized to treat metabolic conditions such DM [204].

Chewing sticks made from certain Acacia species have been used traditionally to maintain dental hygiene and prevent oral infections. The significance of Acacia species in conventional healthcare systems is shown by these activities [205].

3.7.3. Investigation on Phytochemicals

Acacia species contain a variety of secondary metabolites that are responsible for various biological activity, according to phytochemical studies. Flavonoids, tannins, phenolic acids, alkaloids, terpenoids, saponins, and glycosides are the main phytoconstituents found in a variety of species. These substances have strong anti-inflammatory, antibacterial, and antioxidant properties [206].

Tannins and phenolic chemicals are very abundant in AN's bark and pods. Its antioxidant and antihyperglycemic properties are attributed to the presence of catechin, epicatechin, gallic acid, and ellagic acid, according to studies [207].

Similarly, flavonoids, glycosides, and triterpenoids have been found in AL by phytochemical study. These substances are known to have strong antioxidant activity, which aids in shielding tissues against oxidative damage linked to long-term illnesses [208].

Phytoconstituents in Acacia species have been identified and characterized using sophisticated analytical methods such Fourier-transform infrared spectroscopy [FTIR], gas chromatography-mass spectrometry [GC-MS], and high-performance liquid chromatography [HPLC]. These findings support their usage in contemporary pharmaceutical formulations and provide scientific justification for their historic therapeutic purposes [209].

3.7.4. Pharmacological Investigation

The medicinal potential of Acacia species in the treatment of a variety of ailments has been shown by several pharmacological studies. Significant antioxidant, antibacterial, anti-inflammatory, hepatoprotective, and antidiabetic properties of extracts derived from various plant sections have been described in these investigations [210].

AN extracts have shown significant antihyperglycemic action in diabetic animal models, according to experimental research. It is thought that the mechanism of action includes decreasing oxidative stress, inhibiting enzymes that break down carbohydrates, and increasing insulin secretion. Furthermore, this species' antioxidant qualities help to avoid problems from diabetes [211].

Pharmacological research on AL has also shown strong antioxidant and anti-inflammatory properties. These benefits are linked to enhanced cellular antioxidant defense systems and suppression of inflammatory mediators [212].

Acacia species have shown antibacterial efficacy against a variety of pathogenic microbes in addition to their antidiabetic properties. Bark and leaf extracts have been shown to suppress bacterial growth and

lower the risk of infection, underscoring their significance in both conventional and contemporary medicine [213].

The creation of herbal medicines using standardized Acacia extracts has also been investigated recently. The use of Acacia species in the creation of pharmaceutical products is supported by these formulations' increased stability, bioavailability, and therapeutic efficacy [214].

3.8. Methods of Phytochemical and Pharmacognostical Standardization

A crucial first step in guaranteeing the quality, purity, safety, and therapeutic effectiveness of herbal medications is the standardization of medicinal plant ingredients. To verify plant materials, assess their physicochemical characteristics, and pinpoint the bioactive components in charge of pharmacological actions, pharmacognostical and phytochemical standardization techniques are often used. These methods provide a scientific basis for verifying the authenticity of plants and identifying adulteration or replacement in herbal remedies [215].

The initial step in pharmacognostical evaluation is macroscopic examination, which involves the assessment of visible morphological characteristics of plant materials such as color, odor, taste, size, shape, texture, and overall appearance. These parameters serve as primary identification markers and provide a basis for the authentication of crude drugs. In the case of floral materials, diagnostic features such as type of inflorescence, arrangement of flowers, and external morphology play a crucial role in species differentiation. The flowers of AN are characterized by small, bright yellow, globular inflorescences with a soft and fluffy appearance due to numerous stamens. In contrast, AL flowers are creamy white to pale yellow and arranged in elongated spike-type inflorescences. These distinct morphological characteristics serve as reliable criteria for identification and differentiation between the two species and are essential for ensuring the authenticity and quality of the plant material used in further studies[216].

A crucial part of pharmacognostical standards, microscopic examination offers important details about the interior anatomical characteristics of plant tissues. Structures including epidermal cells, vascular bundles, fibers, sclereids, and

calcium oxalate crystals may be seen when transverse slices are examined. By distinguishing distinctive components like lignified fibers and parenchymatous cells, powder microscopy is especially helpful for identifying powdered plant materials. These microscopic features are used as diagnostic indicators for the verification of herbal drugs [217].

Determining characteristics including moisture content, total ash, acid-insoluble ash, water-soluble ash, and extractive values is part of physicochemical standardization. To stop microbial development and deterioration during storage, moisture content measurement is crucial. While extractive values provide an estimate of the soluble bioactive components found in the plant material, ash values show the presence of inorganic contaminants like sand or dirt. These criteria are often used to set guidelines for herbal medication quality control [218].

Secondary metabolites found in plant extracts are quantitatively estimated and qualitatively screened as part of phytochemical standardization. To find substances like alkaloids, flavonoids, tannins, glycosides, saponins, terpenoids, and phenolic compounds, preliminary phytochemical screening is performed using certain reagents. These components operate as chemical indicators for quality evaluation and are in charge of the biological actions of medicinal plants [219].

For phytochemical standardization, sophisticated chromatographic methods including thin-layer chromatography [TLC], high-performance thin-layer chromatography [HPTLC], and high-performance liquid chromatography [HPLC] are often used. These techniques produce distinctive chromatographic fingerprints that guarantee batch-to-batch consistency of herbal materials and allow for the separation, identification, and quantification of specific chemical ingredients. The structural properties of phytoconstituents are also verified using spectroscopic methods such as Fourier-transform infrared [FTIR] spectroscopy and ultraviolet-visible [UV–Vis] spectroscopy [215].

The consistency and dependability of herbal formulations are guaranteed by the combination of pharmacognostical and phytochemical standardization

techniques. The production of safe and efficient herbal pharmaceutical products is greatly aided by these standardized processes, which also improve the scientific validity of medicinal plant research [219].

3.9. Review of the Literature on Pre-formulation & formulation of Herbal Tablets

Because herbal powders often have poor compressibility, a variable particle size distribution, and high hygroscopicity, pre-formulation investigations are a crucial stage in the creation of herbal tablet formulations. In order to guarantee consistency and stability of dosage forms, recent studies have emphasized the need of physicochemical characterisation of herbal extracts before compression [220,221].

According to 2020 research, the compressibility and flow characteristics of herbal powders used for tablet formation were greatly enhanced by optimizing the particle size distribution. Powders with homogeneous particle sizes showed better die filling and less weight fluctuation during compression, according to the scientists [222]. In a similar vein, another study showed that tablet stability and mechanical strength are significantly influenced by moisture content. Herbal pills become less firm and more friable due to excessive moisture [223].

Recent research has extensively examined flow property analysis employing angle of repose, Carr's index, and Hausner ratio. According to research, granulation procedures were needed to improve compressibility and guarantee consistent tablet formation for herbal powders with weak flow properties [224]. Testing for compatibility between excipients and herbal extracts has also been highlighted as a crucial element influencing formulation stability. Certain excipients reacted with polyphenolic substances, reducing their stability during storage, according to spectroscopic investigations [225].

The assessment of herbal excipients in enhancing powder flow and compressibility has also been the subject of recent research. Gums and mucilages are examples of natural binders that have been shown to increase tablet mechanical strength and granule cohesiveness [226].

The mechanical and physical characteristics of herbal pills are largely determined by formulation procedures. Wet granulation is still one of the most used procedures because it improves particle flow and compressibility [227]. Wet granulation decreased friability and increased granule homogeneity in herbal tablet formulations, according to a 2021 study. Additionally, the research showed that adding polymeric binders enhanced tablet hardness and decreased disintegration time [228]. Direct compression, on the other hand, has become more well-liked because of its ease of use and quick processing. Nevertheless, this technique calls for herbal powders with superior flow characteristics [229].

Techniques for dry granulation have been studied for herbal materials that are sensitive to moisture. It was discovered that roller compaction techniques increased granule density and decreased thermolabile phytoconstituent degradation [230]. Furthermore, new research has investigated sophisticated granulation techniques such fluidized-bed granulation, which showed better dissolving properties and uniformity [231].

The use of natural excipients in the manufacturing of herbal tablets has also been extensively studied. Research revealed that gums and starches produced from plants have better tablet disintegration characteristics and better binding qualities [232].

3.9.1. Review of the Literature on Herbal Tablet Evaluation Parameters

To evaluate the performance, stability, and quality of herbal pills, evaluation factors are crucial. The mechanical strength, disintegration behavior, dissolving features, and content homogeneity of herbal dosage forms have all been the subject of recent research [233].

Tests for hardness and friability are often used to assess tablets' mechanical strength. According to a recent study, tablet hardness was greatly increased while acceptable friability limitations were maintained by optimizing compression force [234]. Similarly, research on weight variance found that constant pill weight and dose accuracy were influenced by uniform powder flow [235].

Another important factor affecting the release of medication from herbal pills is disintegration testing. According to studies, adding natural disintegrants such plant mucilage greatly shortened the disintegration time and increased the rate of dissolution [236].

To assess the release behavior of phytoconstituents from herbal pills, dissolution testing has also been extensively studied. According to research, granulation methods outperformed direct compression methods in terms of dissolving properties [237].

Testing for content homogeneity guarantees that active phytoconstituents are distributed consistently across tablets. Optimized mixing methods greatly increased the homogeneity of herbal formulations, according to recent studies [238]. Appropriate packaging materials extended the shelf life of herbal pills, according to stability experiments carried out under accelerated settings [239].

3.9.2. Antidiabetic Activity Experimental Models in vitro & in vivo

The antidiabetic potential of natural items and herbal formulations is often assessed using experimental models. These models provide important information on insulin secretion, glucose metabolism, and pancreatic β-cell defense mechanisms. The creation of trustworthy in-vitro and in-vivo models for evaluating herbal formulations meant to control diabetes has received more attention in recent years [240,241].

Herbal extracts high in polyphenols and flavonoids have been shown by several researchers to exhibit strong antihyperglycemic effects through a variety of mechanisms, such as improved peripheral glucose uptake, inhibition of enzymes that break down carbohydrates, and increased insulin secretion [242]. To verify the therapeutic effectiveness of herbal dosage forms created for antidiabetic purposes, experimental validation utilizing standardized models has become crucial [243].

The significance of integrating both in-vitro and in-vivo models for a thorough assessment of antidiabetic potential has also been highlighted

by recent developments in experimental pharmacology. Research has shown that combining animal-based models with enzyme inhibition tests yields more trustworthy data on the medicinal efficacy of herbal mixtures [244].

Antidiabetic Activity in Vitro Models: To assess the antidiabetic effectiveness of herbal extracts and formulations, in vitro models are used as first screening techniques. These models' affordability, ease of use, and repeatability make them popular. The capacity of herbal extracts to postpone the digestion of carbohydrates and the absorption of glucose has been evaluated using a variety of techniques, including α-amylase and α-glucosidase inhibition experiments [245].

Recent studies have shown that postprandial hyperglycemia is considerably reduced when α-glucosidase activity is inhibited. According to a 2021 investigation, herbal extracts with significant α-glucosidase inhibitory activity shown remarkable antidiabetic potential on par with conventional medications [246]. Similarly, it has been common practice to assess the insulin-mimetic effects of herbal substances by glucose uptake tests employing cultured cell lines including L6 myotubes and adipocytes [247].

Glycation inhibition activity assessment is another widely used in-vitro technique. Inhibiting glycation processes has been shown to be an effective method for reducing long-term problems of diabetes, and advanced glycation end products [AGEs] are a key contributor to diabetic complications [248].

All things considered, in-vitro models provide quick and accurate screening of herbal extracts before in-vivo testing. These techniques are very helpful in identifying possible bioactive substances that have antihyperglycemic effects [240,248].

Antidiabetic Activity in In-vivo Models: The gold standard for assessing the antidiabetic effectiveness of herbal mixtures is still in-vivo models. Comprehensive information on the physiological and

biochemical alterations linked to diabetes may be found in animal models. Antidiabetic research often uses chemically induced diabetic models using streptozotocin [STZ] and alloxan, among other experimental models [249].

Diabetic animals produced by streptozotocin have been widely utilized to simulate insulin insufficiency and pancreatic β-cell loss. Herbal formulations have been shown in many investigations to increase insulin production and dramatically lower fasting blood glucose levels in STZ-induced diabetic rats [241,242]. Similarly, antihyperglycemic efficacy has been assessed by selectively destroying pancreatic β-cells in alloxan-induced diabetes mice [243].

In recent years, diet-induced insulin resistance models have also become more well-liked. By causing insulin resistance and hyperglycemia, high-fat diet [HFD]-induced diabetic animals mimic Type-2 DM. According to research, herbal formulations decreased oxidative stress and enhanced glucose tolerance in these rats [244].

Animal studies often assess a number of biochemical markers, including lipid profile, glycated hemoglobin [HbA1c], liver enzyme levels, and antioxidant enzyme activity, in addition to blood glucose estimates. These metrics provide light on how herbal formulations guard against complications from diabetes [245].

Pancreatic tissue histopathological analysis has also been extensively documented in current literature. Herbal preparations have been shown to protect pancreatic β-cells from oxidative damage and stimulate islet cell regeneration [246].

All things considered, in-vivo experimental models provide thorough proof of the therapeutic potential of herbal formulations and are essential for confirming their effectiveness in the treatment of DM [249].

MATERIALS AND METHODS

4. Materials And Methods

4.1. Collection and Authentication of Plant Material

To guarantee the highest phytoconstituent output, plant materials of AN and AL were gathered from naturally occurring populations in unpolluted areas at the proper blooming or mature stage. To conserve thermolabile components, the gathered plant parts were carefully separated, cleaned with distilled water to get rid of surface impurities, and then shade-dried at room temperature. A mechanical grinder was used to ground the dry material, which was then placed in airtight containers for further examination. A certified taxonomist verified the plant material in an accredited herbarium, where a voucher specimen was stored for later use. Reproducibility and scientific validation of pharmacognostic and pharmacological research were guaranteed by proper identification [250–252].

4.2. Pharmacognostical Evaluation

The identity, purity, and standard properties of the crude medication were determined using pharmacognostical examination. In order to guarantee batch-to-batch consistency and avoid adulteration, these investigations are crucial to the development of herbal drugs. Macroscopic, microscopic, powder, quantitative microscopic, and fluorescence investigations were all included of the examination. Standard pharmacopoeial guidelines and latest verified procedures described in pharmacognosy research were used to examine each parameter. Together, these methods aid in the identification of structural markers and diagnostic characteristics of plant material, guaranteeing its purity and authenticity before extraction and formulation creation [253–255].

4.2.1. Macroscopic Evaluation

During the day, a macroscopic assessment of the crude medication was carried out using visual and sensory observation. Color, odor, taste, form, size, surface roughness, and fracture characteristics were among the parameters that were meticulously recorded. These organoleptic

characteristics are often used in pharmacognostic standardization investigations and provide first identification. To verify the authenticity of the plant material, the observations were matched with verified botanical references. In order to ensure raw material quality for further pharmacological research, such macroscopic profiling is essential in separating authentic pharmaceuticals from adulterants or replacements [253].

4.2.2. Microscopic Evaluation

Plant material was transversely sectioned using a sharp blade and then stained with a safranin and iodine solution for microscopic examination. The slices were examined under a compound microscope after being glycerin-mounted on glass slides. Xylem arteries, phloem tissues, fibers, parenchyma cells, and epidermal structures were among the diagnostic anatomical traits that were meticulously documented. These microscopic features are commonly used in pharmacognostic standardization methods and function as conclusive identification markers for crude medicines. To verify validity, the observed structural arrangement was compared with conventional anatomical descriptions [254,255].

4.2.3. Powder Microscopy

The powdered plant material was examined using powder microscopy to look for distinctive diagnostic pieces. A small quantity of powder was mounted on a slide with glycerin and examined under a microscope. Trichomes, fibers, stone cells, capillaries, calcium oxalate crystals, and starch grains were among the structural components found. When full plant parts are unavailable, these tiny characteristics are crucial for recognizing powdered medications. In herbal medication standardization procedures, powder microscopy is a dependable method for identifying adulteration and guaranteeing quality control [255].

4.2.4. Quantitative Microscopy

Leaf constants such vein islet number, vein termination number, stomatal number, and stomatal index were measured using quantitative microscopy. Fresh leaf samples were examined under a calibrated microscope after being cleaned with chloral hydrate. To guarantee precision and repeatability, measurements were obtained from many areas. These quantitative metrics are often used in the pharmacognostic assessment of medicinal plants and are quite specific for identifying plant species. The findings provide trustworthy botanical identifiers that support herbal raw material verification and quality control [256].

4.2.5. Fluorescence Analysis

Fluorescence analysis was performed to detect characteristic fluorescence behavior of powdered plant material under visible light, UV light at 254 nm, and UV light at 365 nm. Several chemical reagents, including sodium hydroxide, hydrochloric acid, nitric acid, ethanol, and iodine solution, were applied to the powder. The hues of the ensuing fluorescence were noted and examined. Because many phytochemicals display distinctive fluorescence patterns when exposed to UV light, this method is often utilized in the verification of herbal drugs. It provides a quick and accurate way to identify adulteration and chemical fingerprinting of crude medicines [257].

4.3. Physicochemical Evaluation

The quality and purity of the crude medication were assessed physicochemically using established metrics such ash values, extractive values, moisture content, and drying loss. These factors are crucial for evaluating plant material stability, solvent-soluble components, and inorganic contaminants. The investigations were carried out using approved pharmacopoeial techniques that have been documented in previous studies on herbal standardization. These assessments guarantee that the raw material satisfies the quality requirements necessary for the creation of pharmaceutical formulations [257–259].

