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Antidiabetic Potential of *Artemisia vulgaris*: A Comprehensive Literature Review

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ABSTRACT

Diabetes mellitus (DM) is a globally prevalent metabolic disorder characterized by persistent hyperglycaemia. Increasing demand for alternative therapies with fewer side effects has stimulated interest in medicinal plants, including *Artemisia vulgaris* (mugwort), a member of the Asteraceae family traditionally used in the treatment of diabetes. This review critically examines current literature on the phytochemistry, pharmacological actions, and therapeutic potential of *A. vulgaris* in diabetes management. Findings from in vitro, in vivo, and limited clinical studies support its hypoglycaemic effects via mechanisms including inhibition of carbohydrate-digesting enzymes, antioxidant activity, insulin sensitization, and β-cell protection. The review also highlights gaps in research, notably in clinical validation and standardization. Overall, *A. vulgaris* presents a promising complementary agent for diabetes therapy pending further investigation.

Keywords: Antidiabetic Potential, Artemisia vulgaris

1. INTRODUCTION

Diabetes mellitus (DM) is one of the most pressing global health challenges of the 21st century. It is a chronic, multifactorial metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The World Health Organization (WHO) classifies DM into four major types: Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), gestational diabetes mellitus (GDM), and other specific types resulting from genetic defects or secondary causes [1]. Among these, T2DM is the most prevalent, accounting for over 90% of all cases. It is largely associated with insulin resistance, obesity, sedentary lifestyle, and unhealthy dietary habits [2].

According to the 10th edition of the International Diabetes Federation (IDF) Diabetes Atlas (2021), approximately 537 million adults aged 20–79 was living with diabetes globally, and this number is projected to rise to 643 million by 2030 and 783 million by 2045 if current trends continue [3]. In addition to the direct health burden, diabetes is a major risk factor for microvascular complications such as nephropathy, neuropathy, and retinopathy, as well as macrovascular conditions including coronary artery disease and stroke. These complications significantly impact the quality of life and increase the socioeconomic burden worldwide.

Despite the availability of several classes of oral hypoglycaemic agents and insulin formulations, modern pharmacotherapy is not without limitations. Long-term use of synthetic drugs often leads to adverse effects such as weight gain, hypoglycaemia, gastrointestinal disturbances, and even cardiovascular risks [4]. Furthermore, in resource-limited settings, the high cost of continuous pharmacotherapy creates significant barriers to effective disease management. These limitations have spurred increasing global interest in alternative and complementary approaches, especially the use of plant-based therapies in diabetes management.

Medicinal plants have been traditionally used for centuries in various cultures to treat diabetes, often with fewer side effects and lower costs. The WHO recognizes the value of traditional herbal medicine, especially in developing countries where it is frequently the primary source of healthcare [5]. Among the promising herbal candidates, *Artemisia vulgaris* L. (commonly known as mugwort), a plant from the Asteraceae family, has gained attention for its diverse medicinal properties, including antidiabetic activity. Traditionally used in Chinese, Ayurvedic, and European folk medicine, *A. vulgaris* has been employed to treat gastrointestinal disorders, gynaecological problems, fever, and metabolic disorders [6].

Recent pharmacological investigations have reported various biological activities of *A. vulgaris*, such as antioxidant, antimicrobial, anti-inflammatory, and hepatoprotective effects [7]. Notably, preclinical studies have highlighted its potential to modulate blood glucose levels, enhance insulin sensitivity, and protect pancreatic tissues. This review aims to critically explore the botanical

characteristics, phytochemical composition, pharmacodynamics, and antidiabetic efficacy of *A. vulgaris*, providing a comprehensive evaluation of its role as a complementary therapeutic option for diabetes management.

2. Botanical and Pharmacognostical Overview

2.1 Botanical Description

Artemisia vulgaris L., commonly known as mugwort, is an herbaceous, perennial plant native to temperate regions of Asia, Europe, and North America. It belongs to the **Asteraceae** (Compositae) family, which is known for its wide variety of medicinal plants. *A. vulgaris* thrives in a variety of habitats including roadsides, riverbanks, wastelands, and forest edges, especially in nitrogen-rich soils [8].

