

Exploring the Therapeutic Role of *Senna Occidentalis* in Cardiometabolic Diseases: A Systematic Review

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ABSTRACT

Introduction: Cardiometabolic diseases, including diabetes mellitus, obesity, hypertension, and dyslipidaemia, constitute a major global public health challenge due to their increasing prevalence and associated morbidity and mortality. Medicinal plants have attracted considerable attention as alternative therapeutic agents because of their affordability, accessibility, and multi-target pharmacological properties. *Senna occidentalis* (L.) Link is a medicinal plant traditionally used in many African and Asian communities for the management of metabolic and inflammatory disorders.

Objective: This systematic review aimed to evaluate the therapeutic potential of *Senna occidentalis* in the management of cardiometabolic diseases, with emphasis on its phytochemical composition, pharmacological activities, mechanisms of action, efficacy, and safety profile.

Materials and Methods: A systematic literature search was conducted using PubMed, Scopus, ScienceDirect, and Google Scholar databases for studies published up to 2025. Search terms included “*Senna occidentalis*,” “cardiometabolic diseases,” “diabetes,” “obesity,” “hypertension,” and related keywords. Eligible studies included in vitro, in vivo, and clinical studies investigating the metabolic and cardiovascular effects of *S. occidentalis*. Relevant data on phytochemistry, therapeutic effects, mechanisms, and toxicity were extracted and critically reviewed.

Results: Evidence from the reviewed studies demonstrated that *S. occidentalis* possesses significant antidiabetic, antihyperlipidaemic, antioxidant, and anti-inflammatory activities. These pharmacological effects are largely attributed to the presence of bioactive phytochemicals such as flavonoids, alkaloids, saponins, tannins, and phenolic compounds. Mechanistically, the plant was shown to improve glycaemic regulation, modulate lipid metabolism, reduce oxidative stress, and attenuate inflammatory responses. However, evidence supporting its anti-obesity and antihypertensive effects remains limited and inconclusive. Additionally, toxicity concerns, particularly associated with seed consumption and prolonged exposure, were reported in some experimental studies.

Conclusion: *Senna occidentalis* demonstrates promising therapeutic potential in the management of cardiometabolic diseases, especially diabetes mellitus and dyslipidaemia. Nevertheless, the current evidence is largely based on preclinical studies, with limited clinical validation. Further well-designed clinical trials and toxicological investigations are required to establish its safety, efficacy, optimal dosage, and potential for therapeutic standardization.

KEYWORDS: *Senna occidentalis*, diabetes, obesity, hypertension, phytochemicals, cardiometabolic diseases

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1. INTRODUCTION

Cardiometabolic diseases (CMDs) refer to a group of interconnected metabolic conditions that include type 2 diabetes mellitus, obesity, hypertension, cardiovascular diseases (CVD), and related risk factors (Guan et al., 2022). These conditions share underlying risk factors like insulin resistance, dyslipidaemia, hypertension, and chronic inflammation. When considered together, these conditions increase the chance of serious negative consequences, such as heart attack, stroke, and early death (Guan et al., 2022; Kulkarni & Sarin, 2023). Because of their increased prevalence, they constitute major public health challenges and are associated with significant morbidity and mortality (Ralston & Nugent, 2019). Insulin resistance, oxidative stress, persistent low-grade inflammation, and dysregulated lipid metabolism are the main causes of several pathophysiologically related illnesses (Guo *et al.*, 2014).

According to the World Health Organization (WHO), CMDs account for about 32% of all deaths globally (WHO, 2022). As an important component of non-communicable diseases, the development of CMD is linked to various risk factors (WHO, 2022). More than half of the worldwide burden of non-communicable diseases (NCDs) is attributable to the four primary modifiable risk factors for CMDs: unhealthy eating, smoking, excessive alcohol consumption, and physical inactivity (WHO, 2022). These factors have made CMD more widespread and deadlier globally, particularly in low- and middle-income countries (Wang *et al.*, 2023). The expanding prevalence of CMDs highlights the critical need for efficient, affordable, and safer treatment approaches, especially in low- and middle-income nations.

1.2 Management of cardiometabolic diseases and challenges

Despite remarkable advancements in global health care, a statement from the 2009 Institute of Medicine (IOM), National Institutes of Health (NIH), USA Summit on Integrative Medicine and Health of the Public stated that “The disease-driven approach to care has resulted in spiralling costs as well as a fragmented health system that is reactive and episodic as well as inefficient and impersonal.” (Rao, 2018). The statement affirmed that the frequency and prevalence of diseases continue to rise despite advancements in their treatment. The burden and prevalence of diabetes, hypertension, and obesity are rising despite the notable advancements in contemporary CMD management techniques (Akik et al., 2025). In the past few decades, the prevalence of both type 2 diabetes and obesity rates have significantly increased (Sattar et al., 2020). Obesity, type 2 diabetes mellitus, and hypertension together constitute a clinical condition termed metabolic syndrome (MS). Metabolic syndrome, which is a collection of biochemical and clinical abnormalities, raises the risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) (Charles-Davies & Ajayi, 2023). It is a major global clinical and public health concern that is becoming more common.

Worldwide, MS affects more than one billion individuals (Charles-Davies & Ajayi, 2023). Its incidence varies among populations in Africa and can reach 50% or higher. This suggests that there are issues that require an integrative approach to a more cost-effective, outcome-driven, and disease-focused paradigm of illness treatment and prevention. For many decades, traditional medicine practitioners worldwide have used herbal medicine and other phytochemicals and experienced the benefits of their therapeutic qualities (Rao, 2018). In the treatment of CMDs, many classes of drugs and various treatment methods are typically needed. Various drugs utilised in pharmacotherapeutic techniques include antihypertensives for blood pressure regulation, lipid-lowering agents such as statins to manage obesity, antidiabetic agents like sulfonyl ureas for control of diabetes mellitus, Glucose-like petide-1 (GLP-1) receptor agonists for glucose control and weight loss, and icosapent ethyl that reduces cardiovascular adverse events such as obesity and triglycerides (Antwi et al., 2024; Patel et al., 2025). Some of these drugs are either unaffordable, inaccessible, or associated with various adverse effects that make compliance extremely challenging (Jamshidi-kia et al., 2018; Rao, 2018; Shi et al., 2019). In order to ascertain the significance of critical medicinal plants in the prevention, protection, and reversal of cardiometabolic illnesses, numerous studies have examined plant-based dietary patterns as well as specific components (Mullins & Arjmandi, 2021). Because phytochemicals are readily available, inexpensive, and have few or no negative effects, their application as modulators of several cellular pathways to avoid cardiometabolic illnesses seems to be gaining traction (Jamshidi-kia *et al.*, 2018). These phytochemicals work by controlling molecular mechanisms that either interfere with the inflammatory pathways, such as by reducing the production of pro-inflammatory cytokines and other modulators, or synergise with the anti-inflammatory pathways, such as by increasing the production of anti-inflammatory cytokines (Nisar et al., 2023). There are certain disadvantages to consider, even if phytochemicals may aid in the prevention and treatment of illness. These include potential side effects, medication interactions, non-standardisation, and challenges with bioavailability and absorption (Yiwen et al., 2024).

With further research, nutraceuticals, which are products made from food and food ingredients that have nutritional, medical, and health benefits, including disease treatment and prevention (Puri et al., 2022), are expected to play a crucial role in providing well-tested complementary therapies that will be crucial in ensuring affordable healthcare (Rao, 2018). According to studies, nutraceuticals may be able to lessen the increasing prevalence of CMDs. They are also expected to reduce healthcare expenditures, which will be comforting for both the afflicted individual and the relevant authorities (Bruno et al., 2022).