4.3.1. Ash Values

Accurately weighed plant material was burned at 450–600°C in a silica crucible to quantify total ash, acid-insoluble ash, and water-soluble ash. Total ash represents the total inorganic content, while acid-insoluble ash indicates silica and earthy matter. The quantity of inorganic salts soluble in water may be measured with the use of water-soluble ash. When assessing the overall purity, adulteration, and contamination of crude pharmaceuticals, these factors are essential. The results are contrasted with conventional limitations for quality assurance that have been documented in pharmacognosy literature [258,259].

4.4. Extractive Values

Solvents with increasing polarity, such as water, ethanol, and petroleum ether, were used to calculate extractive values. Each solvent was used to macerate a known amount of powdered medication for 24 to 48 hours while being shaken periodically. After the extracts were filtered and dried by evaporation, the yield percentage was computed. Extractive values reveal the chemical makeup of the plant material and show the existence of active phytoconstituents soluble in various solvents. This technique is often used to assess extraction efficiency in herbal standardization research [261,262].

$$\textbf{Extractive Value}\ [\%] = \textbf{Weight of sample/Weight of extract} \times \textbf{100}$$

4.5. Loss on Drying

A carefully weighed sample was heated to 105°C until a consistent weight was achieved in order to calculate the loss on drying. The sample's moisture and volatile components are reflected in the weight loss. One important factor affecting the stability, enzymatic breakdown, and microbiological development of herbal medications is moisture content. The plant material's stability and shelf life are enhanced by maintaining a low moisture level. Pharmacopoeial guidelines for the evaluation of herbal quality generally support this approach [263].

4.6. Moisture Content

Depending on the appropriateness of the sample, either Karl Fischer titration or gravimetric procedures were used to determine the moisture content. The amount of free and bound water in the sample was measured. Microbial contamination and phytoconstituent breakdown might result from excessive moisture in herbal medications. For pharmaceutical formulation to be stable and appropriate, moisture management is crucial. Moisture determination is a crucial quality criterion in the standardization of herbal drugs, according to recent research [264].

4.7. Phytochemical Standardization

To guarantee uniformity in the bioactive components found in the plant material, phytochemical standardization was carried out. Major secondary metabolites, including alkaloids, flavonoids, tannins, and phenolic substances, were analyzed both qualitatively and quantitatively. The antidiabetic action is mostly caused by these phytoconstituents. A crucial stage in the creation of herbal drugs is standardization, which guarantees the repeatability of pharmacological effects. Phytochemical profiling is the basis for quality control in herbal formulations, according to recent research [265–267].

4.8. Preparation of Extract

Soxhlet extraction was performed on the powdered plant material using a hydroalcoholic solvent [ethanol:water 70:30 v/v]. A thimble was filled with between 100 and 500 g of powdered medication, which was constantly withdrawn until it was completely exhausted. To conserve thermolabile components, the extract was concentrated using a rotary evaporator at low temperature and low pressure. For future research, the concentrated extract was dried and kept in airtight containers at 4°C. Herbal pharmacological research has extensively documented this technique, which guarantees the effective extraction of both polar and semi-polar phytoconstituents [268–270].

4.9. Preliminary Phytochemical Screening

Standard qualitative chemical assays were used for preliminary phytochemical screening in order to identify the presence of main phytochemical groups. Alkaloids were tested using Mayer's and Dragendorff's methods, flavonoids using the Shinoda test, tannins using the ferric chloride test, saponins using the foam test, and glycosides using the Keller-Killiani test. The findings verified the existence of bioactive secondary metabolites that have antidiabetic properties. In herbal pharmacological research, these screening techniques are often used as first instruments [271,272].

4.10. Quantitative Estimation

Spectrophotometric techniques were used to quantify the TPC [TPC], TFC [TFC], and total tannin content. TPC was estimated using the Folin-Ciocalteu reagent, TFC was estimated using the aluminum chloride technique, and tannins were estimated using the Folin-Denis method. Gallic acid and quercetin equivalents were used to express the findings. The antioxidant and antidiabetic activity of plant extracts is shown by these quantitative estimates. Antihyperglycemic action is closely associated with high phenolic and flavonoid content [273–275].The TPC of the extract was determined using the Folin–Ciocalteu method, which is based on the reduction of the Folin–Ciocalteu reagent by phenolic compounds under alkaline conditions, resulting in the formation of a blue-colored complex. In the procedure, a known volume of the plant extract was mixed with diluted Folin–Ciocalteu reagent, followed by the addition of sodium carbonate solution. The mixture was incubated at room temperature for a specified time, and the absorbance was measured at 765 nm using a UV–Visible spectrophotometer. The TPC was calculated using a calibration curve prepared with gallic acid and expressed as mg gallic acid equivalents (GAE) per gram of extract.

Similarly, the TFC was estimated using the aluminium chloride colorimetric method, which is based on the formation of a yellow-colored complex between flavonoids and aluminium chloride. In this method, the plant extract was treated with aluminium chloride and potassium acetate, followed by incubation at room

temperature. The intensity of the developed color was measured at 415 nm using a UV–Visible spectrophotometer. The flavonoid content was determined using a calibration curve of quercetin and expressed as mg quercetin equivalents (QE) per gram of extract. These methods provide a reliable estimation of phenolic and flavonoid contents, which are important indicators of the antioxidant potential of plant extracts.

4.11. Chromatographic Analysis

Phytoconstituent measurement and fingerprint profiling were done using TLC, HPTLC, and HPLC methods. HPLC was used for accurate analysis of active ingredients, HPTLC for densitometric quantification, and TLC for initial compound identification. The batch uniformity and chemical standardization of plant extracts are guaranteed by these chromatographic methods. Chromatographic fingerprinting is a crucial quality control method in the creation of herbal drugs, according to recent study [277–281].

4.12. Formulation of Herbal Tablets

In phytopharmaceutical treatment, the use of standardized plant extracts for the production of herbal tablets has been widely reported as an effective approach to improve the accuracy of the dose, stability and compliance of the patients. Recent pharmaceutical studies indicate that direct compression is one of the most commonly used techniques for the preparation of herbal tablets. This is because of its ease of use, less processing and less exposure of phytoconstituents to heat and moisture, which is very important to maintain the stability of thermolabile constituents [250]. [251] The selection of suitable excipients that can improve the powder flow and compressibility characteristics of herbal blends has been found to be important for the successful production of tablets. Superdisintegrants such as sodium starch glycolate and croscarmellose sodium greatly influence the disintegrating efficiency and dissolution performance of herbal tablets. Microcrystalline cellulose has been widely used as a diluent due to its better compressibility and compatibility with plant-derived materials [252].

The use of appropriate binders, in particular polyvinylpyrrolidone, has been shown to enhance the mechanical strength and particle cohesiveness of compressed tablets thereby reducing the chances of breakage of the tablets during handling and transit. Lubricants [e.g., magnesium stearate] and glidants [e.g., talc] are frequently used to improve die filling properties and to decrease interparticle friction during compression and thus to achieve better weight uniformity [253]. Current studies emphasize the significance of pre-compression evaluation of powder blends in terms of bulk density, tapped density, Carr's compressibility index and Hausner's ratio for predicting the flow behavior of herbal mixes during compression . It has been reported that suitable hardness, less friability and rapid disintegration times can be achieved by optimizing the ratios of the excipients along with the compression force to produce tablets with uniform weight distribution. Overall, recent studies indicate that direct compression-based herbal tablet manufacturing is a reliable and repeatable method that could offer stable dosage forms with consistent therapeutic effectiveness when standardized plant extracts are used [254].

4.13. Selection of Excipients

The selection of proper excipients is a very important step during the development of herbal tablet formulations, because the excipients play an important role in powder flow properties, compressibility, stability and drug release behavior. Recent pharmaceutical studies have shown that herbal extracts usually have poor flowability and compressibility because of their fibrous nature and hygroscopic properties, thus the appropriate excipients should be used to improve formulation performance [255]. Microcrystalline cellulose is a commonly used diluent in herbal formulations because of its good compressibility, inertness and ability to enhance tablet hardness without any adverse effect on drug release. Commonly included are superdisintegrants like sodium starch glycolate and croscarmellose sodium which help the tablet to absorb water and swell rapidly leading to faster disintegration of tablets and improved dissolution efficiency [256].

Binders are crucial in imparting mechanical strength to tablets. Polyvinylpyrrolidone [PVP K-30] has been widely reported as a suitable binder

because of its compatibility with phytoconstituents and its ability to improve particle cohesion during compression . Lubricants, such as magnesium stearate, are added in small amounts to ensure that the surfaces of the tablets and the walls of the dies between which they are compressed do not stick or pick during compression. In addition, glidants, such as talc, improve powder flow and provide uniform die filling, leading to consistent tablet weight and uniform drug distribution [257]. The compatibility of herbal extracts with excipients is usually checked by Fourier Transform Infrared [FTIR] spectroscopy or differential scanning calorimetry [DSC] in order to make sure that no chemical interaction occurs that could affect stability or therapeutic efficacy [258]. Selection of excipients should be based on functional requirements and compatibility studies to produce herbal tablets with desirable mechanical strength, rapid disintegration and consistent therapeutic performance [259].

4.14. Method of Tablet Preparation

The direct compression method is well known as a simple and efficient method for the preparation of solid dosage forms with minimum of processing steps. The herbal tablets were prepared by using the direct compression method with standardized extracts of AN / AL . Recent studies have revealed the direct compression technique particularly advantageous for the herbal formulations by minimizing the exposure of the phytoconstituents to moisture and heat, and therefore, preserving the stability and bioactivity of the thermolabile compounds [260]. In this method, accurate weighed quantity of dried herbal extract and selected excipients were individually passed through sieve No. 40 to have uniform particle size distribution and to remove agglomerates. The sieved materials were geometrically diluted and mixed thoroughly to ensure uniform distribution of the active constituents in the powder blend [261].

Lubricants like magnesium stearate and glidants like talc were added in the last stage of blending to minimize friction between powder particles and die walls during compression. The prepared powder blend was then filled in the hopper of rotary tablet compression machine using suitable punches of predetermined diameter. Compression parameters such as compression force and turret speed were optimized to get the tablets with uniform weight, adequate hardness and

minimum friability. It has been reported that mechanical integrity and physical quality of tablets prepared by direct compression technique are significantly affected by careful control of compression pressure and blending time [262,263]. The tablets prepared were visually inspected after compression for any defects such as capping, lamination or sticking and were stored in air tight containers under controlled environmental conditions to protect from moisture and environmental degradation. The direct compression method is still one of the most reliable methods for preparing herbal tablets due to its reproducibility, scalability and consistent tablet quality characteristics [264].

4.15. Optimization of Formulation

The herbal tablet formulation was optimized to get tablets with desired mechanical strength, rapid disintegration and consistent drug release characteristics. In present study, different formulation batches [F1-F6] were prepared by varying the concentration of important excipients like binders and disintegrants while keeping the amount of standardized extract of AN / AL constant. Recent pharmaceutical research emphasizes the crucial role of optimizing excipient concentration in controlling the physicochemical properties and therapeutic efficiency of herbal tablet formulations [265]. A trial based optimization approach using the factorial design principles was utilized to investigate the effect of independent variables such as binder concentration [PVP K-30] and disintegrant concentration [sodium starch glycolate] on dependent parameters such as hardness, friability, disintegration time and dissolution rate [266].

Each batch of formulation was evaluated for flow properties before compression and was subjected to mechanical strength and tablet integrity studies after compression. Research findings show that higher binder concentrations generally lead to increased tablet hardness and reduced friability, but too much binder can cause longer disintegration times and delayed drug release. On the other hand, the increased concentration of super disintegrants favors the faster disintegration of the tablets by increasing the water uptake and swelling capacity in the matrix of the tablets [267]. To get tablets conforming to pharmacopoeial

quality standards, the formulation variables were properly balanced in the optimization process.

Moreover, recent studies have suggested the use of statistical optimization tools in the form of response surface methodology [RSM] or factorial design to determine the most suitable formulation composition with minimum experimental trials. Such methods enhance formulation efficiencies by predicting the interaction between formulation variables and their cumulative effects on tablet performance parameters [268]. On comparative evaluation of all formulation batches the optimized batch was selected on the basis of acceptable hardness, minimum friability [less than 1%], uniform weight variation, rapid disintegration time and satisfactory dissolution profile. The selected optimized formulation was found to be suitable for further in-vitro and in-vivo antidiabetic evaluation studies ensuring reproducibility and consistent therapeutic performance of the developed herbal tablet dosage form [269].

4.16. Evaluation of Herbal Tablets

Prepared herbal tablets were subjected to evaluation for their physical integrity, mechanical strength, uniformity and drug release characteristics. These evaluations are important in the assessment of the quality of the formulated tablets to ensure the tablets meet pharmacopeial specifications and exhibit a uniform quality profile for therapeutic use. The pre-compression and post-compression investigations of the optimized formulation batches were performed according to standard procedures mentioned in recent pharmaceutical research. The parameters of such evaluation provide useful insight into flow behavior of powder blends and performance characteristics of compressed tablets and therefore ensuring reproducibility and reliability of the developed herbal dosage form [270,271].

4.16.1. Pre-compression Parameters

Precompression parameters were employed to determine the flow properties and compressibility behavior of the powder blends before compression into tablets. Good flow properties are required to ensure even die filling during compression and to minimize weight variation

between tablets. Standard pharmacopeial procedures were followed for the evaluation of angle of repose, bulk density, tapped density, Carr's compressibility index and Hausner's ratio of the powder blends of different formulation batches. These parameters are generally accepted as reliable parameters of the flowability and compressibility properties of the powder during the tablet manufacturing process [272].

- **Angle of Repose:** The flowability of the powder blend was determined by measuring the angle of repose by the fixed funnel method. The powder was poured from a funnel held at a fixed height on to a flat surface and formed a conical heap. The measurements of height and radius of the heap were used to obtain the angle of repose by the standard mathematical formula. When the angle of repose value is minimum, then the flow properties of powder blend are better. Good flowability is important for uniform die filling during compression which affects the weight uniformity and dosage accuracy of the tablets [273].
- **Density Bulk :** Bulk density was determined by carefully pouring a known amount of powder into a graduated cylinder without tapping. The volume occupied by the powder was measured and the bulk density was calculated by dividing the mass of the powder by the bulk volume. This parameter gives information about the packing behavior and the porosity of the powder blend. The values of bulk density can be used to determine the appropriate tablet size and compression force needed during the manufacturing process [274].
- **Density [bulk]:** The tapped density was determined by mechanically tapping the graduated cylinder containing the powder blend with a tapped density apparatus until a constant volume was obtained. The last tapped volume was recorded and tapped density was calculated on the basis of it. This parameter is a measure of the degree of packing obtained by mechanical tapping . It is used in the calculation of compressibility indices . The higher the tapped density value, the greater the packing efficiency and lesser inter-particulate void spaces within the powder blend [275].

- **Carr's compressibility index:** The compressibility properties of the powder blend were determined by calculating Carr's compressibility index from the bulk density and tapped density values. This parameter gives information on the tendency of the particles in the powder to consolidate and their cohesion during compression. Lower compressibility index values of powders are considered to be suitable for direct compression methods due to their better flow and compressibility behavior [276].
- **The Hausner Ratio:** The Hausner's ratio was calculated as the ratio of the bulk density to the tapped density. This parameter is widely used to predict the flow properties of powders and is considered to be a reliable indicator of inter-particle friction. The lower the value of Hausner's ratio, the better is the flowability, which is essential for consistent tablet weight and quality during industrial large-scale manufacturing processes [277].

4.16.2. Parameters After Compression.

The physical and mechanical properties of the compressed tablets were evaluated after compression. The tests ensure the tablets are hard enough not to break when handled, packaged and transported. Prepared tablets were evaluated for thickness, hardness, friability, weight variation, disintegration time, dissolution profile and uniformity of drug content by standard pharmacopeial methods. These parameters are important indicators for tablet quality and performance properties [278].

- **Tablet Thickness:** Thickness of the tablet was measured by using a calibrated vernier calipers to maintain uniformity in tablet dimension. Variation in thickness might indicate that the die filling or compression force was not consistent during tablet manufacturing. Tablet thickness uniformity is important for tablet weight uniformity and compatibility with packaging [279].
- **Hardness of Tablet:** The mechanical strength of tablets was evaluated by using a Monsanto hardness tester for the determination of tablet hardness. The hardness should be sufficient to avoid breakage in handling and transport. Tablets with suitable hardness values are more

likely to retain their structural integrity during storage and distribution [280].

- **Tablet Friability:** In order to test for friability, the tablets were placed in a Roche friabilator to determine their resistance to abrasion and mechanical shock. A known number of tablets was rotated at a fixed speed for a fixed time and the percentage loss in weight was determined. Tablets with friability values of <1% are acceptable by pharmacopeial standards [281].
- **Weight Fluctuations:** The uniformity of tablet weight was assessed by weighing individual tablets using analytical balance and by conducting the weight variation test. Uniformity of weight of tablets implies uniformity of active ingredients and accuracy of dosage. The tablets were analyzed for compliance to pharmacopeial limits for standard quality specifications [282].
- **Collapse Moment:** Distilled water was kept at a constant temperature and used for disintegration testing with a USP disintegration test apparatus. Noted time taken for tablets to break into smaller pieces. The rapid disintegration is required to increase the dissolution and to improve the bioavailability of the active ingredients [283].
- **Dissolution Study:** Dissolution testing was performed to evaluate the release behavior of active constituents from the tablets using USP dissolution apparatus [Type II paddle method]. Samples were taken at pre-determined times under controlled conditions of dissolution medium, temperature and rotation speed. The release kinetic profiles were prepared and the release kinetics were determined. Spectrophotometric determination of drug release was performed [284].
- **Content Uniformity of Drug:** The uniformity of drug content was determined by crushing individual tablets and assaying the amount of active constituent by UV-visible spectrophotometer or chromatographic methods. The tablets with the uniform distribution of drug will provide consistent therapeutic performance and will comply with the pharmacopeial standards [285].

