

Chapter

Exploring the Therapeutic Potential from *Moringa oleifera* and *Urtica dioica* Bioactive Compounds in Managing Diabetes and Insulin Resistance

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Abstract

Diabetes is one of the ubiquitous metabolic disorders, indicating increasing chronic blood levels (chronic hyperglycaemia). Its three types are mostly caused by different pathogenic conditions (disorders in the secretion and/or regulation blood sugar insulin levels), often resulting from defects in insulin secretion and abnormal glucose tolerance. In addition, most people with diabetes have type 2 diabetes, which is characterised by insulin resistance and progressive beta-cell failure. Recently, there has been a growing demand for medicinal plants traditionally used to manage diabetes and its complications, as the insulin use is somewhat correlated with side effects. The current chapter focused on two medicinal plants, *Moringa oleifera* and *Urtica dioica*. The chosen plants have shown therapeutic potential as natural diabetes remedies owing to their bioactive compounds. The chosen plants have shown potential as natural diabetes remedies owing to their diverse bioactive compounds range and their effect on insulin resistance and glucose levels. Additionally, they exhibit hypoglycaemic features making them promising candidates for further diabetes management investigation. Besides, because of their bioactive phytochemicals, they do have the ability to prevent the diabetes's onset. Of note, this chapter aims to explore their effects on blood sugar regulation with a focus on managing diabetes potential.

Keywords: insulin, insulin resistance, diabetes, blood glucose, bioactive compounds, *Moringa oleifera*, *Urtica dioica*

1. Introduction

Diabetes and insulin resistance are two common health problems affecting large numbers of people around the world and understanding them is essential to managing them effectively.

On the one hand, the World Health Organization reports that around 537 million adults aged 20–79 will be living with diabetes worldwide in 2021. Moreover, insulin resistance is a precursor to type 2 diabetes, which occurs when the body's cells become less reactive to insulin.

Furthermore, to combat this disease, researchers are making enormous efforts, both in the field of medical biotechnology through drugs and in the phytotherapeutic field and natural compounds through medicinal plants, which have proved highly effective in both prevention and treatment.

This chapter aims to elucidate the therapeutic potential of two anti-diabetic plants, *Moringa oleifera* and *Urtica dioica*. *Moringa oleifera* is rich in bioactive compounds, notably antioxidants, phytosterols, and isothiocyanates, while *Urtica dioica* contains phenolic compounds, flavonoids, and triterpenes. These compounds have a hypoglycemic effect, making them valuable for the prevention and treatment of diabetes.

2. Chemical composition of *Moringa oleifera* and *Urtica*

Aromatic plants (or medicinal herbs) have been used for centuries in traditional medicine [1] and culinary practices due to their potential health benefits. These aromatic plants can be used in various ways, including teas, essential oils, culinary dishes, and herbal remedies [2]. Among these aromatic plants, we find *Moringa oleifera* and *Urtica*, which are known for their medicinal properties [3]. *Urtica* and *Moringa* are two different plants with distinct chemical compositions. Here is an overview of each chemical composition.

2.1 Phytochemicals

The bioactive compounds found in aromatic plants correspond to compounds synthesized by plants and are sometimes present in conjugated forms as glycosides. They originate from the plant's secondary metabolism and act against environmental aggressions [4]. These compounds are divided into five major categories: flavonoids, phenolic acids, lignans, stilbenes, and tannins, most of which are derived from the polymerization of flavonoids. Polyphenols are molecules that have several phenolic groups, meaning they have an aromatic ring with one or more hydroxyl (-OH) groups attached. Both *Moringa oleifera* and *Urtica* contain a variety of bioactive compounds including flavonoids, phenolic compounds, and sterols.

Moringa leaves are indeed an excellent source of vitamins and minerals, including vitamin C, vitamin A, vitamin K, calcium, iron, and potassium [5]. *Urtica* is also a good source of vitamins and minerals, but the content may not be as high as in *Moringa* [6]. Both plants are a source of high-quality plant proteins, containing all essential amino acids, making them useful for supplementing protein intake [7]. Additionally, they are rich in dietary fiber, which can promote good digestive health.

