

Phytochemical Insights and Anti-Diabetic Prospects of *Dolichandrone Falcata*: Current Findings and Future Directions

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ABSTRACT

Dolichandrone falcata, a lesser-explored member of the Bignoniaceae family, it has recently gained attention for its promising ethno pharmacological relevance and potential anti-diabetic properties. Traditionally employed in various indigenous systems of medicine, this plant contains to its diverse Phytoconstituents such as per flavonoids, phenolics, also terpenoids that may donate to its pharmacological actions. Current findings suggest that *D. falcata* exhibits significant antioxidant and glucose-lowering effects demonstrating its possible use in the control of diabetes mellitus. However, comprehensive pharmacological, biochemical, and clinical investigations are still limited. This review consolidates existing knowledge on the phytochemical profile, mechanisms underlying its anti-diabetic activity, and identifies key research gaps. Future studies focusing on bioactive compound isolation, molecular target elucidation, and preclinical validation could pave the way for developing *D. falcata*-based therapeutic agents for diabetes management.

Keywords: *Dolichandrone falcata*, Anti-diabetic activity, Ethnopharmacology, future pharmacological prospects.

INTRODUCTION

In 2019, 463 million individuals worldwide suffered from Diabetes Mellitus (DM). After growing by 62% between 1990 and 2019. By 2045, this number is expected to rise by an additional 51%. [1] A common chronic illness Diabetes mellitus is a major public health issue. Type 2 diabetes (T2DM), also known as non-insulin-dependent diabetic mellitus, prevalence trends and type 1 diabetes (T1DM), also known as insulin-dependent diabetes mellitus, have rarely been studied worldwide. Finding the global patterns in diabetes throughout time and space was our aim. [2] According to recent estimates, 537 million adults worldwide suffer from the illness, and 80% of them reside in nations with low and moderate incomes (LMICs). Furthermore, Diabetes is predicted to continue to have a major global impact and cost, disproportionately affecting low-income nations (LMICs) and the most disadvantaged individuals in high-income countries (HICs). In addition to being environmentally benign, plant-derived medications

are becoming more and more important in medicinal chemistry. Medications made from plants can be used to relieve oxidative stress, lower inflammation, and treat many diseases, such as cancer. [3] The aetiology of diabetes is complex and involves both environmental and genetic factors. The body's cells cannot properly metabolize sugar when diabetes is present because insulin, which regulates blood sugar levels, is less effective in acting on particular tissues. [4] *Dolichandrone Falcata*'s effectiveness against diabetes Rats' blood glucose levels were measured in order to conduct a pharmacological investigation of seem extracts. Rats were given a low dose is 200 mg/kg, a medium dose is 400 mg/kg, and a high dose is 600 mg/kg. To test the extract's anti-diabetic efficacy. The usual guideline for glibenclamide's anti-diabetic efficacy against alloxan-induced diabetes was 10 mg/kg body weight. The extract in water considerably decreased blood sugar levels in rats with diabetes. [5] Hyperglycemia is a hallmark of the endocrine condition known as diabetes mellitus. Numerous studies of oral antihyperglycemic drugs

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derived from plants used in traditional medicine have been carried out, and many of the plants were found to have good activity. [6] Medshingi is the name given to *Dolichandrone falcata* Seem. (Bignoniaceae) in the Toranmal region of Maharashtra, India. It is typically found in hill woods and grows to a height of 20 to 50 feet. It is a small to medium-sized deciduous tree. One significant source for the creation of safe and efficient medications is plant-derived medicine. Strict standardization of their safety and quality is necessary due to their growing use in order to create future pharmaceutical compounds that are more effective. *Dolichandrone falcata* has become a crucial plant in the pharmaceutical and medicinal industries in recent years. [7] *Dolichandrone Falcata* is used to treat anemia, bloody diarrhea, antiviral, analgesic, and antifungal disorders. Seem has long been used utilised for medicinal purposes and a variety of pharmacological effects by indigenous and tribal peoples from all over the world, including India. (1) The one that plant's juice is used to make an antidote for to treat liver disorders and snake venom. (2) Cracks are filled with bark paste. While fruit Paste is added.to scorpions. The bark juice is used to treat menorrhagia and leucorrhea (3) this plant's leaves are utilized as an antioxidant, anti-diabetic, and anti-estrogenic. [8] (4) the decoction of bark is also used to treat nodules. (5) *Dolichandrone falcata* Seem is utilized as Rasayana medications and as a mesh-shingi for Madhuka bites in Ayurveda. (6) The fruit's aqueous extract is used to induce abortion, and the bark is used to poison fish. (7) To treat acute rheumatism, an internal powder infusion is used. (8) You can also use leaves to cleanse swelling. (9) *Falcata Dolichandrone* Stem bark appears to be used to treat epilepsy in Ayurvedic medicine pain, and ulcers. [4]

Hyperglycemia is a typical symptom of a set of metabolic diseases called diabetes mellitus. The heart, blood vessels, nerves, kidneys, and eyes are all harmed by persistent hyperglycemia. *Dolichandrone falcata* leaf juice has long been used to treat diabetes. Rats were used in the study to test an aqueous extract of *Dolichandrone falcata* leaves' anti-diabetic effects because the literature review indicated that the herb's anti-diabetic properties had not yet been investigated. Alloxan caused diabetes, which raised blood glucose levels because β -cells were selectively necrotized.

Diabetic rats' blood glucose levels were significantly lowered by the aqueous extract. There was a strong and dose-dependent anti-diabetic effect. [5, 9] No thorough scientific investigation has been carried out in this area, despite conventional assertions regarding the pharmacological characteristics of *D. falcata* and the successful isolation of bioactive chemicals from it. Determining *Dolichandrone Falcata's* potential to prevent diabetes was the goal of the current investigation. Phytochemical and pharmacological studies have only been conducted on a small percentage of plants. The potential for new discoveries becomes evident when one plant can have thousands of constituents. [7] The scientific validation of plant-based therapies is further strengthened by standardized procedures for phytochemical extraction, isolation, and characterization. The identification and quantification of bioactive compounds have greatly improved thanks to developments in chromatographic and spectroscopic techniques including FTIR, GC-MS, and HPLC. [32]

The Necessity of Research:

The Indian subcontinent is home to the species *Dolichandrone falcata*, which belongs to the Bignoniaceae family. Due to its potential pharmacological properties, this species has long been utilized in a number of local medicinal procedures. This plant has been used historically, although it hasn't been thoroughly studied by scientists. To bridge this gap, a comprehensive study of *D. falcata* is required.

Medicinal Significance: Significance in medicine *D. falcata* may contain bioactive compounds with significant therapeutic potential because it has historically been used to treat ailments like arthritis, inflammation, and gastrointestinal problems. Preliminary studies indicate that the herb possesses anti-inflammatory, antimicrobial, and analgesic properties.