4.17. Antidiabetic Evaluation

The antidiabetic activity of the optimized herbal tablet formulation containing standardized extract of AN / AL was evaluated by in-vitro and in-vivo experimental models. Several experimental approaches should be evaluated to establish the mechanism of antihyperglycemic activity and to validate the therapeutic potential of plant-based formulations. Recent pharmacology research has shown that the combination of enzyme inhibition assays and animal diabetic models can reliably demonstrate the glucose lowering activity and pancreatic protective effects [286]. The present work involved in-vitro α-amylase and α-glucosidase inhibitory assays followed by in-vivo studies on chemically induced diabetic animal models. These methods provide a systematic evaluation of the herbal formulation for its ability to regulate carbohydrate metabolism, improve glucose tolerance and restore pancreatic function [287].

4.17.1. In-vitro Antidiabetic Studies

α-Amylase Inhibition Assay: The inhibition of starch hydrolysis by the herbal extract was determined by a modified colorimetric method for the measurement of α-amylase inhibition [24]. The tablet powder was extracted and dissolved in phosphate buffer and incubated with α-amylase enzyme at controlled temperature conditions. Soluble starch solution was added as substrate after incubation and allowed to react for a certain period of time. The reaction was terminated by the addition of dinitrosalicylic acid [DNS] reagent and heating in a boiling water bath for color development. The absorbance of the obtained solution was measured at the suitable wavelength using UV-Visible spectrophotometer. Enzyme activity was expressed as percentage inhibition relative to control samples. Recently, it has been shown that inhibition of the enzyme α-amylase reduces postprandial hyperglycemia and plays an important role in the management of diabetes [289,290].

α-Glucosidase Inhibition Assay: The anti-glucosidase activity of the herbal extract was measured as an inhibition of formation of glucose from carbohydrate substrates by α-glucosidase inhibition assay. In this method the α-glucosidase

enzyme was incubated with different concentrations of herbal extract at controlled temperature conditions. A synthetic substrate, p-nitrophenyl-α-D-glucopyranoside [pNPG], was added to start the reaction. After incubation, the reaction was terminated by the addition of an alkaline solution and the amount of p-nitrophenol released was measured spectrophotometrically. The inhibitory activity of the extracts was estimated by comparing the absorbance values with control samples. α-Glucosidase inhibition has been shown to delay glucose absorption from the intestine and is a major contributor to the reduction of postprandial blood glucose levels [291,292].

4.17.2. In-vivo Antidiabetic Studies

The in-vivo antidiabetic study was performed to evaluate the therapeutic potential of the optimized herbal tablet formulation in experimental animal models. For herbal drugs, animal studies offer detailed data on pharmacodynamic activity, metabolic regulation and effects on tissue levels. The experimental animals were Wistar albino rats, because of the physiological similarity to the metabolic responses in humans. The animals were housed in the laboratory under controlled conditions of temperature, humidity and light:dark cycles. Ethics approval and consent to participate section The animal experiments were approved by the Institutional Animal Ethics Committee [IAEC] according to the national guidelines for animal research [293, 294].

Experimental Animals: Experimental studies were conducted on healthy adult Wistar albino rats with a body weight of 150–200 g. Animals were housed in polypropylene cages and given standard laboratory diet and water ad libitum. Animals were acclimated to laboratory conditions for at least seven days prior to experimentation. Throughout the study, animal handling and environmental control were performed to reduce stress and variability in experimental results [295].

Induction of Diabetes [STZ] model: Experimental animals were made diabetic by intraperitoneal administration of streptozotocin [STZ]. Animals were fasted overnight before induction of diabetes.

Streptozotocin was dissolved in freshly prepared citrate buffer and administered at an optimized dose based on body weight. Animals were observed for signs of hyperglycemia after administration and blood glucose level was measured 48-72 hours later. Those animals with fasting blood glucose levels above the pre-determined diabetic levels were considered as diabetic and selected for further experimental studies. Chemical induction of diabetes with STZ or alloxan has been reported as a reliable method to study the antidiabetic activity of herbal formulations [296,297].

Experimental Group: Experimental animals were divided into different groups like normal control , diabetic control , standard drug treated group and test formulation treated groups . The herbal tablet formulation was administered orally at a fixed dose according to the body weight. Metformin was used as the standard antidiabetic drug as reference control. Blood glucose levels were checked at different intervals to measure therapeutic response for a fixed duration of the experiment [298].

Estimation of Blood Sugar: Blood glucose measurements were taken from the tail vein at predetermined intervals. Glucose was determined by digital glucometer or biochemical assay kits. The antihyperglycemic effect of herbal tablet formulation was evaluated by periodic monitoring of blood glucose level. The test formulation exhibited significant antidiabetic activity by reducing the blood glucose levels in comparison to diabetic control group [299].

Oral Glucose Tolerance Test [OGTT] : The oral glucose tolerance test was used to assess the efficiency of glucose utilization in treated animals. The animals were fasted overnight and then dosed with a glucose solution by gavage. Blood glucose levels were taken at timed intervals after glucose administration. The groups treated with the compounds showed improvement in glucose tolerance as compared to the diabetic control animals indicating improved glucose metabolism and insulin sensitivity [300].

Biochemical Properties Estimation: Serum biochemical parameters such as total cholesterol, triglycerides, high density lipoprotein [HDL], low density lipoprotein [LDL], glycated hemoglobin [HbA1c] and insulin levels were estimated by standard biochemical assay kits. These parameters are involved in lipid metabolism, glycemia control. The improved biochemical profile indicates the protective effects of herbal formulation against the metabolic complications associated with diabetes [301,302].

Histopathology Studies: Histopathological analysis of pancreatic tissues was carried out to examine the structural alterations associated with diabetes and treatment effects. At the end of the experimental study, animals were humanely sacrificed and pancreatic tissues were collected and fixed in 10% formalin solution. The tissue samples were processed, embedded in paraffin, sectioned by microtome and stained by haematoxylin and eosin stain technique. Microscopic study of the morphology of cells and the integrity of pancreatic β-cells. The restoration of normal pancreatic architecture indicates the protective and regenerative potential of the herbal formulation [303].

4.18. Statistical Analysis

Statistical analysis of the experimental data was performed in order to evaluate the significance and reliability of the observed findings from pre-compression, post compression, in-vitro and in-vivo antidiabetic studies. All experiments were performed in triplicate unless otherwise stated and the results are presented as mean ± standard deviation [SD]. Statistical analysis was done to find out the level of variation between different batches of formulation and experimental groups. Suitable statistical tools are used to confirm the reproducibility and scientific validity of pharmaceutical and pharmacological studies [304].

The analysis of variance [ANOVA] was performed to analyze the differences between multiple experimental groups such as control, standard drug treated and test formulation treated groups. The one-way ANOVA was the main statistical method used to determine statistically significant differences of the mean values

of different experimental groups. If there were significant differences, post hoc multiple comparison tests such as Tukey's test or Dunnett's test were employed to detect the significant differences among groups. These statistical methods are widely recommended in the pharmaceutical and biomedical research for the assessment of efficacy of herbal formulations and determination of treatment response in diabetic models [305, 306].

All statistical calculations were performed using validated statistical software such as GraphPad Prism [version 8.0 or greater] or SPSS statistical software. These software tools allow accurate graphical representation of the experimental data, and also help in interpretation of the results by plotting bar graphs, line graphs and dose-response curves. Statistical significance was defined as $p < 0.05$, the accepted criterion for statistically significant differences between experimental groups. The smaller the p-values, the greater the statistical significance and the better the therapeutic response of the tested herbal formulation [307].

Hypotheses were tested and relationships between formulation variables and performance parameters like dissolution rate, disintegration time and levels of glucose reduction were established using correlation analysis, regression modeling, as and when required. These statistical approaches offer a more holistic perspective on the interaction of formulation components with biological responses. The results obtained were reliable, reproducible and suitable for scientific interpretation and further validation of the developed herbal tablet formulation [308] by systematic application of statistical methods.

RESULTS & DISCUSSION

5. Results

5.1. Pharmacognostical Evaluation Results

Pharmacognostical studies of powder of plant material of AN and AL was carried out to establish its identity, purity and quality parameters. The macroscopic and microscopic characteristics of the plant material were carefully observed and recorded. Diagnostic features are very important in confirming the authenticity of the plant material and preventing adulteration. The powdered drug showed characteristic morphological features in conformity with the standard pharmacognostical descriptions reported for Acacia species. The evaluation helps in the reliability of raw material used for herbal drug formulation and also helps in quality control of herbal tablet preparation.

5.1.1. Macroscopic Evaluation

Macroscopic (organoleptic) evaluation is an important step in pharmacognostical studies, as it helps in the identification and authentication of crude plant materials based on visible characteristics. The flowers of selected Acacia species were examined for their external morphological features such as size, shape, color, odor, taste, texture, and arrangement.

Table 12 Macroscopic evaluation

Parameter	***AN***	***AL***
	Description	
Color	Bright yellow to golden yellow	Creamy white to pale yellow
Size	Small, approximately 1–1.5 cm in diameter	Small, approximately 1–2 cm in length

Shape	Globular (spherical) head	Cylindrical or elongated spike
Inflorescence Type	Capitate (globose head)	Spike
Surface	Soft, fluffy appearance due to numerous stamens	Smooth with fine filamentous structures
Odor	Mild, characteristic	Mild, slightly aromatic
Taste	Slightly astringent	Slightly bitter and astringent
Texture	Soft and powdery on drying	Soft when fresh, fibrous on drying
Arrangement	Flowers arranged in dense spherical clusters on axillary peduncles	Flowers arranged in elongated spikes arising from leaf axils

5.1.2. Microscopic Assessment

Microscopic analysis is an essential component of pharmacognostical studies used for the identification, authentication, and quality assessment of crude plant materials. The microscopic characteristics of Acacia flowers were studied using transverse sections (T.S.) and powder microscopy to identify diagnostic cellular features.

Table 13 Microscopic Evaluation

S. No.	Microscopic Feature	*AN*	*AL*
1	**Epidermis**	Single-layered, compact, thin-walled cells with cuticle	Single-layered, elongated cells with thin cuticle
2	**Calyx**	Parenchymatous cells with chloroplasts	Loosely arranged parenchymatous cells
3	**Corolla**	Thin-walled parenchyma with vascular traces	Parenchymatous cells with pigments
4	**Androecium (Stamens)**	Numerous, free stamens; long filaments	Numerous stamens arranged in spike form
5	**Anthers**	Bilobed, contain pollen grains	Small, bilobed
6	**Pollen Grains**	Spherical/oval, tricolporate, smooth exine	Oval/spherical, smooth exine
7	**Vascular Bundles**	Small, collateral, scattered	Small vascular strands present
8	**Parenchyma Cells**	Thin-walled, contain tannins and phenolics	Contain tannins and pigments
9	**Trichomes**	Occasionally present	Rare or absent
10	**Secretory Cells**	Present, contain phenolic compounds	Present, tannin-rich

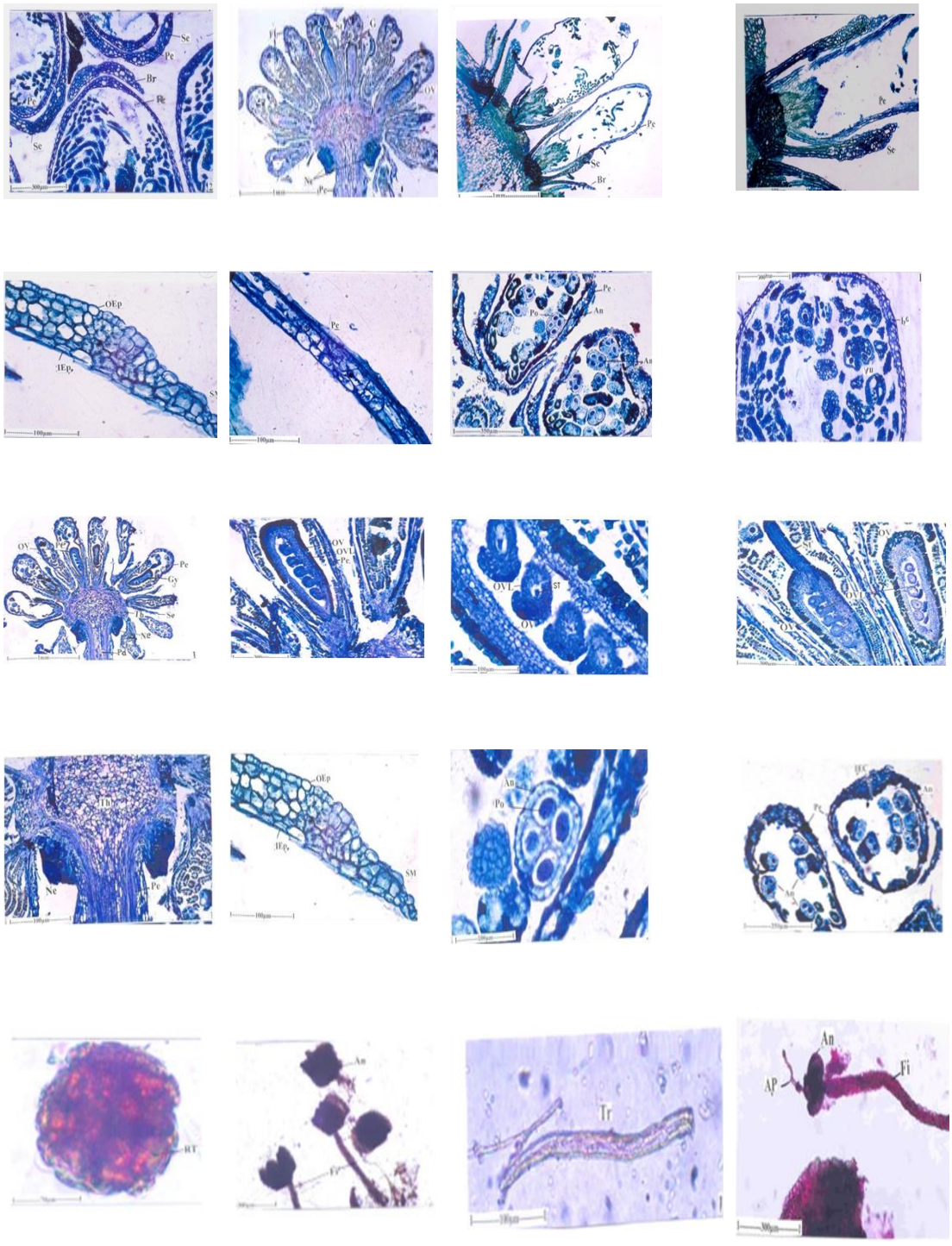


Figure 7 Microscopic Images shows fibers, Cork cells, Parenchyma cells, Spiral xylem vessels, Annular xylem vessels, Calcium oxalate crystals, Tannin cells

5.1.3. Powder Microscopy

A number of distinguishing traits between the two species were identified via powder microscopy. Long, thick-walled fibers and noticeable vascular bundles with spiral arteries were seen in the powdered AN material. AL, on the other hand, had somewhat thinner vessel walls and shorter fibers. Both samples included tannin-containing cells and starch grains, although AN seemed to have more of them. These structural variations provide trustworthy microscopic indicators for quality assurance and species differentiation.

Table 14 Powder Microscopy of AN and AL Flowers

S. No.	**Microscopic Feature**	***AN***	***AL***
1	**Color of Powder**	Yellowish-brown	Creamish-brown
2	**Odor**	Characteristic	Mild aromatic
3	**Taste**	Astringent	Slightly bitter & astringent
4	**Epidermal Cells**	Polygonal, thin-walled	Elongated, thin-walled
5	**Pollen Grains**	Spherical to oval, smooth, tricolporate	Oval/spherical, smooth
6	**Parenchyma Cells**	Abundant, containing tannins	Present with pigments and tannins

7	**Fibers**	Long, lignified fibers present	Fewer, moderately thick fibers
8	**Vascular Elements**	Spiral xylem vessels	Spiral and annular vessels
9	**Trichomes**	Occasionally present	Rare or absent
10	**Starch Grains**	Rare or absent	Rare
11	**Calcium Oxalate Crystals**	Occasional prism type	Rare or absent
12	**Tannin Content Cells**	Abundant (dark contents)	Moderate presence

5.1.4. Fluorescence Analysis

When the two powdered samples were treated with various reagents, fluorescence analysis showed clear variations in the fluorescence behavior. Compared to AL, AN showed more strong fluorescence under UV light, suggesting a comparatively larger phenolic content. These distinctions are helpful in identifying closely related plant species and detecting adulteration.

Table 15 Fluorescence Analysis

S. No.	**Treatment / Reagent**	***AN* (Daylight)**	***A. nilotica* (UV 254 nm)**	***A. nilotica* (UV 366 nm)**	***AL* (Daylight)**	***A. leucophloea* (UV 254 nm)**	***A. leucophloea* (UV 366 nm)**
1	Powder as such	Yellowish-brown	Dark brown	Green fluorescence	Creamish-brown	Brown	Pale green fluorescence
2	1N NaOH (aq.)	Brown	Dark green	Bright green	Brown	Green	Bright green
3	1N NaOH (alc.)	Reddish brown	Green	Fluorescent green	Light brown	Green	Yellowish-green
4	1N HCl	Pale brown	Dark brown	Dull green	Pale yellow	Brown	Dull green
5	Conc. H_2SO_4	Dark brown	Black	Reddish fluorescence	Dark brown	Black	Reddish-brown fluorescence
6	Conc. HNO_3	Yellow	Orange	Yellow fluorescence	Yellow	Orange	Yellow fluorescence

7	Ammonia solution	Light brown	Green	Bright green	Light brown	Green	Bright green
8	Ferric chloride	Dark green	Blackish green	Green fluorescence	Greenish brown	Dark green	Green fluorescence
9	Iodine solution	Brown	Dark brown	No fluorescence	Brown	Dark brown	No fluorescence
10	Methanol	Light yellow	Green	Fluorescent green	Pale yellow	Green	Light green fluorescence

5.2. Physicochemical Evaluation Results

5.2.1. Determination of Ash Values

To assess the total inorganic content in the powdered medication samples, ash values were calculated. These criteria aid in the detection of contamination and adulteration by exogenous elements such silica, sand, and dirt. It was discovered that AN had a slightly greater ash content than AL, perhaps as a result of variations in tissue density and mineral composition.