Regarding bioactive compounds, *Moringa oleifera* contains over 100 compounds. It is rich in antioxidants such as flavonoids, polyphenols, and quercetin (**Figure 1**) which help combat damage caused by free radicals in the body. Its chemical composition also shows the presence of phytosterols and plant compounds like cholesterol,

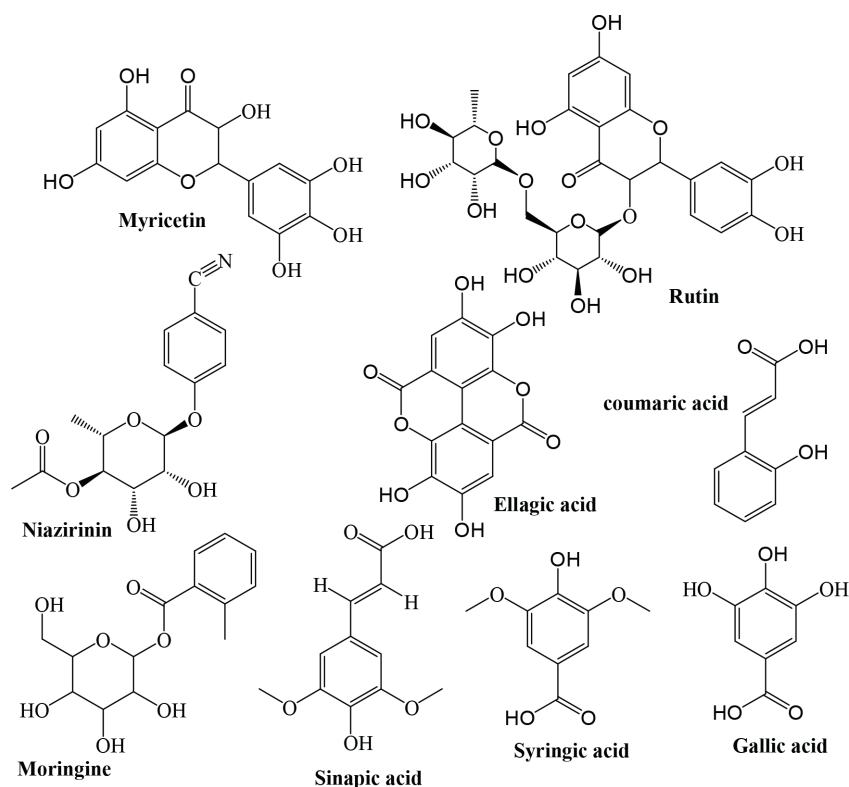


Figure 1.
 Some bioactive compounds in *Moringa oleifera* (MO) [8]. This figure illustrates the diversity of bioactive compounds present in *Moringa*. These compounds display a variety of structural features, including aromatic rings and bicyclic structures with different substituents. The presence of these compounds underlines *Moringa*'s potential as a functional food, suggesting that it is suitable for a wide range of applications in the promotion of health and well-being.

which can help reduce blood cholesterol levels. Other studies have shown that *Moringa* leaves contain glucosinolates with anticancer properties, as well as isothiocyanates that can be used as anti-inflammatories.

Stinging nettles contain lignans like secoisolariciresinol [9], which have potential health benefits, and tannins, which may have unique health benefits, particularly in traditional herbal medicine [10]. In addition to these compounds, studies show that *Urtica* is rich in phenolic compounds, flavonoids, triterpenes, coumarin, and sterols like beta-sitosterol (**Figure 2**).

Finally, studies on the chemical composition of *Moringa* [8] and *Urtica* [11] show that there are several common compounds (**Figure 3**) between these two plants. These common compounds are found in both plants but with varying concentrations.

2.2 Fatty acids

It is worth adding that the essential oil extracted from *Moringa* and *Urtica* seeds is rich in monounsaturated and polyunsaturated fatty acids [12, 13], such as oleic acid and linoleic acid, which are “beneficial for cardiovascular health.”

