



Phytochemical interventions of medicinal plants in the management of diabetes and obesity: A recent therapeutic overview

D'Souza Keith¹, Ketaki Apte², Vivek S. Kumawat², Ansh Chintamaneni¹, Meena Chintamaneni¹, Ujjawal Sharma³, Bunty Sharma⁴, Moyad Shahwan^{5,6}, Ginpreet Kaur^{1*}, Damandeep Kaur⁷, Hardeep Singh Tuli^{8*}

¹Department of Pharmacology, Shobhaben Pratapbhai Patel School of Pharmacy and Technology Management, SVKM'S NMIMS, Mumbai, India.

²SES's R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, India.

³Department of Human Genetics and Molecular Medicine, Central University of Punjab, Bhatinda, India.

⁴Department of Biotechnology, Graphic Era (Deemed to be University), Dehradun, India.

⁵Centre of Medical and Bio-Allied Health Sciences Research, Ajman University, Ajman, United Arab Emirates.

⁶Department of Clinical Sciences, College of Pharmacy and Health Sciences, Ajman University, Ajman, United Arab Emirates.

⁷University Centre for Research and Development (UCRD), Chandigarh University, Mohali, India.

⁸Center of Excellence in Computational Research and Drug Discovery, Department of Bio-Sciences and Technology, Maharishi Markandeshwar Engineering College, Maharishi Markandeshwar (Deemed to be University), Mullana, India.

ARTICLE HISTORY

Received on: 28/05/2025

Accepted on: 19/10/2025

Available Online: 05/12/2025

Key words:

AMPK, PPAR, anti-inflammatory, anti-oxidant, insulin resistance.

ABSTRACT

Over the past four decades, the global surge in diabetes and obesity has given rise to the term “diabesity,” reflecting the strong connection between type 2 diabetes and obesity. This link is correlated with heightened risks of cardiovascular disease, hypertension, and stroke. In light of this escalating health crisis, medicinal plants and natural products, which have long been used in traditional medicine systems, have attracted growing interest for their potential to address diabetes and obesity. This review highlights scientific evidence from preclinical and clinical studies on the efficacy of medicinal plants in treating diabetes and obesity. It focuses on the phytoconstituent responsible for these benefits and supports their traditional therapeutic use while comparing with common therapeutic interventions. Additionally, the review delves into the mechanism of action through which these plants demonstrate their benefits and explores modern formulations that fuse traditional knowledge with current healthcare practices. As diabesity continues to rise globally, understanding the role of medicinal plants in managing this dual condition offers valuable insights into alternative and complementary approaches for comprehensive healthcare.

1. INTRODUCTION

Cardiometabolic diseases (CMDs) encompass a variety of disorders that impair heart function and disturb the body's physiological balance. This group includes conditions

such as coronary artery disease, peripheral vascular disease, stroke, aneurysms, heart attacks, congestive heart failure, hypertension, and others [1,2]. Alarming statistics from the WHO underscore the gravity of CMDs as the primary global cause of mortality, claiming an estimated 17.9 million lives annually [3]. This distressing figure continues to climb, propelled by a myriad of risk factors. Age, sex, medications, and intricate interconnections such as lifestyles, genetics, and environmental influences collectively contribute to the surge in CMD-related fatalities. CMDs are not isolated events but rather complex outcomes of various factors converging to disrupt the cardiovascular and metabolic equilibrium. Lifestyle choices, including diet and physical activity, along with genetic

*Corresponding Author

Ginpreet Kaur, Department of Pharmacology, Shobhaben Pratapbhai Patel School of Pharmacy & Technology Management, SVKM's NMIMS, Mumbai, India, E-mail: ginpreet.kaur@nmims.edu;

Hardeep Singh Tuli, Center of Excellence in Computational Research and Drug Discovery, Department of Bio-Sciences and Technology, Maharishi Markandeshwar Engineering College, Maharishi Markandeshwar (Deemed to be University), Mullana, India. E-mail: hardeep.biotech@gmail.com

predispositions and environmental conditions, play pivotal roles in the progression of these diseases [4–7].

The escalating prevalence of CMDs has brought about an unfortunate surge in global treatment costs, surpassing even the expenditures associated with cancer and diabetes treatments. This unwelcome reality has imposed a substantial economic burden, particularly affecting middle-income and lower middle-income families. The economic strain resulting from CMD treatment has become a pressing global concern in both health and pharmaceutical economics [8–11].

In response to this challenge, concerted efforts are underway to address the root causes and mitigate the risk factors associated with CMDs. A pivotal focus has been placed on tackling diabetes and obesity, recognized as two of the most critical and modifiable risk factors contributing to CMDs. By directing attention towards these specific factors, endeavors are being made to not only alleviate the economic impact but also enhance preventive strategies, ultimately promoting better global health outcomes [12].

In conducting this review, data were sourced from a variety of databases to ensure a comprehensive and robust analysis. PubMed was searched for peer-reviewed articles using keywords focusing on studies published within the last 5 years. ClinicalTrials.gov was used to gather information on ongoing and completed clinical trials relevant to the topic, prioritizing Phase II and III trials. Google Scholar and open-access journals were also utilized to identify additional research, including gray literature and open-access studies not covered in subscription-based databases. Manual searches of reference lists from key studies were performed to capture additional relevant literature. All articles were screened based on inclusion criteria such as relevance, study design, and quality of data.

2. DIABETES AND OBESITY

Diabetes manifests as a family of metabolic disorders distinguished by either insufficient insulin secretion (type 1 diabetes mellitus or T1DM) or resistance to insulin (type 2 diabetes mellitus or T2DM), resulting in high systemic glucose levels alternatively called hyperglycemia [13]. This global health challenge has evolved into an epidemic, claiming over 1.5 million lives, particularly impacting individuals under the age of 70. Projections indicate a worrisome trajectory in the soaring global costs associated with diabetes [14].

The occurrence of type 2 diabetes mellitus (T2DM) is influenced by a constellation of factors, including lifestyle choices, dietary habits, levels of physical activity also including an individual's age and gender. Notably, both T1DM and T2DM carry an augmented risk of being genetically inherited, adding a layer of complexity to their etiology [15–18].

The pathophysiology of T2DM is intricately tied to the malfunctioning or destruction of β -cells and the inhibition of their signaling pathways, potentially influenced by various genetic linkages [19–21]. Currently, oral anti-diabetic drugs like metformin and sitagliptin are available, but lifestyle modifications remain efficacious in managing diabetes [22]. While the direct connections between diabetes and CMDs are not entirely elucidated, factors such as obesity significantly escalate the risk of CMDs [23].

The pathogenesis of T2DM involves intricate mechanistic pathways, with a prominent association with hyperlipidemia and obesity. These factors spark a deluge of events leading to complications such as reactive oxygen species mediated oxidative stress and low-grade inflammation, ultimately culminating in cardiac ailments like arteriosclerosis [24,25]. Another significant pathway implicated in diabetes progression is the tyrosine-serine Protein Kinase C (PKC) pathway, which induces redox stress, contributing to microvascular complications [26].

Additionally, the interaction of sugars with proteins at their freely available amino groups gives rise to Schiff bases, resulting in a rearrangement to form more stable products known as Amadori products, also known as advanced glycation end-products (AGEs). The prevalence of AGEs further exacerbates microvascular complications in diabetes [27]. This multifaceted interplay of hyperlipidemia, obesity, oxidative stress, inflammation, PKC pathway activation, and the formation of AGEs collectively underscores the intricacies of T2DM progression and its associated complications (Fig. 1).

Obesity is defined as an “abnormal buildup of fat that can negatively affect wellness” and occurs when calorie consumption exceeds energy expenditure [28]. In India, data from the National Family Health Surveys (NFHS-4 and NFHS-5) indicate a notable rise in the number of overweight or obese women, rising from 20.6% to 24%. Similarly, the prevalence of obese or overweight men has risen from 18.9% to 22.9% [29,30]. Multiple factors contribute to obesity, including dietary patterns, environmental influences, sedentary lifestyles, social dynamics, and genetic predispositions [31–33].

Population studies emphasize the pivotal roles of dietary habits and physical involvement in the genesis of obesity, with genetic factors together with environmental elements intertwining to characterize it as a modern epidemic. The complexity of these interactions complicates treatment strategies, necessitating a nuanced and multifaceted approach to address the rising epidemic of obesity and its associated health risks. Obesity is frequently associated with a state of low-grade inflammation, a condition that underlies many of its detrimental effects on the cardiovascular system [34]. Additionally, endocrine imbalances, such as hyperthyroidism, Cushing's syndrome, and resistance to leptin effects, contribute to the pathogenesis of obesity [35]. This condition, in turn, acts as a significant risk factor for diabetes, dyslipidemia, and insulin resistance, exacerbating the impact on CMDs [36,37]. The strong association between obesity and hypertension, a prevalent CMD, further emphasizes the profound influence of obesity on cardiovascular health and its related complications [38]. Various treatment strategies are currently available for obesity, ranging from lifestyle modifications and dietary therapy to pharmacotherapy, gene therapy, and surgical interventions. Notably, pharmacotherapy has garnered high acceptance rates among patients, offering a viable avenue for addressing obesity and its associated health challenges. This multifaceted approach acknowledges the intricate interplay of factors contributing to obesity, recognizing that effective intervention necessitates a comprehensive understanding of both its origins and its far-reaching consequences on overall health [39].

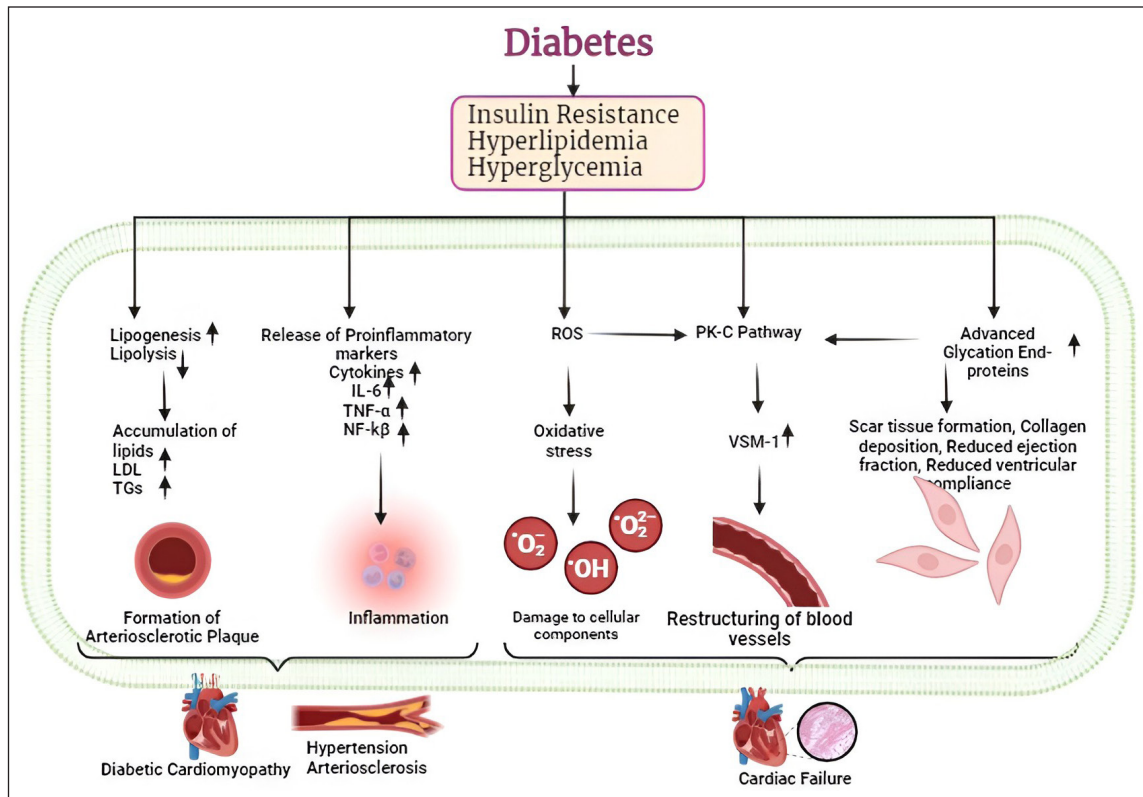


Figure 1. Complications in diabetes mellitus. Lipid accumulation resulting in hyperlipidemia can cause arteriosclerotic plaques. Increased inflammatory markers (IL-6, TNF- α), oxidative damage, and advanced glycation end products (AGEs) contribute to vascular remodeling. Adapted from Poznyak *et al.* [40].

3. PATHWAYS INVOLVED IN DIABETES AND OBESITY

The AMPK pathway serves as the primary regulator of energy metabolism, finely tuned by the adenosine monophosphate (AMP)/adenosine triphosphate ratios. Elevated AMP levels, induced by factors such as exercise or other stimuli, activate the pathway through LKB1, initiating a cascade that controls secondary messengers pivotal in the metabolism of glucose and lipids. Activation leads to upregulating secondary messengers like TBC1D1 and TBC1D4, culminating in increased GLUT4 expression and enhanced glucose uptake (Fig. 2). Conversely, inactivation results in hyperglycemia [41].

This pathway also is essential in modulating lipid levels in obesity. It downregulates acetyl-CoA carboxylase (ACC), resulting in a decrease in the synthesis of fatty acids, and concurrently upregulates desnutrin/adipose triglyceride lipase (ATGL) [42]. Desnutrin/ATGL, a key player in adipose lipolysis, catalyzes the initial step in the breakdown of fats, contributing significantly to the regulation of lipolysis (Fig. 3) [43].

Another pivotal molecular pathway is the PPAR pathway, featuring a family of nuclear receptors. PPARs operate through dual mechanisms: activating genes responsible for glucose and lipid metabolism while concurrently repressing inflammatory pathways, notably NF κ B, commonly implicated in obesity-related inflammation (Fig. 4). Understanding these intricate molecular pathways provides valuable insights into

potential targets for interventions aimed at regulating glucose and lipid metabolism and mitigating the inflammatory aspects associated with obesity [44,45].

As the search for new molecules for the treatment and mitigation of obesity and diabetes has slowed down the focus is shifting towards the various traditional systems of medicines and herbal preparations [46,47]. Phytopharmaceuticals have increased patient tolerance with fewer side effects. Over a quarter of the pharmaceuticals are phyto-derived explaining their increase in its share in the pharmaceutical industry expected to be reaching 550 billion dollars in 2030 [48–50].

4. MEDICINAL PLANTS IN PRE-CLINICAL AND CLINICAL TRIALS

4.1. Bitter Melon/Karela (*Momordica charantia* L.)

4.1.1. Mechanism of action

Bitter melon, popularly referred to as “Karela” in India, has long been renowned for its hypoglycemic effects. Its leaves, stem, and fruits offer many medicinal benefits with its powder form available commercially as a nutraceutical. It is rich in various micronutrients (vitamins and minerals) supporting general metabolic health, and along with various other alkaloids, saponins, flavonoids, and terpenes constitute the main bioactive compounds in bitter melon [51]. *Momordica charantia* polysaccharides (MCP) are a group of heteropolysaccharides present in *M. charantia*

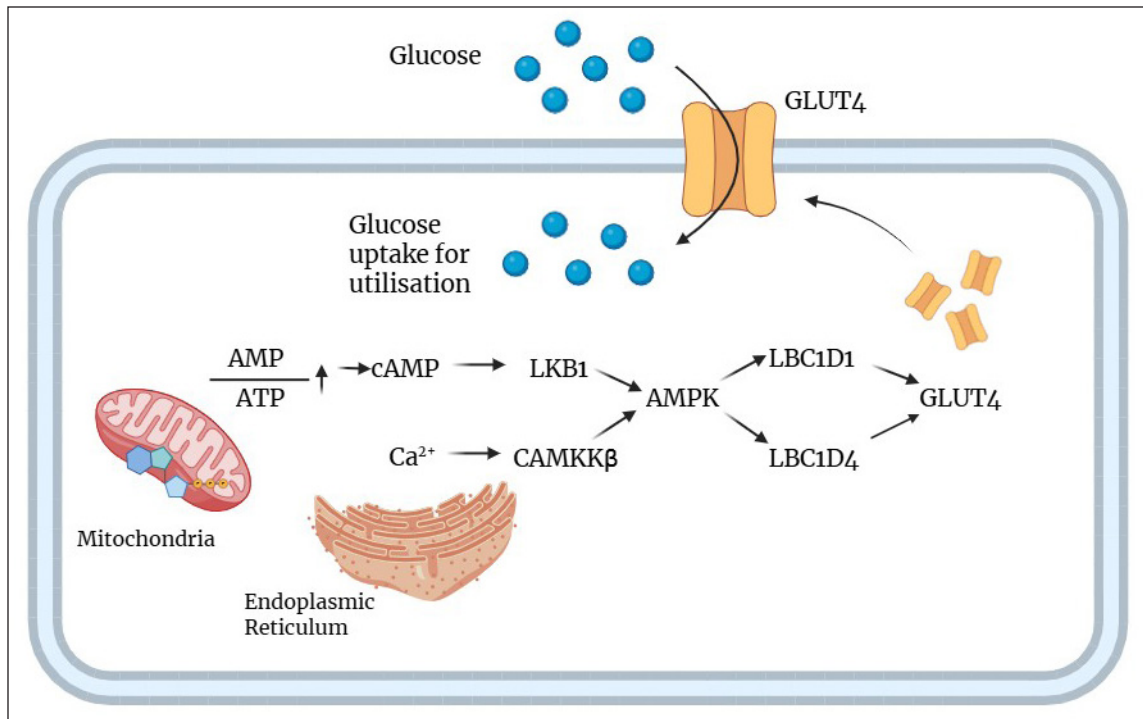


Figure 2. Activation of AMPK signaling pathway resulting in increased levels of LBC1D1 and LBC1D4 which up-regulate the expression of GLUT-4 essential in cells glucose uptake.