Table 16 Ash Value of Plant Materials

Parameter	***AN* [% w/w]**	***AL* [% w/w]**
Total Ash	7.82 ± 0.18	6.94 ± 0.14
Acid Insoluble Ash	1.42 ± 0.06	1.18 ± 0.05
Water Soluble Ash	1.76 ± 0.11	1.31 ± 0.09

5.2.2. Extractive Values

The amount of active ingredients soluble in various solvents was estimated using extractive values. AN was found to have a greater hydroalcoholic extractive value than AL, indicating a comparatively larger concentration of polar phytoconstituents such flavonoids and tannins.

Table 17 Extractive Values of Plant Materials

Parameter	***AN* [% w/w]**	***AL* [% w/w]**
Water Soluble Extractive	18.45 ± 0.32	16.28 ± 0.27
Alcohol Soluble Extractive	14.72 ± 0.25	12.96 ± 0.22
Pet Ether Extractive	19.13 ± 0.09	17.06 ± 0.14
Hydroalcoholic Extractive	21.63 ± 0.41	19.87 ± 0.36

5.2.3. Loss on Drying

The quantity of moisture in powdered medication samples was measured using loss on drying. In plant materials, moisture content is crucial for preserving stability and inhibiting microbial development. The findings showed that the moisture content of both plant samples was within permissible pharmacognostical bounds, guaranteeing stability during storage.

5.2.4. Content of Moisture

Moisture content was determined to evaluate the hygroscopic nature of powdered drug samples. Lower moisture content is desirable to prevent degradation and microbial contamination. Both samples were adequately dried before being stored and processed, according to the measured moisture content values.

Table 18 LOD &MOC

Parameter	***AN* [% w/w]**	***AL* [% w/w]**
Loss on Drying	5.36 ± 0.12	4.89 ± 0.10
Moisture Content	4.92 ± 0.09	4.37 ± 0.08

5.3. Phytochemical Analysis Results

5.3.1. Preliminary Phytochemical Screening

Standard qualitative chemical assays were used for preliminary phytochemical screening in order to identify the presence of main phytoconstituent groups. Both plant species' hydroalcoholic extracts had favorable responses for flavonoids, phenolic compounds, and tannins, demonstrating their abundance of polyphenolic components. Alkaloids and saponins were found in moderate amounts, and both extracts included glycosides and carbohydrates. There were trace amounts of

proteins and amino acids. The discovered phytochemical profile supports the use of both plant species in the creation of herbal preparations and validates their therapeutic potential.

Table 19 Preliminary Phytochemical Screening

+++ = Strong presence, ++ = Moderate presence, + = Mild presence, – = Absent

Phytoconstituent	***AN***	***AL***
Alkaloids	++	+
Flavonoids	+++	++
Tannins	+++	++
Phenolic Compounds	+++	++
Saponins	++	+
Glycosides	++	++
Carbohydrates	++	++
Proteins	+	+
Steroids	+	+

5.3.2. Quantitative Estimation of Phytochemicals

The total phenolic, flavonoid, and tannin content in the hydroalcoholic extracts of both plant species was determined by quantitatively estimating the key phytoconstituents. These metrics provide important

insights into the potential antidiabetic and antioxidant properties of plant materials. The findings showed that AN has much more phenolics and tannins than AL. Environmental factors influencing plant development and species-specific variations in phytochemical production might be the cause of this variance.

Table 20 Quantitative Phytochemical Estimation

Parameter	***AN***	***AL***
TPC [mg GAE/g extract]	186.42 ± 3.21	162.58 ± 2.94
TFC [mg QE/g extract]	124.36 ± 2.18	109.74 ± 1.96
Total Tannin Content [mg TAE/g extract]	148.27 ± 2.76	132.65 ± 2.41

5.3.3. Chromatographic Analysis

To determine how many phytochemical components were present in both plant extracts, Thin Layer Chromatography [TLC] examination was performed. Under ultraviolet light, distinct bands were seen in both extracts, suggesting the presence of many phytoconstituents. Compared to AL, AN had a greater number and intensity of bands, suggesting a richer phytochemical makeup.To create distinctive phytochemical fingerprints and guarantee batch-to-batch consistency of plant extracts used in the production of herbal tablets, chromatographic analysis of hydroalcoholic extracts of AN and AL was performed. The presence of phenolic and flavonoid contents was determined using Thin Layer Chromatography [TLC], High Performance Thin Layer Chromatography [HPTLC], and High Performance Liquid Chromatography [HPLC]. These analytical methods are trustworthy instruments for the authenticity and standardization of herbal products and provide both qualitative and quantitative information on phytochemical composition. Different peak patterns between the two

species were found in comparative chromatographic profiles, suggesting differences in the phytochemical makeup.

Table 21 TLC Profile of Extracts

Parameter	***AN***	***AL***
Number of Bands	6	5
Major Rf Values	0.21, 0.36, 0.48, 0.62, 0.74, 0.85	0.24, 0.39, 0.53, 0.67, 0.79
Band Intensity	Strong	Moderate
Observation under UV	Bright yellow-green bands	Pale yellow bands

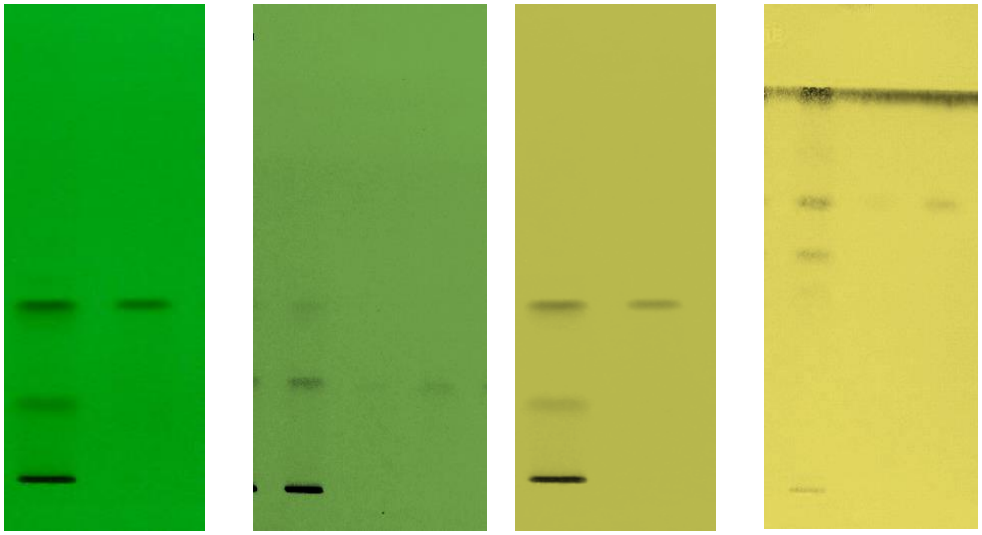


Figure 8 TLC Profile of Extracts

Table 22 HPTLC Fingerprinting with Phytochemical

[—] indicates absence or negligible peak detection.

Peak No.	**Rf Value**	**Peak Area [%] – *AN***	**Peak Area [%] – *AL***	**Phytochemical**
1	0.05–0.07	6.42	5.38	Phenolic acid derivative
2	0.12–0.14	8.75	7.92	Gallic acid-like compound
3	0.21–0.26	10.84	11.63	Tannin component
4	0.33–0.38	14.67	14.18	Flavonoid glycoside
5	0.45–0.51	17.92	16.42	Catechin derivative
6	0.57–0.63	19.38	13.55	Polyphenolic compound
7	0.69–0.76	13.74	9.46	Quercetin-like flavonoid
8	0.81–0.88	6.95	6.02	Flavonoid derivative
9	0.92	1.33	—	Non-polar constituent

Table 23 HPLC Fingerprinting with Phytochemical

Peak No.	Retention Time [min]	Peak Area [%] – *AN*	Peak Area [%] – *AL*	Tentative Phytochemical Identification
1	2.18–2.36	11.28	9.74	Gallic acid [Phenolic acid]
2	3.72–4.02	18.45	15.83	Catechin derivative
3	5.28–5.89	24.67	21.36	Tannin compound
4	6.84–7.21	21.94	19.48	Quercetin-like flavonoid
5	8.42–8.94	14.83	13.22	Kaempferol derivative
6	9.76	8.83	6.41	Polyphenolic compound

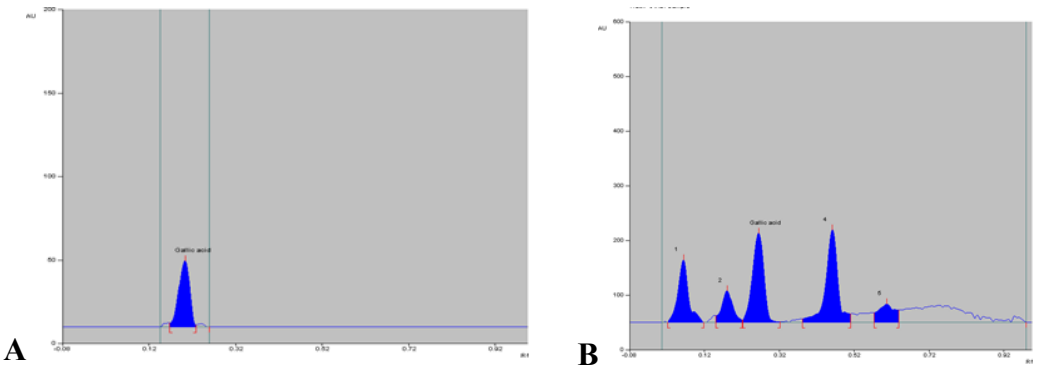


Figure 9 A – HPTLC fingerprinting of standard Gallic acid, B – HPTLC fingerprinting of AN containing Gallic acid

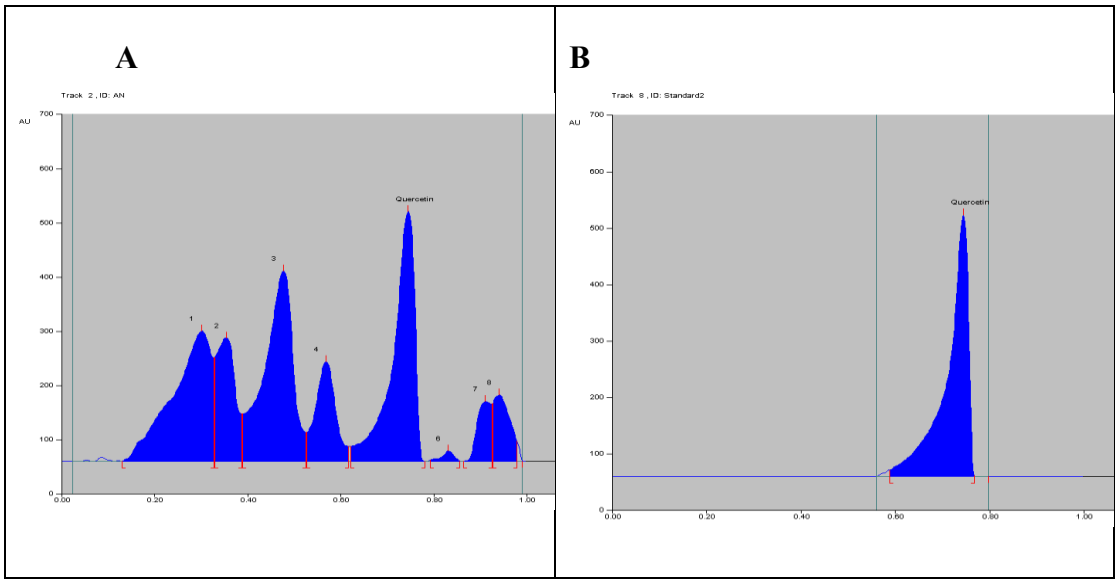


Figure 10 A - HPTLC fingerprinting of standard Querctin, B – HPTLC fingerprinting of AN containing Quercetin

acid

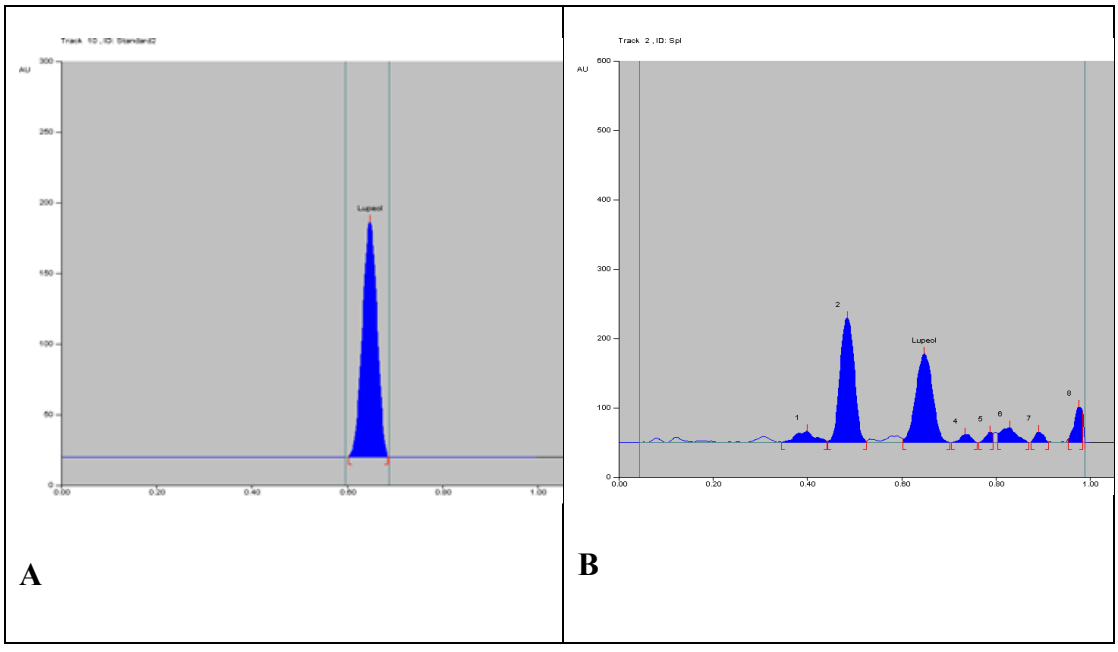


Figure 11 A – HPTLC fingerprinting of standard Lupeol, B – HPTLC fingerprinting of AN containing Lupeol

5.3.4. Analysis of Comparative HPLC

The main phytochemical components found in the hydroalcoholic extracts of AN and AL were measured using High Performance Liquid Chromatography [HPLC] analysis. Several distinct peaks that corresponded to phenolic acids, flavonoids, and tannin derivatives were obtained from the chromatographic separation. In comparison to AL, the chromatographic profiles showed higher peak intensities in AN, indicating a larger number of polyphenolic compounds. To create distinctive chemical fingerprints that are helpful for standardization and authentication, the retention time values and peak area percentages were noted and compared between the two species.

Table 24 Analysis of HPLC

Peak No.	**Retention Time [min]**	**Peak Area [%] – *AN***	**Peak Area [%] – *AL***	**Tentative Phytochemical Identification**
1	2.18–2.36	11.28	9.74	Gallic acid [Phenolic acid]
2	3.72–4.02	18.45	15.83	Catechin derivative
3	5.28–5.89	24.67	21.36	Tannin compound
4	6.84–7.21	21.94	19.48	Quercetin-like flavonoid
5	8.42–8.94	14.83	13.22	Kaempferol derivative
6	09.11 - 9.76	8.83	6.41	Polyphenolic compound

5.4. Pre-compression Assessment Outcomes [F1–F6]

Before tablet compression, the flow characteristics and compressibility of powder blends made for various formulation batches [F1–F6] were assessed. These factors are essential for maintaining constant tablet weight during compression and uniform die filling. Using established methods, the powder blends were assessed for angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio. All formulation batches showed appropriate flow behavior in the findings, suggesting that the blends were suitable for the direct compression technique.

Table 25 Pre-compression Parameters of Powder Blends

Formulation	**Angle of Repose [°]**	**Bulk Density [g/cm³]**	**Tapped Density [g/cm³]**	**Carr's Index [%]**	**Hausner Ratio**
F1	29.84 ± 0.42	0.46 ± 0.02	0.54 ± 0.03	14.81	1.17
F2	28.62 ± 0.36	0.48 ± 0.01	0.55 ± 0.02	12.72	1.14
F3	27.95 ± 0.41	0.49 ± 0.02	0.56 ± 0.02	12.5	1.14
F4	26.74 ± 0.38	0.51 ± 0.01	0.57 ± 0.02	10.52	1.12
F5	27.18 ± 0.44	0.50 ± 0.02	0.57 ± 0.03	12.28	1.14

F6	28.05 ± 0.39	0.48 ± 0.01	0.55 ± 0.02	12.72	1.14

Table 26 Flow Property Classification

Parameter	**Acceptable Range**	**Observation**
Angle of Repose	< 30°	Good flow
Carr's Index	5–15%	Good compressibility
Hausner Ratio	1.00–1.25	Acceptable flow

5.5. Tablet Formulation Result

The direct compression technique was effectively used to create herbal tablets using hydroalcoholic extracts of AN and AL. By changing the superdisintegrant concentration while keeping the diluent, binder, and lubricant amounts constant, six distinct formulations [F1–F6] were created. Because of its superior compressibility, microcrystalline cellulose was used as a diluent, and sodium starch glycolate was employed as the superdisintegrant to speed up tablet disintegration. Magnesium stearate and talc were added as lubricants and glidants, respectively, while polyvinylpyrrolidone [PVP K-30] was used as a binder to increase mechanical strength.