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Conventional pharmacotherapies, although effective, are often associated with adverse effects and limited accessibility in low-resource settings. Consequently, medicinal plants are increasingly explored as alternative therapeutic options (Saad et al., 2017). In addition to being a rich source of new therapeutic molecules, medicinal plants have historically been important in the treatment of metabolic problems. Among these, *Senna occidentalis* (L.) Link (syn. *Cassia occidentalis*), a member of the Fabaceae family, has drawn attention because of its widespread ethnomedical use in South America, Asia, and Africa. The plant's leaves, roots, seeds, and pods have all historically been used to treat haematological disorders, diabetes, inflammation, liver problems, and infections (Lum et al., 2022).

A thorough synthesis of current knowledge is necessary, given the growing interest in plant-based treatments for cardiometabolic disorders and recent data demonstrating *S. occidentalis*'s pharmacological potential. With a focus on *Senna occidentalis*'s phytochemical profile, mechanisms of action, efficacy, and safety, this systematic review critically assesses preclinical and clinical data on the plant's therapeutic potential for the treatment of diabetes, obesity, and hypertension.

2. *SENNA OCCIDENTALIS* AND ITS PHYTOCHEMICAL COMPOSITION

Senna occidentalis, also referred to as coffee senna, is a member of the Fabaceae family. It is found in many tropical and subtropical areas. The plant is commonly known as **Coffee senna**, **Negro coffee**, **Coffee weed**, and **Styptic weed** in English. In Nigeria, *S. occidentalis* is locally known as **Rai dore** or **Sanga-sanga** among the Hausa-speaking population, **Oduduemerema** or **Abo rere** among the Yoruba, and **Akidi agbara** or **Nsiwu muo** among the Igbo ethnic groups. Traditionally, different parts of the plant, including the leaves, roots, seeds, and pods, have been used in the treatment of diabetes, inflammation, liver disorders, infections, haematological disorders, and other chronic ailments (Lum et al., 2022). Figure 2 shows the *Senna Occidentalis* image. The image clearly demonstrates its dense bushy growth pattern, typical of naturally growing *S. occidentalis* populations

2.1 Primary Classes of Phytochemicals

Many of the bioactive phytochemicals found in *Senna occidentalis* have antioxidant and glucose-lowering properties. High amounts of alkaloids, flavonoids, tannins,



Figure 2: Showing the *Senna Occidentalis* plant. (source: <https://italisvital.info/cassia-occidentalis-senna-occidentalis-herbal-profile/>)

saponins, and sugars have been found in a thorough phytochemical screening of *S. occidentalis* root extract, depending on the extract solvent utilised (Lum et al., 2022). Numerous bioactive secondary metabolites found in *Senna occidentalis* (L.) Link contributes to its pharmacological characteristics. Thorough phytochemical examinations of several plant components (roots, leaves, seeds, pods, and stems) have revealed the existence of:

- i. **Flavonoids** – examples include flavonoid glycosides and quercetin; these are powerful antioxidants and may mediate metabolic effects (Lum et al., 2022)
- ii. **Alkaloids** – nitrogenous compounds often linked with antidiabetic and anti-inflammatory activities (Lum et al., 2022)
- iii. **Tannins** – polyphenolic compounds with antioxidant qualities (Lum et al., 2022)

- iv. **Saponins** – foaming glycosides with lipid-lowering and immune-modulating properties (Lum et al., 2022)
- v. **Terpenes and Sterols** – including triterpenes and phytosterols, which may influence cholesterol metabolism (Singh et al., 2019)
- vi. **Glycosides and Anthraquinone Derivatives** – including sennosides-like compounds, which can influence glucose metabolism and digestive motility (Issa et al., 2020)
- vii. **Other constituents** – polysaccharides, fatty oils, and phenolic compounds contributing to biological activity (Singh et al., 2019)

These compounds are responsible for their pharmacotherapeutic roles, especially antioxidant and metabolic effects. Another flavonoid (quercetin) has been isolated exclusively and linked to its antidiabetic and hepatoprotective effects (Lum et al., 2022).

3. METHODS

2.1 Search Strategy

The following electronic databases were searched: PubMed, Scopus, ScienceDirect, and Google Scholar. Search terms included: “*Senna occidentalis* AND diabetes”, “*Senna occidentalis* AND obesity”, “*Senna occidentalis* AND hypertension”, and “Cardiometabolic diseases AND medicinal plants”

2.2 Inclusion Criteria

- i. Experimental (in vitro and in vivo) studies
- ii. Clinical studies
- iii. Studies reporting metabolic outcomes (glucose, lipid profile, blood pressure), including review papers
- iv. Articles published in English

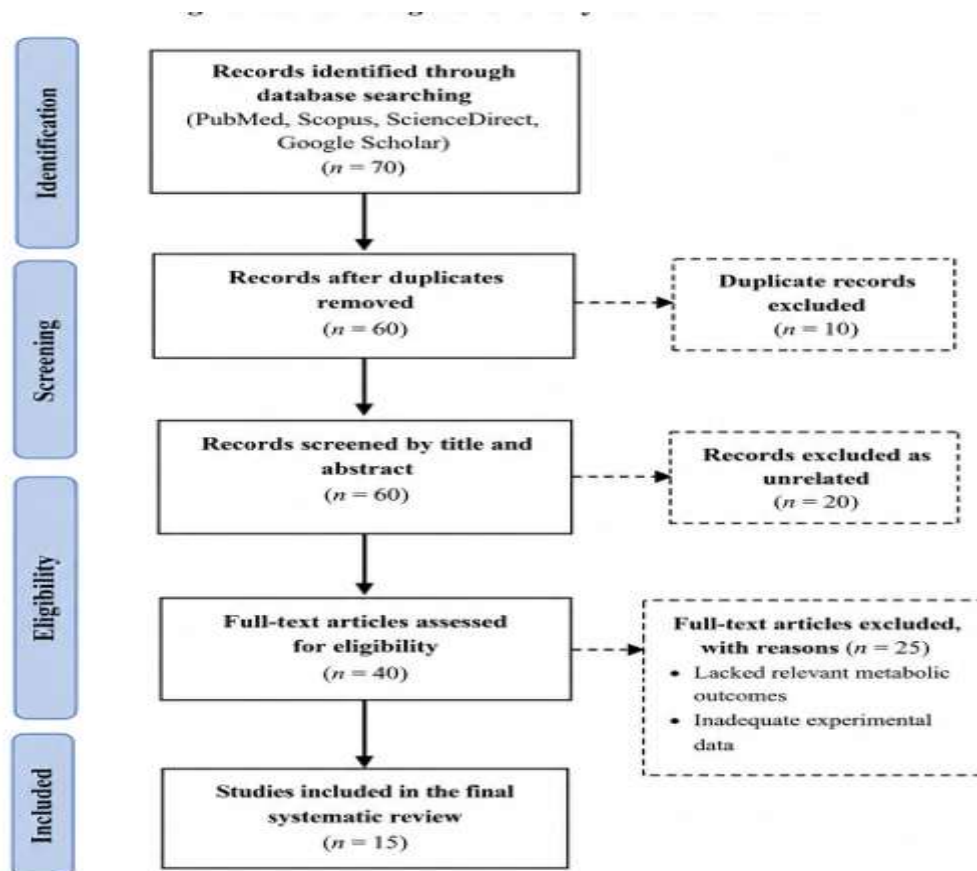
2.3 Exclusion Criteria

- i. Non-peer-reviewed sources
- ii. Studies lacking metabolic endpoints
- iii. Ethnobotanical reports without pharmacological data

2.4 Study Selection

This review followed PRISMA 2020 guidelines for Systematic Reviews.