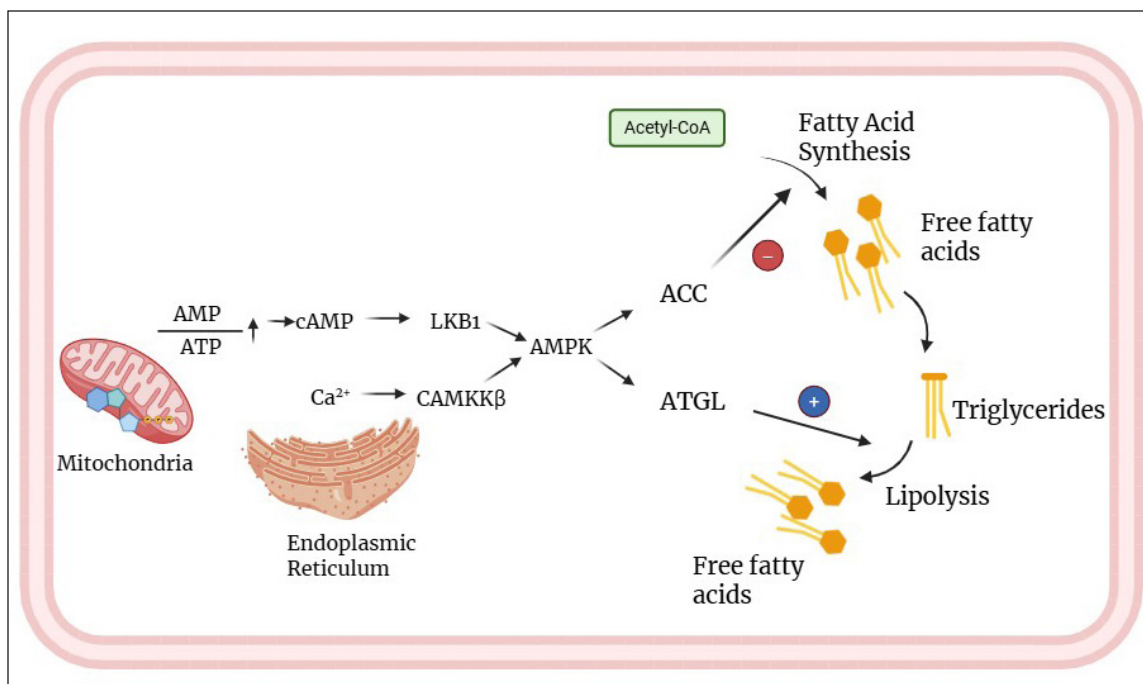


Figure 3. Activation of AMPK to induce ACC which aids in the conversion of acetyl-CoA to FFA for triglycerides. The induction of ATGL prevents the breakdown of triglycerides.

that exert hypoglycemic effects by various mechanisms, particularly it demonstrates immunomodulatory activity by regulating Th1 and Th2 cells, protecting and repairing impaired pancreatic β -cells. It also may serve as an inhibitor

for intestinal α -glucosidase blocking the absorption of glucose into the systemic circulation. At skeletal muscle levels, it may stimulate the uptake of glucose by increasing GLUT-4 expression in a dose-dependent fashion [52].

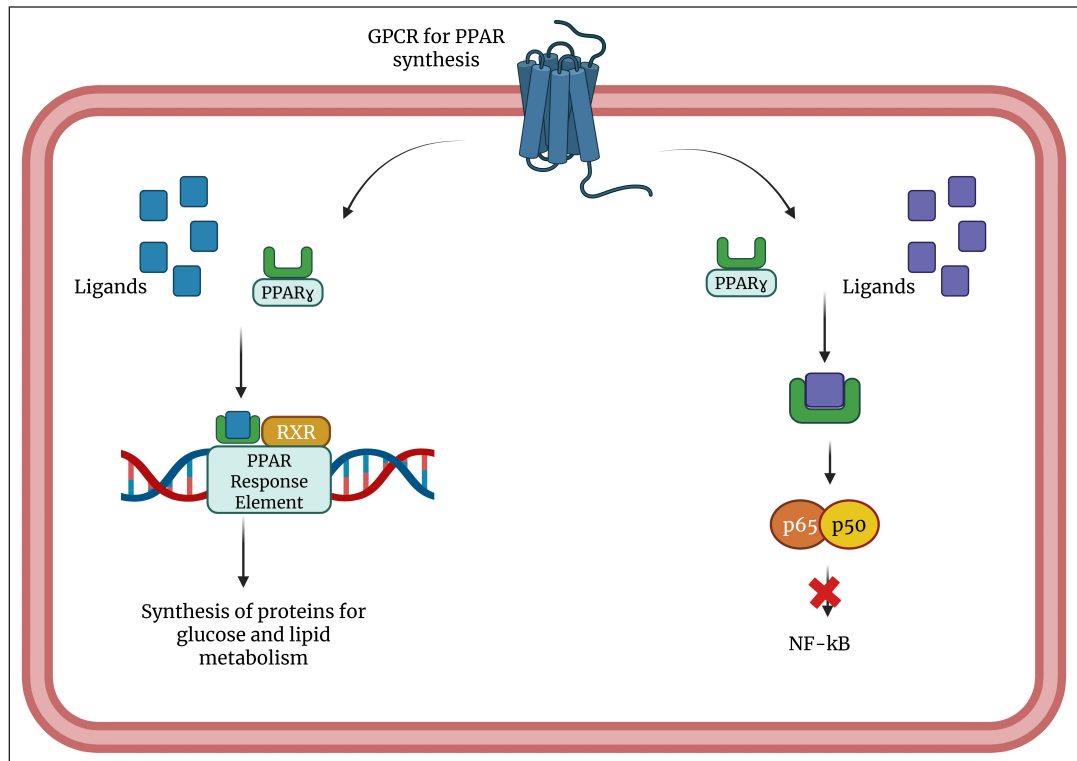


Figure 4. PPAR- γ can function by multiple pathways—(1) once bound to a ligand it heterodimerizes with the RXR element to serve as a promoter to the genes that help to maintain glucose and lipid homeostasis and (2) on its own can inhibit the NF- κ B pathway.

Cucurbitane-type saponin glycosides are another major bioconstituent in *M. charantia*. Amongst these, the triterpenoid saponin *Momocharin* (*charantin*) is believed to be the primary hypoglycemic agent. It shows insulin-like effects such as upregulating the expression of GLUT-4 in skeletal muscle and IRS-1 in the liver cells [53]. Polypeptides in the plant are highly sought-after phytoconstituents due to their multiple activities. Polypeptide-k isolated from the seeds of the plant demonstrated the ability to inhibit both α -glucosidase and α -amylase [54]. Another novel peptide, mcIRBP-1, is a gastric receptor peptide shown to bind at a site on the insulin receptor different from insulin and activate it. Furthermore, it is shown to activate Akt pathways where it phosphorylates and inactivates Protein tyrosine phosphatase 1B, an enzyme responsible for desensitizing insulin receptors [55].

Research indicates that Karela extract selectively inhibits 11 β -hydroxysteroid dehydrogenase1 in a dose-progressive fashion and prevents visceral fat deposition. Inhibition of the enzyme also results in suppressing phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase, key enzymes in hepatic gluconeogenesis. This causes decreased bioenergetics in cells, triggering stress conditions that activate AMPK [56]. The anti-obesity potential of *M. charantia* stems from its ability to suppress the various pathways linked with lipid homeostasis namely PPAR and Sterol regulatory element binding proteins (SREBP) pathways [57]. Inhibiting PPAR is well known for targeting obesity and reducing fat accumulation; while SREBP inhibition is an epigenetic modification that targets cholesterol homeostasis,

reducing levels of triglycerides and cholesterol which allows managing hyperlipidemia [58].

4.1.2. Pre-clinical studies

Momordica charantia juice has been investigated for both the prophylaxis and treatment of T2DM in Streptozotocin (STZ)-induced diabetic rats. Notably, prophylactic administration was found to be more effective in preventing pancreatic β -islet degradation, primarily due to its potent antioxidant properties, which significantly reduced malonyl aldehyde (MDA) levels. This suggests that *M. charantia* extract can delay the onset of diabetes by protecting pancreatic cells from oxidative damage. Furthermore, treatment with *M. charantia* juice led to a significant reduction in blood glucose levels and lipid parameters, including triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL), highlighting its potential role in metabolic regulation [59]. To further enhance its therapeutic efficacy, Olusola Olalekan Elekofehinti developed *M. charantia*-silver nitrate nanoparticles, which demonstrated superior glucose-lowering and lipid-regulating effects compared to conventional extracts. These nanoparticles not only improved antioxidant defense but also offered a key advantage in epigenetic modulation, leading to enhanced insulin secretion. Unlike traditional delivery systems, which often result in suboptimal insulin release, this nanoformulation improved systemic insulin availability, making it a promising approach for more effective diabetes management [60].

The studies incorporated here highlight the vast potential of *M. charantia* bioactive compounds. Liu *et al.*

Table 1. Pre-clinical trials of *M. charantia* and its phytoconstituents.

No.	Animal model	Period of study	Study design and method	Outcomes	Reference to study
1	STZ-induced Wistar rats	21 days	Group 1—Normal control	↓FBG	[59]
			Group 2—Diabetic control	↓TG	
			Group 3—14 days <i>M. charantia</i> juice + induce diabetes and continue treatment for 21 days.	↓TC ↓LDL	
			Group 4—21 days treatment in diabetic rats.	↓MDA	
2	STZ-induced Wistar rats	11 days	Group 1—Normal control	↓FBG	[60]
			Group 2—Diabetes control	↑insulin secretion	
			Group 3— <i>M. charantia</i> nanoparticles (50 mg/kg).	↓TG	
			Group 4—silver nitrate (10 mg/kg).	↓TC	
			Group 5—Metformin (100 mg/kg).	↓LDL	
			Group 6— <i>M. charantia</i> aqueous extract (100 mg/kg).		
3	STZ-induced Sprague Dawley rats	12 weeks	Group 1—Normal control receiving sodium citrate.	↓FBG	[61]
			Group 2—Diabetic control receiving sodium citrate.	↓Total body weight	
			Group 3—Diabetic group receiving 500 mg/kg b.w. of MCP	↓TNF α , IL-6 ↓Neovascularization VEGF	
4	Sprague Dawley rats	8 weeks	Group 1—Normal fed diet (NFD)	↓FBG	[62]
			Group 2—High fat diet (HFD)	↓LBP	
			Group 3—High fat diet + 400 mg/kg b.w. bitter melon powder	↑SCFA producing gut microbiome	
5	<i>db/db</i> mice models	12 weeks	Group 1—Control group	↓FBG	[63]
			Group 2—mcIRB19 treated group	↓HbA1c ↓renal vasculature leakage ↓NF-kB	

Table 2. Clinical trials of *M. charantia* and its phytoconstituents.

Sr. No.	Number of participants	Period of study	Trial design and treatment mode	Outcomes	Reference to study
1	142 T2DM patients	3 months	Group 1—Placebo control	↓FBG	[64]
			Group 2—300 mg bitter melon powder capsules containing 300 ppm mcIRBP-19 peptide given twice a day before meals.	↓HbA1c ↓TG ↓BUN	
			Group 3—0.5 g metformin Group 2—5 mg glibenclamide Group 3—0.5 g metformin + 5 mg glibenclamide. Studied for 1 week and the dose was reduced to half and combined with 200 mg <i>M. charantia</i> extract	↓FBG and post prandial glucose were reduced more with <i>M. charantia</i> extract combination at half dose of oral hypoglycemic	
3	95 T2DM patients	2 weeks	Group 1—Bitter melon powder 2 g/day	↓FBG but lower than glibenclamide	[66]
			Group 2—Bitter melon powder 4 g/day	↓TC/HDL ratio was more significant than glibenclamide	
			Group 3—Glibenclamide 2.5 mg/day	↓Systolic blood pressure	
4	47 Healthy Adults	30 days	Group 1—Placebo control	↓LDL	[67]
			Group 2—300 mg/day bitter melon extract divided into three doses	No changes in HDL and TG	
5	56 Normoglycemic and 26 Hyperglycemic volunteers	—	Blood from both groups was incubated with PEG- <i>M. charantia</i> microspheres at 37°C for 30 minutes	↓blood viscosity	[68]

Table 3. Pre-clinical trials of *B. vulgaris* and its phytoconstituents.

Sr. No.	Animal model	Period of study	Study design and method	Outcomes	Reference to study
1	STZ-induced ICR diabetic rats	2 weeks	Group 1—Control rats Group 2—Glibenclamide treated 10 mg/kg Group 3—Berberine treated 100 mg/kg Group 4—Glibenclamide 10 mg/kg and Berberine treated 100 mg/kg	↑SOD and CAT ↓FBG in groups 2-4	[69]
2	STZ-induced Sprague-Dawley rats	8 weeks	Group 1—Normal control Group 2—Diabetic control Group 3—50 mg/kg b.w. Berberine. Group 4—100 mg/kg b.w. Berberine. Group 5—200 mg/kg b.w. Berberine.	↓FBG ↓creatinine and BUN ↓IL-1 β , IL-6, and MCP-1	[70]
3	STZ-induced Sprague-Dawley rats	8 weeks	Group 1—Diabetic control Group 2—100 mg/kg b.w. Berberine. Group 3—200 mg/kg b.w. Berberine.	↓Apoptosis of Muller cells. ↑SOD and CAT ↓Nf-kB signaling	[71]
4	db/db mouse	5 weeks	Group 1—Normal control. Group 2—150 mg/kg b.w. Berberine Group 3—75 mg/kg b.w. Berberine-ibuprofen co-crystals Group 4—150 g/kg b.w. Berberine-ibuprofen co-crystals	↓FBG ↓TG ↓LDL ↑HDL ↓TNF α , IL-6 and MCP-1	[72]
5	Sprague-Dawley rats	8 weeks	Group 1—NFD rats Group 2—HFD rats Group 3—HFD + vehicle-treated Group 4—HFD + 100 mg/kg b.w. berberine	↓TC ↓TG ↓LDL ↓AST and ALT ↓MTTP and LDL receptors	[73]

Table 4. Clinical trials of *B. vulgaris* and its phytoconstituents.

Sr. No.	Number of participants	Period of study	Trial design and treatment mode	Outcomes	Reference to study
1	97 T2DM patients	2 months	Group 1—1 g Berberine per day Group 2—1.5 g Metformin per day. Group 3—4 mg rosiglitazone per day	↑insulin receptors ↓FBG ↓TG	[72]
2	84 T2DM patients	3 months	Group 1—500 mg berberine/3 times a day Group 2—500 mg metformin/3 times a day Group 3—500 mg berberine/3 times a day + continue original anti-diabetic therapy.	↓HbA1c ↓TC ↓LDL ↓insulin resistance	[73]
3	80 hyperlipidemic patients	12 weeks	Group 1—Berberine treated (500 mg twice/day) Group 2—Placebo treated (500 mg twice/day)	↓TC ↓LDL	[74]
4	63 hypercholesteremia patients	2 months	Group 1—1 g/day Berberine Group 2—20 mg/day simvastatin Group 3—combination of berberine and simvastatin.	↓TC ↓LDL ↑Testosterone	[75]
5	184 NAFLD patients	16 weeks	Group 1—lifestyle improvement. Group 2—15 mg/day pioglitazone + lifestyle improvement. Group 3—0.5 g/ 3 times a day before meals berberine + lifestyle improvement.	↓FBG ↓TC ↓TG ↓LDL ↓AST and ALT ↓Hepatic fat content	[76]

Table 5. Pre-clinical trials of various Brown algae and its phytoconstituents.