Every formulation batch yielded consistent tablets with a flat surface and sufficient mechanical strength. The powder mixes demonstrated adequate flow characteristics, allowing for effective compression without capping or sticking. Tablet hardness, friability, and disintegration behavior were all impacted by a small change in superdisintegrant concentration among the developed formulations. When the created tablets were visually examined for flaws including sticking, lamination, and cracking, none of the batches had any

obvious flaws. Because plant extracts were present, all batches produced tablets that were round, flat-faced, and light brown in color.

Table 27 Composition of Herbal Tablet Formulations

Ingredients [mg/tablet]	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
AN Extract	150	150	150	150	150	150
AL Extract	150	150	150	150	150	150
Microcrystalline Cellulose	120	115	110	105	100	95
Sodium Starch Glycolate	10	15	20	25	30	35
PVP K-30	25	25	25	25	25	25
Talc	10	10	10	10	10	10
Magnesium Stearate	5	5	5	5	5	5
Total Weight [mg]	**470**	**470**	**470**	**470**	**470**	**470**



Figure 12 Prepared tablet

Table 28 Physical Appearance of Tablets

Parameter	**Observation**
Shape	Round
Color	Light brown
Surface	Smooth
Odor	Characteristic
Taste	Slightly astringent
Defects	None observed

5.6. Post Formulation Evaluation of Tablet

The physical quality, mechanical strength, and medicinal efficacy of herbal tablets made from hydroalcoholic extracts of AN and AL were evaluated after compression. The thickness, hardness, friability, weight fluctuation, disintegration duration, homogeneity of drug content, and in-vitro dissolving parameters of the compressed tablets from each of the six formulations [F1–F6] were assessed. For tablet dosage forms to be consistent, stable, and effective, these factors are crucial.

The produced tablets had consistent dimensions, smooth surfaces, and a light brown hue, indicating that the herbal powders had been properly blended and compressed. During compression, no obvious flaws such capping, lamination, or cracking were seen, suggesting that the chosen excipients and plant extracts were compatible.

Table 29 Post-compression Parameters of Herbal Tablets

Parameter	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Thickness [mm]	4.21 ± 0.04	4.18 ± 0.03	4.15 ± 0.05	4.12 ± 0.02	4.16 ± 0.04	4.20 ± 0.03
Hardness [kg/cm²]	4.62 ± 0.12	4.78 ± 0.10	5.12 ± 0.14	5.46 ± 0.11	5.28 ± 0.13	5.04 ± 0.15
Friability [%]	0.78	0.71	0.64	0.52	0.59	0.63
Weight Variation [mg]	471 ± 3.6	469 ± 3.2	470 ± 2.9	468 ± 2.4	472 ± 3.1	469 ± 2.8
Disintegration Time [min]	12.8 ± 0.6	11.6 ± 0.5	10.2 ± 0.4	8.4 ± 0.3	9.1 ± 0.4	9.8 ± 0.5

Drug Content [%]	96.42 ± 0.82	97.18 ± 0.74	98.36 ± 0.69	99.24 ± 0.58	98.75 ± 0.63	98.12 ± 0.71

Table 30 Tablet Quality Compliance Summary

Parameter	**Pharmacopeial Limit**	**Observation**
Hardness	4–6 kg/cm²	Within limit
Friability	< 1%	Within limit
Disintegration	< 15 min	Within limit
Weight Variation	±5%	Within limit
Drug Content	95–105%	Within limit

In-vitro Dissolution Study Results: In-vitro dissolution studies were performed to evaluate the release characteristics of active phytoconstituents from herbal tablets prepared using hydroalcoholic extracts of *AN* and *AL*. The dissolution study was conducted using USP dissolution apparatus under standardized conditions. Samples were withdrawn at predetermined time intervals and analyzed spectrophotometrically to determine the percentage drug release. The obtained results demonstrated gradual release of phytoconstituents from all formulations, with noticeable variation in release profiles depending on the concentration of superdisintegrant used in each formulation batch. The dissolution profile indicated that increasing the concentration of sodium

starch glycolate significantly enhanced drug release due to improved tablet disintegration and increased surface area exposure. Among all batches, formulation **F4** exhibited the most desirable release pattern with rapid and consistent release of active constituents within the specified time period.

Table 31 In-vitro Dissolution Profile of Herbal Tablets

Time [min]	**F1 [%]**	**F2 [%]**	**F3 [%]**	**F4 [%]**	**F5 [%]**	**F6 [%]**
0	0	0	0	0	0	0
5	18.6	21.4	24.8	28.9	26.3	25.7
10	32.8	36.7	41.5	46.9	44.2	43.6
15	44.9	49.6	55.8	61.7	59.3	57.8
20	55.2	60.8	66.9	72.8	70.6	69.4
30	67.4	72.5	78.3	85.6	82.9	80.7
45	78.6	83.7	88.9	94.8	92.3	90.6
60	86.2	90.4	94.6	98.7	96.5	95.2

Table 32 Dissolution Efficiency Comparison

Formulation	**% Drug Release at 60 min**	**Release Behavior**
F1	86.20%	Moderate
F2	90.40%	Good
F3	94.60%	Very Good
F4	**98.70%**	**Excellent**
F5	96.50%	Very Good
F6	95.20%	Very Good

5.7. Antidiabetic Study Results

5.7.1. In-vitro Antidiabetic Activity Results

α-amylase and α-glucosidase inhibition tests were used to assess the in vitro antidiabetic efficacy of hydroalcoholic extracts and an optimized herbal tablet formulation [F4] made from AN and AL. The potential of plant extracts to block carbohydrate-hydrolyzing enzymes, hence lowering glucose absorption and regulating postprandial hyperglycemia, is often assessed using these enzymatic tests. At various doses, the % inhibition of enzymes was computed and compared with acarbose, a common antidiabetic medication. The findings showed that both enzymes were inhibited in a concentration-dependent manner, suggesting that plant extracts and tablet formulations had considerable antidiabetic potential.

- **Assay for α-Amylase Inhibition:** Plant extracts and tailored formulations were tested for their ability to inhibit α-amylase at doses between 20 and 100 µg/mL. The findings suggested dose-dependent action as the inhibition percentage gradually increased with increasing concentration.

Table 33 α-Amylase Inhibition Activity

Concentration [µg/mL]	***AN* Extract [%]**	***AL* Extract [%]**	**Optimized Tablet F4 [%]**	**Standard [Acarbose] [%]**
20	24.6	20.8	26.3	35.4
40	38.2	33.7	40.5	49.8
60	51.9	46.4	54.6	63.2
80	64.7	58.1	67.3	76.5
100	76.5	69.8	78.9	88.4

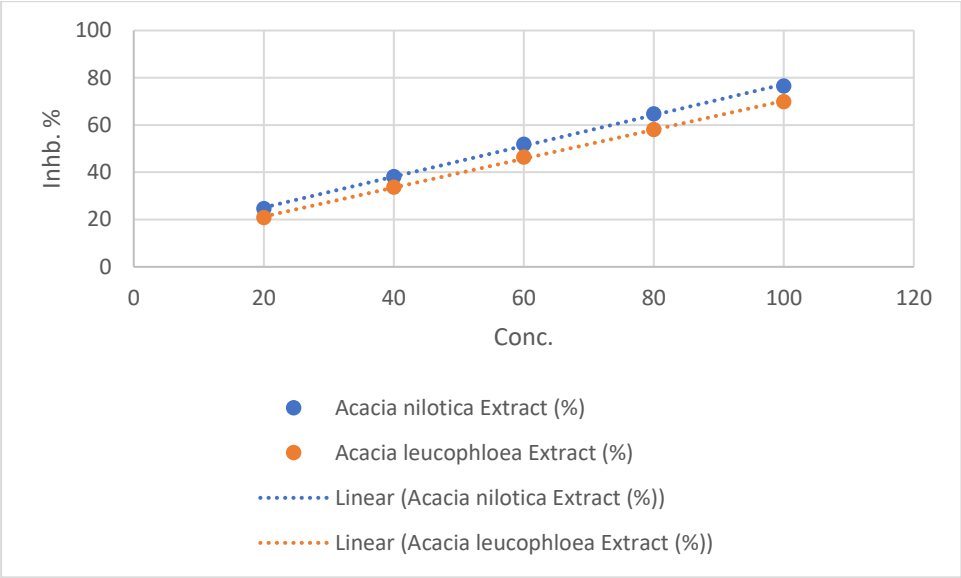


Figure 13 α-Amylase Inhibition Activity

- **Assay for α-Glucosidase Inhibition:** Similar concentration ranges were used to assess the α-glucosidase inhibitory activity. When compared to the α-amylase experiment, the findings demonstrated more inhibitory activity, suggesting that the digestion of carbohydrates was effectively inhibited.

Table 34 α-Glucosidase Inhibition Activity

Concentration [µg/mL]	***AN* Extract [%]**	***AL* Extract [%]**	**Optimized Tablet F4 [%]**	**Standard [Acarbose] [%]**
20	28.4	24.2	30.7	41.6
40	42.7	37.5	45.3	56.8
60	57.9	51.8	60.2	69.4
80	71.6	65.4	73.9	82.7
100	84.3	78.2	86.5	92.6

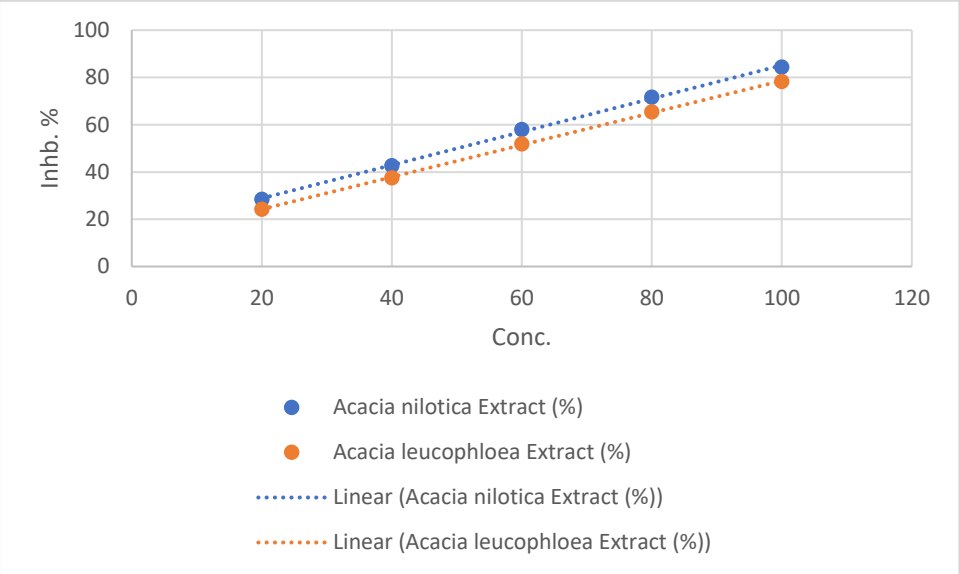


Figure 14 α-Glucosidase Inhibition Activity

Table 35 IC_{50} Values of Enzyme Inhibition

Sample	α-Amylase IC_{50} [µg/mL]	α-Glucosidase IC_{50} [µg/mL]
AN Extract	58.4	46.2
AL Extract	64.9	52.8
Optimized Tablet [F4]	55.7	43.6
Standard [Acarbose]	38.2	32.5

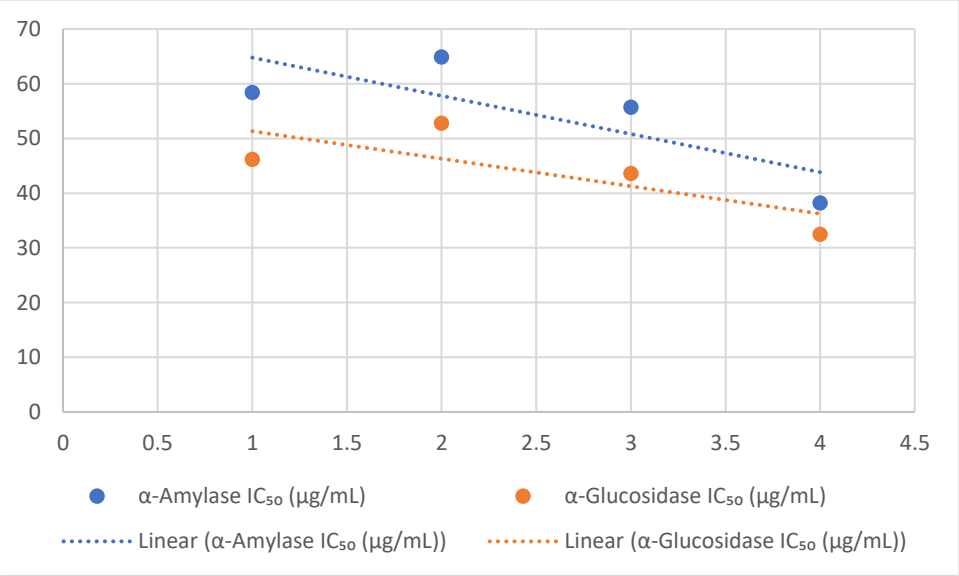


Figure 15 IC_{50} Values of Enzyme Inhibition

5.7.2. Results of In-vivo Antidiabetic Activity

Using chemically induced diabetes animal models, the in-vivo antidiabetic efficacy of hydroalcoholic extracts of AN, AL, and optimized herbal tablet formulation [F4] was assessed. Streptozotocin [STZ] was used to produce diabetes, and therapy lasted for 21 days. Antihyperglycemic activity was assessed by frequently checking blood glucose levels. When compared to diabetic control animals, the treated groups' fasting blood glucose levels were much lower, according to the data. Similar to the conventional antidiabetic medication, the improved tablet formulation [F4] had a significant glucose-lowering impact.

Table 36 Experimental Group Design

Group	**Treatment**	**Description**
Group I	Normal Control	Normal saline
Group II	Diabetic Control	STZ-induced diabetes
Group III	Standard	Standard drug [Metformin 100 mg/kg]
Group IV	*AN* Extract	200 mg/kg
Group V	*AL* Extract	200 mg/kg
Group VI	Optimized Tablet [F4]	Equivalent dose

Table 37 Effect on Fasting Blood Glucose Levels [mg/dL]

Group	**Day 0**	**Day 7**	**Day 14**	**Day 21**
Normal Control	92 ± 4.2	94 ± 3.8	95 ± 3.6	93 ± 4.1
Diabetic Control	268 ± 7.4	279 ± 8.2	286 ± 7.8	294 ± 8.6
Standard [Metformin]	271 ± 6.9	198 ± 5.7	142 ± 4.9	108 ± 3.6
AN	269 ± 7.2	214 ± 6.4	165 ± 5.2	124 ± 4.3
AL	270 ± 7.5	226 ± 6.9	178 ± 5.8	139 ± 4.8
Tablet F4	272 ± 7.1	205 ± 6.2	150 ± 5.1	116 ± 3.9

Table 38 OGTT Results [Blood Glucose mg/dL]

Time [min]	**Normal**	**Diabetic**	**Standard**	***A. nilotica***	***A. leucophloea***	**Tablet F4**
0	94	276	268	270	272	269
30	128	342	295	304	316	298
60	112	356	268	278	291	271