- **Scientific Classification**:
  - **Kingdom**: Plantae
  - **Division**: Magnoliophyta
  - **Class**: Magnoliopsida
  - **Order**: Asterales
  - **Family**: Asteraceae
  - **Genus**: *Artemisia*
  - **Species**: *vulgaris*

Table 1 presents the taxonomical hierarchy and key pharmacognostical characteristics of *Artemisia vulgaris*, highlighting its traditional uses and phytochemical composition.

Table 1. Taxonomical and Pharmacognostical Characteristics of *Artemisia vulgaris*

Feature	Description
Botanical name	*Artemisia vulgaris* L.
Family	Asteraceae
Common name	Mugwort
Habitat	Temperate zones of Asia, Europe, and USA
Plant type	Perennial herb
Leaf morphology	Pinnatifid, green above, silvery below
Flowering	Small, reddish-brown, in panicles
Key phytochemicals	Quercetin, chlorogenic acid, artemisinin
Traditional uses	Antidiabetic, antispasmodic, emmenagogue

Mature *A. vulgaris* plants grow between 1 and 2.5 meters in height. The leaves are deeply pinnatifid, dark green on the upper surface, and covered with a fine layer of silvery hairs on the underside, giving them a unique appearance. The stems are reddish or purplish, and the plant produces small, clustered, yellow to reddish-brown flowers arranged in racemes or panicles. The plant is aromatic, owing to the presence of volatile essential oils concentrated in glandular trichomes.

2.2 Pharmacognostical Features

Pharmacognostical studies provide a scientific basis for identifying and authenticating medicinal plants based on their morphological, anatomical, and histological features. These studies are essential for the quality control of herbal formulations.

2.2.1 Macroscopic Characteristics

- **Stem**: Erect, ribbed, and purplish; cylindrical with numerous branches.

- **Leaves**: Alternate, pinnately lobed with smooth or slightly serrated margins; aromatic due to essential oils.
- **Flowers**: Small, tubular, and occur in panicle inflorescence; yellow to reddish-brown.
- **Odor and Taste**: Aromatic odour and slightly bitter taste.

2.2.2 Microscopic Characteristics

Microscopic analysis of *A. vulgaris* leaf and stem reveals key identifying features:

- **Trichomes**: Non-glandular uniseriate trichomes and glandular trichomes secreting volatile oils.
- **Epidermis**: Covered with cuticle and bear stomata of anomocytic type.
- **Vascular Bundle**: Collateral and open, surrounded by sclerenchymatous tissues.
- **Calcium Oxalate Crystals**: Present as rosettes and druses in mesophyll tissue.

These features are useful for plant identification and ensuring the authenticity of raw material used in formulations [9].

2.3 Traditional and Ethnomedicinal Uses

In traditional medicine systems across Asia and Europe, *A. vulgaris* has been used for its carminative, antiseptic, diuretic, and emmenagogue properties. Notably, its antidiabetic usage is well documented in Ayurveda and Traditional Chinese Medicine (TCM), where it is used to reduce excessive thirst, normalize urine output, and control sugar levels [10].

Traditional formulations include:

- **Decoction of leaves or roots** for lowering blood sugar
- **Powdered leaves** mixed with honey for regulating appetite and digestion.
- **Essential oil massages** for improving circulation and reducing peripheral neuropathy symptoms.

Such practices offer a foundation for scientific validation and pharmacological exploration of *A. vulgaris* in metabolic diseases.

3. Phytochemical Composition of *Artemisia vulgaris*

The pharmacological potential of *Artemisia vulgaris* is largely attributed to its rich and diverse phytochemical profile. The plant contains a complex array of primary and secondary metabolites, many of which are known to exhibit bioactivities relevant to diabetes management, including antioxidant, anti-inflammatory, enzyme-inhibitory, and insulin-sensitizing effects.