The initial database search generated 70 Publications. After duplicate publications were removed, the remaining publications underwent title and abstract screening, resulting in the exclusion of unrelated articles. A total of 60 full-text articles were afterwards evaluated for eligibility. Of these, studies that did not meet the inclusion criteria, such as those lacking relevant metabolic outcomes or sufficient experimental data, were excluded. Eventually, 15 studies were included in the final systematic review. Figure 1 shows the PRISMA flow summary.



Note: The flow diagram is based on PRISMA 2020 guidelines.

Figure 1: PRISMA Flow Summary

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Table 1: Summary of the studies/references included in the review

Author and Year	Study Design	Subject Used	Disease Studied	Outcome
Ahmad et al., 2020	Review article	Phytochemicals/experimental data	Obesity	Described anti-obesogenic mechanisms of phytochemicals including modulation of adipogenesis and lipid metabolism
Alshehri et al., 2022	Review article	Senna species	Oxidative stress and infectious diseases	Reported antioxidant and anti-inflammatory properties of <i>Senna</i> species
Bhatti et al., 2022	Review article	Experimental and clinical studies	Type 2 diabetes mellitus	Highlighted role of oxidative stress in diabetes and therapeutic strategies
Chan et al., 2021	Review article	Natural products	Obesity	Discussed the mechanisms of natural products in obesity management
Di Chiara et al., 2022	Review article	Molecular and clinical evidence	Hypertension	Explained molecular mediators involved in hypertension-related complications
Fathima et al., 2023	Review article	Natural products/phytochemicals	Obesity	Identified molecular mechanisms of anti-obesity natural products
Gadanya & Muhammad, 2018	Experimental study	animal Rats	Dyslipidemia/hyperlipidemia	Aqueous leaf extract of <i>Senna occidentalis</i> showed hypolipidemic effects
Ghaben & Scherer, 2019	Review article	Adipose tissue biology	Obesity/metabolic disorders	Explained adipogenesis and metabolic regulation
Guan et al., 2022	Review article	Experimental and microbiome studies	Cardiometabolic diseases	Bile acids regulate microbiota and immunometabolism
Hall et al., 2024	Review chapter	Human/pathophysiological data	Hypertension	Detailed pathophysiology of hypertension
Hamadjida et al., 2026	Experimental study	animal Alloxan-induced diabetic rats	Diabetes mellitus	<i>Senna occidentalis</i> leaf extract demonstrated antidiabetic activity
Issa et al., 2020	Experimental study	Plant root extract and laboratory assays	Diabetes mellitus	Reported antidiabetic activity of <i>Senna occidentalis</i> root
Kulkarni & Sarin, 2023	Review article	Clinical/metabolic data	Fatty liver disease/metabolic disease	Discussed metabolic impacts of fatty liver disease
Kumar et al., 2022	Experimental study	Animal models and plant extracts	Diabetes mellitus	Demonstrated hepatoprotective and

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Author and Year	Study Design	Subject Used	Disease Studied	Outcome
Lum et al., 2022	Review article	Ethnobotanical and pharmacological studies	Diabetes mellitus	antidiabetic effects of <i>Senna occidentalis</i> Summarized phytochemistry, toxicology, and antidiabetic potential of <i>Senna occidentalis</i>
Ma et al., 2023	Review article	Molecular signalling evidence	Hypertension	Described signaling pathways involved in vascular function and hypertension
Micucci et al., 2020	Review article	Antihypertensive phytocomplexes	Hypertension	Explained antihypertensive mechanisms of medicinal phytocomplexes
Naowaboot & Wannasiri, 2016	Experimental study	animal Animal model	Metabolic disorders	Reported metabolic regulatory effects
Nille et al., 2021	Toxicological review	Senna species studies	Diabetes mellitus	Reviewed toxicity and antidiabetic properties of <i>Senna</i> species
Of et al., 2016	Experimental study	animal Alloxan-induced Wistar rats	diabetic Diabetes mellitus	<i>Senna occidentalis</i> leaf supplement reduced blood glucose and improved biochemical markers
Onakpa & Ajagbonna, 2012	Experimental study	animal Alloxan-induced albino mice	diabetic Diabetes mellitus	Leaf extract exhibited antidiabetic effects
Onukwuli et al., 2024	Review article	Phytochemical studies	Diabetes mellitus	Reviewed mechanisms and efficacy of phytochemicals in diabetes management
Patil & Patil, 2025	Review article	Experimental/metabolic evidence	Obesity	Discussed oxidative stress and inflammation in obesity
Poulios et al., 2024	Review article	Phytochemicals	Obesity	Highlighted molecular anti-obesity mechanisms of phytochemicals
Ramachandran & Saravanan, 2015	Experimental study	animal Diabetic rats	Diabetes mellitus	Asiatic acid improved glucose uptake through PI3K/Akt and GLUT4 signaling
Saad et al., 2017	Book/review	Medicinal plants and phytochemicals	Diabetes and obesity	Summarized mechanisms, efficacy, and safety of anti-diabetic and anti-obesity plants
Shahzadi et al., 2024	Computational/network pharmacology study	Fabaceae species	Hypertension	Molecular docking suggested

Author and Year	Study Design	Subject Used	Disease Studied	Outcome
Singh et al., 2019	Review article	<i>Senna occidentalis</i> studies	Multiple diseases/cardiometabolic disorders	antihypertensive potential of phytochemicals Reviewed chemistry and biological activities of <i>Senna occidentalis</i>
Venkatesan et al., 2025	Review article	Experimental inflammatory studies	and Insulin resistance/type 2 diabetes	Discussed inflammation and oxidative stress in insulin resistance
Wang & Wang, 2017	Review article	Pancreatic β -cell studies	Diabetes mellitus	Explained role of oxidative stress in β -cell dysfunction and regeneration
Yakubu et al., 2021	Experimental phytochemical study	Ethanol extract fractions	Oxidative stress/metabolic disorders	Demonstrated antioxidant activities and phytochemical composition of <i>Senna occidentalis</i>

4.1 Antidiabetic Potential of Senna occidentalis

Diabetes mellitus is a chronic metabolic disease brought about as a result of persistent hyperglycaemia due to decreased insulin secretion, insulin resistance, or both (Hamadjida et al., 2026). The hunt for safer and more potent therapeutic molecules, especially from medicinal plants, has accelerated due to the rising prevalence of diabetes worldwide (Hamadjida et al., 2026). Among these, the *Fabaceae* family member *Senna occidentalis* (previously *Cassia occidentalis*) has garnered a lot of interest due to its ethnomedical use in the treatment of diabetes and related metabolic illnesses throughout South America, Asia, and Africa (Lum et al., 2022). Through a variety of biochemical mechanisms, the plant appears to have antihyperglycemic, antihyperlipidemic, antioxidant, and pancreatic protective actions, according to experimental data from in vitro and in animal research (Hamadjida et al., 2026). By focusing on oxidative stress, inflammation, insulin signalling, glucose metabolism, and lipid metabolism, the compounds of the plant are thought to work in concert with the plant's antidiabetic properties (Lum et al., 2022). The strongest evidence exists for antidiabetic effects. With very little clinical confirmation, *Senna occidentalis* (L.) Link has been extensively studied for its antidiabetic qualities, especially in preclinical (in vitro and in animal) investigations. The information that is now available indicates that the plant has antioxidant, hypoglycaemic, and antihyperlipidemic properties, all of which are essential for managing diabetes mellitus and its consequences (Lum et al., 2022).