Preservation and Sustainable Utilization: *Dolichandrone falcata* is an important species that contributes to the area's biodiversity in its natural settings. However, overuse for medical purposes puts the resource's sustainability at risk.



Financial Potential: Particularly in rural areas where the plant is widespread, *D. falcata* offers a significant opportunity for economic growth given the growing demand for natural products and traditional cures globally. Understanding plant traits and producing standardized extracts or products can lead to new economic opportunities. Research can aid in the development of cultivation techniques, providing an additional economic stream for the community [24]

2. BOTANICAL PROFILE AND ETHNOPHARMACOLOGY

2.1 DOLICHANDRONE FALCATA

Regarding the Plant:

2.1.1 *Dolichandrone falcata* seem is the botanical name.

Bignoniaceae is the family. There are three types: red, white, and black.

2.1.2 Common Names:

- Manchingi, Bhersing, and Medshing in Marathi.
- Hindi Hawar
- In Tamil, Kadatathi, Kattuvarsana and Kaddalatti.
- Godmurki, Muduvudure and Udure in Kannada
- Chittivoddi, Chittiniruviddi, and Telugu Oddi.
- Mesasrnga and Visanika in Sanskrit.

2.1.3 Classification by Taxonomy:

- Synonym: *Bignonia Falcata*, *Bignonia Spathacea*, *Markhamia Falcata*
- Common Name: Medshingi, Meshsa-Sringi
- Biological Source: The tree is tiny and deciduous.

- Bignoniaceae family
- Kingdom: Plantae
- Order: Lamiales
- Class: Tracheophytes
- Class: Eudicots
- Class: Asterids
- Dolichandrone genus, the species is *D. Falcata*
- Fruit, leaves, roots, bark, and flowers are among the parts of plants that are used.
- The regions that are used are Rajasthan, Maharashtra, and Karnataka.
- The Medical System Used In Sowa-Rigpa, Ayurveda, folk medicine, and siddha
- Material Type: Plant
- Substance Class: diverse in structure
- Source: organism. [4]

2.1.4 Distribution:

The *Dolichandrone falcata* tree is quite common in Bihar, the Deccan plateau, and Central India.

2.1.5. Description:

The deciduous *Dolichandrone falcata* tree can reach heights of 6 to 15 meters. Simple pinnate leaves with Leaflets opposite subobicular to ovate, base cuneate, pubescent or glabrous, sometimes very briefly acuminate, and uneven sides. The corolla is a white tube that is quite narrow at the base and progressively enlarges upward; the calyx is hairy and mucronate at the apex of the terminal few flowered racemes. Capsules are glabrous, sub quadrangular, and significantly falcately curved. Rectangle seed with wings on both ends. The plants bear fruit from June to December and bloom from April to May. [11]





Fig 1: Whole Plant

2.2 Ethno medicinal Uses of Plant

The entire plant is recognized to have therapeutic qualities, as are some sections of it, such as the leaves, stem, and roots. It has long been used by India's and other nations' indigenous and tribal populations. Ayurveda also mentions the plant's bark and leaves' therapeutic properties. [12] It has been demonstrated that the entire plant, as well as some of its specialised parts, such as the stem, roots, and leaves, have therapeutic properties. It has long been used by tribal and indigenous people in India and other nations. The bark and leaves of this plant have medicinal properties, according to Ayurveda. Bark decoction is used to treat nodules by the Bhil tribes in the Kota district of Rajasthan. To reduce edoema, a paste made from neem leaves is used. Snake and scorpion bites can be healed with three applications of fruit paste and bark paste mixed with water. The tribes of the Kota region use leaf juice and water to treat snake bites. According to medical folklore, this herb has anti-snake venom properties. [13] Information gleaned from ethnobotanical studies of according to woods in the states of Madhya Pradesh and Bihar, liver disorders are treated with *Dolichandrone falcata* in the Ayurvedic medical system. The identification of the biological compounds present in each herbal remedy ensures the phytochemical purity of the remedy. Thus, the current study was carried out to determine the qualitative and quantitative characteristics of *Dolichandrone falcata*'s fruit, bark, and leaves. [14]

2.3 Morphology Description (Habit):

Dolichandrone falcata is also known as "Markhamia" falcata, "Medhshing" in Hindi, or "Mesasninghi" in

Sanskrit, which translates to "look like a sheep horn, showing in Plate." A tree is considered medium in size when it reaches a height of fifteen meters. Robustly blooming, with a dense canopy. This medium-sized tree belongs to the Bignoniaceae family. It has a lot of flowers and thick foliage. In the evening, creamy white flowers with a potent scent bloom, and in the morning, they fall (Plate). The fruits, leaves, and bark have medicinal properties. Woodland areas, botanical gardens, and municipal gardens should all have this tree planted. Leaflets, which can be glabrous or pungent, provide an option. They are 1.3–3.8 in length and 1.1–3.8 in width. They are typically oblong or suborbicular, with rounded or cuneate bases, and their sides are asymmetrical. The lateral leaflets' petioles are extremely short, measuring only 0 to 0.5 mm in length, and the main nerves are noticeable on the underside. [8]

2.3.1 Leaves:

The leaves' anti-inflammatory properties have been demonstrated to be caused by the presence of n-hexadecenoic acid, a chemical with anti-inflammatory properties. The percentage of n-hexadecenoic acid in the methanol and chloroform extracts is 24% and 9.24%, respectively. The leaves' naturally occurring tocopherol, a derivative of tocopherol, and vitamin E antioxidants also contribute to this quality. Long-chain unsaturated fatty acids are known to have antibacterial properties. Fatty acids also play an important role in antibacterial food additives. [13] The plant's natural biosynthesis of vitamin E may use this compound as a precursor. The potential of *Dolichandrone falcata* as a medicinal plant substitute in pharmaceuticals and drug formulations is evident from the study. *Dolichandrone falcata* leaf juice has long been used to treat diabetes. The anti-diabetic potential of the herb has not yet been investigated, according to the literature review. Therefore, an aqueous extract of *Dolichandrone falcata* leaves was used to test the extract's anti-diabetic activity in rats. The selective necrosis of β -cells caused by alloxan resulted in diabetes, which raised blood glucose levels. In rats with diabetes, the aqueous extract significantly lowered blood glucose levels. Significant and dose-dependent anti-diabetic effects were observed. [5]