Sr. No.	Animal model	Period of study	Study design and method	Outcomes	Reference to study
1	C57BL/6 mice	6 weeks	Group 1—Normal control Group 2—Diabetic control Group 3—Diabetic group treated with 300 mg/kg b.w. fucoxanthin	↓FBG ↑insulin levels ↑GLP-1 activation ↑β-cell proliferation.	[77]
2	C57BL/KsJ-db/db mice	6 weeks	Group 1—Normal control Group 2—0.2%w/w fucoxanthin Group 3—0.4%w/w fucoxanthin Group 4—0.02% w/w Metformin	↓body weight ↓FBG ↑insulin sensitivity ↓TC and TG ↓gluconeogenesis	[78]
3	C57BL/6J mice	12 weeks	Group 1—NFD control Group 2—HFD control Group 3—HFD + 0.05%w/w fucoxanthin Group 4—HFD + 0.1%w/w fucoxanthin	↓body weight ↓LDL ↑HDL ↓ Firmicutes ↑Bacteroidetes	[79]
4	STZ-induced Wistar rats	4 weeks	Group 1—Normal untreated group. Group 2—Normal treated with 60 mg/kg b.w. phlorotannins Group 3—Diabetic untreated group. Group 4—Diabetic treated with 60 mg/kg b.w. phlorotannins	↓FBG ↓TC ↓TG ↑β-cell proliferation.	[80]
5	STZ-induced Sprague Dawley rats	1 day	Group 1—Normal control Group 2—Epalrestat 50 mg/kg b.w. Group 3—Fucosterol 30 mg/kg b.w.	↓FBG ↓glycogenolysis ↓sorbitol accumulation in lenses	[81]

Table 6. Clinical trials of various brown algae and its phytoconstituents.

Sr. No.	Number of participants	Period of study	Trial design and treatment mode	Outcomes	Reference to study
1	48 overweight participants	8 weeks	Group 1—Placebo control Group 2—500 mg tablets containing kelp powder given 30 times a day.	↓BMI ↓body fat ↓LDL	[82]
2	80 overweight participants	24 weeks	Group 1—Placebo control Group 2—400 mg Seaweed polyphenol capsules	↑antioxidative activity ↓obesity-induced DNA damage	[83]
3	28 patients with metabolic syndrome	90 days	Group 1—Magnesium stearate capsules Group 2—12 mg fucoxanthin capsules before breakfast.	↑insulin secretion ↓TG ↓BP ↓BMI and waist circumference	[84]
4	42 NAFLD patients	24 weeks	Group 1—Placebo control Group 2—Treatment group (825 mg low molecular weight fucoxanthin + 825 mg fucoxanthin)	↓FBG ↓TC and TG ↑hepatocytes protection ↑leptin and adiponectin expression	[85]
5	113 non-diabetic NAFLD patients and 38 with normal fat liver	16 weeks	Divided into 11 groups with placebo control and increasing doses of fucoxanthin and pomegranate seed oil.	↓BMI and waist circumference ↓liver fat and enzyme activity ↑resting state energy expenditure	[86]

[52] extracted MCP from *M. charantia* and administered it to T1DM rats, where it reduced the fasting blood glucose (FBG) levels with a progressive loss in body weight after the 12-

week period. Further analysis revealed that MCP was able to lower cytokines (TNF α and IL-6) by NF-kB suppression and neovascularization by vascular endothelial growth factor

Table 7. Pre-clinical trials of *N. sativa* and its phytoconstituents.

Sr. No.	Animal model	Period of study	Study design and method	Outcomes	Reference to study
1	STZ-induced Albino rats	2 months	Group 1—Normal control Group 2—Diabetic control Group 3—Diabetic rats + Metformin 8.5 mg/kg IP Group 4—Diabetic rats + <i>N. sativa</i> oil 0.5 ml/kg IP Group 5—Diabetic rats + Aqueous extract of <i>N. sativa</i> 3 mL/kg IP	↓FBG ↓HbA1c ↓TG ↓LDL ↓TC	[87]
2	Wistar Albino rats	8 weeks	Group 1—Normal control Group 2—Diabetic control Group 3—Diabetic rats + Metformin 100 mg/kg b.w. Group 4—Diabetic rats + Vitamin E 100 mg/kg b.w. Group 5—Diabetic rats + <i>N. sativa</i> oil 2.5 ml/kg	↓Blood urea nitrogen ↓Bax ↓caspase-9 ↑Bcl-2	[88]
3	Male Wistar rats	12 weeks	Group 1—Normal control Group 2—HFD control Group 3—HFD + <i>N. sativa</i> oil-treated diabetic group Group 4—HFD + atorvastatin treated Group 5—HFD + L-carnitine treated	↓body weight ↓hepatic steatosis and hepatic injury	[89]
4	Sprague Dawley rats	18 weeks	Group 1—NFD rats Group 2—HFD control Group 3—HFD + 20 mg/kg b.w. thymoquinone Group 4—HFD + 40 mg/kg b.w. thymoquinone Group 5—HFD + 5 mg/kg b.w. orlistat	↓FBG ↑AMPK ↓body weight ↓SREBP ↓C/EBP- α ↓TC, TG, and LDL	[90]
5	Wistar rats	21 days	Group 1—Normal control Group 2—Diabetic control Group 3—Metformin 150 mg/kg Group 4—Metformin nanocapsules 80 g/kg Groups 5–7—Thymoquinone (20, 40, and 80 mg/kg) Groups 8–10—Thymoquinone nanocapsules (20, 40, and 80 mg/kg) Group 11—Empty nanocapsules shells	↑bioavailability ↓FBG ↓LDL ↓TG ↓TC ↑HDL	[91]

(VEGF) downregulation in the eye, which proved beneficial in mitigating the risks of diabetic retinopathy, a common complication in older patients [61]. Bitter melon powder demonstrated the ability to also improve the gut microbiome, particularly the short chain fatty acids (SCFAs) producing microbes—*Blautia*, *Lactococcus*, and *Allobaculum*. SCFA like butyrate and propionate help prevent gut inflammation as seen in obesity. SCFA has a beneficial role in preventing glucose spikes and regulating cholesterol and blood pressure levels in CMD. It also decreased lipopolysaccharide-binding protein (LBP), a potential biomarker for inflammation and insulin resistance [62]. mcIRB-19 was analyzed to decrease blood glucose levels and it showed positive effects and together with its other insulin mimetic activities, it reduced inflammation and immune reactions at the nephron level to decrease the incidence of diabetic nephropathy [62] (Table 1).

4.1.3. Clinical studies

mcIRB19 was further extended to human trials in DM patients, which received 600 ppm of peptide daily. After 3-month intervention, the FBG and HbA1c levels were significantly lower than those of the control group. It also demonstrated lower TG and blood urea nitrogen (BUN); the latter associated with diabetic nephropathy. Although the study showed promising effects in lowering FBG, the study didn't fully exclude the effect of patients' hypoglycemic medications and further analysis would be required to study the other effects too [64].

In a study comparing bitter melon vs oral hypoglycemic glibenclamide, it was found that bitter melon at 2–4 g was not very effective just alone when compared to glibenclamide. However, significant and better results were found in lowering TC to high-density lipoprotein (HDL) ratio in the 4 g bitter

Table 8. Clinical trials of *N. sativa* and its phytoconstituents.

Sr. No.	Number of participants	Period of study	Trial design and treatment mode	Outcomes	Reference to study
1	117 pre-diabetic patients	6 months	Group 1—Lifestyle modification.	↓FBG	[92]
			Group 2—Metformin 500 mg twice a day.	↓TC, TG, and LDL	
			Group 3— <i>N. sativa</i> oil 450- mg capsule twice a day.	↑HDL ↑SIRT expression	
2	63 chronic kidney disease patients in stages 3 and 4	12 weeks	Group 1—Conservative treatment	↓FBG	[93]
			Group 2—Conservative treatment + <i>N. sativa</i> oil 2.5 ml/day	↓BUN ↑GFR and urine output Normal physiological ion concentrations	
3	120 neuropathic patients	8 weeks	Group 1—Placebo control	↓pain, numbness, and alternate sensations.	[94]
			Group 2— <i>N. sativa</i> ointment 10%w/w		
			Group 3—300 mg gabapentin		
4	46 overweight or obese women	8 weeks	Group 1—Placebo control.	↓TC, TG, and LDL	[95]
			Group 2—2000 mg <i>N. sativa</i> /day	↓leptin ↓IL-1 β ↓IL-6	
5	39 overweight or obese women	8 weeks	Group 1—Placebo control.	↓TC, TG, and LDL	[96]
			Group 2—2000 mg <i>N. sativa</i> /day	↓Systolic BP	

melon treated group, highlighting the antiatherogenic risk of the plant [65]. The combination studies of *M. charantia* extract were studied with oral hypoglycemics metformin and glibenclamide. It was found that the combination of half doses of metformin and glibenclamide with *M. charantia* extract was more pronounced in lowering FBG and post-prandial glucose by 10%–21%, respectively, than full doses of metformin and glibenclamide without extract underscoring the augmented hypoglycemic effect of *M. charantia* with various anti-diabetic drugs [66].

In the context of treating cardiovascular complications of diabetes and obesity, *M. charantia* extract was found to reduce LDL levels significantly even in healthy personal mostly attributed to its fiber content, which was confirmed by normal HDL and TG levels. Even at low doses of 300 mg/day, it was effective but the small sample size may warrant for additional studies [67]. Another study focused on polyethylene glycol (PEG) microspheres laded with *M. charantia* demonstrated that it reduced the viscosity of blood in hyperglycemic patients. In individuals with diabetes, blood viscosity is often elevated, potentially increasing the risk of cardiovascular complications and microvascular damage. While PEGylation itself cannot lower blood viscosity, the *M. charantia* fraction may exert these effects via insulin mimetic or anti-oxidant potential [68] (Table 2).

4.2. Barberry (*Berberis vulgaris*)

4.2.1. Mechanism of action

Barberries are the fruits of *B. vulgaris* which have a long-standing role in the treatment of various cardiovascular

disorders. It is rich in flavonoids, lignans, coumarins, and terpenes that play a role in providing anti-oxidant and anti-inflammatory effects but its true value lies in its alkaloids namely the Isoquinoline class which includes berberine, berbamine, palmatine, and jatrorrhizine [97]. Polyphenols in barberry have potent anti-oxidant activity to prevent lipid peroxidation in CMD as well as some Angiotensin-converting enzyme inhibitory activity to lower hypertension [98].

Berberine is the most sought-after candidate for this species. It can effectively activate the AMPK pathway, leading to improved glucose control and reduced lipid accumulation [99]. Moreover, it can non-competitively inhibit α -amylase and competitively inhibit α -glucosidase to prevent absorption of glucose from the brush border epithelium of the intestine [100]. Finally, it prevents hepatic gluconeogenesis, a feature attributed to the inhibition of PEPCK and G6Pase [101] which when coupled with decreased expression of PPAR-Y and SREBP prevents adipocyte differentiation and results in weight loss thereby averting obesity and its complications [102].

Palmatine and Jatrorrhizine were also effective by similar mechanisms. They caused increased metabolism in adipocytes by epigenetic modulation downregulating FAS and preventing cholesterol synthesis and absorption. Jatrorrhizine showed the most potent epigenetic regulation than the other two alkaloids and had more pronounced effects in treating hyperlipidemia [103,104].

Beyond its effects on metabolism, berberine demonstrates potential in heart health. It inhibits potassium channels and elevates calcium levels, positioning itself as a treatment candidate for heart failure [105]. Berberine also exhibits noteworthy anti-arrhythmic and anti-platelet

Table 9. Pre-clinical trials of *O. sanctum* and its phytoconstituents.

Sr. No.	Animal model	Period of study	Study design and method	Outcomes	Reference to study
1	Male Long-Evans rats (14 weeks old, weighing 180–220 g)	28 days	Group 1—Placebo control Group 2—Type-1 diabetes-induced rats Group 3—Type-2 diabetes-induced rats	↑glucose transport ↓Intestinal disaccharide activity ↓glucose absorption ↑Total antioxidant status ↓Fasting serum glucose	[106]
2	Male Wistar rats weighing between 180 and 220 g	6 weeks	Group 1—Placebo control Group 2—2% dietary OS Group 3—2% dietary OS before induction of experiment	↓blood glucose on pretreatment ↓elevated AST and ALT	[107]
3	Inbred Charles-Foster albino rats (160–180 g) and Swiss albino mice (20–25)	10 days	Group 1—Diabetic rats	↑collagen turnover and stabilization ↑breaking strength of healed wounds ↓blood glucose ↓cholesterol ↑wet tissue weight ↑protein per gram tissue ↓triglycerides	[108]
4	Forty-two male Wistar rats of body weight 170–200 g	21 days	Group 1—(NC) normal saline for placebo Group 2—OSE given to healthy rats (N+OSE) Group 3—(DC) normal saline to diabetic rats Group 4—(D+G) gliclazide to diabetic rats Group 5—(D+OSE) OSE to diabetic rats Group 6—(D+G+OSE) OSE and gliclazide to diabetic rats	↑body weight ↑glucose metabolism in the liver ↓lipids and triglycerides ↑ serum glucose and HbA1c ↓bilirubin ↓elevated AST and ALT ↓oxidative stressors ↓tissue necrosis ↑ pancreatic islet, liver, and regenerating cells	[109]
5	40 male rats, aged 4 to 5 months weighing 200–300 g	14 days	Group 1—control Group 2—Sham group Group 3—OS to healthy rats Group 4—diabetes-induced rats Group 5—OS to diabetic rats	↓IL-1B immunoreactivity ↑ blood glucose ↓degeneration of kidney tissue	[110]

aggregation activities, emphasizing its broad therapeutic potential in cardiovascular conditions [111, 112].

4.2.2. Pre-clinical studies

Berberine demonstrated a significant reduction in FBG levels in diabetic rats, though its efficacy was lower than that of the reference drug, glibenclamide. Additionally, the combination of berberine and glibenclamide exhibited limited synergistic effects in lowering FBG than stand-alone; however, it contributed to enhanced antioxidant activity by increasing the expression of SOD and CAT [69]. At higher doses (above 100–200 mg/kg b.w.), berberine effectively reduced inflammation by inhibiting Toll-like receptor 4 (TLR4) and NF-κB signaling in podocytes, thereby playing a protective role in mitigating the progression of diabetic

nephropathy [70]. These anti-oxidant and anti-inflammatory effects of berberine can also help to prevent early apoptosis in Muller cells (retinal glial cells) to prevent diabetic retinopathy [71].

Berberine suffers from low bioavailability which often limits its potential to treat metabolic syndrome. Wang *et al.* [72] prepared a co-crystal of berberine-ibuprofen which demonstrated potentiated effects such as improved fat metabolism and decreased insulin resistance leading to weight loss in db/db mice. Moreover, it inhibits NF-κB more strongly than berberine alone reducing pro-inflammatory cytokines and low-grade inflammation [72].

In the realm of non-alcoholic fatty liver disease (NAFLD), berberine was found to inhibit microsomal triglyceride transfer protein (MTTP) and LDL receptor expression which

Table 10. Clinical trials of *O. sanctum* and its phytoconstituents.

Sr. No.	Number of participants	Period of study	Trial design and treatment mode	Outcomes	Reference to study
1	60 patients with T2DM	90 days	Group 1—glibenclamide administered to diabetic patients Group 2—glibenclamide with OS treatment for diabetic patients	↓fasting blood sugar ↓post prandial mean blood glucose level ↓HbA1c ↓hypoglycemic episodes	[113]
2	30 over-weight participants (BMI > 2) Age group - 17–30 years	8 weeks	Group 1—250 mg tulsi extract capsule Group 2—no intervention	↑HDL-C ↓lipids and triglycerides ↓BMI ↓plasma insulin	[114]
3	20 type 2 diabetic patients	2 months	Group 1—Tulsi aqueous extract Group 2—control	↑HDL-C ↓fasting blood sugar ↓total cholesterol ↓LDL	[115]
4	90 non-insulin dependent male diabetic subjects in the age group of 40–60 years	3 months	Group 1—Tulsi powder Group 2—neem powder Group 3—mixture of tulsi and neem powder in a capsule form	↓blood pressure ↓diabetic symptoms	[116]

lowered the lipid accumulation in the liver as demonstrated by reduced aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. This also results in significantly reducing the levels of TC, TG, and LDL [73] (Table 3).

4.3. Clinical studies

Berberine is as effective in increasing insulin receptor expression when compared to hypoglycemic drugs such as metformin and rosiglitazone which results in a reduction of FBG. When compared to these two drugs it was more effective in lowering TG and TC levels in hyperlipidemia. When combined with metformin, the FBG and HbA1c levels decreased further than monotherapy and LDL levels were also significantly lower than baseline [117,118].

While studying the lipid-lowering effects of berberine, Zhao *et al.* [73] reported that berberine effectively lowered TC and LDL levels while it increased testosterone levels in men. Significant levels of testosterone are associated with a lower risk of CMD. This study however doesn't fully represent the anti-atherogenic effects of berberine namely as the subject selection didn't include patients of T2DM or known cardiovascular disorders and secondly didn't consider women in the study and their hormonal interactions [74]. Kong *et al.* [75] combined berberine with Simvastatin—an HMG-CoA reductase inhibitor; the anti-lipid profile included the reduction of LDL and TG; the latter being reduced due to upregulation of hepatic LDL receptors. It also showed to decrease fat accumulation and risk of steatohepatitis [75].