3.1 Classes of Phytochemicals

3.1.1 Flavonoids

Flavonoids are a major class of polyphenolic compounds found abundantly in *A. vulgaris*. These include **quercetin, rutin, luteolin, apigenin, and kaempferol** [11]. Flavonoids are known to modulate several biological targets involved in diabetes such as oxidative stress markers, glucose transporters, and inflammatory cytokines. Quercetin, for example, has been reported to inhibit α-glucosidase and aldose reductase, enhance insulin secretion, and protect pancreatic β-cells from oxidative damage [12].

3.1.2 Phenolic Acids

Phenolic acids such as **caffeic acid, chlorogenic acid, ferulic acid, and syringic acid** are potent antioxidants and are known to reduce oxidative stress-induced β-cell damage [13]. These compounds also inhibit glucose absorption in the intestine and improve glucose utilization in peripheral tissues.

3.1.3 Terpenoids and Sesquiterpene Lactones

A. vulgaris contains several **monoterpenes and sesquiterpene lactones**, including **artemisinin**, **camphor**, **cineole**, **borneol**, and **thujone** [14]. These compounds exhibit antimicrobial, anti-inflammatory, and hepatoprotective effects. In diabetic models, these terpenoids help maintain liver function and reduce lipid peroxidation.

3.1.4 Essential Oils

Essential oils extracted from *A. vulgaris* include a mixture of volatile compounds such as **1,8-cineole, camphor, α-thujone, and β-thujone** [15]. While thujone is considered toxic at high concentrations, in small, regulated amounts, the essential oils contribute to the plant's anti-inflammatory and digestive-stimulating actions.

3.1.5 Other Constituents

- **Saponins**: Known for their role in reducing blood cholesterol and improving glucose uptake.
- **Tannins**: Exhibit protein-precipitating and antioxidant properties, potentially helping in glycation control.
- **Alkaloids and Coumarins**: Exhibit vasodilatory and mild diuretic effects, possibly beneficial in diabetic nephropathy and hypertension [16].

Table 2 summarizes the key phytoconstituents of *A. vulgaris* along with their reported antidiabetic mechanisms.

Table 2. Phytoconstituents of *A. vulgaris* and Their Reported Antidiabetic Actions

Phytoconstituent	Type	Antidiabetic Mechanism	Reference
Quercetin	Flavonoid	Enhances insulin secretion, antioxidant, enzyme inhibition	[12]
Chlorogenic acid	Phenolic acid	Delays glucose absorption, antioxidant	[13]
Luteolin	Flavonoid	Anti-inflammatory, GLUT4 translocation	[11]
Artemisinin	Sesquiterpene	Pancreatic protection, anti-inflammatory	[6]
Cineole & camphor	Essential oils	Antioxidant, anti-inflammatory	[15]

3.2. Phytochemical Basis of Antidiabetic Activity

The antidiabetic potential of *Artemisia vulgaris* is strongly associated with its rich phytochemical profile. It contains a variety of bioactive compounds, particularly flavonoids (e.g., quercetin, luteolin), phenolic acids (e.g., chlorogenic acid), and sesquiterpene lactones such as artemisinin [17,18]. These constituents exert multiple mechanisms of action relevant to diabetes management.

Pharmacologically, AV demonstrates inhibition of key digestive enzymes—α-glucosidase and α-amylase—thereby reducing postprandial glucose spikes. Additionally, its high antioxidant activity contributes to the neutralization of reactive oxygen species (ROS), which are implicated in pancreatic β-cell damage and insulin resistance [19]. AV also exhibits insulin-mimetic properties by enhancing glucose transporter (GLUT-4) translocation and insulin receptor substrate-1 (IRS-1) signaling pathways in peripheral tissues, promoting effective glucose uptake [20].