Fig 2: Photograph of Leaves and Flowers of Dolichandrone Falcata

2.3.2 Fruits:

This study showed that DFFM and DFFEAF had a variety of pharmacological characteristics, specifically their anti-inflammatory and antinociceptive effects. Tannins, glycosides, and steroids were among the compounds found by phytochemical screening; it has been proposed that these compounds work in concert to produce the observed activities. Consequently, our findings support the conventional wisdom that *Dolichandrone falcata* fruits have the ability to cure a variety of ailments, and the plant's possible pharmacological characteristics warrant more research. [5, 13]



Fig 3: Photograph of Fruits of Dolichandrone Falcata

2.4 Utilising Microscopy

The transverse portion of a pamphlet about *Dolichandrone Falcata* Seem showed the cuticle-lined epidermis. There was a noticeable dorsiventral structure in the transverse section. A single layer of the epidermal cell was visible, encased in a thick layer

of cuticle. The epidermis was fractured by unicellular trichomes. Anomocytic stomata include Amphistomatic stomata. The cuticle upper epidermis consisted of spherical cells that ranged in diameter from 15 to 22 to 30 micrometres. Spherical cells with a diameter ranging from 15 to 22 to 30 micrometres comprised the cuticle upper epidermis. Mesophyll has spongy tissues and palisade cells. In a single layer just beneath the upper and lower epidermis were palisade cells, which were long, thin-walled cells with a diameter of 22 to 30 52 to 220 micrometres. A polygonal, 9–12 layer was visible on the underside of the tissues of the spongy parenchyma. On the outside of the vascular bundle, there were patches of sclerenchyma cells that measured 10 to 15 × 10 to 15 micrometres. Phloem surrounded the vascular bundle, which was organised as a ring of xylem. [14]

3. PHYTOCHEMICAL INSIGHTS

3.1 Extraction and Analysis Methods

Phenolic compounds, flavonoids, resins, glycosides, and tannins are examples of pharmacologically active chemicals that augment the medicinal significance of plants. There are many plant species that could be studied, but the choice of plant material is crucial to the final success of any investigation into bioactive plant constituents. In order to isolate these bioactive compounds and obtain pure compounds, a range of separation techniques are commonly used, such as column chromatography, High-Performance Liquid Chromatography (HPLC), flash chromatography, and thin-layer chromatography (TLC). [10]

3.1.1 Plant Material



Several studies on oral antihyperglycemic agents derived from plants used in traditional medicine have been carried out, and many of the plants have been found to have good activity [10]. Following that, airtight polythene covers were used to store the finely powdered samples. Now, 20 milliliters of distilled water were added to a conical flask containing 0.1 grams of each powder sample. To guarantee adequate extraction, the setup was left to stand for about 30 minutes before being filtered into different conical flasks. [12] How does *Dolichandrone falcata* appear? Plants belonging to the Bignoniaceae family were collected from the Savitribai Phule Pune University campus in Ganeshkhind, Pune. At the Botanical Survey of India, Western Circle, Koregaon Park, Pune, and Maharashtra, the herbaria were prepared and validated. [15]

3.1.2 Pharmacognostic Evaluation

In accordance with AOAC guidelines, Pharmacognostic parameters were determined. Among the parameters were Extractive values fractions soluble in water and alcohol. The three ash values are total ash, acid-insoluble ash, and water-soluble ash. Moisture content is the amount lost during drying. For crude plant material, these assessments offer standards for standardization and quality control.

3.1.3 Extraction and Isolations of Crude Drug:

Hexane, ethyl acetate, ethanol, and distilled water were the solvents used in this reproducible extraction; the solvent-to-powder ratio was 10:1 (v/w). The maceration period for each solvent was 48 hours at room temperature. Whatman? The filtration process was carried out using No. 1 filter paper. A rotary evaporator was used to concentrate the extracts at a lower pressure. The percentage yield was calculated using the formula (weight of extract / weight of dried plant powder) × 100. [32]

The *Dolichandrone falcata* Seem's aerial parts were cleaned, left to cool at room temperature in the shade prior to being ground using a home mixer into a powder. A powdered sample weighing 100 g was macerated in 1000 mL petroleum ether and thoroughly shaken to eliminate lipids, oil, and fatty acids. A variety of solvents, including methanol, alcohol, ethyl acetate, water, acetone extract, and petroleum ether extract, were used in Soxhlet extraction to remove the coarsely powdered medication. After drying the insoluble residue, 1000 mL of ethanol was used for a 72-hour Soxhlet extraction. The *Dolichandrone falcata* Leaves Extract (DFLE) was vacuum-concentrated in a rota evaporator after 72 hours of post-incubation and stored in a refrigerator at 2 to 4 degrees Celsius for future research. [4, 15]

3.1.4 Analysis Methods

The standard procedures for various phytochemicals were used to qualitatively screen crude medications for their active ingredients. It must be noted that the Spectrophotometer System was used to estimate the total phenol and total flavonoid. [12]

Table: Pharmacognostic Analysis of *Dolichandrone Falcata*. [31]

Sr. No.	Particulars	Result
1.	Alcohol Extractive value	68.70 %
2.	Water Extractive value	100%
3.	Ash value	40%
4.	Moisture	65%



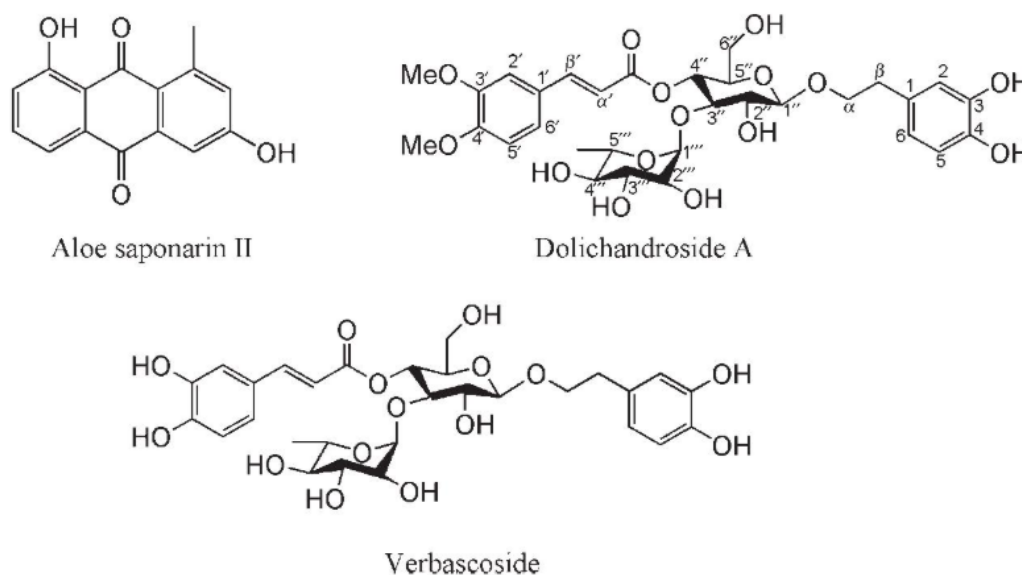


Fig: The structure of the newly isolated active compounds from *D. falcata*, including Dolichandrosidase A. The new substance, Dolichandroside A, was found to be an amorphous white powder. In primary screening, Aloe saponarin II, Dolichandroside A, and Verbascoside show promise as Active ingredients for DPPH free radical scavenging and α -glucosidase inhibition. ^[36]