4.1.1 Preclinical Evidence
4.1.1.1 In Vivo Animal Studies

Most of the available evidence comes from experimental animal models, especially alloxan- or streptozotocin-induced diabetic rats.

4.1.1.1.1 Hypoglycaemic Effects

Several studies have demonstrated that extracts of *S. occidentalis* significantly reduce blood glucose levels. Ethanolic root extracts administered at 200 mg/kg showed significant hypoglycaemic activity in animal models of diabetes produced by streptozotocin and alloxan, comparable to standard drugs such as glibenclamide (Lum et al., 2022). In certain investigations, methanolic and aqueous leaf extracts have shown a significant hypoglycaemic effect on par with conventional antidiabetic medications (Issa et al., 2020). Results also indicated that various extract concentrations (200, 300, and 450 mg/kg) exhibit a dose-dependent hypoglycaemic effect in an alloxan-induced diabetic mouse model (Onakpa & Ajagbonna, 2012). Male albino rats were used to test the antidiabetic effects of methanolic and aqueous extracts of the aerial parts of *S. occidentalis* (L.) Link (leaves, seed, and stem) at a concentration of 3000 mg/kg on alloxan-induced hypoglycaemia. The aqueous extracts of aerial portions were found to have a strong hypoglycaemic impact (Hamadjida et al., 2026; Gidado et al., 2016). The glucose-lowering effects may result from either enhanced insulin secretion, improved peripheral glucose uptake, delayed intestinal glucose absorption, or suppression of hepatic gluconeogenesis (Lum et al., 2022).

4.1.1.1.2 Possible Molecular Mechanisms of Anti-Diabetic Action

Figure 3 summarises the possible molecular mechanisms associated with the potential therapeutic benefits of *Senna Occidentalis* in the management of Diabetes Mellitus.

4.1.1.1.2.1 Enhancement of Insulin Secretion and β -Cell Protection

Oxidative stress contributes significantly to pancreatic β -cell destruction in diabetes mellitus (Wang & Wang, 2017). The antioxidant-rich phytoconstituents of *Senna occidentalis* may preserve pancreatic β -cell integrity and improve endogenous insulin secretion. This antioxidant effect may prevent oxidative injury to pancreatic tissues and preserve insulin-producing cells (Hamadjida et al., 2026). The proposed mechanism involves scavenging reactive oxygen species (ROS), reducing lipid peroxidation and increasing endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) (Wang & Wang, 2017)

4.1.1.1.2.2 Improvement of Insulin Sensitivity

One proposed mechanism is the activation of insulin signalling pathways that improve glucose uptake in peripheral tissues such as skeletal muscle and adipose tissue (Lum et al., 2022). The likely pathways include:

i. Phosphoinositide-3-kinase/protein kinase-B (PI3K/Akt) Signalling Pathway

Insulin receptor activation stimulates phosphoinositide 3-kinase (PI3K) and Akt signalling, resulting in increased glucose transport into cells (Ramachandran & Saravanan, 2015).

ii. GLUT4 Translocation

Enhanced translocation of glucose transporter-4 (GLUT4) to the plasma membrane increases cellular glucose uptake (Ramachandran & Saravanan, 2015).

Although direct mechanistic studies on *Senna occidentalis* are limited, the flavonoid-rich profile of the plant suggests potential modulation of these pathways similar to other medicinal plants with established anti-diabetic properties (Ahmad et al., 2020; Lum et al., 2022).

4.1.1.1.2.3 Activation of AMPK Pathway

AMP-activated protein kinase (AMPK) is a critical cellular energy sensor involved in glucose and lipid metabolism and regulation (Onukwuli et al., 2024). Possible activation of AMPK by phytochemicals in *Senna occidentalis* may increase glucose uptake, enhance fatty acid oxidation, suppress hepatic glucose production, and improve insulin sensitivity (Lum et al., 2022). AMPK activation also reduces hepatic lipogenesis and contributes to better metabolic control in type 2 diabetes mellitus. While direct AMPK studies on *Senna occidentalis* remain sparse, structurally related phytochemicals identified in the plant are known AMPK modulators (Lum et al., 2022)

4.1.1.1.2.4 Antioxidant Mechanisms

Oxidative stress plays a major role in diabetic complications, including nephropathy, neuropathy, and cardiovascular disease (Bhatti et al., 2022).

Senna occidentalis demonstrates strong antioxidant activity through the reduction of malondialdehyde (MDA) (Yakubu et al., 2021), enhancement of endogenous antioxidant defence systems and neutralisation of free radicals (Alshehri et al.,

2022). The antioxidative effects are largely attributed to flavonoids and phenolic compounds in *Senna occidentalis* (Lum et al., 2022)

4.1.1.1.2.5 Anti-Inflammatory Effects

Chronic low-grade inflammation contributes to insulin resistance and β -cell dysfunction (Venkatesan et al., 2025). Bioactive compounds in *Senna occidentalis* are shown to suppress inflammatory mediators and reduce inflammatory signalling

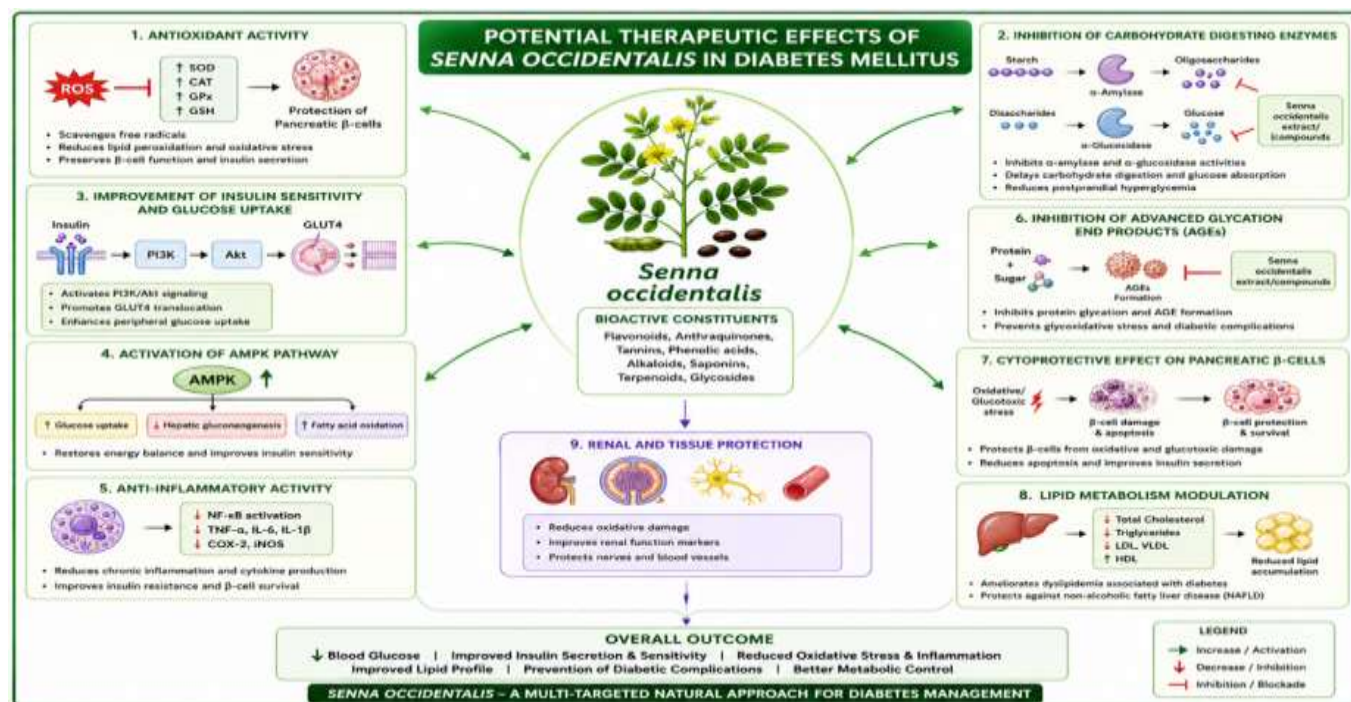


Figure 3: Summary of the possible molecular mechanisms associated with the potential therapeutic benefits of *Senna Occidentalis* in the management of Diabetes Mellitus

pathways. This reduction may improve insulin sensitivity and reduce the progression of diabetic complications (Hamadjida et al., 2026).