Recent studies further support these findings. Shafique et al. (2020) confirmed a strong correlation between total phenolic content and antioxidant capacity in AV extracts [21], while Singh et al. (2021) reported significant upregulation of GLUT-4 and IRS-1 expression in AV-treated diabetic models [22].

4. Mechanisms of Antidiabetic Action

A. vulgaris acts through multiple pharmacological mechanisms to exert its antidiabetic effects. These mechanisms work synergistically to lower blood glucose levels, improve insulin function, reduce oxidative stress, and prevent diabetic complications.

4.1 Inhibition of Carbohydrate-Hydrolysing Enzymes

The postprandial spike in blood glucose is largely influenced by enzymatic digestion of carbohydrates by **α-amylase** and **α-glucosidase**. Inhibiting these enzymes is a well-established strategy for managing Type 2 diabetes.

- **In vitro studies** have shown that ethanolic and aqueous extracts of *A. vulgaris* inhibit both enzymes in a concentration-dependent manner [23].

- At 500 µg/mL concentration, *A. vulgaris* extract demonstrated over **65% inhibition of α-glucosidase**, with IC_{50} values comparable to standard drug acarbose [24].

This inhibition slows down the breakdown of complex carbohydrates into glucose, resulting in a moderated post-meal glycaemic response.

4.2 Antioxidant and Free Radical Scavenging Activity

Oxidative stress is a key contributor to the progression of diabetes and its complications. It arises due to the overproduction of reactive oxygen species (ROS) and the failure of endogenous antioxidant systems.

- Flavonoids and phenolic acids in *A. vulgaris* neutralize free radicals and **enhance endogenous antioxidant enzyme activity**, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [25].

- **DPPH and ABTS assays** revealed strong antioxidant potential of *A. vulgaris* extracts with high total phenolic and flavonoid content [26].

These activities protect pancreatic β-cells from oxidative injury and delay the onset of complications like neuropathy, nephropathy, and retinopathy.

4.3 Enhancement of Insulin Sensitivity

Insulin resistance is the hallmark of Type 2 diabetes. Several constituents in *A. vulgaris*, especially flavonoids and terpenoids, improve insulin action:

- Experimental studies show that *A. vulgaris* increases the **expression of insulin receptor substrate-1 (IRS-1)** and **GLUT-4 transporters**, facilitating glucose uptake in skeletal muscle and adipose tissue [27].

- Improvement in **insulin signalling pathways** results in lower circulating glucose and improved metabolic profiles in diabetic rats [28].

4.4 Hypolipidemic and Hepatoprotective Effects

Dyslipidaemia and hepatic dysfunction are common in diabetic patients. *A. vulgaris* has shown to:

- **Lower serum triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL)**

- **Increase high-density lipoprotein (HDL)** levels in diabetic animal models [29]

- Restore liver glycogen content and normalize hepatic enzyme markers (ALT, AST, ALP), suggesting **hepatoprotective effects** [30]

These benefits are vital for preventing cardiovascular complications in long-term diabetic patients.

4.5 Pancreatic β-cell Protection and Regeneration

Loss of pancreatic β-cell mass and function is a key event in the development of both Type 1 and Type 2 diabetes.

- Histological studies in diabetic rats treated with *A. vulgaris* showed **reduced cellular necrosis**, **preservation of islet architecture**, and **increased insulin secretion** [31].

- The plant's **antioxidant and anti-inflammatory effects** play a central role in protecting β-cells from glucotoxicity and lipotoxicity.

5. Preclinical and In Vitro Evidence: A Critical Appraisal

Scientific validation of the antidiabetic potential of *Artemisia vulgaris* (AV) has predominantly emerged from a growing body of **in vitro** and **in vivo** research. These studies have focused on the pharmacodynamic attributes of various AV extracts, highlighting its multi-targeted approach in modulating hyperglycaemia and associated metabolic dysfunctions. The literature strongly supports the plant's ability to influence multiple diabetic targets, making it a compelling candidate for further translational research.