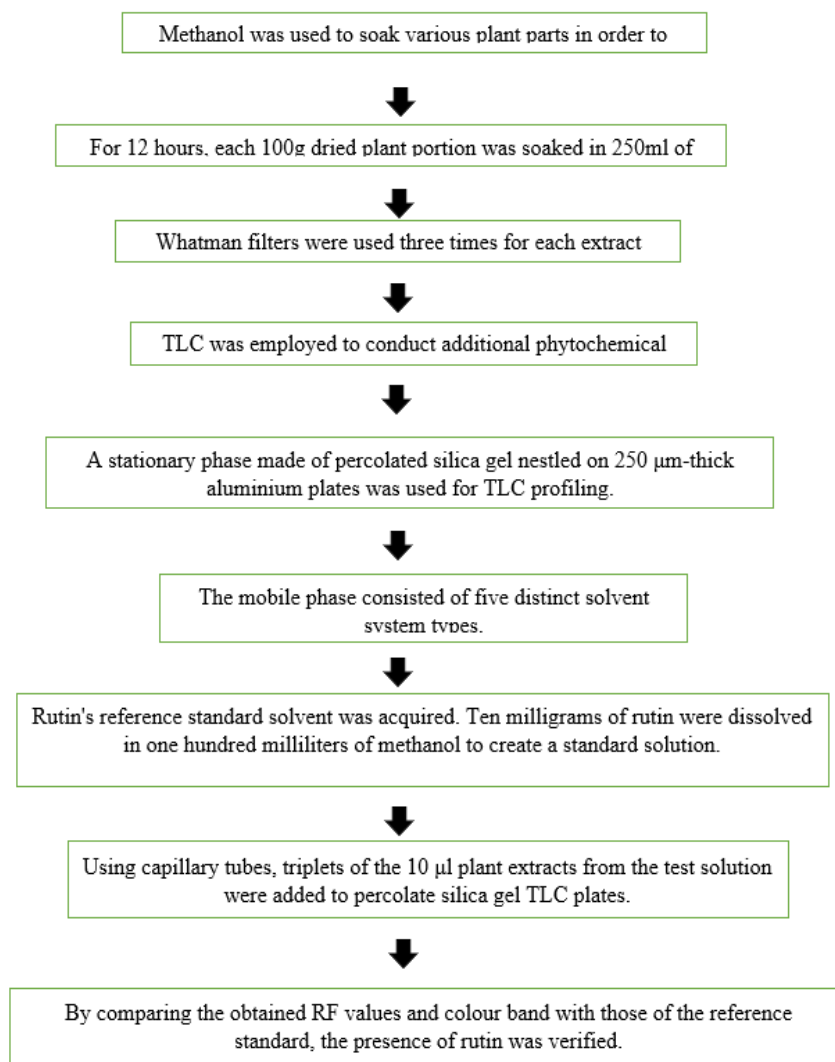
3.1.5 Common Solvents and Reagents

Numerous chemical components found in *Dolichandrone falcata* have been identified in multiple extracts. Both methanol and acetone extract contain the alkaloids. Alcoholic and aqueous extracts of terpenoids are analyzed. All types of extracts, including aqueous, alcohol, methanol, and ethyl acetate, contain tannins. ^[8] The following analytical-grade chemicals and reagents were purchased locally: Glacial acetic acid, methanol, ethanol, dichloromethane, n-hexane, ethyl acetate. All analytical-grade chemicals and reagents, including n-

Butanol, hydrochloric acid, pyridine, toluene, anisaldehyde, calcium chloride, copper sulphate, ferric chloride, Follin's reagent, conc. sulphuric acid, phenolglucinol, iodine, lead acetate, magnesium chloride, mercuric chloride, Ninhydrin, nitric acid, Ruthenium red, sodium acetate, sodium iodide, sodium hydroxide, sodium nitroprusside, hide powder, Folin Ciocalteu reagent, sodium bicarbonate, gallic acid, and all other compounds and reagents. ^[16]

3.1.6 Chromatographic Profiling

3.1.6.1 Thin Layer Chromatography (TLC) parts were soaked in methanol to create extracts.



A. Thin layer chromatography (TLC) was performed using the specified techniques.

B. Tests were conducted on a number of solvent systems.

C. The proportion of methanol to ethyl acetate to chloroform (6:2:2) establishes the optimal solvent system.

D. at 254 nm, the spots were detected by UV light. ^[8]

3.1.7 HPLC Technique

HPLC is a natural product isolation technique that is used in analytical chemistry and phytochemicals to identify, quantify, and purify the mixture's constituent parts. ^[17, 18]

Taking all of these factors into account, the current study aims to determine the phytochemical analysis of

Dolichandrone falcata leaves and bark that elicits anti-oxidant and anti-diabetic activity. ^[19, 20]

3.2 Major Phytochemical Classes in *D. Falcata*

Numerous phytochemical classes, such as alkaloids, phenolic compounds, terpenoids, glycosides, flavonoids, and saponins, are present in *Dolichandrone falcata*.

3.2.1 *Dolichandrone Falcata* Phytochemical Screening: Petroleum ether, ethanol, and water extract all contain alkaloids, based on the preliminary screening of leaf extracts for phytochemicals. Water extract, ethanol, flavonoids, glycosides, and saponins include carbohydrates and proteins as well. Steroids and oils are present in petroleum ether extract.

▪ Alkaloids:



Initial phytochemical screening of fruit and bark extracts revealed that alkaloids were present in methanol, alcohol, and ethyl acetate extracts. Saponins can be found in aqueous and alcohol extracts.

▪ Terpenoids:

The terpenoids include extracted from ethyl acetate, methanol, acetone, and water. Saponins are found in extracts from tobacco, ethyl acetate, and water.

▪ Tannins:

Aqueous, methanol, alcohol, and ethyl acetate extracts include tannins. All extracts do not include steroids. Methanol, alcohol, or ethyl acetate extracts can be used to remove tannins from plants.