Yan *et al.* [76] conducted a multicentre parallel randomized control trial of berberine for NAFLD. Berberine along with lifestyle improvement was found to be more effective than lifestyle modification alone and pioglitazone treatment. It lowered liver fat content and systemic levels of TC, TG, and

LDL while significantly lowering the FBG. Though the exact mechanism is not fully elucidated, epigenetic modulation in lowering MTTP and LDL receptors is often given the credit [76] (Table 4).

4.4. Brown algae (Phaeophyceae)

4.4.1. Mechanism of action

Marine ecosystems are a rich source of bioactive compounds, brown seaweeds such as *Laminaria japonica* and *Undaria pinnatifida*, stand out for their diverse therapeutic potential. Traditionally consumed for their nutritional value, they have recently drawn scientific attention to their role in metabolic health. The key phytoconstituents—fucoxanthin, fucoidans, phlorotannins, alginates, and bromophenols—work through multiple mechanisms to support glucose regulation, lipid metabolism, and inflammation control.

Fucoidan, a sulfated polysaccharide contributes to metabolic balance by preventing inflammation via the Nf-kB pathway and anti-oxidant potential protecting oxidative damage to β -cells, which in turn improves insulin secretion; fucoidans are also responsible for insulin-sensitizing actions due to activation of P13K/Akt pathway in cells [119].

Fucoxanthin, a carotenoid found in brown seaweeds, promotes fat metabolism by activating uncoupling protein-1 (UCP1) in white adipose tissue, shifting it toward a more energy-burning state. It also regulates AMPK and PPAR- γ , improving insulin sensitivity and reducing fat accumulation. By enhancing GLUT4 expression, fucoxanthin facilitates glucose uptake, helping to stabilize blood sugar levels [120,121].

Phlorotannins like eckol and dieckol, a unique class of polyphenols found in brown algae, support glycemic control by inhibiting α -glucosidase and α -amylase, enzymes involved

Table 11. Clinical trials of *M. koenigii* and its phytoconstituents.

Sr. No.	Animal model	Period of study	Study design and method	Outcomes	Reference to study
1	Thirty healthy adult male Sprague Dawley rats	30 days	Group 1—(NC1) control	↑islet cell histology	[122]
			Group 2—(NC2) 400 mg/kg MK	↑reversal of body weight loss	
			Group 3—(DC) diabetic control	↓blood glucose	
			Group 4—(MK-200) 200 mg/kg MK	↓oxidative stress	
			Group 5—(MK-400) 400 mg/kg MK	↑renal function	
2	Male albino Wistar rats weighing about 160–180 g	30 days	Group 1—control	↑protein levels	[123]
			Group 2—diabetic control	↓blood glucose	
			Group 3—200 mg/kg MK to diabetic rats	↓ blood urea, uric acid, and creatinine	
			Group 4—glibenclamide to diabetic rats	↑Body weight	
3	Male Albino rabbits Weight - 1.00–1.5 kg	6 hours	Group 1—control	↑glucose tolerance	[124]
			Group 2—diabetic control	↓blood glucose	
			Group 3—200 mg/kg MK to diabetic rats		
			Group 4—300 mg/kg MK to diabetic rats		
			Group 5—400 mg/kg MK to diabetic rats		
			Group 6—tolbutamide to diabetic rats		
4	Adult male Wistar Rats (weighing 150–200 g)	30 days	Group 1—control	↑potentiation of insulin	[125]
			Group 2—diabetic control	↓fasting blood sugar	
			Group 3—50 mg/kg mahanimbine to diabetic rats	↓lipid profile	
			Group 4—100 mg/kg mahanimbine to diabetic rats	↓post prandial hyperglycemia	
			Group 5—0.50 mg/kg glibenclamide to diabetic rats	↑ alpha-amylase and alpha-glucosidase inhibition	
5	Adult Wistar Albino rats weight - 150–250 grams	30 days	Group 1—control	↑memory and learning	[126]
			Group 2—diabetic control	↓fasting blood sugar	
			Group 3—donepezil to diabetic rats	↓lipid profile	
			Group 4—200 mg/kg ethanolic extract of MK to diabetic rats	↓oxidative injury	
			Group 5—400 mg/kg ethanolic extract of MK to diabetic rats	↑spontaneous motor activity	
			Group 6—200 mg/kg aqueous extract of MK to diabetic rats		
			Group 6—400 mg/kg aqueous extract of MK to diabetic rats		

in carbohydrate digestion [127]. This results in a slower release of glucose into the bloodstream, preventing rapid spikes in blood sugar. Phlorotannins also help regulate fat metabolism by downregulating SREBP-1c and FAS, genes involved in lipid synthesis [128].

Sterols also contribute to these metabolic effects. One such sterol majorly found in brown algae is fucosterol which by inhibition of pancreatic lipase is able to prevent breakdown and absorption of dietary fats [129]. It also is known to reduce lipid accumulation in adipocytes namely by PPAR γ and CEBP α downregulation [130]. Research also indicates the anti-diabetic potential of these sterols by improving insulin sensitivity by inhibiting PTP-1B expression [131].

4.4.2. Pre-clinical studies

The various phytoconstituent effects have been summarized here in general. Fucoidans were able to exert

protective effects on the β islet cells effectively improving insulin production. The study also revealed the role of fucoidan in improving GLP-1 levels which improved insulin secretion via AMPK and Sirt expression [77].

Zhang *et al.* [78] studied the various pathways of fucoxanthin in diabetes while comparing its effects to metformin. Like metformin fucoxanthin was able to lower FBG levels while modulation insulin secretion in a dose-dependent fashion. Fucoxanthin supplementation also showed positive effects on the lipid profile such as lowering TG and TC levels while decreasing the body weight making it beneficial in obesity. Fucoxanthin was shown to act via a multitude of pathways including the inactivation of PEPCCK and G6Pase in the liver and activating GSK3 β to inhibit gluconeogenesis [78]. Sun *et al.* [79] studied the anti-inflammatory effects of fucoxanthin in treating obesity. While the decrease in lipid parameters was significant like the previous study, fucoxanthin supplementation

Table 12. Clinical trials of *M. koenigii* and its phytoconstituents.

Sr. No	Number of participants	Period of study	Trial design and treatment mode	Outcomes	Reference to study
1	45 women	45 days	Group 1—control	↓fasting blood sugar	[132]
			Group 2—curry leaves extract 5 mg/kg	↓random blood sugar level	
			Group 3—curry leaves extract 10 mg/kg	↓HbA1c levels	
2	60 patients	20 days	Group 1—control	↓fasting blood sugar	[133]
			Group 2—curry leaves extract 5 mg/kg	↓Post-prandial blood sugar	
			Group 3—curry leaves extract 10 mg/kg		
3	70 patients	30 days	Group 1—diabetic control	↓post prandial sugar level	[134]
			Group 2—curry leaves powder for diabetic patients		

resulted in a decreased incidence of hepatic steatosis. The main reason believed was the gut microbiome regulation by downregulating Firmicutes and upregulating Bacteroidetes. This helped to maintain a beneficial gut microbiome producing SCFA preventing intestinal inflammation and control of lipid parameters [79].

Phlorotannins from *Sargassum linifolium* were screened for their antidiabetic potential. The major effect was to reduce the oxidative stress resulting in the protection of the β -islet cells. Insulin sensitivity was improved via AMPK activation while the lipid levels of TG and TC were concurrently lowered [80]. Fucosterol was examined in diabetic control by Yeon Sil Lee *et al.* where it lowered the FBG and inhibited glycogenolysis in the liver. Hyperglycemia converts excessive glucose to sorbitol via the polyol pathway which is responsible for neuro and nephropathies in diabetes complications. When compared to the aldose reductase inhibitor epalrestat, it was shown to decrease the sorbitol levels significantly in the lenses which could turn out useful in diabetic retinopathy but the insignificant decrease in sorbitol accumulation in RBC and sciatic nerves warrants for more comprehensive studies for longer durations [81] (Table 5).

4.4.3. Clinical studies

Kombu or Japanese kelp (*Laminaria japonica*) is one of the most emerging nutraceuticals in this category due to its rich source of carotenoids and polyphenols. Supplementation of kelp powder was shown to decrease the body fat percentage in Japanese obese men while in women it didn't demonstrate significant results when compared to control due to strong hormonal regulation already contributing to lower fat percentages. However, kelp powder lowered the serum levels of TC namely LDL in both groups decreasing atherogenic risk [82]. A polyphenol-rich extract of *Ascophyllum nodosum* indicated a modest decrease in lymphocyte DNA damage in obese individuals. Plasma and urine analysis studies identified various metabolites of phlorotannins such as pyrogallols, phloroglucinols, and eckol derivatives highlighting their role in preventing oxidative DNA damage commonly linked with obesity [83].

Fucoanthin administration in patients with metabolic syndrome demonstrated lower BMI and waist circumference levels. It also showed a positive impact in lowering hypertension

often linked with these disorders and triglyceride levels. It also showed improved insulin secretion often linked to its β -islet protective activity [84]. When combined with low molecular weight fucoidans, fucoxanthin demonstrated excellent hepatoprotective activity mainly via reducing oxidative damage and cytokine-induced inflammation in hepatocytes. Enhanced leptin and adiponectin expression due to this combination results in better fat expenditure in adipocytes and decreased insulin resistance as demonstrated by lower FBG, TG, and TC levels [85]. Xanthigen, a combination of fucoxanthin and pomegranate seed oil was screened in NAFLD patients. 300 mg pomegranate seed oil + 2.4 mg fucoxanthin dose showed the most significant beneficial effects such as improving the resting state energy expenditure compared to placebo. The anti-oxidative and anti-inflammatory activities of both constituents showed improved synergistic activity to serve as hepatoprotective [86] (Table 6).

5. BLACK CUMIN SEEDS/KALONJI (*NIGELLA SATIVA*)

5.1. Mechanism of action

Nigella sativa, commonly known as Kalonji or black cumin, stands out due to its rich phytochemical profile. Traditionally valued in various healing systems, this tiny black seed harbors a powerful blend of bioactive compounds including terpenes such as thymoquinone (the major constituent), isoquinoline alkaloids like nigellidine and nigellimine, saponins, and polyphenols [135].

Thymoquinone (TQ) and its derivatives, thymohydroquinone and dithymoquinone, are powerful activators of the Nrf2 pathway, enhancing cellular antioxidant defenses by upregulating catalase and glutathione. This antioxidant boost plays a crucial role in mitigating oxidative stress and inflammation, key contributors to metabolic dysfunction. Additionally, these compounds effectively suppress the TLR4 signaling pathway, reducing pro-inflammatory cytokine production. This dual mechanism not only protects pancreatic β -cells, thereby enhancing insulin secretion but also helps regulate hepatic glucose metabolism by inhibiting gluconeogenesis. Furthermore, their activation of the AMPK pathway enhances insulin sensitivity and promotes glucose uptake in cells [136,137]. Moreover, it contributes to its anti-obesity effects by inhibiting adipocyte differentiation, lipid accumulation, and downregulating PPAR γ [138]. Enomoto *et*

al. [139] analyzed the methanolic portion of *N. sativa* which revealed various terpenes such as 2-(2-methoxypropyl)-5-methyl-1,4-benzenediol, thymol carvacrol which showed fibrinolytic activity comparable or higher than aspirin, a useful characteristic to treat thrombosis in CMDs [139].

Nigella sativa also contains triterpenoid saponins hederagenin, and α -hederin, which have a beneficial role in preventing autophagy in cancer cells. Recently it has also been noted that these saponins can upregulate UCP-1 expression via PPAR-Y modulation to promote thermogenesis and browning in 3T3L1 adipocytes [140]. *Nigella sativa* oil is now regarded as a functional oil due to its high contents of omega 3 polyunsaturated fatty acids (PUFA) such as linoleic acids and a few others in marginal quantities. These PUFAs are often linked to lower insulin resistance and LDL and TG levels preventing arteriosclerosis risk [141,142].

5.1.1. Pre-clinical studies

The effects of *N. sativa* have been compared to standard metformin treatment. It was found that 0.5 ml/kg *N. sativa* oil was more effective than its aqueous extract and metformin treatments in reducing FBG and HbA1c levels as well as lipid profiles of TG, TC, and LDL [87]. Ayaz *et al.* [88] reported that *N. sativa* oil was more of a nephroprotective than vitamin E and metformin supplementation as shown by the lower BUN levels. *N. sativa* oil downregulated apoptotic proteins like Bax, caspase-3, and caspase-9 while upregulating anti-apoptotic Bcl-2 indicating its role in preventing diabetic nephropathy complications [88]. Esmail *et al.* [89] studied the effects of three drugs namely atorvastatin, L-carnitine, and *N. sativa* oil in reducing hepatic-induced injury in NAFLD. Both *N. sativa* and L-carnitine decreased body weight reducing visceral fat deposition. Histopathological analysis of the liver highlighted that *N. sativa* was able to prevent hepatic injury better than atorvastatin possibly via the anti-inflammatory and anti-oxidant activities often attributed to thymoquinone. This could open the doors for a combination of *N. sativa* and L-carnitine in the future for the treatment of NAFLD [89].

Thymoquinone supplementation effectively ameliorated diabetes parameters in HFD rats. It is shown that it reduced C/EBP- α and SREBP expression similar to orlistat (an anti-hyperlipidemic drug as pancreatic lipase inhibitor) reducing fat accumulation and body weight. This is often associated with reduced FBG and improved AMPK signaling. The plasma lipid profile was also lower than the orlistat treatment group [90]. Thymoquinone often suffers from low bioavailability limiting its effects. Rani *et al.* [91] prepared various doses of thymoquinone-nanocapsules and compared it with metformin-nanocapsules. The drug release profile of thymoquinone was greatly increased due to increased solubility and permeability. When compared to metformin-nanocapsules it was equivalent to reducing FBG but had a more pronounced effect than the latter to decrease levels of C, TG, and LDL while significantly increasing HDL cholesterol [91] (Table 7).

5.1.2. Clinical studies

Limited clinical studies have been conducted on *N. sativa* for diabetes and obesity but the current trials

demonstrate the potential of this plant. In comparison with lifestyle modification and metformin treatment in pre-diabetic patients *N. sativa* was statistically equivalent to metformin in lowering the FBG levels and improving the Sirt-1 expression leading to improved insulin secretion. The lipid profile of only *N. sativa* was found to be significant than the other two groups lowering TG, TC, and LDL while also significantly elevation HDL [92]. Ansari *et al.* [93] studied the effects of *N. sativa* oil supplementation in chronic kidney disease patients in comparison with conservative management treatment (insulin, torsemide, telmisartan, iron, calcium, vitamin D3, and erythropoietin). *Nigella sativa* significantly decreased FBG and BUN nitrogen levels. Compared to control, it also improved the GFR and urine output levels and maintained serum electrolytes of Na⁺, K⁺, and Ca²⁺ at normal physiological levels [93]. Seyed-Ali Khodaie *et al.* [94] studied the effects of *N. sativa* ointment on treating peripheral neuropathy. After receiving the treatments, the patients were asked to fill out a michigan neuropathy screening instrument questionnaire to assess their pain. The results revealed a greater relief in the *N. sativa* group than in gabapentin to alleviate the symptoms of leg cramps, skin prickling, foot numbness, and pain during walking. While the study showed effects in alleviating symptoms, the study still requires further investigations into the mechanisms and biochemical parameter changes to explain the effects [94].

Razmpoosh *et al.* [95] conducted two separate clinical trials to demonstrate the cardio-beneficial properties of *N. sativa* in overweight and obese women. *Nigella sativa* significantly lowered leptin LDL, TC, and TG levels, reducing lipid accumulation and improving cardiovascular health. Additionally, it downregulated pro-inflammatory cytokines IL-6 and IL-1 β , mitigating systemic inflammation and endothelial dysfunction. The reduction in systolic BP further contributed to cardiovascular protection, alleviating hypertension-related risks. These findings highlight the potential of *N. sativa* in promoting heart health through lipid regulation, anti-inflammatory effects, and blood pressure control [95,96] (Table 8).

6. HOLY BASIL (*OCIMUM SANCTUM*)

6.1. Mechanism of action

Ocimum sanctum, also known as Holy Basil is regarded as the Queen of Herbs with anti-inflammatory, antidiabetic, antimicrobial, hepatoprotective, radioprotective, neuroprotective, anticancer, and notably, mosquito repellent properties, being some of its many roles. Its leaves contain various phytoconstituents including but not limited to eugenol, caryophyllene, ursolic acid, rosmarinic acid, and flavonoids. Due to its antioxidant nature, an extract of *O. sanctum* helps to increase the insulin sensitivity in pancreatic cells [143]. Even though its exact mechanism is still unclear, the antiglycemic effect of *O. sanctum* can be attributed to its role in the stimulation of pancreatic beta cells by modification of the passage of intracellular calcium. Eugenol present as 67%–73% of the composition of the leaf constitutes to be a major component showing alpha-glucosidase inhibition activity. It prevents the glucose moiety in the body from binding to serum albumin protein. A supporting action in diabetes management

is its antioxidant character as it upregulates enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase in addition to being a potent free radical scavenger [144].