4.1.1.1.2.6 Modulation of Lipid Metabolism

Dyslipidaemia commonly accompanies diabetes mellitus. Studies suggest that *Senna occidentalis* can reduce total cholesterol, Lower triglycerides, Decrease LDL cholesterol, and increase HDL cholesterol (Gadanya & Muhammad, 2018). This antihyperlipidemic effect may involve the regulation of lipid-metabolising enzymes and improved insulin action (Lum et al., 2022).

4.1.1.1.2.7 Histopathological Evidence

Histological investigations in diabetic animal models treated with *Senna occidentalis* extracts have shown regeneration of pancreatic islets, reduced hepatic degeneration, and improved renal architecture (Issa et al., 2020).

4.1.1.1.3 Phytochemical-Driven Mechanisms

The observed antidiabetic effects are attributed to bioactive compounds such as flavonoids, Alkaloids, Saponins, Tannins, and terpenes. These compounds act synergistically to improve glucose uptake, enhance insulin sensitivity, and modulate carbohydrate metabolism (Lum et al., 2022). Phytochemical isolation studies have identified quercetin, a flavonoid, from *S. occidentalis* extracts. Quercetin is known to possess antidiabetic and antioxidant properties. It may contribute to glucose regulation and β -cell protection (Kumar et al., 2022).

4.1.1.2 In Vitro Evidence

Although limited, in vitro studies suggest that the inhibition of enzymes involved in carbohydrate digestion (e.g., α -amylase, α -glucosidase) (Nille et al., 2021), antioxidant activity through free radical scavenging, *S. occidentalis* may

protect pancreatic β -cells from oxidative damage and preserve insulin secretion. This has been shown through different assays such as Nitric oxide scavenging assay, Lipid peroxidation inhibition assay, e.tc (Nille et al., 2021). These mechanisms support its role in controlling postprandial hyperglycaemia. Oxidative stress-induced β -cell apoptosis contributes to impaired insulin secretion in diabetes mellitus. Cell culture studies indicate that antioxidant-rich extracts of *S. occidentalis* may improve β -cell viability, reduce oxidative damage, prevent apoptosis and enhance insulin secretory function. The Potential cellular targets include mitochondrial oxidative pathways, caspase signalling, and NF- κ B inflammatory pathways (Lum et al., 2022). Insulin resistance is closely associated with dysregulated lipid metabolism and adipocyte dysfunction. In vitro adipocyte studies indicate that phytochemicals from *S. occidentalis* may reduce lipid accumulation, suppress adipogenesis, improve lipid metabolism and reduce oxidative injury in adipocytes. This is possible by targeting molecular pathways such as PPAR- γ , SREBP-1c, and AMPK signalling (Ahmad, Friar, Sufyan, et al., 2020). Recent in silico and molecular docking studies have evaluated the interaction of *S. occidentalis* phytochemicals with diabetic molecular targets. Potential targets that may improve diabetes include α -glucosidase, α -amylase, DPP-4, PPAR- γ , AMPK, and GLUT4-related proteins (Nille et al., 2021). Several flavonoids and anthraquinones demonstrated favourable binding affinities, supporting experimental findings from enzyme inhibition assays.

4.1.1.3 Clinical Evidence/Human Studies

Currently, there is no robust randomised controlled trial (RCT) evaluating *S. occidentalis* in humans with diabetes. No

standardised clinical dosage or formulation. Most evidence remains preclinical, limiting direct clinical translation.

4.1.1.4 Ethnomedicinal Evidence

Despite limited clinical trials, traditional medicine systems report the use of leaves, roots, and seeds in managing diabetes and related metabolic disorders, with widespread use in Africa, Asia, and South America. These traditional practices provide a basis for scientific investigation but require clinical validation (Lum et al., 2022).

4.1.1.5 Comparative Efficacy

Compared with standard antidiabetic drugs, the hypoglycaemic effect of *S. occidentalis* is moderate but significant. It may act as an adjunct therapy rather than a replacement for conventional drugs. Its multi-target mechanism (antioxidant + metabolic regulation) is advantageous in managing complex metabolic disorders.

4.2 Anti-Obesity Potential of *Senna Occidentalis*

Traditional medicine systems in Africa and India employ *S. occidentalis* preparations for weight reduction and metabolic regulation, suggesting potential anti-obesity activity that warrants scientific investigation (Lum et al., 2022).

4.2.1 Phytochemical Constituents Relevant to Anti-Obesity Activity

The therapeutic potential of *S. occidentalis* is attributed to its diverse phytochemical composition. Major compounds identified include Flavonoids, Anthraquinones, Tannins, Alkaloids, Saponins, Terpenoids, Glycosides, and Phenolic compounds. These phytochemicals possess significant antioxidant, anti-inflammatory, lipid-lowering, and glucose-regulating properties that may influence obesity-related metabolic pathways (Lum et al., 2022). Flavonoids and polyphenols, in particular, are recognised for their ability to regulate adipocyte differentiation, improve insulin sensitivity, and suppress inflammatory signalling in obesity (Poulios et al., 2024)

4.2.2 Pathophysiology related to obesity

Chronic positive energy balance causes excessive triglyceride storage in adipose tissue, which leads to obesity. Important pathogenic mechanisms consist of a rise in adipogenesis, diminished lipolysis, low-grade chronic inflammation, oxidative stress and damage, dysfunction of the mitochondria, resistance to insulin, and dysregulation of appetite signalling. At the molecular level, obesity involves multiple signalling pathways, including:

- iv. AMP-activated protein kinase (AMPK)
- v. Peroxisome proliferator-activated receptor gamma (PPAR- γ)
- vi. Sterol regulatory element-binding protein-1c (SREBP-1c)
- vii. Nuclear factor-kappa B (NF- κ B)
- viii. PI3K/Akt pathway
- ix. Adipokine signalling

Potential anti-obesity agents include natural phytochemicals that can target these pathways.(Ahmad, Friar, Vohra, et al., 2020).

4.2.3 Experimental Evidence Supporting Anti-Obesity Potential of *Senna Occidentalis*

Even though direct anti-obesity studies on *S. occidentalis* remain limited, several experimental findings strongly support its therapeutic relevance in obesity management.

4.2.3.1 Antihyperlipidemic Activity

Animal studies have demonstrated that *S. occidentalis* extracts significantly reduce Total cholesterol, Triglycerides, Low-density lipoprotein (LDL), Very-low-density lipoprotein (VLDL), while increasing high-density lipoprotein (HDL) (Ahmad et al., 2020; Lum et al., 2022). Dyslipidemia is a hallmark of obesity; therefore, these lipid-lowering effects suggest anti-obesity potential (Lum et al., 2022).