▪ Cardiac Glycoside:

All extracts, with the exception of water, contain cardiac glycosides. Terpenoids were also found in ethyl acetate and aqueous extracts. Steroid chemicals can be found in both acetone extract and methanol. ^[20]

▪ Flavonoids:

Extracts of alcohol, methanol, acetone, and water include flavonoids. Plant parts contain flavonoid chemicals in large quantities. They are polyphenolic substances. They influence the colour and aroma of plants" One of the many functions of flavonoids is the

production of blue, red, and yellow pigmentation in flowers and other plant parts. Additionally, recent research has shown that the flavonoids rutin and Chrysin can be employed as antifertility and anti-cancer agents. Such basic study will aid in identifying the particular phytochemical that can be used to treat incurable illnesses like AIDS and cancer. Using the TLC method, certain flavonoids (Rutin) will be identified.

Principle: Phloroglucinol in the vanillin reagent reacts with flavonoids in an acidic media to generate a reddish-brown hue.

▪ Phenols:

The kingdom of plants is rich in phenols, which are aromatic chemicals with hydroxyl groups. They are found throughout the entire plant. It is well known that phenols provide plants with resilience to pests and diseases. Tannins, flavonols, and other substances are examples of phenols. The Folin-Ciocalteu reagent can be used to measure total phenol.

Principle: Molybdenum blue is a blue complex that is created when phenols and phosphomolybdic acid react in an alkaline medium using the Folin-Ciocalteu reagent. ^[12]

3.3 Phytochemical Preliminary Test ^[8]

1] Test for Carbohydrates:

TEST	OBSERVATION	INFERENCE
1 Molish Test: Add a millilitre of H ₂ SO ₄ and a few drops of alpha naphthol to the sample extract.	The violet ring signifies	Presence of carbohydrates.
2 Fehling's Test: Fehling A 1:1 mixture of A solution and Fehling B is used.	Brick red colouration indicates	Presence of reducing sugar.
3 Benedict's Test: The mixture is heated in a water bath after Benedict's reagent is added.	A red precipitate show	Absence of monosaccharide's
4. Barfoed test combining the test solution with an equivalent amount of Barfoed's reagent	No red precipitate was seen.	Absence of monosaccharide's



2] The Test for Sugar

Test	Observation	Inference
1. Test for Pentose Sugar Two drops of HCL and phloroglucinol crystals are added to the test solution.	Red colour absent	Pentose sugar absent
2. Test for Hexose Sugar Heat the Salviano's reagent in a water bath for two to three minutes, then add 1.5 millilitres of test solution.	Red colour is absent	Hexose sugar absence

3] The Test for Proteins

TEST	OBSERVATION	INFERENCE
1. Biuret Test. Combining the test solution via email with 4% NaOH and 1% Cuso4 solution	Violet colour appeare	Presence of protein
2. Millin Test 3 millilitres of Millins solution added to a test solution.	Show red colour	Presence of protein

4] The Test for Alkaloids

Test	Observation	Inference
1. Dragendorff Test: Add a few drops of Dragendorff reagent to the test solution.	Orange or brown ppt is formed	Presence of alkaloids
2. Mayer's Test: Add Mayer's reagent and 2–3 millilitres of test solution.	It gives ppt	Presence of alkaloids
3. Hager's Reagent: Add Hager's reagents to the test mixture.	Give yellow ppt	Presence of alkaloids

4. ANTI-DIABETIC PROSPECTS ^[20]

Diabetes is one of the most prevalent metabolic diseases worldwide. The World Health Organisation (WHO) estimates that the global incidence of adult diabetes was 9% in 2014, and four out of five diabetes-related deaths take place in low- or middle-income nations. Type 1 diabetes is characterised by insufficient insulin production by pancreatic b-cells, as opposed to type 2 diabetes (T2D), also known as non-insulin dependent diabetes mellitus (NIDDM), which is characterised by insulin resistance and elevated blood glucose. Resistance to insulin,

hyperinsulinemia, decreased insulin synthesis, and decreased glucose absorption and insulin utilisation are the outcomes of type 2 diabetes. The enzyme A-glucosidase, which hydrolyses starches and absorbs glucose, is found in the brush border of the small intestine and the pancreas, respectively. Individuals who suffer from type 2 diabetes are more likely to experience long-term issues such as blindness, hypertension, neuropathy, atherosclerosis, hyperlipidaemia, slow-healing wounds, vascular diseases, and renal failure. Evidence is mounting that a-glucosidase inhibitors help T2D patients' blood glucose levels rise more quickly by slowing down the



rate at which carbohydrates are absorbed and digested. Krentz and Bailey claim that type 2 diabetes can be effectively managed by strongly inhibiting intestinal α -glucosidase and slightly inhibiting pancreatic α -amylase. [21]

Fasting blood glucose levels, which are commonly used to diagnose diabetes, do not accurately predict postprandial hyperglycemia (PPHG), the most reliable marker of the metabolic abnormality that causes Type 2 Diabetes (T2D). Because PPHG is associated with type 2 diabetes, diabetes-related macro- and microvascular complications, and cardiovascular disease (CVD), it is imperative to prevent it. To treat pre-diabetic conditions and type 2 diabetes, drugs that reduce PPHG are therefore crucial. Another consequence of prolonged PPHG is postprandial oxidative stress (PPOS). The hallmark of PPOS is the body's increased vulnerability to oxidative damage after consuming a high-fat or high-carb meal. It is linked to a higher risk of obesity, diabetes, and atherosclerosis. The idea that PPHG is linked to PPOS and a higher risk of CVD is now supported by data, and that using the α -glucosidase inhibitor acarbose to lower PPHG has positive effects. Moreover, it is well known that natural compounds like acarbose, which slow down the absorption of

carbohydrates and mimic pharmaceutical medications, have been used to treat diabetes. [22] Diet and exercise are two essential factors that can help manage type-2 diabetes. [23]

4.1 Evaluation of Anti-Diabetic Potential in Vitro

4.1.1 Assessment of α - Amylase Inhibition Activity:

Before adding a starch solution to investigate in vitro amylase inhibition, after allowing the test sample to react with the α -amylase enzyme, it is temporarily allowed to sit at room temperature. Sodium chloride, sodium phosphate buffer, and potatoes were used to make a starch solution. We then brought it to a quick boil. The α -amylase solution was made by mixing the α -amylase with the same buffer. [24] We mixed equal amounts of 3, 5-dinitro salicylic acid (DNS) solution and sodium potassium tartrate tetrahydrate solution to make the colorimetric reagent. We added α -amylase solution after combining test samples of acarbose at various doses with starch solution. The combination was then kept at 25°C in an incubator to react with the starch solution. The DNS reagent-containing mixture was cooked for fifteen minutes in a boiling water bath. [25]