Orientin and vicenin are two flavonoids in Holy Basil, beneficial as antioxidants, using the same mechanism of targeting harmful free radicals and providing cellular defense against radiation. As a cell protectant, it acts on human erythrocytes in a dose-dependent manner to prevent oxidative stress-induced damage. Its function as an antioxidant allows a broad application in diseases such as colon cancer by peroxidation and neutralization of the carcinogen dimethyl hydrazine. Orientin has a vast unexplored potential in neuroprotection owing to its antioxidant, anti-inflammatory, and radioprotective properties. It has shown significant improvement in trials against neurodegeneration-associated pain, by inhibition of interleukins 1 and 6 and also shows an effect on various pathways such as TLR-4 and NF-KB [145]. *Ocimum sanctum* can be made into various formulations in order to improve the bioavailability, and ease of administration, reduce chances of drug-herb or her-herb interaction, or for a targeted release mechanism. A lyophilized leaf powder of Tulsi produced a pronounced effect on the blood glucose levels, HbA1c, and other biochemical parameters when compared with the control and glibenclamide-treated rats. The researchers concluded that the effect of *O. sanctum* may not be due to the action of a single phytochemical but in turn, a synergistic effect of multiple phytochemicals present either in a single plant or a structured combination of several herbal agents [146]. Silver nanoparticles of *O. sanctum* and *Ocimum basilicum* using its aqueous leaf extracts were tested *in vitro* for antidiabetic activity by Malapermal *et al.* [147] phytotherapy is preferred over synthetic alternatives, due to the outcome being similar to the chemical counterparts, but without the side effects. Both plants exhibit higher alpha-amylase inhibitory activity, paired with the technologically advanced nanoparticle delivery will aid in its faster transport across cell membranes and may exhibit a sustained effect in the body. Additionally, the green synthesis of a medicinally active phytochemical eliciting an euglycemic response paves a path for cheaper and more beneficial treatment options for hyperglycemia [147].

6.1.1. Pre-clinical studies

An extract of *O. sanctum* administered to alloxan-induced diabetic albino rats showed that it successfully reduced the peak glucose levels in glucose-fed hyperglycemic animals [148]. Streptozocin-induced type 1 type 2 diabetic rats with obesity and insulin resistance were tested for oral glucose resistance, gut motility and absorption, glucose uptake, disaccharide, and antioxidant activity after administration of *O. sanctum* by *in situ* perfusion. According to a study by Hannan *et al.* [106] preclinical trials of nicotinamide and streptozocin-induced diabetic rats showed a positive response to tulsi extract. Several comparative studies have been conducted to measure the effectiveness of allopathic medication in conjunction with traditional and herbal sources. The antidiabetic effect of OS on measuring rat cells for serum and glucose contents concluded that glucose secretion and insulin levels in 3T3-L1 cells were increased. This represents

that OS can be successfully used in diabetes management as an adjunct to chemotherapy [106]. OS also contributes to antidyslipidemic effects in addition to hyperglycemia. To ascertain and quantify this, Suanarunsawat and Songsak [107] conducted a study where alteration of elevated blood glucose levels was observed after 3 weeks of treatment with OS. 2% white dietary *O. sanctum* was administered to STZ-induced diabetic rats. Serum triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol, serum AST, serum ALT, and creatinine levels were examined. It normalized the lipid profile and creatinine, and reduced the elevated ALT and AST levels. The action of *O. sanctum* improves glucose regulation in type 2 diabetic rats by delaying carbohydrate digestion and enhancing insulin circulation in the body. OS supplementation either before or after diabetic induction can reverse dyslipidemia and glomerular filtration. Thus, pretreatment of subjects with white OS can be a therapeutic addition to antidiabetic treatment options [107]. Delayed wound healing is a common occurrence in diabetic patients, leading to oxidative stress and inefficient collagen synthesis. The wound healing capacity of diabetic rats was examined after administration of 400 mg/kg OS ethanolic extract. Antioxidant, free radical, inflammatory markers as well as serum blood glucose and cholesterol testing of granulated wound ulcer tissue was performed. Examination of wound ulcers of albino rats treated with OS not only reduced the blood glucose levels but also aided in wound healing. OS increased antioxidant activity and reduced inflammation and oxidative damage in order to enhance wound healing. OS promotes the formation of connective tissue and antioxidant action, concurrently decreasing blood glucose levels [108]. A combination therapy of traditional alternatives with drugs for diabetes has shown a lot of promise. OS is to be used synergistically with gliclazide poses to be an effective treatment option. A comparison of OS-supplemented alloxan-induced diabetic rats on gliclazide with rats on monotherapy of gliclazide or OS was conducted by Ramzan *et al.* [109] Biochemical and histopathological examination of pancreatic and liver tissues for anti-hyperglycemic effect was conducted for alloxan-induced diabetic rats. Assessment of blood glucose levels, lipid profile, and tissue contents showed a marked improvement in insulin secretion and islet cells. The antioxidant activity of OS in conjunction with gliclazide was effective in ameliorating oxidative stress-mediated damage to the liver. Use of OS as an adjunct to first-line gliclazide achieved sustained hypoglycemic effect [109]. *Ocimum sanctum* extract was administered at 200 mg/kg for the diabetic group to examine immunohistochemical and structural changes in the kidneys. Assessing the effect of OS on the liver pathology led to an enhanced understanding of the role of inflammatory cytokines in diabetic patients. This is one of the leading causes of diabetic nephropathy, with various levels of OS being deposited at particular junctures in the kidney as time progressed. OS reduced kidney damage that normally occurs in diabetic rats, showing an influence on IL-1B secretion. IL-1B levels were lower in the OS-treated group as compared to the diabetic group, affirming its involvement as an anti-diabetic agent [110] (Table 9).

6.1.2. Clinical studies

Ocimum sanctum acted as a successful adjuvant when administered with oral hypoglycemic agents by reducing the safety profile of the treatment. The incidence of hypoglycemic episodes in the test group receiving the combination therapy was significantly lower than that in the control group. This affirms that *O. sanctum* shows synergistic effects when administered with prescription medication when recommended to a moderately diabetic patient [149]. A study was carried out to ascertain the efficacy of OS in addition to glibenclamide as an anti-hyperglycemic agent. Glibenclamide is a sulfonylurea which stimulates the release of insulin from the pancreas. When administered in conjunction with OS 250 mg capsule to a diabetic patient, lowered the HBA1c levels in both fasting and post-prandial testing as compared to glibenclamide alone. Haemoglobin and fasting blood glucose showed better and long-term control of glycemic levels in patients. Significant prolonged glycemic control during the study as well as during follow-up checks proves this combination therapy to show fewer hypoglycemic cases and sustained control over diabetes [113]. A study by Satapathy *et al.* [114] tackles the obesity epidemic by proposing the inclusion of Tulsi capsules twice a day for overweight patients. A randomized, parallel-group, open-label pilot study was designed for obese subjects to evaluate the role of *O. sanctum*. Twice daily supplementation of OS capsules led to significant improvement in body weight, BMI, plasma insulin levels, and other biochemical parameters. Thus, *O. sanctum* stands to be an easily available, cost-effective, and beneficial constituent for obesity treatment, with lowered side effects [114]. The effect of several medicinal aqueous extracts including *Ocimum sanctum* was studied to assess its antihyperlipidemic and anti-diabetic effect on diabetic patients in Bengal. An aqueous extract of tulsi lowered not only the total cholesterol and LDL but also significantly increased the HDL levels in the patients of rural Bengal, exhibiting excellent anti-diabetic and hypolipidemic effects. Thus, OS significantly reduced both glycemic and lipidemic levels in the patients [115]. Kochhar *et al.* [116] studied the effect of tulsi and neem, as monotherapy and in combination to alleviate diabetic symptoms and blood pressure in non-insulin dependent males who were diagnosed with diabetes. The study findings included positive markers where diabetic symptoms such as polydypdia, polyphagia, tiredness, frequent urination were significantly reduced in all treated groups. Blood pressure reduction and diabetic symptoms observed and reported by the patient indicated a positive change after neem and tulsi supplementation [116] (Table 10).

6.2. Curry leaves (*Murraya koenigii*)

6.2.1. Mechanism of action

This medicinal herb functions as an antidiabetic agent by facilitating the uptake and breakdown by cells when either glycogenesis increases or gluconeogenesis/glycogenolysis is reduced. *Murraya koenigii* contains carbazole alkaloid, which has proven anti-hyperglycemic and anti-hyperlipidemic activity [122]. Another study by Dineshkumat *et al.* [115] has isolated the carbazole alkaloid, called mahanimbine, responsible for the antioxidant activity and pancreatic beta-cell protective

activity, exhibiting a therapeutic benefit for a diabetic body. Additionally, it showcases a free radical scavenging activity which is essential in regulating insulin levels and preventing insulin resistance in the body.

6.2.2. Pre-clinical trials

In an effort to understand the effect of *M. koenigii* on histopathological and biochemical changes in the kidneys and pancreas of diabetic rats, a study was conducted in Malaysia by Al-Ani *et al.* [122] The pathological changes in pancreatic islet cells and kidneys of diabetic rats were reversed after treatment with MK extract. Aqueous extract of MK led to a dose-independent fall in glucose levels, and improvement in islet morphology associated with an increase in body weight. It was responsible for a significant lowering in the blood glucose levels in treated rats as compared to the control group. This therapy displayed hypoglycemic as well as hepatoprotective effects [122]. Comparison of the effect of *Murraya koenigii* on STZ-induced diabetic rats with a well-known glibenclamide treatment for hyperglycemia showed a decrease in blood glucose and an increase in blood insulin levels by MK. This can be attributed to the improved action of the beta cells of islets of Langerhans to release insulin. Administration of an aqueous extract of curry leaves to STZ-induced diabetic rats showed a better response than the glibenclamide-tested group. It also showed a positive effect on levels of hemoglobin which usually decrease in a diabetic patient. The antihyperglycemic property of MK has also resulted in enhancing the levels of a protein related to a decrease in proteolysis and an increase in protein synthesis due to an increase in insulin levels. Creatinine, uric acid levels, and other metabolic factors affecting kidney function were reported to be high in diabetic rats, which were lowered after the administration of the extract. Thus, MK has shown an all-round enhanced activity as a diabetogenic agent [123]. Diabetes-induced rabbits were tested for blood glucose levels after administration of tolbutamide and MK extract in respective groups for comparison of the effect of *M. koenigii* on alloxan-induced diabetic rabbits for hyperglycemia. The aqueous extract of MK showed a marked lowering of blood sugar levels in just 4 hours, with a 300 mg/kg dose showing a response identical to the drug tolbutamide, and holds promise in its role as an anti-diabetic agent. Thus, MK is an effective and promising diabetogenic agent, which can be recommended as an adjunct dietary therapy for the treatment of hyperglycemia [124]. Mahanimbine is a carbazole alkaloid, especially found in *M. koenigii* plant leaves. Estimation of biochemical parameters for the antihyperglycemic role of mahanimbine obtained from MK leaves was performed by Dineshkumar *et al.* Pre-treatment and post-treatment blood samples were compared, where the effect of mahanimbine showed significantly lowered fasting blood glucose, triglycerides, LDL, and total cholesterol. Delayed degradation of complex carbohydrates by inhibition of alpha-amylase and alpha-glucosidase activity is an avenue for managing post-prandial hyperglycemia is exhibited by mahanimbine. Mahanimbine extract can be used in individuals with an imbalanced lipid profile and cardiovascular complications, who are diabetic patients due to its antihyperglycemic and antihyperlipidemic

properties [125]. Bhupatiraju *et al.* [126] conducted a trial for the evaluation of behavioral and biochemical parameters of diabetes-induced cognitive disability models of rats on the administration of *M. koenigii*. Improved memory and learning in diabetic rats as well as spontaneous motor activity indicates a nootropic effect due to the interaction of various phytoconstituents such as flavonoids, anthocyanin glycosides, triterpenoids, and phytosterols. A 400 mg/kg dose of MK extract exhibited a comparative effect with the synthetic complex donepezil, and thus can be utilized as a potent adjuvant in the treatment of neurodegenerative diseases in a diabetic patient. A concurrent increase in body weight of the animal in all studies on administration of a hypoglycemic agent follows the mechanism which enhances glucose metabolism. Long term chronic use of MK ethanolic extract may play a role in preventing cognitive decline and reducing oxidative damage in the diabetic nervous system [126] (Table 11).

6.3. Clinical trials

A controlled randomized trial to determine the therapeutic potential of the capsule of curry leaf extract in the regulation of blood glucose levels and HbA1c in diabetic patients focusing on the female diabetic population showed a consistent result as that of previous animal trials taken place, with a significant improvement in HbA1c levels followed by random blood sugar levels and fasting blood sugar levels. The study also measured the high magnesium content in the curry leaves, which may have made a contribution to regulating insulin function. The results denoted a long-term decrease in HbA1c levels and reduced elevated fasting glucose levels [132]. Curry leaves being a natural source of carbazole alkaloids, pose to be a highly helpful alternative to allopathic medicines which cause complications in later stages due to damage to kidneys and liver. In this study, on observing the blood sugar among diabetic patients before and after their treatment with curry leaves powder, it was concluded that consumption of curry leaves has successfully reduced the blood sugar levels without any side effects [134]. Jadhav and Dhudum [133] assessed fasting blood sugar and post-prandial blood sugar in diabetic patients by treating them with 12 g of curry leaves powder. Descriptive and inferential statistics determined a significant difference in the average levels of sugar before and after the administration of MK powder [133] (Table 12).

7. FUTURE PROSPECTIVES

Regulatory challenges, quality control, and standardization are critical hurdles in the clinical adoption of medicinal plant formulations. The variability in bioactive compound composition due to differences in plant species, geographical location, harvesting conditions, and extraction methods complicates standardization [150]. Regulatory bodies such as the FDA and EMA require stringent quality assurance, including batch-to-batch consistency, stability, and safety evaluations, yet the lack of globally harmonized guidelines leads to discrepancies in approval processes across regions. Additionally, the presence of contaminants, adulterants, and variable potency necessitates robust analytical techniques,

such as high-performance liquid chromatography and mass spectrometry, to ensure quality control [151]. Establishing pharmacopeial standards and good manufacturing practices for herbal medicines is essential to enhance their reliability, safety, and therapeutic efficacy, ultimately facilitating their integration into mainstream healthcare [152].

Combining phytochemicals with conventional anti-diabetic and anti-obesity drugs offers a multi-targeted approach that enhances therapeutic efficacy, enables dose reduction, and minimizes side effects. Preclinical and clinical studies have demonstrated significant benefits, including the ability of *M. charantia* to reduce the required dosage of hypoglycemic agents, to synergistic combinations of phytoconstituents, such as thymoquinone and L-carnitine, in NAFLD. Beyond these examples, bioactive compounds such as berberine, fucoxanthin, and polyphenols have been reported to improve insulin sensitivity, regulate lipid metabolism, and exert anti-inflammatory effects when combined with standard pharmacotherapies, offering a more holistic strategy for metabolic disease management.

Beyond their synergistic potential with conventional drugs, these phytochemicals also hold promise as standalone nutraceuticals for metabolic health. These plant-derived bioactives have demonstrated glucose-lowering, lipid-regulating, and anti-inflammatory properties, making them viable options for individuals seeking natural alternatives or adjuncts to pharmaceutical interventions. Their ability to modulate key metabolic pathways, enhance mitochondrial function, and support gut microbiota balance underscores their potential as preventive and therapeutic agents in diabetes and obesity management. However, optimizing bioavailability and understanding long-term safety remain critical areas for further research.

8. CONCLUSION

Medicinal plants stand as a reservoir of diverse phytoconstituents, each endowed with a broad spectrum of functions that hold significant promise in healthcare. The ongoing exploration of these botanical wonders is marked by a surge in both pre-clinical and clinical trials, aiming to unravel the therapeutic potential of various phytochemicals in managing an array of diseases and disorders. However, it remains crucial to acknowledge that, despite their natural origins, herbal medicines are not exempt from side effects, necessitating a judicious approach to their utilization.

The relentless pursuit of understanding and harnessing the healing properties of medicinal plants has led to a continuous influx of herbal drugs into the pharmaceutical market. This expanding repertoire of phyto-therapies enriches the options available for healthcare practitioners and patients alike. With each new herbal remedy that undergoes scrutiny and validation, the compendium of plant-based treatments grows, offering a diverse array of alternatives in the pursuit of holistic health.