5.1 In Vivo Evidence from Animal Studies

The majority of preclinical research on *A. vulgaris* has utilized rodent models of diabetes, especially **streptozotocin (STZ)-** and **alloxan-induced diabetes**, which simulate Type 1 and insulin-deficient Type 2 diabetes pathophysiology. These models offer insight into glucose-lowering potential, β-cell protection, and secondary metabolic improvements.

5.1.1 Glycaemic Control and Insulin Secretion

- **Rani and Singh (2014)** demonstrated that AV leaf extract, administered orally at 200 and 400 mg/kg for 14 days in STZ-induced diabetic rats, significantly reduced fasting blood glucose and improved glucose tolerance, with effects comparable to glibenclamide [32].

- In a study by **Ahmed et al. (2013)**, AV ethanolic extract showed dose-dependent antihyperglycemic effects in alloxan-induced diabetic mice, with significant recovery in plasma insulin levels and pancreatic weight, suggesting enhanced insulin biosynthesis or secretion [33].

5.1.2 Glycogen Restoration and Gluconeogenesis Inhibition

- Diabetic rats often present with depleted hepatic glycogen stores due to increased gluconeogenesis and decreased glycogenesis. AV-treated rats exhibited significant restoration of liver and skeletal muscle glycogen content, indicating enhanced peripheral glucose utilization and hepatic glucose storage [24].

5.1.3 Lipid Modulation and Cardiometabolic Benefits

- AV extract has shown considerable improvement in lipid profiles. **Ahmad et al. (2018)** reported that AV treatment led to reductions in total cholesterol, triglycerides, and LDL-C, while increasing HDL-C in diabetic rats, thus potentially reducing the risk of atherosclerosis and cardiovascular events [35].

Table 3. Summary of In Vivo Studies on Antidiabetic Activity of *A. vulgaris*

Study (Year)	Animal Model	Extract Type & Dose	Duration	Key Findings
Rani & Singh (2014)	STZ-induced rats	Aqueous extract, 400 mg/kg	14 days	↓Fasting glucose, ↑Insulin, ↓Lipids
Ahmed et al. (2013)	Alloxan-induced mice	Methanolic extract, 300 mg/kg	21 days	↑Pancreatic mass, ↑Insulin levels
Kumar et al. (2017)	STZ-induced rats	Hydroalcoholic extract	28 days	β-cell protection, normalized liver enzymes

5.1.4 Hepatoprotective and Renoprotective Effects

- STZ and alloxan cause hepatic and renal oxidative damage. Studies reveal normalization of liver enzymes (AST, ALT, ALP) and improved serum creatinine and urea levels in AV-treated groups, suggesting hepatoprotective and nephroprotective activities [36].

5.1.5 Histopathological Recovery of Pancreatic Tissue

- Histological analysis in AV-treated diabetic rodents revealed preservation of islet architecture, reduction in necrosis, and increased β-cell density. **Kumar et al. (2017)** confirmed that AV exerts protective effects against STZ-induced pancreatic injury, indicating its potential for β-cell regeneration [37].

5.2 In Vitro Mechanistic Studies

In vitro studies serve as essential tools to identify specific molecular mechanisms through which AV confers its antidiabetic effects. These studies offer detailed understanding of bioactivity at the enzymatic and cellular levels.

5.2.1 Inhibition of α-Glucosidase and α-Amylase

- The inhibition of digestive enzymes, particularly α-amylase and α-glucosidase, is a recognized approach for controlling postprandial hyperglycemia.

- **Agrawal and Rathore (2019)** demonstrated that ethanolic extracts of AV achieved up to 66.25% α-glucosidase inhibition at 500 µg/mL, with an IC_{50} comparable to acarbose, a standard antidiabetic drug [37]. This suggests potential for AV as a natural postprandial glucose regulator.

5.2.2 Antioxidant Properties and ROS Scavenging

- AV extracts exhibit strong antioxidant activity, as evidenced by DPPH, ABTS, and FRAP assays.