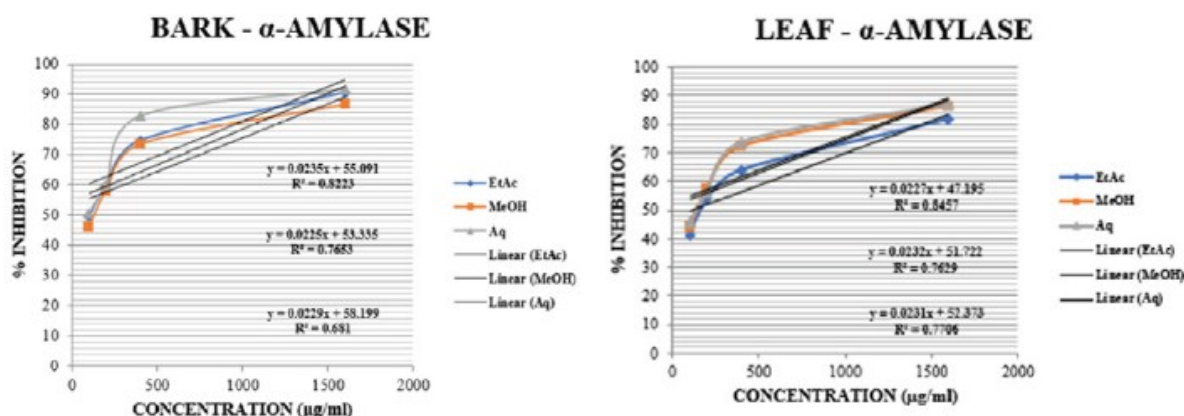


Fig: Bark and Leaf of α -Amylase Inhibition Activity [28]

4.1.2 Evaluation of the Inhibitory Activity of α -glucosidase:

A glucose reagent was added, and the quantity of glucose that the α -glucosidase enzyme releases from maltose was estimated by measuring its absorbance at

540 nm. The IC₅₀ and percentage of inhibition were calculated. To measure the inhibition activity of the α -glucosidase enzyme, the enzyme solution was incubated with phosphate buffer containing test samples of various connections in maltose solution for one hour at 37°C. [26]



Sr.no. Extract	Solvent	Plant Part	IC ₅₀ (µg/mL) For α -Glucosidase inhibition
Acarbose (Standard)	-----	-----	23.75
D. Falcata Leaf EtAc	Ethyl acetate	Leaf	63.56
D. Falcata Leaf MeOH	Methanol	Leaf	63.47
D. Falcata Leaf Aq	Aqueous	Leaf	57.89
D. Falcata Bark EtAc	Ethyl acetate	Bark	48.78
D. Falcata Bark MeOH	Methanol	Bark	57.30
D. Falcata Bark Aq	Aqueous	Bark	44.97

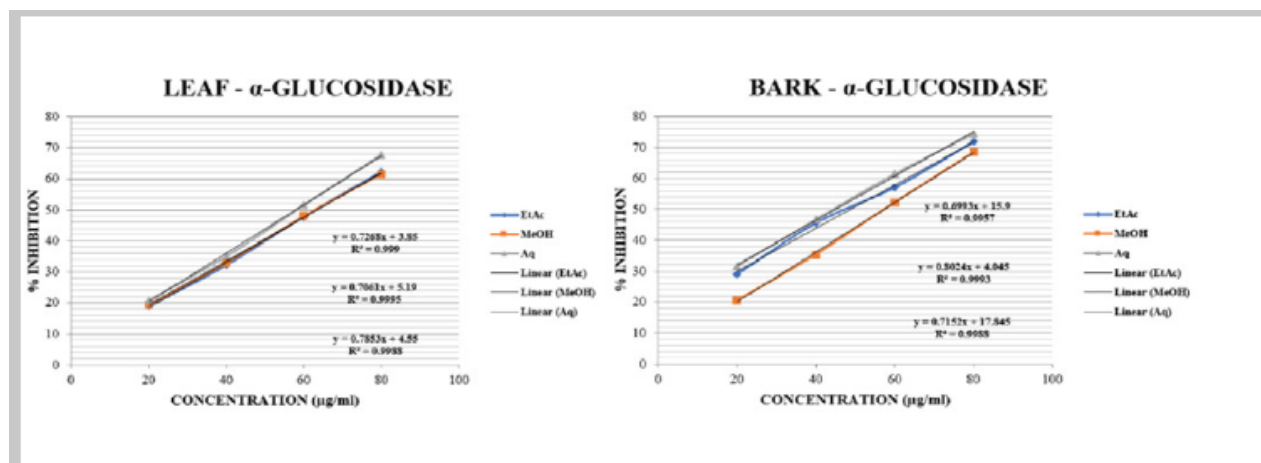


Fig: Fig: Bark and Leaf of α -Glucosidase Inhibition activity

4.1. In Vitro Investigations of Glucose Absorption and Insulin Secretion

Insulin secretion, target organ glucose uptake, and food absorption are only a few of the glucose metabolic routes that oral anti-diabetic medications might affect. Modern treatment focusses on incretins and transcription factors like peroxisome proliferator activated receptors, or PPAR. Glucose transporters and insulin receptors have not been the focus of anti-diabetic medication. [28, 29]

4.1.4 Qualification of Insulin Released by ELISA:

Apoptosis, glucotoxicity, autoimmunity, and insulin resistance are just a few of the physiological and pathological conditions that are linked to pancreatic cell regulation, which is necessary for insulin secretion and glucose homeostasis. Permanent damage and pancreatic cell death, which lead to a disruption in glucose homeostasis, are among the primary causes of diabetes. The pancreatic cell line RIN-5F was used to measure insulin secretion activity. Diabetes mellitus is a group of chronic metabolic diseases characterised by elevated blood glucose levels brought on by either the body's resistance to the effects of insulin, its incapacity to

produce insulin, or both. Nine. Type 1 diabetes, caused by autoimmune beta cell loss in the pancreas and characterised by a total lack of insulin production, is one of four clinically distinct types of this category of conditions. Gestational diabetes, a type of glucose intolerance that some pregnant women experience; type 2 diabetes, which arises when the body becomes more resistant to the action of insulin and is unable to produce enough insulin to overcome the resistance; and several other types of diabetes brought on by particular genetic defects in the function of insulin or beta-cells, pancreatic disorders, medications, or chemical toxicity. The main focus of this discussion is type 2 diabetes. 90–95% of all cases of diabetes that are diagnosed are type 2 diabetes. The seventeenth Insulin resistance is a prevalent early sign of type 2 diabetes. Over time, the pancreas may produce less or no insulin because the body is unable to produce enough of it to overcome the resistance. [37, 38, and 39]

4.2 Mechanisms of Antidiabetic Action

- Enhancement of insulin secretion or β -cell regeneration.
- Glucose uptake stimulation in peripheral tissues.