In parallel with the utilization of well-known herbal remedies, concerted efforts are underway to extract and investigate newer combination therapies of phytochemicals, further diversifying the pharmacological arsenal derived from nature. This ongoing exploration is fueled by the recognition that the untapped potential of medicinal plants extends beyond

the compounds already familiar to us. As science delves deeper into the intricate biochemistry of these botanical sources, novel phytoconstituents are identified, paving the way for innovative therapeutic interventions.

As we move forward, a thoughtful, science-backed approach to phytotherapy will ensure that these age-old remedies continue to offer safe, effective, and accessible options in the evolving landscape of medicine

9. LIST OF ABBREVIATIONS

AGE, Advanced Glycation End products; ALT, Alanine Aminotransferase; AMP, Adenosine monophosphate; AMPK, Adenosine Monophosphate Kinase; AST, Aspartate Aminotransferase; BUN, Blood urea nitrogen; C/EBP- α , CCAAT/Enhancer binding protein alpha; CAT, Catalase; CMD, Cardiometabolic disorders; FAS, Fatty acid synthase; FBG, Fasting blood glucose; G6Pase, Glucose-6-Phosphatase; GSH, Glutathione; HbA1c, Glycated hemoglobin; HDL, High-density lipoprotein; IL-6, Interleukin-6; LDL, Low-density lipoprotein; MAD, Malonyl aldehyde; MCP, Momordica Charatin polysaccharide; MK, *Murraya koenigii*; NAFLD, Non-Alcoholic fatty liver disease; NF-kB, Nuclear Factor Kappa B; OS, *Ocimum sanctum*; PEPCK, Phosphoenolpyruvate carboxykinase; PPAR, Peroxisome proliferator-activated receptors; PTP-1B, Protein Tyrosine Phosphatase 1B; ROS, Reactive oxygen species; SBP, Systolic blood pressure; SCFA, Short-chain fatty acids; SOD, Superoxide dismutase; SREBP, Sterol regulatory element binding protein; STZ, Streptozocin; T2DM, Type 2 diabetes mellitus; TC, Total cholesterol; TG, Triglycerides; TNF- α , Tumor necrosis factor-alpha; UCP-1, Uncoupling protein 1

10. AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

11. CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

12. FINANCIAL SUPPORT

There is no funding to report.

13. ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

14. DATA AVAILABILITY

All data generated and analyzed are included in this research article.

15. PUBLISHER'S NOTE

All claims expressed in this article are solely those of the authors and do not necessarily represent those of the publisher, the editors and the reviewers. This journal remains neutral with regard to jurisdictional claims in published institutional affiliation.

16. USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declare that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, *et al.* Heart Disease and Stroke Statistics—2018 Update: a report from the American Heart Association | Circulation. 2018 [cited 2025 Mar 22];137(12):e67–492. Available from: <https://www.ahajournals.org/doi/10.1161/cir.0000000000000558>
2. Flora GD, Nayak MK. A brief review of cardiovascular diseases, associated risk factors and current treatment regimes. *Curr Pharm Des.* 2019 [cited 2025 March 22];25(38):4063–84. Available from: <https://pubmed.ncbi.nlm.nih.gov/31553287/>
3. Luo Y, Liu J, Zeng J, Pan H. Global burden of cardiovascular diseases attributed to low physical activity: an analysis of 204 countries and territories between 1990 and 2019. *Am J Prev Cardiol.* 2024;17:100633. doi: <https://doi.org/10.1016/j.ajpc.2024.100633>
4. Rodgers JL, Jones J, Bolleddu SI, Vanthenapalli S, Rodgers LE, Shah K, *et al.* Cardiovascular risks associated with gender and aging. *J Cardiovasc Dev Dis.* 2019 [cited 2025 Mar 22];6(2):19. Available from: https://www.researchgate.net/publication/332730389_Cardiovascular_Risks_Associated_with_Gender_and_Aging
5. Sharifi-Rad J, Rodrigues CF, Sharopov F, Docea AO, Can Karaca A, Sharifi-Rad M, *et al.* Diet, lifestyle and cardiovascular diseases: linking pathophysiology to cardioprotective effects of natural bioactive compounds. *Int J Environ Res Public Health.* 2020 Mar 30;17(7):2326. doi: <https://doi.org/10.3390/ijerph17072326>
6. Hajar R. Genetics in cardiovascular disease, heart views off. *J. Gulf Heart Assoc.* 2020;21:55–6. doi: https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS_140_19
7. Bhatnagar A. Cardiovascular pathophysiology of environmental pollutants. *American J Physiol Heart Circulatory Physiol.* 2004 Feb [cited 2025 Mar 22];286(2):H479–85. Available from: <https://journals.physiology.org/doi/full/10.1152/ajpheart.00817.2003>
8. Tarride JE, Lim M, DesMeules M, Luo W, Burke N, O'Reilly D, *et al.* A review of the cost of cardiovascular disease. *Can J Cardiol.* 2009 Jun [cited 2025 Mar 22];25(6):e195–202. Available from: https://www.researchgate.net/publication/26301306_A_review_of_the_cost_of_cardiovascular_disease
9. Dunbar SB, Khavjou OA, Bakas T, Hunt G, Kirch RA, Leib AR, *et al.* Projected costs of informal caregiving for cardiovascular disease: 2015 to 2035: a policy statement from the American Heart Association. *Circulation.* 2018 May 8 [cited 2025 Mar 22];137(19):e558–77. Available from: <https://www.ahajournals.org/doi/10.1161/CIR.0000000000000570>
10. Gheorghe A, Griffiths U, Murphy A, Legido-Quigley H, Lamptey P, Perel P. The economic burden of cardiovascular disease and hypertension in low- and middle-income countries: a systematic review. *BMC Public Health.* 2018 Dec;18:1–1. Available from: <https://bmcpublihealth.biomedcentral.com/articles/10.1186/s12889-018-5806-x>
11. Leon BM, Maddox TM. Diabetes and cardiovascular disease: epidemiology, biological mechanisms, treatment recommendations

- and future research. *World J Diabetes*. 2015 Oct 10;6(13):1246–58. doi: <https://doi.org/10.4239/wjd.v6.i13.1246>
12. Luengo-Fernandez R, Walli-Attaei M, Gray A, Torbica A, Maggioni AP, Huculeci R, *et al.* Economic burden of cardiovascular diseases in the European Union: a population-based cost study. *Eur Heart J*. 2023 Dec 1 [cited 2025 Mar 22];44(45):4752–67. Available from: <https://academic.oup.com/eurheartj/article/44/45/4752/7251239>
 13. Kharroubi AT, Darwish HM. Diabetes mellitus: the epidemic of the century. *World J Diabetes*. 2015 Jun 25 [cited 2025 Mar 22];6(6):850. Available from: <https://pubmed.ncbi.nlm.nih.gov/26131326/>
 14. WHO. Diabetes. Geneva, Switzerland: WHO; 2025 [cited 2025 Mar 22]. Available from: https://www.who.int/health-topics/diabetes#tab=tab_1
 15. Bommer C, Sagalova V, Heesemann E, Manne-Goehler J, Atun R, Bärnighausen T, *et al.* Global economic burden of diabetes in adults: projections from 2015 to 2030. *Diabetes Care*. 2018 May;41(5):963–70. doi: <https://doi.org/10.2337/dc17-1962>
 16. Alanazi NH, Alsharif MM, Rasool G, Alrowaili ABH, Alrowaili AMZ, Aldaghmi AS, *et al.* Prevalence of diabetes and its relation with age and sex in Turaif city, northern Saudi Arabia in 2016–2017. *Electron Physician*. 2017 Sep 25;9(9):5294–7. doi: <https://doi.org/10.19082/5294>
 17. Sami W, Ansari T, Butt NS, Hamid MRA. Effect of diet on type 2 diabetes mellitus: a review. *Int J Health Sci (Qassim)*. 2017 Apr-Jun;11(2):65–71.
 18. Dean L, McEntyre J. The genetic landscape of diabetes. Bethesda, MD: National Center for Biotechnology Information (US); 2004.
 19. Muoio DM, Newgard CB. Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. *Nat Rev Mol Cell Biol*. 2008 Mar;9(3):193–205. doi: <https://doi.org/10.1038/nrm2327>
 20. Halban PA, Polonsky KS, Bowden DW, Hawkins MA, Ling C, Mather KJ, *et al.* β -cell failure in type 2 diabetes: postulated mechanisms and prospects for prevention and treatment. *Diabetes Care*. 2014 Jun;37(6):1751–8. doi: <https://doi.org/10.2337/dc14-0396>
 21. Frayling TM. Genome-wide association studies provide new insights into type 2 diabetes aetiology. *Nat Rev Genet*. 2007;8(9):657–62. doi: <https://doi.org/10.1038/nrg2178>
 22. Marín-Peñalver JJ, Martín-Timón I, Sevillano-Collantes C, Del Cañizo-Gómez FJ. Update on the treatment of type 2 diabetes mellitus. *World J Diabetes*. 2016 Sep 15;7(17):354–95. doi: <https://doi.org/10.4239/wjd.v7.i17.354>
 23. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals: does the clock for coronary heart disease start ticking before the onset of clinical diabetes?. *Jama*. 1990 Jun 6;263(21):2893–8. doi: <https://doi.org/10.1001/jama.1990.03440210043030>
 24. Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, *et al.* The role of inflammation in diabetes: current concepts and future perspectives. *Eur Cardiol*. 2019 Apr;14(1):50–9. doi: <https://doi.org/10.15420/eur.2018.33.1>
 25. Giacco F, Brownlee M. Oxidative stress and diabetic complications. *Circ Res*. 2010 Oct 29 [cited 2025 Mar 22];107(9):1058–70. Available from: <https://www.ahajournals.org/doi/10.1161/circresaha.110.223545>
 26. Pan D, Xu L, Guo M. The role of protein kinase C in diabetic microvascular complications. *Front Endocrinol (Lausanne)*. 2022 Aug 17 [cited 2025 Mar 22];13:973058. Available from: <https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2022.973058/full>
 27. Singh VP, Bali A, Singh N, Jaggi AS. Advanced glycation end products and diabetic complications. *Korean J Physiol Pharmacol*. 2014 Feb;18(1):1–14. doi: <https://doi.org/10.4196/kjpp.2014.18.1.1>
 28. WHO. Obesity. Geneva, Switzerland: WHO; 2025 [cited 2025 Mar 22] Available from: <https://www.who.int/health-topics/obesity>
 29. NFHS. NFHS-4 (2014–2015). New Delhi, India: Ministry of Health & Family Welfare, Government of India; 2025 [cited 2025 Mar 22]. Available from: <https://www.nfhsiips.in/nfhsuser/nfhs4.php>
 30. NFHS. NFHS-4 (2014–2015). New Delhi, India: Ministry of Health & Family Welfare, Government of India; 2025 [cited 2025 Mar 22]. Available from: <https://www.nfhsiips.in/nfhsuser/nfhs5.php>
 31. Oranika US, Adeola OL, Egbuchua TO, Okobi OE, Alrowaili DG, Kajero A, *et al.* The role of childhood obesity in early-onset type 2 diabetes mellitus: a scoping review. *Cureus*. 2023 Oct 31;15(10):e48037. doi: <https://doi.org/10.7759/cureus.48037>
 32. Ersoy C, Imamoglu S, Tuncel E, Erturk E, Ercan I. Comparison of the factors that influence obesity prevalence in three district municipalities of the same city with different socioeconomic status: a survey analysis in an urban Turkish population. *Prev Med*. 2005 Feb;40(2):181–8. doi: <https://doi.org/10.1016/j.ypmed.2004.05.018>
 33. Singh RK, Kumar P, Mahalingam K. Molecular genetics of human obesity: a comprehensive review. *C R Biol*. 2017 Feb;340(2):87–108. doi: <https://doi.org/10.1016/j.crvi.2016.11.007>
 34. Latorre J, Lluch A, Ortega FJ, Gavalda-Navarro A, Comas F, Morón-Ros S, *et al.* Adipose tissue knockdown of lysozyme reduces local inflammation and improves adipogenesis in high-fat diet-fed mice. *Pharmacol Res*. 2021 Apr;166:105486. doi: <https://doi.org/10.1016/j.phrs.2021.105486>
 35. Park HK, Ahima RS. Endocrine disorders associated with obesity. *Best Pract Res Clin Obstet Gynaecol*. 2023;90:102394. doi: <https://doi.org/10.1016/j.bpobgyn.2023.102394>
 36. Ritchie SA, Connell JM. The link between abdominal obesity, metabolic syndrome and cardiovascular disease. *Nutr Metab Cardiovasc Dis*. 2007 May;17(4):319–26. doi: <https://doi.org/10.1016/j.numecd.2006.07.005>
 37. Gutiérrez-Cuevas J, Galicia-Moreno M, Monroy-Ramírez HC, Sandoval-Rodríguez A, García-Bañuelos J, Santos A, *et al.* The role of NRF2 in obesity-associated cardiovascular risk factors. *Antioxidants (Basel)*. 2022 Jan 26;11(2):235. doi: <https://doi.org/10.3390/antiox11020235>
 38. Din-Dzietham R, Liu Y, Bielo MV, Shamsa F. High blood pressure trends in children and adolescents in national surveys, 1963 to 2002. *Circulation*. 2007 Sep 25;116(13):1488–96. doi: <https://doi.org/10.1161/CIRCULATIONAHA.106.683243>
 39. Prashar D. Current treatment strategies for obesity including Indian scenario. *Asian J Pharm* 2016;10(3):3. doi: <https://doi.org/10.22377/ajp.v10i03.774>
 40. Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The diabetes mellitus–atherosclerosis connection: the role of lipid and glucose metabolism and chronic inflammation. *Int J Mol Sci*. 2020;6;21(5). doi: <https://doi.org/10.3390/ijms21051835>
 41. O’Neill HM. AMPK and exercise: glucose uptake and insulin sensitivity. *Diabetes Metab J*. 2013 Feb [cited 2025 Mar 22];37(1):1–21. Available from: <https://pubmed.ncbi.nlm.nih.gov/articles/PMC3579147/>
 42. Galic S, Loh K, Murray-Segal L, Steinberg GR, Andrews ZB, Kemp BE. AMPK signaling to acetyl-CoA carboxylase is required for fasting- and cold-induced appetite but not thermogenesis. *Elife*. 2018 Feb 13;7:e32656. Available from: <https://pubmed.ncbi.nlm.nih.gov/29433631/>
 43. Kim SJ, Tang T, Abbott M, Viscarra JA, Wang Y, Sul HS. AMPK phosphorylates desnutrin/ATGL and hormone-sensitive lipase to regulate lipolysis and fatty acid oxidation within adipose tissue. *Mol Cell Biol*. 2016 Jun 29 [cited 2025 Mar 22];36(14):1961–76. Available from: <https://pubmed.ncbi.nlm.nih.gov/articles/PMC4936063/>
 44. Chiarelli F, Di Marzio D. Peroxisome proliferator-activated receptor-gamma agonists and diabetes: current evidence and future perspectives. *Vasc Health Risk Manag*. 2008;4(2):297–304. doi: <https://doi.org/10.2147/VHRM.S993>