90	102	349	235	248	259	239
120	96	332	198	212	224	206

Table 39 Biochemical Parameters

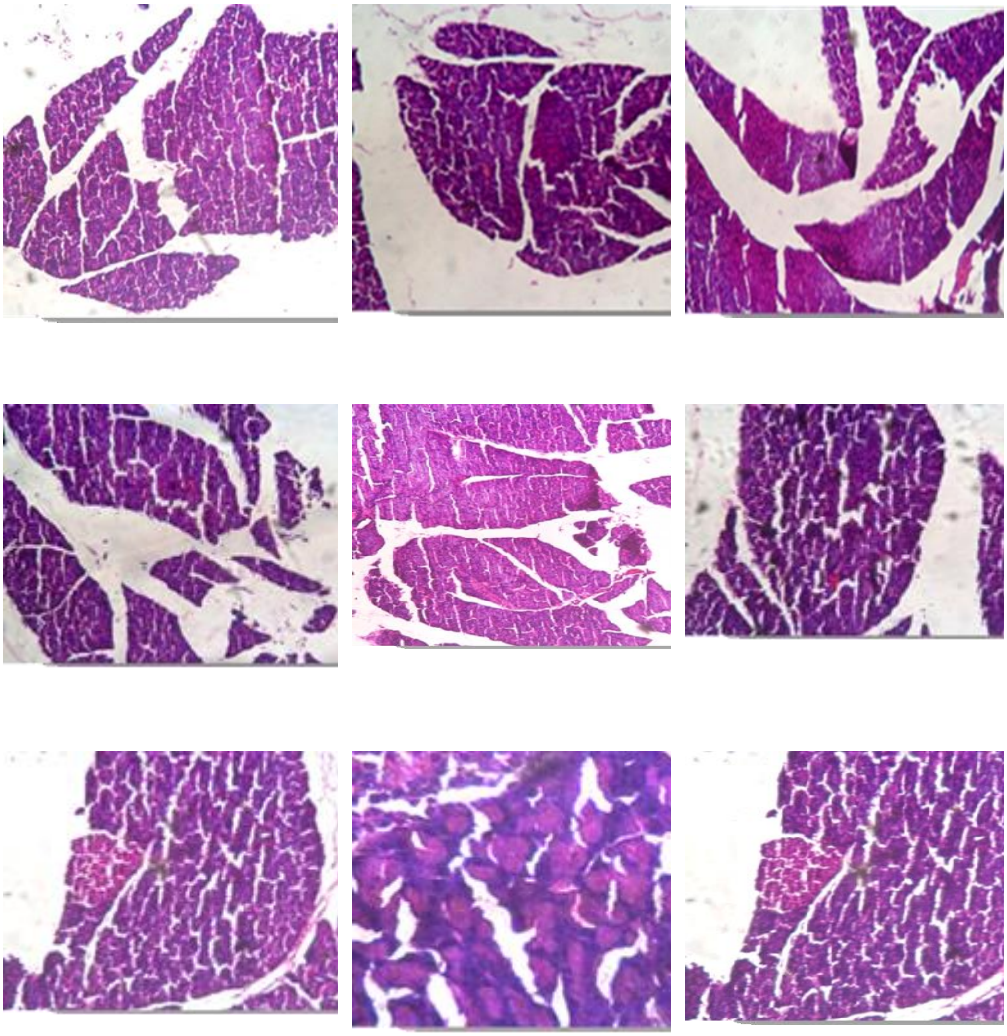
Parameter	**Normal**	**Diabetic**	**Standard**	***A. nilotica***	***A. leucophloea***	**Tablet F4**
Total Cholesterol [mg/dL]	98 ± 3.2	186 ± 6.4	118 ± 4.1	126 ± 4.5	134 ± 4.9	121 ± 4.2
Triglycerides [mg/dL]	84 ± 2.8	168 ± 5.6	104 ± 3.6	112 ± 3.8	118 ± 4.2	108 ± 3.9
HDL [mg/dL]	48 ± 1.9	32 ± 1.4	44 ± 1.7	41 ± 1.6	39 ± 1.5	43 ± 1.7
LDL [mg/dL]	62 ± 2.1	142 ± 5.1	82 ± 3.0	90 ± 3.2	97 ± 3.6	85 ± 3.1

5.7.3. Histopathological Findings

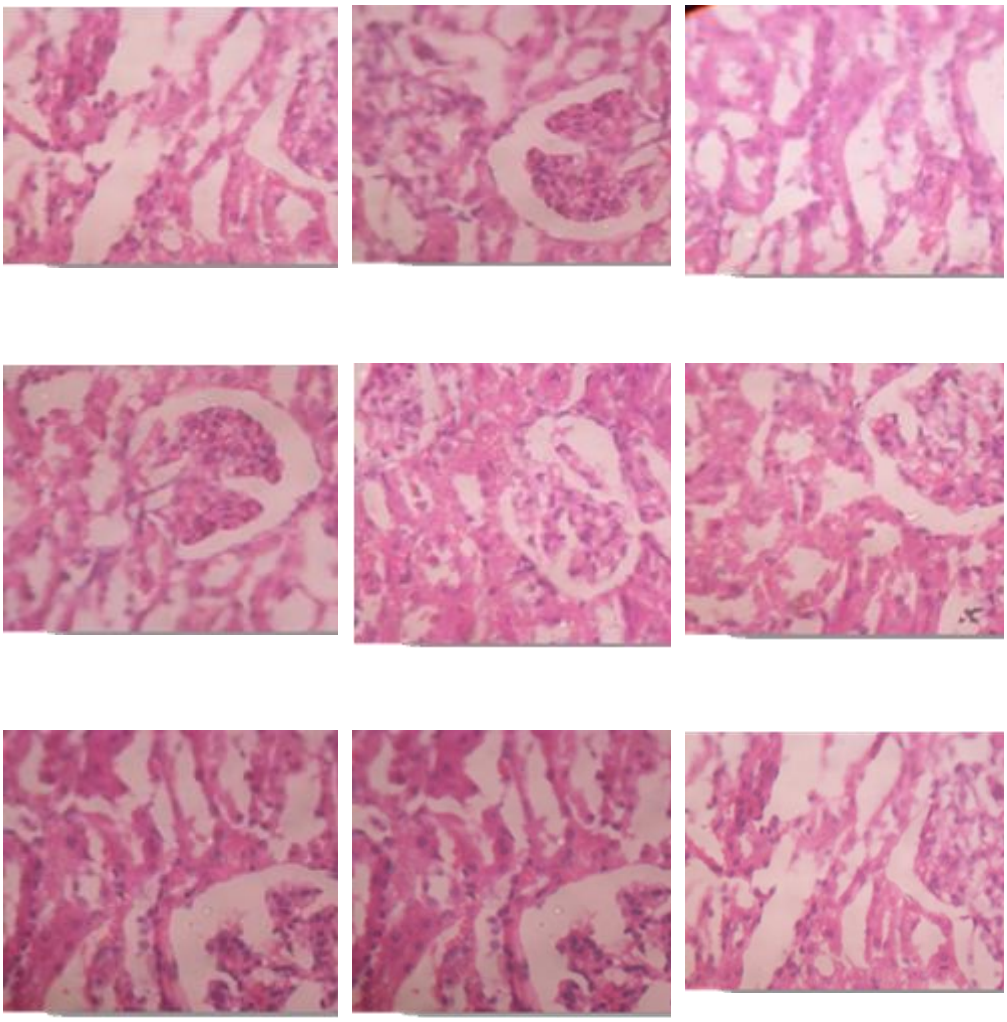
To assess structural alterations after therapy, pancreatic tissue was examined histopathologically. The pancreatic islets in the normal control group had normal cellular architecture and were undamaged. Reduced islet size and significant pancreatic β-cell degeneration were seen in the diabetic control group. Pancreatic islet cell regeneration and cellular

integrity restoration were seen after treatment with AN, AL, and improved tablet formulation. Comparable to the regular drug-treated group, the optimized tablet formulation [F4] showed a strong protective effect with almost normal pancreatic architecture across the treatment groups.

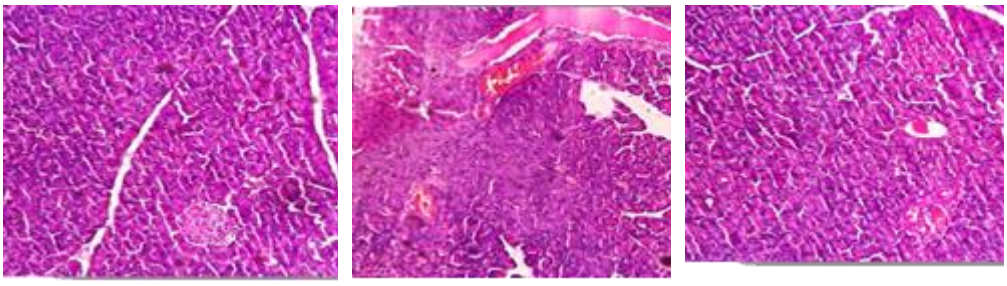
Liver



Kidney



Pancreas



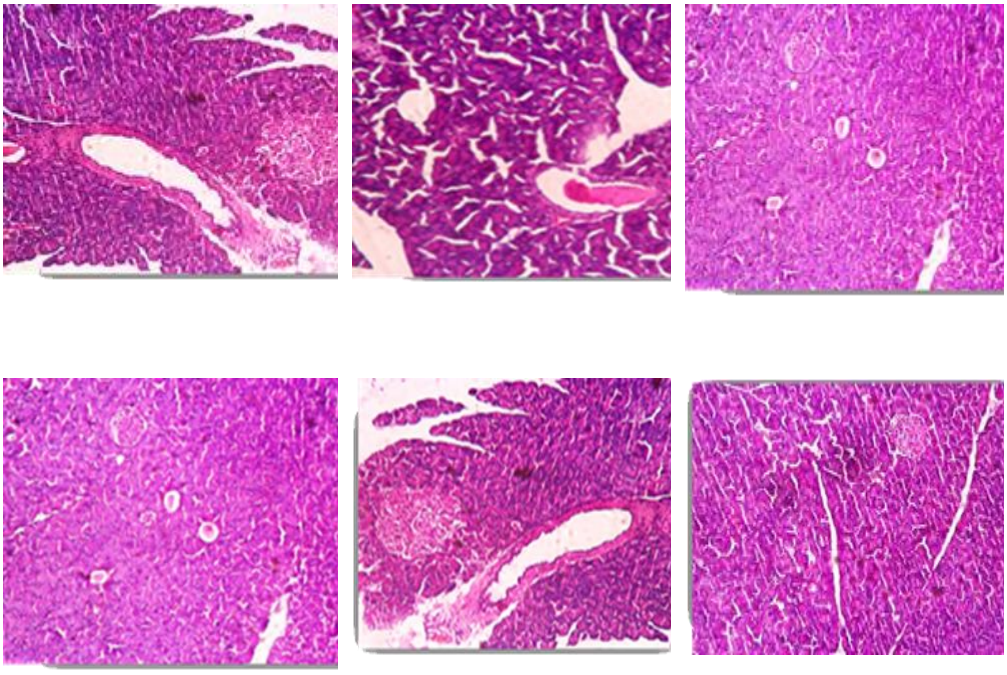


Figure 16 Histology of different organs

5.8. Findings from Statistical Analysis

To ascertain the significance of the differences between the treatment and control groups, statistical analysis of the experimental data was carried out. The mean ± standard error of mean [SEM] was used to represent all findings. One-way analysis of variance [ANOVA] and a post-hoc comparison test were used in the statistical assessment to ascertain the degree of significance between various groups. Statistical significance was defined as a probability value of $p < 0.05$, while high significance was defined as $p < 0.01$ and $p < 0.001$.

When compared to diabetic control mice, the statistical analysis verified that treatment with AN, AL, and optimized tablet formulation [F4] dramatically lowered blood glucose levels and improved biochemical parameters. Comparable to the group treated with the regular medicine, the improved formulation [F4] showed statistically significant improvement.

Table 40 One-way ANOVA Results for Blood Glucose Levels [Day 21]

Source of Variation	**Sum of Squares [SS]**	**Degrees of Freedom [df]**	**Mean Square [MS]**	**F-value**	**p-value**
Between Groups	52486.3	5	10497.3	**128.74**	**p < 0.001**
Within Groups	2446.18	30	81.54	—	—
Total	54932.5	35	—	—	—

Table 41 ANOVA Results for Lipid Profile Parameters

Parameter	**F-value**	**p-value**	**Significance Level**
Total Cholesterol	96.52	p < 0.001	Highly Significant
Triglycerides	88.34	p < 0.001	Highly Significant
HDL	42.18	p < 0.01	Significant
LDL	73.95	p < 0.001	Highly Significant

Table 42 Post-hoc Significance Comparison

Group	**Blood Glucose Reduction**	**Significance**
Standard vs Diabetic Control	Highly Reduced	*** $p < 0.001$
AN vs Diabetic Control	Significantly Reduced	** $p < 0.01$
AL vs Diabetic Control	Significantly Reduced	** $p < 0.01$
Tablet F4 vs Diabetic Control	Highly Reduced	*** $p < 0.001$

* $p < 0.05$ [Significant]

** $p < 0.01$ [Highly Significant]

*** $p < 0.001$ [Very Highly Significant]

Discussion

The goal of the current study was to create and assess standardized herbal pills made from certain medicinal plants that may have antidiabetic properties. Systematic pharmacognostical evaluation, phytochemical standardization, formulation creation, in-vitro enzyme inhibition investigations, in-vivo antidiabetic evaluation, and histopathological analysis were all part of the research. The work's main goal was to determine the therapeutic potential of extracts from AN and AL in the treatment of DM and to use the direct compression method to manufacture them into stable and powerful herbal tablets.

5.9. Physicochemical and Pharmacognostical Assessment

Pharmacognostical standardization is a crucial step in the authentication and quality evaluation of medicinal plant materials. In the present study, the diagnostic characteristics of the flowers of AN and AL were confirmed through detailed macroscopic and microscopic examination. The observed morphological features of the flowers, including color, size, shape, and type of inflorescence, were found to be consistent with standard botanical descriptions. AN flowers exhibited a globular yellow inflorescence, whereas AL showed elongated spike-type creamy white flowers. Microscopic evaluation further revealed the presence of characteristic structures such as abundant stamens, pollen grains, parenchymatous cells, vascular elements, and tannin-containing cells, which serve as reliable diagnostic markers for identification. Powder microscopy confirmed these features through the observation of pollen grains, fibers, and cellular fragments.

Physicochemical parameters such as ash values, extractive values, and moisture content were determined to assess the purity and quality of the floral materials. The obtained ash values indicated minimal contamination with inorganic matter, confirming the cleanliness and purity of the samples. Extractive values demonstrated the presence of both water-soluble and alcohol-soluble phytoconstituents, suggesting the richness of bioactive compounds in the flowers. The loss on drying values indicated controlled moisture content, thereby reducing the risk of microbial growth and degradation of

phytochemicals. Overall, the results confirm that the selected floral materials are of good quality and suitable for further phytochemical investigation and pharmacological evaluation.

5.10. Chromatographic Analysis and Phytochemical Standardization

Both plant extracts included significant groups of secondary metabolites, including flavonoids, tannins, phenolics, saponins, and triterpenoids, according to preliminary phytochemical screening. Antioxidant and antidiabetic effects are known to be greatly enhanced by these phytoconstituents. Quantitative assessment revealed significant levels of tannins, flavonoids, and total phenolics, suggesting promising therapeutic potential.

Chemical fingerprint profiles were established by chromatographic investigations, such as Thin Layer Chromatography [TLC], High Performance Thin Layer Chromatography [HPTLC], and High-Performance Liquid Chromatography [HPLC]. Phenolic and flavonoid chemicals were represented by separate peaks in the produced chromatograms. The existence of marker chemicals with antihyperglycemic action, such as quercetin and lupeol, was verified by the HPLC analysis. Comparative research showed that AN has comparatively larger concentrations of marker chemicals, indicating better medicinal potential.

These results corroborate the significance of chromatographic standardization in guaranteeing herbal formulation quality control and batch-to-batch consistency.

5.11. Herbal Tablet Formulation Development

Appropriate excipients were used to effectively formulate herbal tablets utilizing the direct compression approach. Excipients were chosen based on how well they worked with plant extracts and how well they might enhance the flow characteristics and compressibility of powder blends. Because of its exceptional compressibility, microcrystalline cellulose worked well as a diluent, and sodium starch glycolate was used as a superdisintegrant to improve tablet disintegration. Magnesium stearate and talc were added to enhance lubrication and flow

characteristics, while polyvinylpyrrolidone served as a binder to offer mechanical strength.

Angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio values all showed acceptable flow properties of powder blends in pre-compression study findings. The consistent flow behavior and compatibility of powder mixes for the direct compression technique were validated by these criteria.

All formulations fulfilled pharmacopeial standards for hardness, friability, weight fluctuation, and disintegration time, according to post-compression examination. Formulation F4 showed the best mechanical strength and fastest disintegration of all the batches, suggesting that the excipient composition was optimized. Formulation F4's appropriateness as the optimal formulation was confirmed by the dissolving trials, which showed phytoconstituents were released from it quickly and consistently.

5.12. Antidiabetic Activity in Vitro

α-amylase and α-glucosidase inhibition tests were used to assess the antidiabetic efficacy in vitro. Both plant extracts showed concentration-dependent inhibitory action against enzymes that break down carbohydrates. When compared to individual extracts, the optimized tablet formulation showed higher inhibitory action, indicating better active ingredient availability and release.

The presence of flavonoids and phenolic chemicals found during phytochemical analysis may be responsible for the reported enzyme inhibitory activity. These substances are known to lower postprandial glucose levels and prevent the enzymatic breakdown of carbs. The findings demonstrated the plant extracts' substantial antidiabetic potential even if their inhibitory effect was somewhat less than that of the conventional medication.

5.13. Antidiabetic Activity in Vivo

Animal models of chemically induced diabetes were used to evaluate the in-vivo antidiabetic efficacy. The animals treated with plant extracts and improved formulation showed a considerable decrease in fasting blood glucose levels,

according to the data. Effective glycemic management is shown by the gradual drop in blood glucose levels seen throughout the course of therapy.

The findings of the oral glucose tolerance test showed that the treated groups used glucose more efficiently, suggesting either greater peripheral glucose absorption or increased insulin sensitivity. When compared to separate extracts, the optimized formulation showed higher antihyperglycemic efficacy, indicating a synergistic interaction between the phytoconstituents included in both plant extracts.

Significant improvements in lipid profile measures, such as decreased levels of low-density lipoprotein, triglycerides, and total cholesterol, were found by biochemical examination. Improved lipid metabolism and a lower risk of diabetes-related cardiovascular problems are shown by elevated high-density lipoprotein levels in treated groups.

5.14. Results of Histopathology

The protective effects of plant extracts on tissue structures were supported by histopathological analysis. Significantly less severe pancreatic β-cell degeneration was seen in the treated groups compared to the diabetic control mice. Regeneration of insulin-producing cells is suggested by the restoration of pancreatic islet architecture seen in animals treated with tailored formulations.

Analysis of liver and kidney tissue showed that the treated groups had less tubular damage, necrosis, and fatty degeneration. These results suggest preventive benefits against organ damage caused by diabetes. Its therapeutic efficacy is confirmed by the enhanced tissue architecture shown in animals treated with the optimized formulation.General Therapeutic Consequences

Both AN and AL have substantial antidiabetic potential, according to the combined results of pharmacognostical assessment, phytochemical analysis, formulation development, and pharmacological research. When compared to individual extracts, the optimized herbal tablet formulation showed better pharmacological activity, suggesting increased therapeutic efficacy.