4.2.3.2 Antioxidant and anti-inflammatory Activity

Oxidative stress and chronic low-grade inflammation significantly contribute to obesity-induced metabolic dysfunction (Patil & Patil, 2025). *Senna occidentalis* extracts have been associated with reductions in lipid peroxidation, increases in superoxide dismutase (SOD) and catalase (CAT), and elevations in glutathione (GSH) levels. These antioxidant effects may attenuate adipocyte dysfunction and obesity-associated inflammation (Lum et al., 2022). Chronic low-grade inflammation caused by pro-inflammatory cytokines and adipose tissue macrophages is also a hallmark of obesity. Bioactive compounds in *S. occidentalis* may suppress inflammatory mediators, such as TNF- α , interleukin-6 (IL-6), NF- κ B signalling and Cyclooxygenase pathways. Reduction of inflammatory signalling may improve insulin sensitivity and metabolic homeostasis (Fathima et al., 2023).

4.2.4 Possible Molecular Mechanisms of Anti-Obesity Action

Figure 4 summarises the possible molecular mechanisms underlying the potential therapeutic benefits of *Senna Occidentalis* in the management of Obesity.

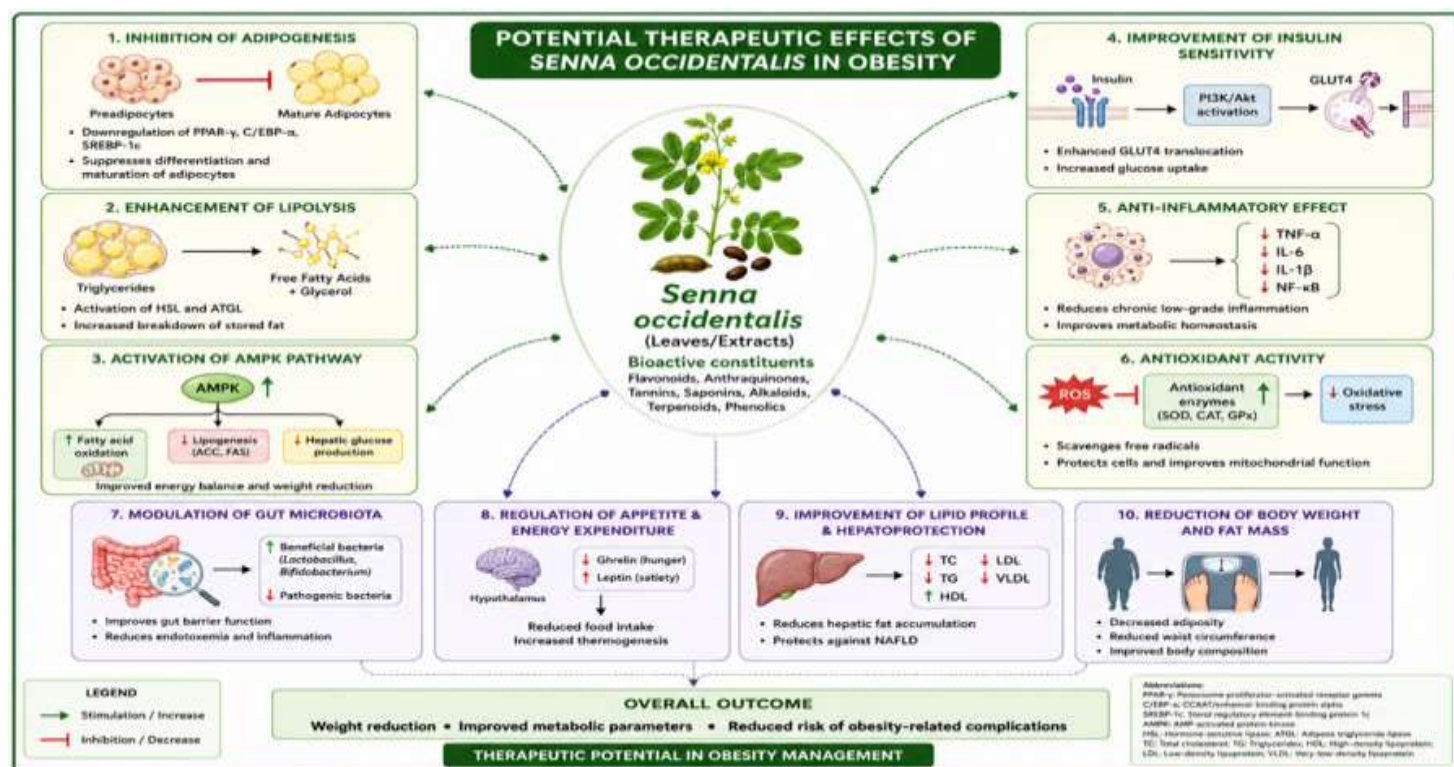


Figure 4: Summary of possible molecular mechanisms underlying the potential therapeutic benefits of *Senna Occidentalis* in the management of Obesity.

4.2.4.1 Activation of the AMPK Pathway

As a master regulator of cellular energy homeostasis, activation of the AMPK pathway enhances fatty acid oxidation, suppresses lipogenesis, improves insulin sensitivity, increases glucose uptake, and promotes mitochondrial biogenesis. Like other plant-derived anti-obesity substances, *S. occidentalis* contains polyphenols and flavonoids that may activate AMPK signalling (Ahmad et al., 2020).

4.2.4.2 Inhibition of Adipogenesis

Adipogenesis involves the differentiation of preadipocytes into mature adipocytes.

Key transcription factors involved include PPAR- γ , C/EBP α , SREBP-1c (Ghaben & Scherer, 2019). Phytochemicals from *S. occidentalis* may suppress adipocyte differentiation by downregulating these transcription factors. Suppression of adipogenesis reduces fat accumulation and adipocyte hypertrophy (Ahmad, Friar, Vohra, et al., 2020).

4.2.4.3 Enhancement of Lipolysis

Lipolysis is the breakdown of triglycerides into free fatty acids and glycerol. Potential mechanisms involved in lipolysis include activation of hormone-sensitive lipase (HSL), upregulation of adipose triglyceride lipase (ATGL), and increased catecholamine signalling. These effects may contribute to reduced adipose tissue mass (Chan et al., 2021). Leptin, triglycerides, hepatic triglycerides, serum total cholesterol, serum insulin, and increased blood glucose levels significantly decreased in mice fed a high-fat diet and given an aqueous extract of senna. Additionally, fatty acid synthase,

acetyl-CoA carboxylase, and lipid buildup in liver tissue were decreased (Naowaboot & Wannasiri, 2016).