45. Stienstra R, Duval C, Müller M, Kersten S. PPARs, obesity, and inflammation. *PPAR Res.* 2007;2007:95974. doi: <https://doi.org/10.1155/2007/95974>
46. Aumeeruddy MZ, Mahomoodally MF. Traditional herbal medicines used in obesity management: a systematic review of ethnomedicinal surveys. *J Herbal Med.* 2021 Aug 1;28:100435. doi: <https://doi.org/10.1016/j.hermed.2021.100435>
47. Rizvi SI, Mishra N. Traditional Indian medicines used for the management of diabetes mellitus. *J Diabetes Res.* 2013;2013(1):712092. doi: <https://doi.org/10.1155/2013/712092>
48. Saad B, Zaid H, Shanak S, Kadan S, Saad B, Zaid H, *et al.* Prevention and treatment of obesity-related diseases by diet and medicinal plants. In: *Anti-diabetes and Anti-obesity medicinal plants and phytochemicals.* Cham, Switzerland: Springer; 2017. doi: https://doi.org/10.1007/978-3-319-54102-0_4
49. Bhusnure OG, Shinde MC, Vijayendra SSM, Gholve SB, Giram PS, Birajdar MJ. Phytopharmaceuticals: an emerging platform for innovation and development of new drugs from botanicals. *J Drug Deliv Ther.* 2019;9(3). doi: <https://doi.org/10.22270/jddt.v9i3-s.2940>
50. Nath RA, Kityania SI, Nath DE, Talkadar AD, Sarma GA. An extensive review on medicinal plants in the special context of economic importance. *Asian J Pharm Clin Res.* 2023 [cited 2025 Mar 22];16(2):6–11. Available from: https://www.researchgate.net/publication/368565227_AN_EXTENSIVE_REVIEW_ON_MEDICINAL_PLANTS_IN_THE_SPECIAL_CONTEXT_OF_ECONOMIC_IMPORTANCE
51. Gayathry KS, John JA. A comprehensive review on bitter gourd (*Momordica charantia* L.) as a gold mine of functional bioactive components for therapeutic foods. *Food Prod Process Nutr.* 2022;4:10. doi: <https://doi.org/10.1186/s43014-022-00089-x>
52. Liu J, Lei Y, Guo M, Wang L. Research progress on the hypoglycemic effects and mechanisms of action of *Momordica charantia* polysaccharide. *J Food Biochem.* 2023;2023(1):8867155. Available from: <https://onlinelibrary.wiley.com/doi/10.1155/2023/8867155>
53. Wang HY, Kan WC, Cheng TJ, Yu SH, Chang LH, Chuu JJ. Differential anti-diabetic effects and mechanism of action of charantin-rich extract of Taiwanese *Momordica charantia* between type 1 and type 2 diabetic mice. *Food Chem Toxicol.* 2014 Jul;69:347–56. doi: <https://doi.org/10.1016/j.fct.2014.04.008>
54. Ahmad Z, Zamhuri KF, Yaacob A, Siang CH, Selvarajah M, Ismail A, *et al.* *In vitro* anti-diabetic activities and chemical analysis of polypeptide-k and oil isolated from seeds of *Momordica charantia* (bitter gourd). *Molecules.* 2012 Aug 10;17(8):9631–40. doi: <https://doi.org/10.3390/molecules17089631>
55. Lo HY, Ho TY, Li CC, Chen JC, Liu JJ, Hsiang CY. A novel insulin receptor-binding protein from *Momordica charantia* enhances glucose uptake and glucose clearance *in vitro* and *in vivo* through triggering insulin receptor signaling pathway. *J Agric Food Chem.* 2014 Sep 10;62(36):8952–61. doi: <https://doi.org/10.1021/jf5002099>
56. Blum A, Loerz C, Martin HJ, Staab-Weijnitz CA, Maser E. *Momordica charantia* extract, a herbal remedy for type 2 diabetes, contains a specific 11 β -hydroxysteroid dehydrogenase type 1 inhibitor. *J Steroid Biochem Mol Biol.* 2012 Jan;128(1-2):51–5. doi: <https://doi.org/10.1016/j.jsbmb.2011.09.003>
57. Wu S, Huang C, Chen YR, Huang HC, Huang WC, Lai YH. *Momordica charantia* leaf extract reduces hepatic lipid accumulation and diet-induced dyslipidemia in zebrafish through lipogenesis and beta-oxidation. *J Funct Foods.* 2021 Dec 1;87:104857. doi: <https://doi.org/10.1016/j.jff.2021.104857>
58. Franckhauser S, Bosch F. Transgenic animal models and the metabolic syndrome. In: *The metabolic syndrome at the beginning of the XXI Century: a genetic and molecular approach.* Elsevier; 2005. 67–82 pp. doi: <https://doi.org/10.1016/B978-84-8174-892-5.50004-8>
59. Mahmoud MF, El Ashry FE, El Maraghy NN, Fahmy A. Studies on the antidiabetic activities of *Momordica charantia* fruit juice in streptozotocin-induced diabetic rats. *Pharm Biol.* 2017 Dec;55(1):758–65. doi: <https://doi.org/10.1080/13880209.2016.1275026>
60. Elekofehinti OO. *Momordica charantia* nanoparticles potentiate insulin release and modulate antioxidant gene expression in pancreas of diabetic rats. *Egypt J Med Hum Genet.* 2022 Mar 14;23(1):63. doi: <https://doi.org/10.1186/s43042-022-00282-0>
61. Liu J, Liu Y, Sun J, Guo Y, Lei Y, Guo M, *et al.* Protective effects and mechanisms of *Momordica charantia* polysaccharide on early-stage diabetic retinopathy in type 1 diabetes. *Biomed Pharmacother.* 2023 Dec;168:115726. doi: <https://doi.org/10.1016/j.biopha.2023.115726>
62. Bai J, Zhu Y, Dong Y. Modulation of gut microbiota and gut-generated metabolites by bitter melon results in improvement in the metabolic status in high fat diet-induced obese rats. *J Funct Foods.* 2018 Feb 1;41:127–34. doi: <https://doi.org/10.1016/j.jff.2017.12.050>
63. Liao PY, Lo HY, Liu IC, Lo LC, Hsiang CY, Ho TY. A gastro-resistant peptide from *Momordica charantia* improves diabetic nephropathy in db/db mice via its novel reno-protective and anti-inflammatory activities. *Food Funct.* 2022 Feb 21;13(4):1822–33. doi: <https://doi.org/10.1039/D1FO02788C>
64. Hsu PK, Pan FFC, Hsieh CS. mclRBP-19 of Bitter melon peptide effectively regulates diabetes mellitus (DM) patients' blood sugar levels. *Nutrients.* 2020 Apr 28;12(5):1252. doi: <https://doi.org/10.3390/nul2051252>
65. Inayat U Rahman, Khan RU, Khalil Ur Rahman, Bashir M. Lower hypoglycemic but higher antiatherogenic effects of bitter melon than glibenclamide in type 2 diabetic patients. *Nutr J.* 2015 Jan 26;14:13. doi: <https://doi.org/10.1186/1475-2891-14-13>
66. Tongia A, Tongia SK, Dave M. Phytochemical determination and extraction of *Momordica charantia* fruit and its hypoglycemic potentiation of oral hypoglycemic drugs in diabetes mellitus (NIDDM). *Indian J Physiol Pharmacol.* 2004 Apr;48(2):241–4.
67. Kinoshita H, Ogata Y. Effect of bitter melon extracts on lipid levels in Japanese subjects: a randomized controlled study. *Evid Based Complement Alternat Med.* 2018 Nov 8 [cited 2025 Mar 12];2018:4915784. Available from: <https://pubmed.ncbi.nlm.nih.gov/30532795/>
68. França EL, Ribeiro EB, Scherer EF, Cantarini DG, Pessôa RS, França FL, *et al.* Effects of *Momordica charantia* L. on the blood rheological properties in diabetic patients. *Biomed Res Int.* 2014;2014:840379. [cited 2025 Mar 12]. Available from: <https://pubmed.ncbi.nlm.nih.gov/24672797/>
69. Chatuphonprasert W, Lao-Ong T, Jarukamjorn K. Improvement of superoxide dismutase and catalase in streptozotocin-nicotinamide-induced type 2-diabetes in mice by berberine and glibenclamide. *Pharm Biol.* 2013;524:419-27. Available from: <https://www.tandfonline.com/doi/abs/10.3109/13880209.2013.839714>
70. Zhu L, Han J, Yuan R, Xue L, Pang W. Berberine ameliorates diabetic nephropathy by inhibiting TLR4/NF- κ B pathway. *Biol Res.* 2018 Mar 31;51(1):9. doi: <https://doi.org/10.1186/s40659-018-0157-8>
71. Zhai J, Li Z, Zhang H, Ma L, Ma Z, Zhang Y, *et al.* Berberine protects against diabetic retinopathy by inhibiting cell apoptosis via deactivation of the NF- κ B signaling pathway. *Mol Med Rep.* 2020 Nov;22(5):4227–35. doi: <https://doi.org/10.3892/mmr.2020.11505>
72. Wang M, Xu R, Liu X, Zhang L, Qiu S, Lu Y, *et al.* A co-crystal berberine-ibuprofen improves obesity by inhibiting the protein kinases TBK1 and IKK ϵ . *Commun Biol.* 2022 Aug 12;5(1):807. doi: <https://doi.org/10.1038/s42003-022-03776-0>
73. Chen P, Li Y, Xiao L. Berberine ameliorates nonalcoholic fatty liver disease by decreasing the liver lipid content via reversing the abnormal expression of MTTP and LDLR. *Exp Ther Med.* 2021 Oct;22(4):1109. doi: <https://doi.org/10.3892/etm.2021.10543>
74. Zhao JV, Yeung WF, Chan YH, Vackova D, Leung JYY, Ip DKM, *et al.* Effect of berberine on cardiovascular disease risk factors:

- a mechanistic randomized controlled trial. *Nutrients*. 2021 Jul 26;13(8):2550. doi: <https://doi.org/10.3390/nu13082550>
75. Kong WJ, Wei J, Zuo ZY, Wang YM, Song DQ, You XF, *et al.* Combination of simvastatin with berberine improves the lipid-lowering efficacy. *Metabolism*. 2008 Aug;57(8):1029–37. doi: <https://doi.org/10.1016/j.metabol.2008.01.037>
 76. Yan HM, Xia MF, Wang Y, Chang XX, Yao XZ, Rao SX, *et al.* Efficacy of berberine in patients with non-alcoholic fatty liver disease. *PLoS One*. 2015 Aug 7;10(8):e0134172. doi: <https://doi.org/10.1371/journal.pone.0134172>
 77. Yu WC, Chen YL, Hwang PA, Chen TH, Chou TC. Fucoidan ameliorates pancreatic β -cell death and impaired insulin synthesis in streptozotocin-treated β cells and mice via a Sirt-1-dependent manner. *Mol Nutr Food Res*. 2017 Oct;61(10). doi: <https://doi.org/10.1002/mnfr.201700136>
 78. Zhang Y, Xu W, Huang X, Zhao Y, Ren Q, Hong Z, *et al.* Fucoxanthin ameliorates hyperglycemia, hyperlipidemia and insulin resistance in diabetic mice partially through IRS-1/PI3K/Akt and AMPK pathways. *J Funct Foods*. 2018 Sep 1;48:515–24. doi: <https://doi.org/10.1016/j.jff.2018.07.048>
 79. Sun X, Zhao H, Liu Z, Sun X, Zhang D, Wang S, *et al.* Modulation of gut microbiota by fucoxanthin during alleviation of obesity in high-fat diet-fed mice. *J Agric Food Chem*. 2020 May 6;68(18):5118–28. doi: <https://doi.org/10.1021/acs.jafc.0c01467>
 80. Gheda S, Hamouda RA, Naby MA, Mohamed TM, Al-Shaikh TM, Khamis A. Potent effect of phlorotannins derived from *Sargassum linifolium* as antioxidant and antidiabetic in a streptozotocin-induced diabetic rats model. *Appl Sci*. 2023;13(8):4711. doi: <https://doi.org/10.3390/appl13084711>
 81. Lee YS, Shin KH, Kim BK, Lee S. Anti-diabetic activities of fucosterol from *Pelvetia siliquosa*. *Arch Pharm Res*. 2004;27(11):1120–2, Nov. 2004, doi: <https://doi.org/10.1007/BF02975115>
 82. Aoe S, Yamanaka C, Ohtoshi H, Nakamura F, Fujiwara S. Effects of daily kelp (*Laminaria japonica*) intake on body composition, serum lipid levels, and thyroid hormone levels in healthy Japanese adults: a randomized, double-blind study. *Mar Drugs* 2021;19(7):352. doi: <https://doi.org/10.3390/md19070352>
 83. Baldrick FR, Kevin M, Maria I, Chris S, Tanya M, Kate M, *et al.* Impact of a (poly)phenol-rich extract from the brown algae *Ascophyllum nodosum* on DNA damage and antioxidant activity in an overweight or obese population: a randomized controlled trial. *Am J Clin Nutr*. 2018;108(4):688–700. doi: <https://doi.org/10.1093/ajcn/nqy147>
 84. López-Ramos A, González-Ortiz M, Martínez-Abundis E, Pérez-Rubio KG. Effect of fucoxanthin on metabolic syndrome, insulin sensitivity, and insulin secretion. *J Med Food* 2023;26(7):521–527. doi: <https://doi.org/10.1089/jmf.2022.0103>
 85. Shih PH, Shiue SJ, Chen CN, Cheng SW, Lin HY, Wu LW, *et al.* Fucoidan and fucoxanthin attenuate hepatic steatosis and inflammation of NAFLD through modulation of leptin/adiponectin axis. *Mar Drugs* 2021;19(3):148. doi: <https://doi.org/10.3390/md19030148>
 86. Abidov M, Ramazanov Z, Seifulla R, Grachev S. The effects of Xanthigen in the weight management of obese premenopausal women with non-alcoholic fatty liver disease and normal liver fat. *Diabetes Obes Metab*. 2010;12(1):72–81. doi: <https://doi.org/10.1111/j.1463-1326.2009.01132.x>
 87. Al Jamal A. Effects of *Nigella sativa* and metformin on HbA1C, glucose tolerance and lipid profile of diabetic rats. *J Chem Pharm Sci*. 2024;12(1):6–9. doi: <https://doi.org/10.30558/jchps.20191201002>
 88. Ayaz H, Kaya S, Seker U, Nergiz Y. Comparison of the anti-diabetic and nephroprotective activities of vitamin E, metformin, and *Nigella sativa* oil on kidney in experimental diabetic rats. *Iran J Basic Med Sci*. 2023;26(4):395–399. doi: <https://doi.org/10.22038/IJBMS.2023.68051.14876>
 89. Esmail M, Anwar S, Kandeil M, El-Zanaty AM, Abdel-Gabbar M. Effect of *Nigella sativa*, atorvastatin, or L-Carnitine on high fat diet-induced obesity in adult male Albino rats. *Biomed Pharmacother*. 2021;141:111818. doi: <https://doi.org/10.1016/j.biopha.2021.111818>
 90. Ramineedu K, Sankaran KR, Mallepogu V, Rendedula DP, Gunturu R, Gandham S, *et al.* Thymoquinone mitigates obesity and diabetic parameters through regulation of major adipokines, key lipid metabolizing enzymes and AMPK/p-AMPK in diet-induced obese rats. *3 Biotech*. 2024;14(1):16. doi: <https://doi.org/10.1007/s13205-023-03847-x>
 91. Rani R, Dahiya S, Dhingra D, Dilbaghi N, Kim KH, Kumar S. Improvement of antihyperglycemic activity of nano-thymoquinone in rat model of type-2 diabetes. *Chem Biol Interact*. 2018;295:119–132. doi: <https://doi.org/10.1016/j.cbi.2018.02.006>
 92. Mostafa TM, Hegazy SK, Elnaidany SS, Shehabeldin WA, Sawan ES. *Nigella sativa* as a promising intervention for metabolic and inflammatory disorders in obese prediabetic subjects: a comparative study of *Nigella sativa* versus both lifestyle modification and metformin. *J Diabetes Complications* 2021;35(7):107947. doi: <https://doi.org/10.1016/j.jdiacomp.2021.107947>
 93. Ansari ZM, Nasiruddin M, Khan RA, Haque SF. Protective role of *Nigella sativa* in diabetic nephropathy: a randomized clinical trial. *Saudi J Kidney Dis Transplant Off Publ Saudi Cent Organ Transplant Saudi Arab*. 2017;28(1):9–14. doi: <https://doi.org/10.4103/1319-2442.198093>
 94. Khodaie SA, Nikkha H, Namiranian N, Abotorabi M, Askari M, Khalilzadeh SH, *et al.* Topical *Nigella sativa* L. product: a new candidate for the management of diabetic peripheral neuropathy. *Inflammopharmacology*. 2024;32(1):551–9. doi: <https://doi.org/10.1007/s10787-023-01338-2>
 95. Razmpoosh E, Safi S, Mazaheri M, Khalesi S, Nazari M, Mirmiran P, *et al.* A crossover randomized controlled trial examining the effects of black seed (*Nigella sativa*) supplementation on IL-1 β , IL-6 and leptin, and insulin parameters in overweight and obese women. *BMC Complement Med Ther*. 2024;24(1):22. doi: <https://doi.org/10.1186/s12906-023-04226-y>
 96. Razmpoosh E, Safi S, Nadjarzadeh A, Fallahzadeh H, Abdollahi N, Mazaheri M, *et al.* The effect of *Nigella sativa* supplementation on cardiovascular risk factors in obese and overweight women: a crossover, double-blind, placebo-controlled randomized clinical trial. *Eur J Nutr*. 2021;60(4):1863–74. doi: <https://doi.org/10.1007/s00394-020-02374-2>
 97. Mokhber-Dezfuli N, Saeidnia S, Gohari AR, Kurepaz-Mahmoodabadi M. Phytochemistry and pharmacology of berberis species. *Pharmacogn Rev*. 2014 Jan;8(15):8–15. doi: <https://doi.org/10.4103/0973-7847.125517>
 98. Şensu E, Kasapoğlu KN, Gültekin-Özgülven M, Demircan E, Arslaner A, Özçelik B. Orange, red and purple barberries: Effect of *in-vitro* digestion on antioxidants and ACE inhibitors. *Lwt*. 2021 Apr 1;140:110820. doi: <https://doi.org/10.1016/j.lwt.2020.110820>
 99. Jin Y, Liu S, Ma Q, Xiao D, Chen L. Berberine enhances the AMPK activation and autophagy and mitigates high glucose-induced apoptosis of mouse podocytes. *Eur J Pharmacol*. 2017 Jan 5;794:106–14. doi: <https://doi.org/10.1016/j.ejphar.2016.11.037>
 100. Zhao J, Wang Z, Karrar E, Xu D, Sun X. Inhibition mechanism of berberine on α -amylase and α -glucosidase *in vitro*. *Starch-Stärke*. 2022 Mar;74(3-4):2100231. doi: <https://doi.org/10.1002/star.202100231>
 101. Xia X, Yan J, Shen Y, Tang K, Yin J, Zhang Y, *et al.* Berberine improves glucose metabolism in diabetic rats by inhibition of hepatic gluconeogenesis. *PLoS One*. 2011 Feb 3;6(2):e16556. doi: <https://doi.org/10.1371/journal.pone.0016556>
 102. Ilyas Z, Perna S, Al-Thawadi S, Alalwan TA, Riva A, Petrangolini G, *et al.* The effect of Berberine on weight loss in order to prevent obesity: a systematic review. *Biomed Pharmacother*. 2020 Jul;127:110137. doi: <https://doi.org/10.1016/j.biopha.2020.110137>
 103. Ekeuku SO, Pang KL, Chin KY. Palmatine as an agent against metabolic syndrome and its related complications: a review.