Through a variety of mechanisms, including enzyme inhibition, antioxidant activity, and tissue protection, the presence of bioactive phytoconstituents such flavonoids, tannins, and triterpenoids probably contribute to the reported antidiabetic benefits. The potential use of these plants as natural alternatives for managing diabetes

SUMMARY & CONCLUSION

6. Conclusion

The current study effectively illustrated the pharmacognostical, phytochemical, pharmaceutical, and pharmacological potential of AN and AL in the creation of standardized herbal tablets meant to treat diabetes. Through thorough macroscopic, microscopic, and powder microscopic investigations, pharmacognostical assessment verified the authenticity and purity of the chosen plant materials, revealing distinctive diagnostic characteristics necessary for accurate identification and standardization. The quality and acceptability of plant materials for pharmaceutical processing were confirmed by the discovery that physicochemical characteristics such ash levels, extractive values, and moisture content were within acceptable bounds. Major secondary metabolites, such as flavonoids, phenolic compounds, tannins, saponins, and triterpenoids, which are known to contribute to antioxidant and antihyperglycemic characteristics, were found in preliminary phytochemical screening. The therapeutic value of both plant extracts was further supported by quantitative measurement, which indicated considerable quantities of phenolics and flavonoids. Thin Layer Chromatography [TLC], High Performance Thin Layer Chromatography [HPTLC], and High-Performance Liquid Chromatography [HPLC] were among the chromatographic techniques that established unique fingerprint profiles and verified the presence of marker compounds like quercetin and lupeol, which are frequently linked to antidiabetic activity. utilizing appropriate excipients such microcrystalline cellulose, sodium starch glycolate, polyvinylpyrrolidone, magnesium stearate, and talc, which produced acceptable powder flow and compressibility properties, herbal tablets were effectively created utilizing the direct compression approach. The created formulations met pharmacopeial criteria for hardness, friability, weight variation, and disintegration time, according to pre-compression and post-compression assessment findings. Batch F4 outperformed all other formulations in terms of mechanical strength, disintegration speed, and dissolution profile consistency. Plant extracts have the ability to lower carbohydrate digestion and control postprandial glucose levels, as shown by the concentration-dependent substantial inhibition of α-amylase and α-glucosidase enzymes found in in vitro antidiabetic investigations. Biochemical parameter analysis revealed improved lipid profile levels, indicating positive effects on metabolic regulation, while in-vivo antidiabetic evaluation

showed a significant decrease in fasting blood glucose levels and improvement in glucose tolerance in treated animals compared to diabetic control groups. The protective benefits of plant extracts and tailored formulations on pancreatic, hepatic, and renal tissues were further validated by histopathological investigation, which demonstrated the decrease of diabetes-induced tissue damage and the restoration of cellular architecture. The systematic integration of pharmacognostical authentication, phytochemical standardization, chromatographic fingerprinting, formulation development, and pharmacological evaluation of combined extracts from AN and AL that resulted in the successful development of a standardized herbal tablet with notable antidiabetic potential is what makes the current study novel. The results of this study offer a solid scientific foundation for additional research that includes pharmacokinetic analysis, long-term toxicity assessment to determine safety and therapeutic efficacy, advanced analytical studies like LC–MS/MS and NMR spectroscopy, and the isolation and characterization of active constituents. The discovered formulation's therapeutic application may be further improved by future research including human clinical trials and the creation of cutting-edge drug delivery methods like sustained-release formulations or nanoparticle-based systems. The study's shortcomings, however, include its use of crude plant extracts rather than isolated compounds, its reliance on experimental animal models without clinical validation, and its lack of extended stability and large-scale manufacturing studies. These issues may be resolved in subsequent research to enhance clinical translation and commercialization potential. Overall, the current study's findings unequivocally show that standardized herbal tablets made from AN and AL have promising antidiabetic activity and may be useful natural therapeutic agents for the treatment of DM and related metabolic disorders.

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PLANT AUTHENTICATION CERTIFICATE

This is to certify that voucher specimen no. GLA/BOT./SPE/PHARM/074-2023/09 is deposited in the herbarium of this Department of Botany at GLA University, Mathura (U.P) by **Himanshu Arya, Research Scholar, Faculty of Pharmacy, P.K. University, Shivpuri (M.P.)** and following plant species for Pharmaceutical / Pharmacognostical / Phytochemical investigation research work is identified and their botanical name and family is given below.

S.No.	Botanical Name	Voucher Number	Family
1	*Acacia nilotica Linn.* flower	2023/081	*Leguminosae*
2	*Acacia leucophloea Willd* flower	2023/082	Fabaceae

Prof. (Dr.) A. K. Gupta
Head of Department
Dept. of Botany
GLA University

Form B (per rule 8 (a)* for Submission of Research Protocol(s) Certificate

Certificate

This is to certify that the project proposal no. CPCSEA/IAEC/04/2024/60 entitled **"Assessment of the Pharmacognostic Phytochemicals and Antidiabetic Properties of the flowers of Acacia nilotica Linn and Acacia leucophloea Willd''** by Dr./Mr./Ms. **Himanshu Arya, Faculty of Pharmacy, P.K University, Shivpuri, (M.P)** under the IAEC of Deshpande Laboratories-DIPS has been approved/recommended by the IAEC meeting held on 25/04/2024 and Adult healthy **Wistar rats Nos.100** have been sanctioned under this. CPCSEA No.1581/PO/Re/S/10/CPCSEA.

Authorized by Name Signature Date

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Assessment of the Pharmacognostical Phytochemicals and Antidiabetic properties of the *Acacia nilotica Linn and Acacia leucophloea Willd* : A Comprehensive Review

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ABSTRACT

The plant Acacia arabica, also called babul, is native to Egypt and is found across the tropical and subtropical plains of India, Sri Lanka, and Sudan. It is a member of the Fabaceae family. Nearly every component of it—root, bark, leaves, flowers, gum, pods, etc.—is utilized in medicine. Furthermore, reports of polyphenolic substances in bark and pods have also been recorded. A. arabica is used in traditional medicine to treat bleeding disorders, prolapse, leucorrhea, and other conditions. Experimental research on the plant revealed antihypertensive, antispasmodic, antibacterial, antifungal, and antioxidant properties. The goal of this study is to thoroughly examine and highlight the pharmacological, phytochemical, and ethnomedical applications of Acacia arabica that have been documented to far. Astringency, tonicity, wound healing, aphrodisiac, expectorant, resolvent, and antispasmodic actions are only a few of the medicinal properties of A. nilotica. A. nilotica is a potential source of a variety of bioactive compounds with distinct pharmacological properties and therapeutic uses, according to published publications' in vivo, in vitro, and clinical research. Among the several pharmacological activities include anti-inflammatory, analgesic, antibacterial, antidiabetic, and antihypertensive properties. According to this review, scientific studies have shown that A. nilotica has medicinal effects.

KEYWORDS: Phytochemical, pharmacological, ethnomedicine, A. nilotica, antidiabetic, Anti-inflammatory

1. INTRODUCTION

With the exception of pancreas transplantation, maintaining normoglycemia, preventing diabetic complications, and managing other pathological features are challenging despite the various therapeutic options now available for diabetes mellitus. But finding the necessary donor is challenging and quite costly. As a result, there is a clear need for alternative medicine sources and diabetes treatment methods. Research on traditional antidiabetic herbs for diabetes prevention and treatment has been determined to be the most effective approach.

Due to the fact that several botanical preparations have been shown to have positive benefits on diabetes management, including increased insulin production, improved insulin binding, reduction of glucose absorption, etc. Numerous herbal supplements have been investigated and employed as possible treatment tools for diabetes and its associated problems.

Only a tiny percentage of the approximately 600 traditional plant remedies for diabetes that have been documented in India have undergone scientific and medical investigation to determine their effectiveness. Certain herbal extracts have been shown to have an antidiabetic impact in Type-II diabetes models in both humans and animals. The most researched in this area and often used medicinal plants for diabetes therapy are listed below. Aloe vera, Momordica charantia, Azardiractha indica, Panax sps, Gymea sylvestre, Trigonella foenum-graecum, Pterocarpus marsupium, and Syzigium cumini. Coccinia cordifolia, Phyllanthus emblica, and Allium sps. Due to its antidiabetic properties, Acacia nilotica and Acacia leucophloea blossoms are crucial in this situation. Thus, the current study's goal is to identify the phytoconstituents found in the blooms of Acacia nilotica and Acacia leucophloea and assess their potential as antidiabetic agents.

1.1. Epidemiology of Diabetes mellitus

Because epidemiology sheds light on risk factors, prevalence patterns, and disease burden, it is essential to comprehending and treating diabetes. Epidemiological research makes it easier to spot trends and changes in the prevalence of diabetes. Large-scale research also identifies risk variables that influence the pathophysiology of the illness. These studies take into account a variety of factors, including environmental factors, lifestyle choices, food habits, and genetics.

Type 1 diabetes, an autoimmune disorder primarily affecting children and young adults, accounts for about 10% of all diabetes cases globally. In contrast, type 2 diabetes, which affects

90–95% of people with diabetes, is more common among adults and is linked to insulin resistance. The global prevalence of diabetes has been on a sharp rise. In 2000, approximately 2.8% of the world's population was affected by diabetes, a figure projected to increase to 4.4% by 2030. This alarming rise is driven by sedentary lifestyles, unhealthy diets, and an aging global population.

In the United States, diabetes affects a significant portion of the population. According to the January 2011 National Diabetes Fact Sheet, 25.8 million people, accounting for 8.3% of the U.S. population, were diagnosed with diabetes. Of these, 1.9 million new cases were reported among adults aged 20 and above. The prevalence rates for men and women stood at 11.8% and 10.8%, respectively. Global estimates predict that the total number of diabetes cases could double within 20 years, reaching 180 million.

The prevalence of diabetes varies across countries and economic regions. In wealthier nations, diabetes is more common among individuals aged 60 and above, whereas in developing countries, it affects people aged 40 to 60. By 2030, diabetes prevalence is expected to increase by 54%, reflecting an annual growth rate of 2.2%, nearly double the global population growth rate. Alarmingly, China and India are projected to have the highest diabetes burden, with a combined total of approximately 154 million affected individuals.

The prevalence of diabetes also differs across regions and population groups. For example, the prevalence rate among the Indian diaspora (2.2%) is higher than that of European populations (1.2%). Within India, southern states like Tamil Nadu report a higher prevalence (10.4%) compared to Maharashtra (8.4%) and Jharkhand (5.3%). Regionally, diabetes prevalence rates vary from 12.1% in North America to 8.1% in Europe, 4% in Africa, and 1% in Asia.

Multiple logistic regression analyses have identified several key risk factors for diabetes. Age, male sex, urban residence, family history of diabetes, hypertension, abdominal and generalized obesity, and socioeconomic status have all been significantly associated with an increased risk of developing diabetes. Additionally, similar risk factors, including age, family history, obesity, hypertension, and socioeconomic status, have been linked to the development of prediabetes (Wild et al., 2004).

1.2. Classification of diabetes

Diabetes mellitus is broadly classified into two primary types: type 1 and type 2 diabetes. Type 1 diabetes, also known as juvenile diabetes, is characterized by a severe deficiency of insulin due to the autoimmune destruction of pancreatic β-cells. In contrast, type 2 diabetes is marked by insulin resistance combined with inadequate insulin production. Type

1 diabetes accounts for approximately 5–10% of the global diabetic population, making it significantly less common than type 2 diabetes. The autoimmune nature of type 1 diabetes is evidenced by the presence of specific autoantibodies. These include islet cell autoantibodies, insulin autoantibodies, glutamic acid decarboxylase (GAD) autoantibodies, and autoantibodies targeting tyrosine phosphatase proteins IA-2α and IA-2β. These autoantibodies serve as biomarkers indicating immune-mediated destruction of pancreatic β-cells. Additionally, genetic predisposition plays a vital role in the development of type 1 diabetes. The condition is strongly associated with the Human Leukocyte Antigen (HLA) system, particularly the DQA and DQB gene variants, which are key genetic contributors to disease susceptibility.

Each person with type 1 diabetes has a variable rate of β cell distraction. Children and newborns showed rapid cell death, whereas adults showed gradual cell death. Compared to hyperglycemia, ketoacidosis was the initial sign of the illness in children and adolescents. Others had mild hyperglycemia when fasting, which quickly progresses to severe hyperglycemia and ketoacidosis. There is no known because for certain type 1 diabetics, who have persistent insulinopenia, are at risk for ketoacidosis, and show no signs of autoimmunity, all of which are characteristics of idiopathic diabetes. Multiple genetic predispositions and poorly defined environmental variables contribute to the autoimmune damage of diabetes. Additionally, these people are at risk for developing other autoimmune diseases (Mayorov et al., 2011).

1.3. Type 2 Diabetes

Insulin resistance and a relative lack of insulin production are characteristics of type 2 diabetes. The majority of people with type 2 diabetes are fat, and insulin resistance is a result of obesity. The exact aetiology of this kind of diabetes is unknown, and there is no indication of autoimmune distraction in the β cells. One of the factors contributing to the development of type 2 diabetes is an elevated proportion of body fat, which is mostly distributed in the abdominal area, in individuals who are not obese. Because hyperglycemia develops slowly and is typically recognized after additional issues have occurred, this kind of diabetes is often not diagnosed for a long time.Type 2 diabetes is more prevalent across all ethnic groups and has a strong hereditary component. Nevertheless, the disease's genetic makeup is more nuanced and unclear: The development of diabetes mellitus involves multiple interconnected physiological dysfunctions, which contribute to abnormal glucose metabolism. These key mechanisms include: a) Reduced Insulin Secretion: The β-cells of the islets of Langerhans in the pancreas produce insufficient amounts of insulin, leading to impaired glucose uptake by cells. b)

Excessive Glucagon Release: The α-cells of the pancreatic islets secrete an abnormally high amount of glucagon, promoting increased blood glucose levels. c) Enhanced Hepatic Glucose Production: The liver increases gluconeogenesis and glycogenolysis, resulting in elevated glucose release into the bloodstream. d) Neurotransmitter Imbalance and Insulin Resistance in the Brain: Disruption of brain neurotransmitter signaling reduces the body's ability to regulate glucose and contributes to insulin resistance. e) Increased Fat Breakdown (Lipolysis): Excessive lipolysis releases free fatty acids into the bloodstream, which further exacerbates insulin resistance. f) Elevated Renal Glucose Reabsorption: The kidneys increase the reabsorption of glucose, which prevents its excretion in urine, leading to higher blood glucose levels. g) Reduced Incretin Response: The small intestine shows a diminished incretin effect, thereby decreasing insulin secretion in response to meals. h) Impaired Glucose Uptake in Peripheral Tissues: Skeletal muscle, liver, and adipose tissue exhibit reduced glucose uptake due to insulin resistance, resulting in hyperglycemia (Ojha et al., 2019).

1.4. Plant Profile

1.4.1. Ethnobotanical description

A. nilotica L. is a perennial tree that grows to a height of 2.5–10 m. With dark to black stems, branches extend out to produce a thick, flat, or rounded crown. The bark is rich red-brown, tough, and cracked. In young trees, axillary pairs of thin, straight, light grey spines (thorns) typically measure 3–12 pairs and are 5–5.7 cm long. Pinnae are 2-11 pairs, with 7-25 pairs of leaflets per pinnae; leaves are bipinnate, 30-40 mm long, and frequently include 1-2 petiolar glands.

At the nodes of both leafy and leafless branchlets, peduncles gathered. Profusion of golden yellow flowers in globules with a diameter of 1.2 to 1.5 cm. Pods are 5–15 cm long on a pedicel, straight or slightly curved, and 0.5–1.2 cm broad. The constrictions between the seeds resemble a string of pearls, and when they are young and indehiscent, they are soft; when they mature, they become hard and black. The smooth, sub-circular, deep blackish-brown seeds have an areole that is 6-7 mm long and 4.5-5 mm diameter. The bark is thick and cracked, with a scattering of branches. The plant contains the sticky, orange-brown resinous material [11, 13-16].

1.4.2. Classification

Vernacular names

Bengal - Babla

English	-	Indiangum, Arabictree, Babultree
Hindi	-	Babula, Babura, Kirkar
Kananda	-	Karijali. Gobbli
Malayalam	-	Karivelan, karuvelum
Tamil	-	Karuvelamaram, Karivelei, Karuvael,
Telugú	-	Nallatumma, Tumma, Tuma

Acacia leucophloea willd Taxonomical Classification

Kingdom	- Plantae
Phyllum	-Tracheophyta
Class	-Equisetopsida C. Agardh Order Fabales
Family	-Fabaceae Genus Acacia
Species	-Acacia leucophloea (Roxb.) Willd.

1.5. Medicinal properties of *A. nilotica* in traditional medicine

1.5.1. Extract of pods (Aqaqia): When the uterus and anus emerge, the pod extract helps to push them back and avoid leucorrhea [7, 11, 13, 15, 22]. Additionally, it helps with istarkha rehm, or vaginal laxity [7]. If applied topically, it tightens the perineum [13]. Redirecting the diseased stuff that is headed toward the organ is also beneficial [11]. Haemorrhagic diarrhea is prevented by it [7]. When combined with roghan gul (rose oil), it inhibits infantile diarrhea [10, 15]. When administered externally to the body, it results in dryness [13]. If applied topically to the skin in conjunction with gulab (rose), it stops sweat from smelling bad [11, 13].