4.2.4.4 Regulation of Appetite and Energy Expenditure

The central nervous system, gastrointestinal hormones, adipokines, and metabolic signalling pathways interact to regulate appetite, which is a complicated physiological process. Type 2 diabetes, metabolic syndrome, and obesity are all greatly impacted by dysregulation of appetite. Scientists are becoming more interested in medicinal plants with appetite-modulating qualities as possible therapeutic agents for managing obesity. Natural phytochemicals may influence hypothalamic pathways controlling hunger and satiety. Possible mechanisms include modulation of Leptin, Ghrelin, Neuropeptide Y (NPY), and Melanocortin signalling. Additionally, phytochemicals may stimulate thermogenesis through brown adipose tissue activation (Ahmad et al., 2020). By lowering oxidative stress and inflammation linked to obesity-induced leptin resistance, *S. occidentalis* may increase leptin sensitivity. Improved leptin signalling may reduce food intake, increase satiety, and improve metabolic regulation (Fathima et al., 2023). Ghrelin is the primary hunger-stimulating hormone produced mainly in the stomach. Through modulation of glucose metabolism and gastrointestinal activity, *S. occidentalis* may indirectly suppress ghrelin secretion or reduce ghrelin-mediated appetite stimulation. This may contribute to reduced caloric intake and improved body weight control (Lum et al., 2022). Insulin acts centrally as an appetite-regulating hormone. *Senna occidentalis* possesses antihyperglycemic and insulin-

sensitising activities that may improve hypothalamic insulin signalling. Improved insulin signalling may enhance satiety, reduce hyperphagia, and improve metabolic homeostasis (Lum et al., 2022). AMP-activated protein kinase (AMPK) is a key regulator of cellular energy balance and feeding behaviour. Peripheral AMPK activation may increase energy expenditure, enhance fatty acid oxidation, and reduce adiposity. Although hypothalamic AMPK activation can stimulate appetite, peripheral metabolic improvements may overall contribute to better appetite control and body weight reduction (Ahmad et al., 2020).

4.2.4.5 Modulation of Gut Microbiota

Emerging evidence indicates that obesity is associated with gut dysbiosis. Polyphenolic compounds may enhance beneficial gut bacteria, reduce endotoxemia, improve intestinal barrier integrity, and decrease systemic inflammation. Although direct microbiome studies on *S. occidentalis* are lacking, its phytochemical profile suggests possible prebiotic and microbiota-modulating effects (Poulios et al., 2024).

4.2.4.6 Improvement of Insulin Resistance

Insulin resistance is central to obesity-related metabolic dysfunction. Potential mechanisms include enhanced PI3K/Akt signalling, increased GLUT4 translocation, reduced inflammatory cytokines, and improved mitochondrial function. *Senna Occidentalis* has been associated with improving insulin sensitivity, which may reduce adipose tissue expansion and metabolic syndrome progression (Lum et al., 2022).

4.2.4.7 Hepatoprotective Effects and Obesity

Obesity is strongly associated with non-alcoholic fatty liver disease (NAFLD).

Studies have shown hepatoprotective effects of *S. occidentalis* extracts by reduction of oxidative stress, stabilisation of liver enzymes, and prevention of hepatic lipid accumulation. These effects may contribute to improved metabolic health in obesity (Lum et al., 2022).

Senna occidentalis's antioxidant, antihyperlipidemic, anti-inflammatory, insulin-sensitising, and hepatoprotective properties show great therapeutic potential in the treatment of obesity. Numerous molecular pathways implicated in adipogenesis, lipid metabolism, oxidative stress, and chronic inflammation may be targeted by its rich phytochemical composition, including flavonoids, tannins, terpenoids, and anthraquinones.

Direct experimental and clinical research particularly addressing obesity is still scarce, even though existing evidence substantially supports its metabolic benefits. Additionally, careful dose standardisation and safety assessment are required due to toxicological concerns. However, *S. occidentalis* is a viable option for the creation of anti-obesity medications in the future and merits more molecular and clinical research.

4.3 Therapeutic Potential of *Senna occidentalis* in the Management of Hypertension

Plant-derived phytotherapeutics with multitarget cardiovascular activities are receiving more attention because traditional antihypertensive treatments, such as ACE inhibitors, calcium channel blockers, beta-blockers, and diuretics, are effective but may cause side effects like electrolyte imbalance, cough, fatigue, orthostatic hypotension, and metabolic disturbances (Micucci et al., 2020).

Recent Pharmacological investigations show that *Senna Occidentalis* may have therapeutic potential against hypertension by modulating oxidative stress, vascular inflammation, endothelial dysfunction, and metabolic abnormalities (Lum et al., 2022).

4.3.1 Phytochemical Constituents Relevant to Antihypertensive Activity

Phytochemical investigations have identified numerous bioactive compounds in *S. occidentalis*, including Flavonoids, Anthraquinones, Phenolic acids, Tannins, Alkaloids, Saponins, Glycosides, Terpenoids, and Xanthones. Several of these compounds possess established cardiovascular protective effects, such as antioxidant activity, vasodilation, anti-inflammatory activity, and endothelial protection (Singh et al., 2019). Recent network pharmacology studies identified compounds such as Dihydrokaempferol, Flavan-3-ol, Germichrysone, and Epiafzelechin as potential antihypertensive agents targeting inflammatory and vascular signalling pathways (Shahzadi et al., 2024).

4.3.2 Pathophysiology of Hypertension

Hypertension results from complex interactions involving increased peripheral vascular resistance, endothelial dysfunction, oxidative stress, RAAS activation, chronic vascular inflammation, sympathetic nervous system activation, and vascular remodelling (Hall et al., 2024). Main molecular mediators include Angiotensin II, endothelin-1, reactive oxygen species (ROS), NF- κ B, TNF- α , IL-6, calcium channels, and nitric oxide (NO) (Di Chiara et al., 2022; Ma et al., 2023). Phytochemicals capable of modulating these pathways are considered promising therapeutic agents for hypertension management (Micucci et al., 2020).

4.3.3 Potential Molecular Mechanisms of Antihypertensive Action

Figure 5 summarises the possible molecular mechanisms of the antihypertensive potential of *Senna Occidentalis*.

4.3.3.1 Antioxidant Activity

Oxidative stress contributes significantly to endothelial dysfunction and vascular injury in hypertension (Di Chiara et al., 2022). *Senna occidentalis* possesses strong antioxidant properties through scavenging of reactive oxygen species and enhancement of endogenous antioxidant enzymes. *S. occidentalis* may increase superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), while

reducing lipid peroxidation and oxidative vascular injury (Lum et al., 2022).

4.3.3.2 Enhancement of Nitric Oxide Bioavailability

Nitric oxide (NO) is an important vasodilator synthesised by endothelial nitric oxide synthase (eNOS) (Di Chiara et al., 2022). Phytochemicals in *S. occidentalis* may improve endothelial NO production and reduce oxidative degradation of NO. Improved NO signalling promotes vasodilatation, reduced vascular resistance, and improved endothelial function (Micucci et al., 2020).

4.3.3.4 Anti-Inflammatory Activity

Chronic vascular inflammation contributes to hypertension progression and vascular remodelling. Studies indicate that phytochemicals from *S. occidentalis* may suppress TNF- α , IL-6, IL-1 β , and NF- κ B signalling. This may improve vascular elasticity and endothelial integrity (Shahzadi et al., 2024).

4.3.3.4 Modulation of Renin–Angiotensin–Aldosterone System (RAAS)

The RAAS plays a central role in blood pressure regulation. Potential mechanisms by which *S. occidentalis* may regulate RAAS include reduced angiotensin II signalling, suppression of ACE activity, and decreased aldosterone-mediated sodium retention. Although direct experimental studies remain limited, network pharmacology analyses support interactions between *S. occidentalis* phytochemicals and RAAS-related pathways (Shahzadi et al., 2024).

4.3.3.5 Calcium Channel Modulation

Intracellular calcium regulates vascular smooth muscle contraction. Phytochemicals from *S. occidentalis* may interfere with calcium influx into vascular smooth muscle cells. Reduction of calcium-mediated vasoconstriction may promote arterial relaxation and reduce peripheral resistance, causing a reduction in blood pressure.