- Inhibition of enzymes that hydrolyse carbohydrates (α -amylase, α -glucosidase).
- Antioxidant protection against pancreatic β -cell damage.
- Decrease of oxidative stress and improvement of the lipid profile.
- Control of hepatic enzymes involved in the metabolism of glucose

4.2.1 Inhibition of Carbohydrate-Digesting Enzymes ^[22, 30]

Phenolic compounds and other phytoconstituents may suppress the α -amylase and α -glucosidase enzymes, which would postpone the intestinal absorption of glucose and the breakdown of carbohydrates. Aim for α -amylase and α -glucosidase. Impact: Decreased hyperglycemia after meals.

4.2. Enhanced Sensitivity to Insulin (Peripheral Mechanism) ^[31, 33]

Polyphenols and triterpenoids have the potential to increase GLUT4 translocation in fat and skeletal muscle by turning on the PI3K/Akt signaling pathway and enhancing insulin receptor (IR) phosphorylation. Improved peripheral cell uptake of glucose. The PI3K/Akt pathway and insulin receptor substrate (IRS) are the targets. Impact: Better utilization of glucose by cells.

4.2.3 Enhancement of Insulin Secretion (Pancreatic Mechanism) ^[32]

Flavonoids, alkaloids, and glycosides found in *Dolichandrone falcata* are phytochemicals that may increase the quantity of insulin that the pancreatic β -

cells secrete. This happens by altering ATP-sensitive K^+ channels and raising intracellular Ca^{2+} , which causes the exocytosis of insulin granules. Target of the Pancreas: β -cells. Impact: Reduced blood glucose due to increased insulin release

4.2.4 Antioxidants and Anti-inflammatory Action ^[31, 32]

Dolichandrone falcata has potent antioxidants (tannins, flavonoids) that prevent β -cell damage and lessen oxidative stress. Insulin resistance-related inflammatory cytokines (TNF- α , IL-6) are decreased when the NF- κ B pathway is inhibited.

Target: ROS and the NF- κ B pathway scavenging mechanisms.

Impact: decreased insulin resistance and protection of β -cells.

4.2.5 Suppression of Hepatic Gluconeogenesis ^[31, 34]

Key gluconeogenic enzymes in the liver, such as PEPCK and G6Pase, can be down regulated by certain alkaloids and flavonoids.

Target: G6Pase and PEPCK genes.

Impacts: Reduced production of glucose by the body.

4.2.6 Modulation of Lipids Metabolism ^[33]

Extracts from plants control AMPK (AMP-activated protein kinase), which encourages the oxidation of fatty acids and inhibits lipogenesis. Goal: AMPK signaling. Improved glucose homeostasis and lipid profile are the results.

Table: Mechanism of Antidiabetic Action

Mechanism	Molecular Target	Biological Effects
B-cell Stimulation	K^+ / Ca^{2+} channels	↑ Insulin secretion
Insulin Sensitization	IRS, PI3K/Akt, GLUT4	↑ Glucose uptake
Enzyme Inhibition	α -Amylase, α -Glucosidase	↓ Glucose absorption
Hepatic Modulation	PEPCK, G6Pase	↓ Gluconeogenesis
Antioxidant defence	ROS, NF- κ B	β -cell protection
Lipid Regulation	AMPK	Improved glucose-lipid balance



5. SAFETY AND TOXICOLOGICAL PROFILE OF DOLICHANDRONE FALCATA

5.1 Toxicological Warning: Its bark paste is used as a fish poison on broken or dislocated bones, and its bark juice is used to treat leucorrhea and menorrhagia. The plant's leaves have been converted into chrysin-7-rutinoside. Effects of *D. falcata* stem-bark methanol extract (DFBM), ethyl acetate extract (DFBEA), and isolated component DFB on anxiety. Were investigated in this work using animal models. [42] Pregnant women should avoid the plant at all costs because its fruits are used to induce abortions and indicate strong uterine-stimulating activity. Additionally used as a fish toxin, the bark may have ichthyotoxic (fish-killing) qualities. [43]

5.2 Phytochemical Basis: Phytochemical screening is used to identify Amino acids, alkaloids, flavonoids, saponins, phenolics, terpenoids, cardiac glycosides, and steroids. Numerous classes of compounds, including cardiac glycosides and alkaloids, are known to exhibit dose-dependent toxicity. [44]

5.3 Safety Assessment and Risk Management:

Determining Safety Margins: Toxicokinetics compares the exposure levels at which side effects manifest to those anticipated in humans at therapeutic or environmental exposure levels in Identification of Toxic Metabolites to ascertain a drug's or chemical's safety margin: Researchers can identify and measure toxic metabolites that may be responsible for negative effects by using toxicokinetic studies. To evaluate a substance's overall safety, it is essential to comprehend how these metabolites are formed and eliminated. **Non-Clinical Risk Assessment:** Based on animal research, TK data are utilized to forecast possible human risks. Researchers can more accurately determine the applicability of findings on animal toxicity to humans by comparing toxicokinetics profiles across species. [40]

5.3.1 Preclinical Toxicological Testing:

Lethal dose 50, or LD_{50} , is a conventional indicator of acute toxicity that is the dose at which half of test animals perish. The highest dosage at which no negative effects are noticed is known called the NOAEL (No-Observed-Adverse-Effect Level),

which is the basis for figuring out human exposure limits. Repeated dose toxicity: To evaluate the effects of prolonged administration, animals are given the drug over the course of days or months. [6]

5.4. Studies Using Animal Models That Demonstrate Pharmacologic Responses But Few Toxicities Endpoints:

In one study, oral doses of 100–300 mg/kg of the ethanolic leaf extract of *D. Falcata* were applied to a rat model of haemorrhoids (an anti-inflammatory model), and the outcomes demonstrated a reduction in inflammatory markers. There was no overt toxicity in that model reported by the study. [45] Numerous biologically active substances, such as vitamin E derivatives, phytol, and octadecanoic acid, are found in the leaves according to a GC-MS phytochemical profiling study. These compounds may have both positive and negative effects. [42]

5.5. No Toxicology or Human Safety Studies: "No dedicated toxicology or safety trials on humans have been reported," according to the review article on *D. falcata*. [8] I couldn't find any published human safety or toxicology trials for *D. falcata*.

5.6. Safety and Toxicological Gaps in Dolichandrone Falcata

- There is no thorough acute toxicity study of *D. falcata* in healthy animals that identifies LD_{50} , organ toxicities, maximum tolerated dose, etc.
- *D. falcata* has not been the subject of any published sub-chronic or chronic toxicity studies (such as 90-day feed studies) that evaluate histopathology, reproductive toxicity, mutagenicity, or multiple organ systems in animals.
- There are no specific studies on *D. falcata*'s toxicity to animal reproduction or development.
- There are no human clinical safety data (no Phase I trials, no controlled safety monitoring).