When used orally or as an enema, it induces constipation [7, 13]. It helps with hemorrhagic diarrhea and intestinal abrasions [7, 11, 13]. It keeps the joints from becoming flabby [7]. Along with gulab and aas, it can be used externally to anus irritation [10]. It cures eye problems and improves and fortifies eyesight [7, 11, 15]. It relieves erysipelas and conjunctivitis and is also used in pterygium medications [7, 13, 15]. It stops hair loss and turns hair black [7, 11, 13, 15, 19]. It helps with cold-induced cracks and provides a clear complexion [7]. It is appropriate for those with dysentery and diarrhea [15]. All bleeding disorders can benefit from it [11, 13, 15]. When combined with gulab and aas, it lessens excessive perspiration [10, 11, 13, 16]. When used with egg white, it helps with fire burns, pimples, whitlow (paronychia), and heated swellings [7, 8, 13, 15, 16]. In the form of zaroor (powder), it helps with oral ulcers and

bleeding gums [7]. It helps with premature ejaculation and spermatorrhea [18, 19]. Bilious diarrhoea is prevented [11]. The powdered pods are beneficial in treating urogenital problems and impotence [23].

1.5.2. Flowers: It works well as a remedy for insanity and as a tonic for diarrhea and dysentery. It has been observed that the blooms lower body temperature [14]. Flowers and bark in powdered form are helpful for seminorrhea and early ejaculation [18].

1.5.3. Leaves: The leaves' decoction is used as an astringent for the intestines, to treat bronchitis, to mend fractures, and to treat eye conditions [14]. Children's injured eyes were treated with bruised leaves. Burnt leaf paste works well as an itch reliever [9]. Tender leaves mashed into a pulp are used as a wash for hemorrhagic ulcers and wounds, and as a gargle for spongy gums and sore throats [9].

. An astringent, leaves extract is injected to relieve the irritation of acute leucorrhea and gonorrhea. Additionally, damaged leaves that have been made into a poultice and applied on ulcers have astringent and stimulating properties [4]. When the tender leaves and growing tips are mixed into a paste with water and sugar and taken in the morning and evening, it acts as a cough-relieving demulcent [4]. When diarrhea occurs, the tender leaves that have been crushed into a pulp are used as an astringent [12].

1.5.4. Bark: The bark is a potent astringent with a high tannin content; its decoction is frequently used as a mouthwash and gargle for syphilitic and malignant conditions [4]. Bark infusion (1½ ounces to 1 pint water) is administered twice daily in amounts of 1½ to 2 ounces to those with diabetes mellitus and persistent diarrhea. When conjunctivitis occurs, the eye is irrigated with a mixture of milk and bark juice [4]. Bark decoction is frequently used as an astringent remedy for uterine prolapse, gonorrhea, cystitis, vaginitis, and leucorrhea [9].

1.5.5. Gum: When a fever is accompanied by diarrhea and dysentery, quinine and powdered gum might be helpful [4]. It also helps with diabetes [23] and eliminates bleeding as well as vaginal and urine discharges. In situations of fever that are worsened by diarrhea and dysentery, powdered gum combined with quinine is helpful; it is also administered to burns and scalds when combined with egg white [9].

1.5.6. Fruits: In cases of opthalmia and dysentery, the fruits are prescribed. [14].

1.5.7. Seeds: Seed extract was discovered to have overall bodily vigor [28].

1.5.8. Root: Root powder helps heal wounds, relieve burning sensations, and treat leucorrhea [30]. [31] Many plant components are used to treat leprosy, cholera, syphilis, earaches, hair

loss, and dysentery [23]. When the sensitive growing tips are rubbed into a paste with water and sugar, they have a demulcent effect and can help with coughing. [4]

1.6 Chemical constituents:

Stearic acid, kaempferol-3-glucoside, isoquercetin, and leucocyanidin are found in flowers, whereas 32% of tannin is found in leaves and fruits [27, 32]. Twenty percent of the bark is tannin. Several polyphenolic substances have been found and reported, including gallic acid, (+) dicatechin, quercetin, and ∞-amyrin and ß-sitosterol [9, 33]. [23, 32] Additionally, sucrose is present in the bark [2, 32]. Tannin is also present in babul pods, ranging from 12–19% in the whole pod to 18–27% after the seeds are removed. Gallic acid, m-digallic acid, (+) catechin, and robidandiol are among the polyphenols found in pods; other polyphenols include chlorogenic acid, m-digallic acid, and galloylated flavan-3-4-diol [4, 33].

L-arabinose, galactose, and moisture make up 1.8% of the gum. Four aldobiouronic acids and L-rhamnose. L-arabinose, 3-O-ß-L-arabinopyranosyl, and arabinose are also present [4, 32, 33]. In addition, it includes oxidative enzymes, calcium, polysaccharides, potassium, sugar, moisture, ash, magnesium salts, and malic acid [9, 32]. Chlorides are found in wood [5]. The following values (dry basis) were obtained from the seeds' analysis. Moisture 8.83, total ash 4.7, calcium 673.0, phosphorous 420.0, iron 4.95, niacin 3.17, ascorbic acid 4.51, thiamine 0.24 mg/100 ml, crude protein 26.5, fat 3.3, N-free extract 62.9, and crude fiber 2.7.

Histidine 3.7, lysine 4.3, methionine 0.4, cystine 0.49, leucine 8.8, valine 4.2, and threonine 3.39/16 g are the essential amino acid makeup of the seed protein. When seeds are extracted using petroleum ether, brownish oil (6.7%) is produced. Saturated acids make up 27.4%, oleic acid 30.5%, and linoleic acid 42.1% of the oil [27]. Both have 32% tannin [34], and gallic acid is also present in fruit [23]. Hentriacontane, lapachol, n-hentriacontanol, sitosterol, octacosanol, betulin, and ß-amyrin are all found in the root [30, 33]. Stearic acid, leucocyanidin, isoquercetin, and kaempferol-3 glucoside are all found in flowers [32].

1.7. Pharmacological Activity

1.7.1 Antihypertensive activity: A methanol extract of Acacia nilotica pods was found by Gilani et al. (1999) to have a reduction in arterial blood pressure at doses ranging from 3 to 30 mg/kg. Additionally, it inhibits force rate concentration in rabbits and guinea-pigs by blocking calcium channels [30]. According to Amos S. et al. (1999), the isolated guinea-pig ileum exhibits spasmogenic activity when exposed to an aqueous extract of Acacia nilotica seeds. An increase in calcium influx that causes muscular spasm might be the mechanism [36].

1.7.2 Antimutagenic activity: According to Arora S. et al. (2003), Acacia nilotica acetone extract shown antimutagenic action against sodium azide, the S9-dependent mutagen 2-aminofluorene (2AF), and direct acting NPD mutagens. The plate incorporation method is used to ascertain this mutagenic activity. Several strains of Salmonella typhimurium are used in the Ames Salmonella histidine reversion test [37].

1.7.3 Antibacterial activity: In a comparative analysis of the antimicrobial activity of Acacia species and A. nilotica, Mohan Lal Saini et al. (2008) found that the methanolic extract of the former showed the highest activity against Salmonella typhi, Staphylococcus aureus, and Escherichia coli (bacteria); Candida albicans and Aspergillus niger (fungus) [38].

A research by Deshpande SN (2013) on the ethanol and petroleum ether extract of Acacia nilotica stem bark revealed the highest antibacterial activity against Salmonella paratyphi B, Escherichia coli, Staphylococcus aureus, Proteus vulgaris, Proteus mirabilis, and Klebsiella pneumonia. The findings demonstrate that both extracts had an inhibitory effect on the aforementioned pathogens. However, the ethanol extract was more active than the comparable petroleum ether extract [39].

Using the agar diffusion technique, Banso A. (2009) demonstrated the antibacterial efficacy of the Acacia nilotica extracts against Shigella sonnei, Escherichia coli, Bacillus subtilis, Streptococcus viridians, and Staphylococcus aureus. Although Bacillus subtilis is the most vulnerable to the plant extract, this investigation demonstrates antibacterial action against all of the aforementioned species [41].

1.7.4 Antifungal activity: According to the findings of Mahesh B et al. (2008), the antifungal activity of Acacia nilotica methanolic and aqueous extracts ranges from 34.27±1.45 to 93.35±1.99 [42].

1.7.5 Antiviral activity: The plant's crude leaf extract demonstrated in vitro antiviral efficacy against the Turnip mosaic virus, according to Singh R et al. (1972). On the hosts Chenopodium amaranticolor (93.77%) and C. album (80.2%), the number of lesions decreased [43].

1.7.5 Antimicrobial activity: The antibacterial activity of methanolic and aqueous extracts of Terminalia chebula, Mimusops elengi, Achyranthes aspera, Acacia catechu, Acacia arabica, and Glycyrrhiza glabra was evaluated against six dental infection microorganisms, including Candida albicans, Lactobacillus acidophilus, Staphylococcus aureus, Staphylococcus mutans, Staphylococcus salivarius, Staphylococcus sanguis, Staphylococcus salivarius, Staphylococcus salivarius, Staphylococcus aureus, Staphylococcus aureus, and

Staphylococcus mutans. Synergistic antibacterial effects were demonstrated by these plants' phytochemical studies [44].

Khan R (2009) investigated the antimicrobial properties of crude ethanolic extracts of five plants against ATCC strains of Streptococcus mutans, Klebsiella pneumoniae, Candida albicans, and multidrug resistant (MDR) strains of Escherichia coli, as well as various microorganism stains. A. nilotica has a minimum inhibitory concentration range of 9.75-313ÂµÂg/ml [45]. Acacia nilotica has been shown to have antimicrobial action against S. aureus, B. subtilis, and E. coli by Mashram N et al. (2009). The leaf and bark extracts were most effective against E. Coli and had zones of inhibition ranging from 7.5–16 mm and 8–15.5 mm, respectively [46].

1.7.5 Antidiabetic (Hypoglycemic effect) activity: Wadood A et al (1989) examined the A. nilotica ssp. Normal rats given indica for a week showed a hypoglycemic effect (blood sugar decreased by 25.05%), however alloxanized diabetic rats showed no discernible hypoglycemic effect (blood sugar decreased by 2.14%). Legumes' direct or indirect stimulation of the islets of Langerhans' β-cells to secrete more insulin was the cause of their hypoglycemic effect [47].

1.7.6 Antioxidant activity: Agrawal S. (2010) investigated the antioxidant activity of a plant's methanolic extract, finding that it was 9.88 µg/ml [48]. According to Sultana B. (2007), several bark extracts from Acacia nilotica linn showed a range of 49% to 87% DPPH radical scavenging activity and a 44–90% suppression of linoleic acid oxidation [49].

Singh R. (2010) investigated the fractionation of methanol extract and extracted a fraction, AN-2, which was determined to be a coumarin derivative, or umbelliferone, using spectroscopic methods such as mass spectroscopy and NMR. The DPPH, site-specific and non-site-specific deoxyribose, chelating power, reducing power, and lipid peroxidation tests were among the antioxidative activities that were investigated and carried out in vitro. Umbelliferone's antioxidative action was shown to be dose dependent up to 100 µg/ml before leveling off without causing any further activity to rise. Umbelliferone's isolation and antioxidant capacity from A. Nilotica have never been documented before [50].

1.7.7 Antidiarrhoeal Activity: According to Agunua A. et al. (2005), they looked at the usage of medicinal plants—Acacia nilotica, Acanthospermum hispidum, Gmelina arborea, Parkia biglobosa, and Vitex doniana—in Kaduna State, Nigeria, for the treatment of diarrhea. The perfused isolated rabbit jejunum and castor oil-induced diarrhea in mice were the subjects of this investigation. Although this was not consistent across all plants, it was typically seen that the aqueous methanol extracts (0.5, 1.0, 2.0, and 3.0 mg/ml) had a dose-dependent reaction in the isolated rabbit jejunum. At low dosages (0.5, 1.0 mg/ml), Gmelina arborea and Vitex

doniana exhibited concentration-dependent relaxation; but, at higher doses (2.0, 3.0 mg/ml), they did not exhibit any discernible relaxation. Biphasic effects were seen in other extracts. For instance, 3.0 mg/ml of Acacia nilotica soon induced contraction after initial relaxation. Extracts of Acacia nilotica and Parkia biglobosa (100, 200 mg/kg) demonstrated 100% protection against castor oil-induced diarrhea, but Vitex doniana exhibited a dose-dependent effect. [51]

1.7.8 Antiplasmodial activity: The antiplasmodial activity of A. nilotica's aqueous root extract in mice was examined. Organization for Economic Cooperation and Development (OECD) guideline 423 was used to investigate the extract's acute toxicity. Chloroquine-sensitive Plasmodium berghei NK 65-infected mice were used to study the suppressive activity, curative, and preventive effects. There were five groups, each with five mice. Ten milliliters of distilled water per kilogram of body weight was given to group 1, which served as the control; 100, 200, and 400 milligrams of extract per kilogram of body weight were given to groups 2, 3, and 4, respectively; and five milligrams of chloroquine per kilogram of body weight was given to group 5.

Oral administration was used for the dosages. In the suppressive, curative, and preventive assays, the extract demonstrated considerable, dose-dependent chemo-suppressive action against the parasite at all dosages. This is similar to the group that received chloroquine treatment. In comparison to the untreated group, the extract also increased the average survival duration of the treated mice. In mice, the extract's oral median lethal dosage (LD_{50}) was 5000 mg/kg body weight. The study's findings demonstrated the anti-plasmodial efficacy and safety of Acacia nilotica's aqueous root extract [54].

CONCLUSION

Since ancient times, Acacia arabica has been used in traditional medicine to cure a variety of illnesses. Its antidiabetic, antihypertensive, antispasmodic, antibacterial, antifungal, antiplaque, antioxidant, antiplasmodic, antiviral, catalytic, and galactagogue properties have all been demonstrated in experimental research. The conventional medical system's assertions have been validated by scientific research. To make it a mainstream medication, more thorough clinical studies are required to investigate its therapeutic potential.

Actually, experimental research work have looked at a number of pharmacological characteristics, such as antioxidant, antidiabetic, and anti-inflammatory qualities. The species' abundance in secondary metabolites, including as terpenoids, polyphenols, and alkaloids, has also been shown in several investigations. These provide credence to its extensive use in

conventional medicine. However, it should be noted that there is a dearth of study on the fractionation and isolation of its constituent parts.

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Abstract

Acacia nilotica Linn and *Acacia leucophloea* Willd: Hidden Jewel of Medicinal Use

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Acacia nilotica Linn (syn. *Acacia arabica*), commonly known as babul, is a significant medicinal plant belonging to the Fabaceae family. Indigenous to regions such as Egypt, India, Sri Lanka, and Sudan, nearly every part of this plant—including its root, bark, leaves, flowers, gum, and pods—is employed in traditional medicine. It has been historically used to treat a wide array of ailments, including bleeding disorders, prolapse, leucorrhea, and various infections. Its documented therapeutic properties are extensive, encompassing astringent, tonic, wound-healing, aphrodisiac, expectorant, resolvent, and antispasmodic actions. Scientific investigations have further validated these uses, revealing that *A. nilotica* possesses potent antihypertensive, antibacterial, antifungal, and antioxidant properties, largely attributed to its rich content of polyphenolic compounds found in the bark and pods.

This comprehensive review aims to consolidate and critically evaluate the existing scientific literature on the pharmacological, phytochemical, and ethnomedical profiles of *Acacia nilotica* and its relative, *Acacia leucophloea* Willd, with a particular emphasis on their antidiabetic potential. A growing body of evidence from *in vivo*, *in vitro*, and clinical studies confirms that *A. nilotica* is a promising source of diverse bioactive compounds with distinct pharmacological activities. These include significant anti-inflammatory, analgesic, antibacterial, antidiabetic, and antihypertensive effects.

In conclusion, this review synthesizes compelling scientific evidence that establishes *Acacia nilotica* and *Acacia leucophloea* as medicinally valuable species. Their extensive history in traditional medicine is strongly supported by modern phytochemical and pharmacological research. The potent antidiabetic activity demonstrated in experimental models, alongside a broad spectrum of other therapeutic actions, positions these plants as excellent candidates for the development of novel natural therapeutics and justifies further investigation into their bioactive constituents and mechanisms of action.

Abstract

Pharmacognostical Study of flower of *Acacia nilotica* Linn and *Acacia leucophloea* Willd

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The present pharmacognostical investigation was undertaken to evaluate key quality-control parameters of the flowers of Acacia nilotica and Acacia leucophloea (Family: Leguminosae), two medicinal plants traditionally used for treating leucorrhea, skin ailments, diabetes, diarrhea, dysentery, ulcers, and wounds. Due to increasing concerns regarding contamination, adulteration, and compromised safety in herbal raw materials, establishing standardized pharmacognostical parameters has become essential. Following WHO guidelines, the study assessed primary physicochemical constants, including total ash, acid-insoluble ash, water-soluble ash, alcohol-soluble extractive, water-soluble extractive, and loss on drying, to ensure identity, purity, and quality of the crude drugs.

Both plant samples were shade-dried, powdered, and subjected to analytical evaluations. Total ash was determined by incineration of the powdered drug at temperatures not exceeding 450°C, representing the total inorganic matter present. Acid-insoluble ash was quantified by boiling the total ash with hydrochloric acid to measure silica and other insoluble impurities. Water-soluble ash was calculated by dissolving ash in water and measuring the soluble portion, thereby helping to identify the presence of foreign inorganic matter. Extractive values were determined by maceration using alcohol and water separately to estimate the amount of bioactive and soluble constituents present in each solvent system. Loss on drying was measured to determine moisture content, which plays a crucial role in preventing microbial growth and degradation of plant materials.

These pharmacognostical parameters provide essential benchmarks for the standardization of *A. nilotica* and *A. leucophloea* flowers. Establishing such scientifically validated quality profiles supports reliable identification, minimizes adulteration, and ensures consistent therapeutic efficacy of herbal formulations derived from these species. The study contributes to the development of standardized herbal raw materials for safe and effective traditional medicinal preparations.