4.3.3.5 Improvement of Lipid Metabolism

Hypertension is commonly associated with dyslipidaemia and atherosclerosis. Experimental evidence indicates that *S. occidentalis* may reduce LDL cholesterol, lower triglycerides, and increase HDL cholesterol. This may improve lipid metabolism and may reduce arterial stiffness and cardiovascular risk (Lum et al., 2022).

4.3.3.6 Endothelial Protection and Vascular Remodelling

Hypertension induces structural changes in blood vessels, including smooth muscle hypertrophy, collagen deposition, and reduced arterial elasticity (Ma et al., 2023). Bioactive compounds in *S. occidentalis* may inhibit vascular remodelling through antioxidant and anti-inflammatory effects (Lum et al., 2022). Potential targets include MAPK signalling, vascular endothelial growth factor-A (VEGFA) pathways, serine/threonine kinase 1 (AKT1) signalling, and matrix metalloproteinases (MMPs) (Shahzadi et al., 2024).

4.3.3.7 Computational and Molecular Docking Evidence

Recent network pharmacology and molecular docking studies demonstrated strong binding interactions between *S. occidentalis* phytochemicals and hypertension-related molecular targets. Key targets identified include Toll-like receptor-4 (TLR4), mitogen-activated protein kinase 14 (MAPK14), MMP9, VEGFA, Heat shock protein 90kDa alpha (cytosolic), member A1 (HSP90AA1), and AKT1. Compounds such as dihydrokaempferol and flavan-3-ol showed favourable binding affinities and potential antihypertensive activity (Shahzadi et al., 2024).

4.3.3.8 Potential Cardioprotective Benefits

The antihypertensive properties of *S. occidentalis* may contribute to protection against atherosclerosis, stroke, left ventricular hypertrophy, heart failure, and renal injury. Its antioxidant and anti-inflammatory properties may provide broader cardiovascular protection beyond blood pressure reduction (Micucci et al., 2020).

Senna occidentalis's antioxidant, anti-inflammatory, vasodilatory, antihyperlipidemic, and endothelium-protecting properties show significant therapeutic potential in the treatment of hypertension. Its phytochemical components, such as terpenoids, anthraquinones, phenolics, and flavonoids, seem to have the ability to alter several molecular pathways related to blood pressure control and vascular dysfunction.

Enhancing nitric oxide bioavailability, reducing oxidative stress and inflammation, regulating RAAS activity, preventing calcium-mediated vasoconstriction, and improving vascular remodelling are some possible antihypertensive processes. However, before therapeutic application can be established, clinical validation and thorough toxicological assessment are still required, despite promising pharmacological and computational data.

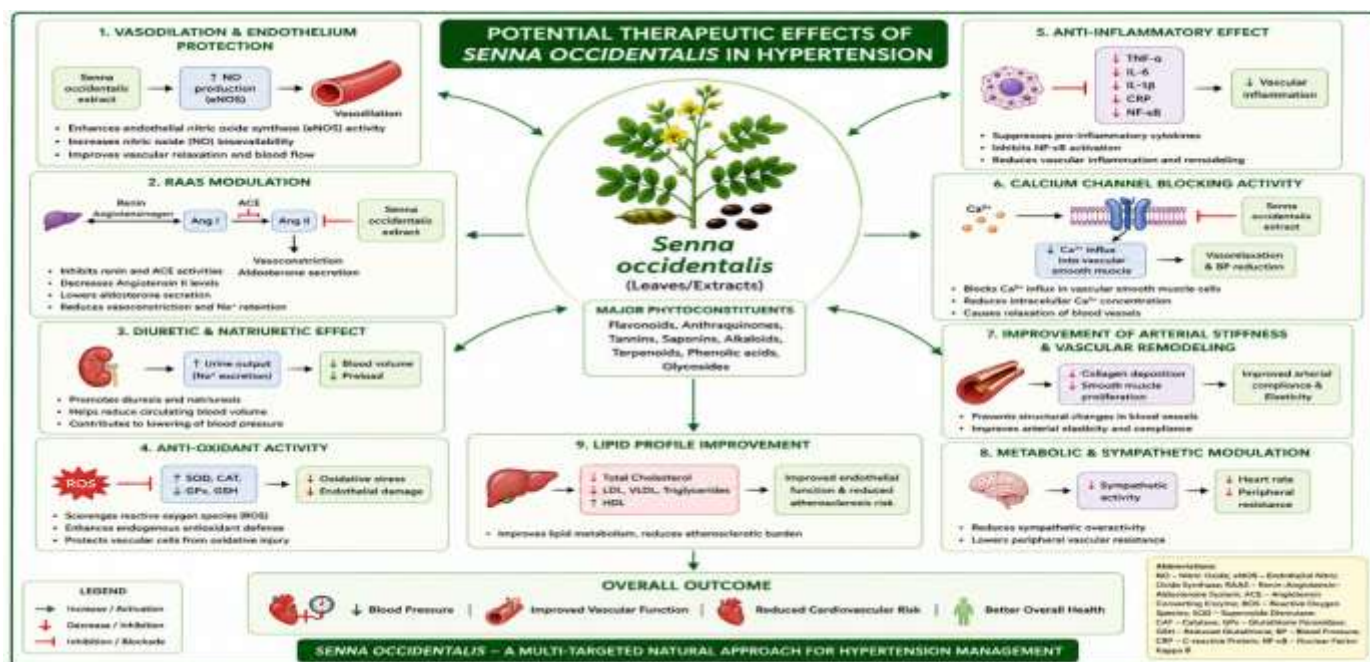


Figure 5: Summary of possible molecular mechanisms underlying the potential therapeutic benefits of *Senna Occidentalis* in the management of Hypertension.

5. DISCUSSION

This review highlights that *Senna occidentalis* possesses multi-target pharmacological properties relevant to cardiometabolic diseases. *Senna occidentalis* has significant medicinal promise for the treatment of obesity, hypertension, diabetes mellitus, and other cardiometabolic disorders. Its extensive phytochemical composition, which includes flavonoids, anthraquinones, tannins, phenolics, alkaloids, terpenoids, and saponins, is largely responsible for its pharmacological actions. The plant modulates oxidative stress, inflammation, insulin signalling, adipogenesis, endothelial dysfunction, lipid metabolism, vascular tone, and neurohormonal control to provide multitarget effects. AMPK activation, PI3K/Akt signalling, GLUT4 translocation, NF-κB suppression, nitric oxide increase, RAAS regulation, and calcium channel inhibition are possible molecular pathways implicated. These integrated mechanisms position *S. occidentalis* as a promising phytotherapeutic candidate for cardiometabolic disease management

Strength of Evidence

According to the evidence currently available, *Senna occidentalis* has comparatively poor anti-obesity and antihypertensive effects, moderate lipid-lowering effects, and substantial antidiabetic activity.

6. LIMITATIONS

However, despite encouraging experimental evidence, significant challenges remain regarding toxicity, extract standardisation, pharmacokinetics, and clinical validation

7. FUTURE RESEARCH DIRECTIONS

Future translational studies combining molecular pharmacology, omics technologies, toxicological evaluation,

and randomised clinical trials are essential to establish the safety and therapeutic efficacy of *S. occidentalis* in cardiometabolic medicine.

8. CONCLUSION

Senna occidentalis is a promising medicinal plant with significant antidiabetic and cardiometabolic regulatory potential. Its effects are largely mediated through antioxidant, anti-inflammatory, and lipid-modulating pathways. However, clinical validation and safety evaluation remain critical gaps, limiting its current therapeutic application.

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