- **Shafique et al. (2020)** established a direct correlation between the high total phenolic content (TPC) and flavonoid concentration of AV and its free radical scavenging potential, supporting its ability to combat oxidative stress in diabetic conditions [38].

5.2.3 Cell-Based Glucose Uptake and Insulin Signaling

- In 3T3-L1 adipocyte models, AV enhanced glucose uptake via stimulation of GLUT-4 translocation, even in the absence of insulin, indicating insulin-mimetic properties [39].

- Furthermore, AV has been shown to upregulate insulin receptor substrate-1 (IRS-1) and activate the PI3K/Akt pathway, essential for insulin signal transduction [40].

6. Clinical Evidence and Human Application: Gaps and Opportunities

Despite strong pharmacological and preclinical evidence, the clinical application of *Artemisia vulgaris* (AV) in human populations remains limited and underexplored. Most available clinical information stems from polyherbal formulations where AV is used in combination with other botanicals, making it difficult to isolate its specific therapeutic contributions [41]. This lack of targeted human studies presents a significant barrier to integrating AV into standardized diabetes care protocols.

6.1 Traditional and Ethnopharmacological Context

AV has a longstanding presence in traditional medical systems including Ayurveda, Traditional Chinese Medicine (TCM), and various European herbal practices. Historically, it has been used to manage symptoms that overlap with diabetic manifestations, such as polyuria, fatigue, and peripheral neuropathy [42].

Common ethnomedicinal preparations include:

- **Leaf decoctions**, administered orally to lower blood sugar levels.

- **Essential oil-based massages**, traditionally used for improving circulation and relieving diabetic neuropathy.

- **Powdered herb formulations**, employed as adjuncts to lifestyle and dietary interventions.

These uses highlight the broad therapeutic potential of AV and its utility in addressing not just hyperglycemia, but also diabetes-associated complications through holistic approaches [43].

6.2 Clinical Trials and Observational Studies

To date, the clinical evidence supporting AV's antidiabetic efficacy in humans is sparse and primarily confined to observational reports or studies involving multi-herb interventions.

A pilot study conducted by Devi et al. (2019) investigated the effect of a polyherbal formulation containing *Artemisia vulgaris*, *Momordica charantia*, *Trigonella foenum-graecum*, and *Gymnema sylvestre* in patients with Type 2 Diabetes Mellitus (T2DM). Over an 8-week treatment period, the study observed significant reductions in fasting blood glucose and HbA1c levels [44]. However, due to the complex nature of the formulation, the specific role of AV could not be conclusively determined.

Currently, **no randomized controlled trials (RCTs)** evaluating AV as a **monotherapy** in diabetic patients have been published. Moreover, existing human studies lack critical design elements such as standardized extract usage, defined dosage ranges, and appropriate control groups. This represents a substantial gap in translational research [45].

7. Safety and Toxicological Profile

Ensuring the safety of phytotherapeutic agents is essential before recommending them for widespread clinical use. *Artemisia vulgaris* (AV), while traditionally considered safe, requires comprehensive toxicological evaluation, particularly when used in concentrated forms like essential oils or standardized extracts.

7.1 Preclinical Toxicity

Preclinical toxicity studies in animal models have shown AV to have a favorable safety profile. Acute and sub-chronic oral administration of AV extracts in rats, as per OECD guidelines, demonstrated no mortality or signs of toxicity up to 2000 mg/kg [46]. Histopathological analysis of major organs—including liver, kidney, and pancreas—revealed no structural or functional abnormalities, supporting the plant's safety at therapeutic doses [47].

7.2 Thujone Content and Caution

Essential oils derived from AV are known to contain α- and β-thujone, monoterpenes associated with neurotoxicity when consumed in high concentrations or over prolonged periods. Thujone exerts its toxic effects primarily through GABA_A receptor antagonism, which may lead to convulsions, neuroexcitation, or hepatotoxicity [48]. Regulatory authorities such as the European Medicines Agency (EMA) and the U.S. FDA recommend strict limits on thujone content in food and medicinal products [49]. Therefore, caution is advised for the long-term use of AV essential oil preparations, and proper standardization protocols must be established to monitor thujone levels in clinical products.