- No evaluations of the safety of particular formulations (e.g., of isolated compounds, enhanced extracts, novel delivery systems).
- Lack of bioavailability and pharmacokinetic information, which is crucial for safety (e.g., metabolites, elimination, and the duration of active compounds).
- Although they cannot be applied directly to *D. falcata*, there are indications of reproductive effects in a related species that raise concerns.

5.6.1. Proxy Warnings from Related Organism

In one study, male rats received 100, 300, and 600 mg/kg of aqueous flower extract for 48 days. *Dolichandrone serrulata* (a different species in the same genus). While no significant histopathological damage was discovered, some liver/kidney biochemical markers (ALT, ALP, and creatinine) showed changes, albeit within normal ranges. ^[46]

This implies that some doses of the genus may impact liver/kidney parameters, even though *D. falcata* is not one of them. Male rats of a different plant were given a methanol extract at a dose of 100 mg/kg for 60 days, *Dendrophthoe falcata* (a mistletoe parasitic plant of a different genus), experienced reproductive toxicity (reduced sperm count, motility, and testicular size). ^[47] Although not directly related, it raises questions about possible toxicity to reproduction in medicinal plants with comparable activity.

5.6.2. *D. Falcata* Safety Implication

In light of the gaps, the following suggestions and practical implications are offered to anyone thinking about using *D. falcata* (for research or therapeutic development):

- Until further information is available, assume safety: While low-to-moderate doses in animals might seem safe, higher doses, long-term use, and human exposures can be harmful.
- It is crucial to perform the entire toxicology battery when creating a formulation for human use, such as an extract for anti-diabetic purposes, including acute,

sub-acute, chronic, reproductive, genotoxicity, organotoxicity, and pharmacokinetics.

- Due to the lack of safety data, exercise caution when dealing with patient groups such as children, pregnant or nursing women, and those with liver or kidney impairments.
- In any animal or human trial, keep an eye on the following standard safety parameters: haematology, major organ histopathology, kidney function (creatinine, BUN), liver enzymes (ALT/AST), and reproductive endpoints, if applicable.
- Start with lower doses than those used in pharmacology studies (less than 100 mg/kg in animals, for example) and increase them gradually.

- Any negative events should be fully documented and reported (for future data building).
- Because some extracts exhibit cytotoxic activity, toxicity may occur at higher dosages or with specific extract types (even beneficial in cancer models but potentially harmful in normal tissue).
- Be aware of the possibility of herb-drug interactions: If the plant extract has hormone-modulating properties (such as anti-estrogenic properties reported in the literature) or inhibits or induces metabolising enzymes, interactions with other medications may occur.

7. RESEARCH GAPS & FUTURE PROSPECTS

7.1. Absence of Substantial Phytochemical Isolation Research

- Although compounds are isolated in one paper (Isolation of Dolichandroside A), the scope is limited.
- Review articles mention numerous other extracts (leaf, bark, fruit, etc.) and families of compounds (flavonoids, glycosides, alkaloids, terpenoids) that have not been fully isolated or described in relation to their anti-diabetic effects. ^[8]
- **Future Prospects:** Systematic phytochemical research aimed at *D. falcata* for anti-diabetic leads, such as isolating all significant flavonoids or phenolics and testing them in cell models, enzyme assays, insulin signalling, etc.



7.2. Limited Molecular and Mechanistic Research

- There is little research on insulin secretion, insulin sensitivity, glucose uptake, signalling pathways (e.g., PI3K/AKT, AMPK), molecular docking, and in vivo diabetic animal models with appropriate mechanistic endpoints. The majority of the work that is currently available focusses on enzyme inhibition (α -amylase/ α -glucosidase) and free-radical scavenging.
- **Future Prospect:** Examine the mechanistic endpoints (β -cell protection, insulin receptor signalling, oxidative stress, and inflammation), analyse both type 1 and type 2 diabetes models in vivo, and profile isolated molecules using ADME and molecular docking.

7.3. Need for Formulation Development to Improve Bioavailability

- A proof-of-concept study rather than an appropriate in vivo bioavailability/bio efficacy study is the focus of one work that employs nanoparticle (CuO) formulation. There are no published formulation studies that focus on the anti-diabetic compounds of *D. falcata* that are intended for oral administration, controlled release, or phytosome/lipid formulation.
- **Future Prospect:** Formulate active extracts or compounds from *D. falcata* in optimal forms (such as Nano-emulsions, liposomes, or phytosome) and assess their pharmacokinetics, bioavailability, and in vivo effectiveness using diabetic animal models.

7.4. Opportunities for Clinical Validation

- To date, there have been no human or clinical trials documented for the treatment of diabetes using *D. falcata* extracts or compounds; the work is preclinical (in vitro enzyme assays, limited in vivo).
- **Future Prospect:** Create pilot clinical trials (Phase I/II) in diabetic or pre-diabetic

populations to assess safety, tolerability, pharmacokinetics, and preliminary efficacy (glucose/insulin markers) once there is adequate safety and in vivo efficacy data.

8. UPCOMING SCOPE:

1. To put it briefly, the phytochemical components that cause hypoglycemia should be isolated and confirmed.
2. *Dolichandrone falcata* may be used for future animal research (in-vivo evaluation). Plant extract has been shown to have hypoglycemic potential.
3. Investigating combination treatments using currently available anti-diabetic drugs to possibly improve effectiveness and reduce negative effects.
4. Customizing treatment strategies to optimize therapeutic results based on unique patient profiles and hereditary variables.
5. When these two extracts are combined, they may have synergistic effects that improve each extract's unique hypoglycemic qualities and offer a more thorough method of treating diabetes mellitus.

9. CONCLUSION

A promising medicinal plant with significant ethno pharmacological significance and mounting evidence of its potential to prevent diabetes is *Dolichandrone falcata*. Numerous phytochemicals, including flavonoids, alkaloids, tannins, and phenolic compounds, are present, which implies that their therapeutic effects could be attributed to a variety of mechanisms, such as increased insulin sensitivity, antioxidant activity, and glucose metabolism modulation. Comprehensive study on its bioactive components, molecular targets, and pharmacokinetic properties is still lacking, despite intriguing results from basic pharmacological trials. To confirm its effectiveness and safety, further research should focus on mechanistic studies, well-designed in vivo and clinical tests, and the isolation and characterisation of active elements. The creation of *D. falcata*-based formulations as innovative, plant-derived treatments for the treatment of diabetes may eventually be made



easier by fusing traditional knowledge with contemporary pharmacological research.

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