- Drug Des Devel Ther. 2020 Nov 17;14:4963–74. doi: <https://doi.org/10.2147/DDDT.S280520>
104. He H, Deng J, Yang M, An L, Ye X, Li X. Jatrorrhizine from *Rhizoma Coptidis* exerts an anti-obesity effect in db/db mice. *J Ethnopharmacol.* 2022 Nov 15;298:115529. doi: <https://doi.org/10.1016/j.jep.2022.115529>
105. Wang YX, Zheng YM. Ionic mechanism responsible for prolongation of cardiac action-potential duration by berberine. *J Cardiovasc Pharmacol.* 1997 Aug;30(2):214–22. doi: <https://doi.org/10.1097/00005344-199708000-00010>
106. Hannan J, Ojo O, Rokeya L, Khaleque J, Akhter M, Flatt P, *et al.* Actions underlying antidiabetic effects of *Ocimum sanctum* leaf extracts in animal models of type 1 and type 2 diabetes. 2015;5:1–12. doi: <https://doi.org/10.9734/EJMP/2015/11840>
107. Suanarunsawat T, Songsak T. Anti-hyperglycaemic and anti-dyslipidaemic effect of dietary supplement of white *Ocimum Sanctum* Linnean before and after STZ-induced diabetes mellitus. *Int J Diabetes Metab.* 2005 Jan;13(1):18–23. doi: <https://doi.org/10.1159/000497569>
108. Murthy S, Gautam MK, Goel S, Purohit V, Sharma H, Goel RK. Evaluation of *in vivo* wound healing activity of *Bacopa monniera* on different wound model in rats. *Biomed Res Int.* 2013;2013:972028. doi: <https://doi.org/10.1155/2013/972028>
109. Ramzan TA, Aslam BI, Muhammad FA, Faisal MN, Hussain AS. Influence of *Ocimum sanctum* (L.) extract on the activity of gliclazide in alloxan-induced diabetes in rats. *Rev Chim.* 2020;71(10):101–10. doi: <https://doi.org/10.37358/RC.20.11.8379>
110. Yildiz SE, Bakir B, Asker H, Sari EK. The effects of the Basil (*Ocimum sanctum*) Treatment on the tumor necrosis factor- α and Interleukin 1 β release in the kidney tissue of the diabetic rats. *Kafkas Univ Vet Fak Derg.* 2021;27(3):315–22. doi: <https://doi.org/10.9775/kvfd.2021.25359>
111. Wang LH, Yu CH, Fu Y, Li Q, Sun YQ. Berberine elicits anti-arrhythmic effects via IK1/Kir2.1 in the rat type 2 diabetic myocardial infarction model. *Phytother Res.* 2011 Jan;25(1):33–7. doi: <https://doi.org/10.1002/ptr.3097>
112. Marin-Neto JA, Maciel BC, Secches AL, Gallo Júnior L. Cardiovascular effects of berberine in patients with severe congestive heart failure. *Clin Cardiol.* 1988 Apr;11(4):253–60. doi: <https://doi.org/10.1002/clc.4960110411>
113. Somasundaram G, Manimekalai K, Salwe KJ, Pandiamunian J. Evaluation of the antidiabetic effect of *Ocimum sanctum* in type 2 diabetic patients. *Int J life Sci Pharma Res.* 2012 Jul;5:75–81.
114. Satapathy S, Das N, Bandyopadhyay D, Mahapatra SC, Sahu DS, Meda M. Effect of Tulsi (*Ocimum sanctum* Linn.) supplementation on metabolic parameters and liver enzymes in young overweight and obese subjects. *Indian J Clin Biochem.* 2017 Jul;32:357–63. doi: <https://doi.org/10.1007/s12291-016-0615-4>
115. Dineshkumar B, Analava M, Manjunatha M. Antidiabetic and hypolipidaemic effects of few common plants extract in type 2 diabetic patients at Bengal. *Int J Diabetes Metab.* 2010 Feb;18(2):59–65. doi: <https://doi.org/10.1159/000497694>
116. Kochhar A, Sharma N, Sachdeva R. Effect of supplementation of Tulsi (*Ocimum sanctum*) and Neem (*Azadirachta indica*) leaf powder on diabetic symptoms, anthropometric parameters and blood pressure of non insulin dependent male diabetics. *Studies on Ethno-Medicine.* 2009 Jan 1;3(1):5–9.
117. Yin J, Xing H, Ye J. Efficacy of berberine in patients with type 2 diabetes mellitus. *Metabolism.* 2008 May;57(5):712–7. doi: <https://doi.org/10.1016/j.metabol.2008.01.013>
118. Zhang H, Wei J, Xue R, Wu JD, Zhao W, Wang ZZ, *et al.* Berberine lowers blood glucose in type 2 diabetes mellitus patients through increasing insulin receptor expression. *Metabolism.* 2010 Feb;59(2):285–92. doi: <https://doi.org/10.1016/j.metabol.2009.07.029>
119. Liu Y, Xu Z, Huang H, Xue Y, Zhang D, Zhang Y, *et al.* Fucoidan ameliorates glucose metabolism by the improvement of intestinal barrier and inflammatory damage in type 2 diabetic rats. *Int J Biol Macromol.* 2022 Mar 15;201:616–29. doi: <https://doi.org/10.1016/j.ijbiomac.2022.01.102>
120. Maeda H, Hosokawa M, Sashima T, Funayama K, Miyashita K. Fucoxanthin from edible seaweed, *Undaria pinnatifida*, shows antiobesity effect through UCP1 expression in white adipose tissues. *Biochem Biophys Res Commun.* 2005 Jul 1;332(2):392–7. doi: <https://doi.org/10.1016/j.bbrc.2005.05.002>
121. Mohibullah M, Haque MN, Sohag AAM, Hossain MT, Zahan MS, Uddin MJ, *et al.* A systematic review on marine algae-derived fucoxanthin: an update of pharmacological insights. *Mar Drugs.* 2022 Apr 22;20(5):279. doi: <https://doi.org/10.3390/md20050279>
122. Al-Ani IM, Santosa RI, Yankuzo MH, Saxena AK, Alazzawi KS. The antidiabetic activity of curry leaves “*Murraya Koenigii*” on the glucose levels, kidneys, and islets of Langerhans of rats with Streptozotocin induced diabetes. *Makara J Health Res.* 2017 Aug 18;21(2):4. doi: <https://doi.org/10.7454/msk.v21i2.7393>
123. Arulselvan P, Senthilkumar GP, Sathish Kumar D, Subramanian S. Anti-diabetic effect of *Murraya koenigii* leaves on streptozotocin induced diabetic rats. *Die Pharmazie-An Int J Pharm Sci.* 2006 Oct 1;61(10):874–7.
124. Kesari AN, Gupta RK, Watal G. Hypoglycemic effects of *Murraya koenigii* on normal and alloxan-diabetic rabbits. *J Ethnopharmacol.* 2005 Feb 28;97(2):247–51. doi: <https://doi.org/10.1016/j.jep.2004.11.006>
125. Mitra A, Mahadevappa M. Antidiabetic and hypolipidemic effects of mahanimbine (carbazole alkaloid) from *Murraya koenigii* (rutaceae) leaves. *Int J Phytomed.* 2010;2:22–30.
126. Bhupatiraju L, Bethala K, Goh KW, Dhaliwal JS, Siang TC, Menon S, *et al.* Influence of *Murraya koenigii* extract on diabetes induced rat brain aging. *J Med Life.* 2023 Feb;16(2):307. doi: <https://doi.org/10.25122/jml-2022-0151>
127. Gisbert M, Franco D, Sineiro J, Moreira R. Antioxidant and antidiabetic properties of phlorotannins from *Ascophyllum nodosum* seaweed extracts. *Molecules.* 2023 Jun 23;28(13):4937. doi: <https://doi.org/10.3390/molecules28134937>
128. Kim AT, Park Y. Trifluhalol A, a phlorotannin from the brown algae *Agarum cribrosum*, reduces adipogenesis of human primary adipocytes through Wnt/ β -catenin and AMPK-dependent pathways. *Curr Res Food Sci.* 2023 Nov 22;7:100646. doi: <https://doi.org/10.1016/j.crf.2023.100646>
129. Hannan MA, Sohag AAM, Dash R, Haque MN, Mohibullah M, Oktaviani DF, *et al.* Phytosterols of marine algae: Insights into the potential health benefits and molecular pharmacology. *Phytomedicine.* 2020 Apr;69:153201. doi: <https://doi.org/10.1016/j.phymed.2020.153201>
130. Jung HA, Jung HJ, Jeong HY, Kwon HJ, Kim MS, Choi JS. Anti-adipogenic activity of the edible brown alga *Ecklonia stolonifera* and its constituent fucosterol in 3T3-L1 adipocytes. *Arch Pharm Res.* 2014 Jun;37(6):713–20. doi: <https://doi.org/10.1007/s12272-013-0237-9>
131. Jung HA, Bhakta HK, Min BS, Choi JS. Fucosterol activates the insulin signaling pathway in insulin resistant HepG2 cells via inhibiting PTP1B. *Arch Pharm Res.* 2016 Oct;39(10):1454–1464. doi: <https://doi.org/10.1007/s12272-016-0819-4>
132. Farooq M, Ul Ain I, Aysha Ifikhar Z. Investigating the therapeutic potential of aqueous extraction of curry plant (*Murraya koenigii*) leaves supplementation for the regulation of blood glucose level in type 2 diabetes mellitus in female human subjects. *Pak J Pharm Sci.* 2023 Mar 1;36(2):601–5.
133. Jadhav KV, Dhudum B. Effectiveness of curry leaves powder on blood sugar level among diabetic patients. *SCOPUS IIPHRD CITATION SCORE.* 2019 Jul;10(7):388. doi: <https://doi.org/10.5958/0976-5506.2019.01597.3>

134. Gaikwad V. Effectiveness of curry leaves on blood sugar level among diabetic clients. *Group*. 2018;2(O1):O2.
135. Hussain S, Rukhsar A, Iqbal M, ul Ain Q, Fiaz J, Akhtar N, *et al.* Phytochemical profile, nutritional and medicinal value of *Nigella sativa*. *Biocatal Agric Biotechnol*. 2024;60:103324. doi: <https://doi.org/10.1016/j.bcab.2024.103324>
136. Abdelrazek HM, Kilany OE, Muhammad MA, Tag HM, Abdelazim AM. Black seed thymoquinone improved insulin secretion, hepatic glycogen storage, and oxidative stress in streptozotocin-induced diabetic male wistar rats. *Oxid Med Cell Longev*. 2018;2018:8104165. doi: <https://doi.org/10.1155/2018/8104165>
137. Darakhshan S, Pour AB, Colagar AH, Sisakhtnezhad S. Thymoquinone and its therapeutic potentials. *Pharmacol Res*. 2015;95–96:138–158. doi: <https://doi.org/10.1016/j.phrs.2015.03.011>
138. Shahbodi M, Emami SA, Javadi B, Tayarani-Najaran Z. Effects of thymoquinone on adipocyte differentiation in human adipose-derived stem cells. *Cell Biochem Biophys*. 2022;80(4):771–779. doi: <https://doi.org/10.1007/s12013-022-01095-z>
139. Enomoto S, Asano R, Iwahori Y, Narui T, Okada Y, Singab AN, *et al.* Hematological studies on black cumin oil from the seeds of *Nigella sativa* L. *Biol Pharm Bull*. 2001;24(3):307–310. doi: <https://doi.org/10.1248/bpb.24.307>
140. Choi SM, Lee HS, Lim SH, Choi G, Choi CI. Hederagenin from hederia helix promotes fat browning in 3T3-L1 adipocytes. *Plants* 2024;13(19):2789. doi: <https://doi.org/10.3390/plants13192789>
141. Tulukcu E. A comparative study on fatty acid composition of black cumin obtained from different regions of Turkey, Iran and Syria. *Afr J Agric Res*. 2011;6(4):892–5. Feb. 2011, doi: <https://doi.org/10.5897/AJAR10.286>
142. Bayram SŞ, Kızıltan G. The role of omega-3 polyunsaturated fatty acids in diabetes mellitus management: a narrative review. *Curr Nutr Rep*. 2024;13(3):527–551. doi: <https://doi.org/10.1007/s13668-024-00561-9>
143. Samanth M. The chemical constituents of *Ocimum sanctum* and its pharmacological applications: a review. In: Min HS, editor. *Recent developments in chemistry and biochemistry research*. Tarkeshwar, India: BP International; 2025. Vol. 11, pp. 119–52. doi: <https://doi.org/10.9734/bpi/rdcbr/v11/4371>
144. Pradhan D, Biswasroy P, Haldar J, Cheruvanachari P, Dubey D, Rai VK, *et al.* A comprehensive review on phytochemistry, molecular pharmacology, clinical and translational outfit of *Ocimum sanctum* L. *South Afr J Bot*. 2022;150:342–60. doi: <https://doi.org/10.1016/j.sajb.2022.07.037>
145. Raza Ishaq A, A S El-Nashar H, M Al-Qaaneh A, Asfandyar, Bashir A, Younis T. Younis, Orientin: a natural glycoside with versatile pharmacological activities. *Nat Prod Res*. 2025 Jan 5:1–23. doi: <https://doi.org/10.1080/14786419.2024.2436119>
146. Jadaramkunti UC. Hypoglycemic activity of lyophilized tulsi leaf powder and its protective role association with the antioxidant and antidyslipidemic properties in alloxan-induced diabetic rats. *World J Pharm Res*.
147. Malapermal V, Botha I, Krishna SBN, Mbatha JN. Enhancing antidiabetic and antimicrobial performance of *Ocimum basilicum*, and *Ocimum sanctum* (L.) using silver nanoparticles. *Saudi J Biol Sci*. 2017 Sep;24(6):1294–305. doi: <https://doi.org/10.1016/j.sjbs.2015.06.026>
148. Vats V, Grover JK, Rathi SS. Evaluation of anti-hyperglycemic and hypoglycemic effect of *Trigonella foenum-graecum* Linn, *Ocimum sanctum* Linn and *Pterocarpus marsupium* Linn in normal and alloxanized diabetic rats. *J Ethnopharmacol*. 2002 Jan;79(1):95–100. doi: [https://doi.org/10.1016/S0378-8741\(01\)00374-9](https://doi.org/10.1016/S0378-8741(01)00374-9)
149. Kharat P, Kurane S. *Ocimum Sanctum* Linn Extract As An Adjuvant Therapy For Effective Glycaemic Control In Type II Diabetes Mellitus. *J Pharm Negat Results*[Internet]. 2022;13(8):412–7. doi: <https://doi.org/10.47750/pnr.2022.13.S08.055>
150. Panossian A. Challenges in phytotherapy research. *Frontiers in pharmacology*. 2023 May 31;14:1199516. doi: <https://doi.org/10.3389/fphar.2023.1199516>
151. Wang H, Chen Y, Wang L, Liu Q, Yang S, Wang C. Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. *Front Pharmacol*. 2023 Sep 25;14:1265178. doi: <https://doi.org/10.3389/fphar.2023.1265178>
152. Rodríguez Villanueva J, Martín Esteban J, Rodríguez Villanueva L. Pharmacological activities of phytomedicines: a challenge horizon for rational knowledge. *Challenges*. 2018 Mar 23;9(1):15. doi: <https://doi.org/10.3390/challe9010015>

How to cite this article:

Keith D, Apte K, Kumawat VS, Chintamaneni A, Chintamaneni M, Sharma U, Sharma B, Shahwan M, Kaur G, Kaur D, Tuli HS. Phytochemical interventions of medicinal plants in the management of diabetes and obesity: A recent therapeutic overview. *J Appl Pharm Sci*. 2026;16(01):046-069. DOI: 10.7324/JAPS.2025.217666