7.3 Human Safety

Human safety data specific to AV remains limited. However, formulations containing AV as one component—particularly polyherbal capsules used in diabetes or inflammation management—have shown good tolerability in clinical settings. No serious adverse events have been reported in short-term use [50]. Nonetheless, long-term human studies, especially involving monotherapy, are required to establish AV's complete safety profile across diverse populations, including those with hepatic, renal, or neurological conditions.

8. Research Gaps and Future Directions

Although *Artemisia vulgaris* holds promise as an adjunct or alternative therapy in diabetes management, several research areas require immediate attention to enable clinical translation.

8.1 Clinical Trials and Dose Optimization

There is currently a lack of robust, randomized controlled trials (RCTs) examining AV as a monotherapy in diabetic populations. Existing studies either lack placebo controls or involve multiple herbal components, making it difficult to attribute observed effects directly to AV. Well-designed RCTs with clearly defined endpoints such as HbA1c reduction, fasting glucose control, and insulin sensitivity are essential [51].

Moreover, there is insufficient data on the optimal therapeutic dose, dose-response relationships, and duration of action. Establishing these parameters through pharmacokinetic and pharmacodynamic studies will guide evidence-based dosing in clinical practice [52].

8.2 Extract Standardization and Quality Control

The efficacy of AV extracts depends on several factors, including the plant's geographical origin, time of harvest, and method of extraction. These factors significantly affect the concentrations of bioactive phytochemicals such as flavonoids, terpenoids, and sesquiterpene lactones. Without standardized formulations, reproducibility remains a major challenge. Developing validated quality control techniques—such as HPLC or LC-MS/MS fingerprinting—will help ensure consistency and therapeutic reliability [53].

8.3 Long-Term Safety and Toxicological Profiling

Beyond acute toxicity, comprehensive long-term toxicological evaluations are lacking. These should include assessments of reproductive, genotoxic, carcinogenic, and chronic toxicity. Additionally, the potential neurotoxicity of thujone-containing preparations should be carefully monitored through repeated-dose and cumulative toxicity studies [48,54].

8.4 Mechanistic and Biomarker-Based Validation

Although preclinical evidence suggests mechanisms such as α-glucosidase inhibition, insulin sensitization, and oxidative stress reduction, these effects require confirmation in human trials using validated biomarkers. These include:

- HbA1c and fasting insulin
- HOMA-IR (Homeostatic Model Assessment for Insulin Resistance)
- Proinflammatory cytokines (e.g., IL-6, TNF-α)
- Oxidative stress indicators (e.g., malondialdehyde, glutathione, catalase) [55]

These markers will provide insight into the therapeutic pathways modulated by AV.

8.5 Bioavailability Enhancement and Novel Delivery Systems

Many bioactive compounds in AV, such as quercetin and artemisinin, have poor aqueous solubility and low oral bioavailability. Advances in delivery systems—such as phytosomes, liposomes, solid lipid nanoparticles, and polymer-based carriers—may improve the absorption, stability, and therapeutic index of these compounds [56].

9. Conclusion

Artemisia vulgaris is a pharmacologically rich, traditionally validated medicinal plant with multi-targeted antidiabetic properties. Its flavonoids and phenolic acids contribute to blood glucose regulation, insulin sensitization, and protection of pancreatic β-cells. Preclinical and in vitro studies from the last five years reinforce its therapeutic potential and mechanistic plausibility. However, clinical translation remains limited due to the lack of monotherapy trials, standardized formulations, and long-term safety data.

Future research must prioritize randomized controlled trials, toxicological evaluations (especially for thujone content), and biomarker-based efficacy studies. With these gaps addressed, *A. vulgaris* may emerge as a reliable and safe adjunct in integrative diabetes management.

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