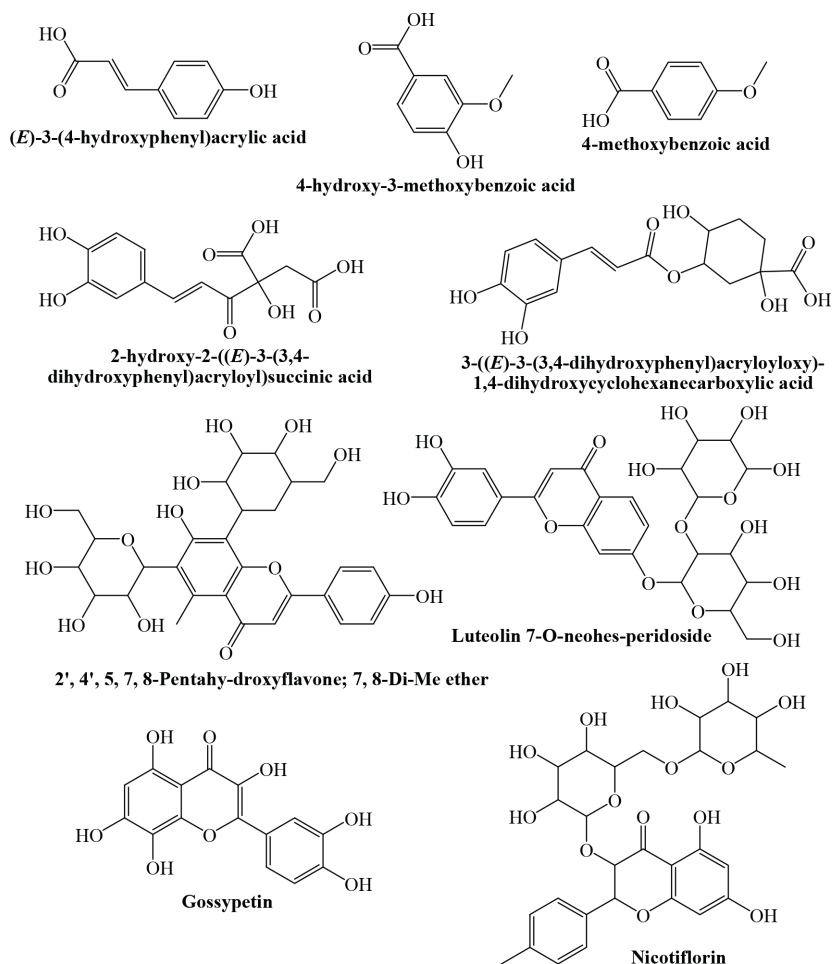


Figure 2.

Some bioactive compounds isolated from *Urtica dioica* (UD) [11]. The figure highlights the main aromatic compounds present in *Urtica*, also known as stinging nettle. These compounds encompass a wide range of phytochemicals, the most notable representatives of which are flavonoids and phenolic acids. Flavonoids and phenolic acids are well known for their medicinal properties, notably their antioxidant, anti-inflammatory and antimicrobial effects. These constituents are highly valued in traditional phytotherapy for their therapeutic potential. *Urtica* is traditionally used for its antiviral activities and anti-inflammatory properties. The antiviral effects are particularly important, as they contribute to *Urtica*'s ability to fight viral infections. In addition, its anti-inflammatory properties help relieve inflammatory conditions such as arthritis and allergies. Overall, the presence of these aromatic compounds in *Urtica* underlines its medicinal importance and supports its traditional use as a remedy for a variety of ailments.

2.2.1 Diabetes

Diabetes is a multifaceted condition closely linked to disturbances in insulin metabolism. This section aims to elucidate the chronological progression, diagnostic procedures, associated complications, and diabetes therapeutic approaches to promote a more comprehensive understanding of this disease. Moreover, the synthesis of the information presented here is summarized in **Figure 1**, which delineates the different stages of diabetes based on dynamic changes in the functionality of pancreatic β -cells, which play an essential role in the secretion of the hormone insulin. Besides the insulin resistance effect on diabetes complications, other hormones are implied in the blood's unbalanced glucose concentration, especially cortisol and ghrelin.

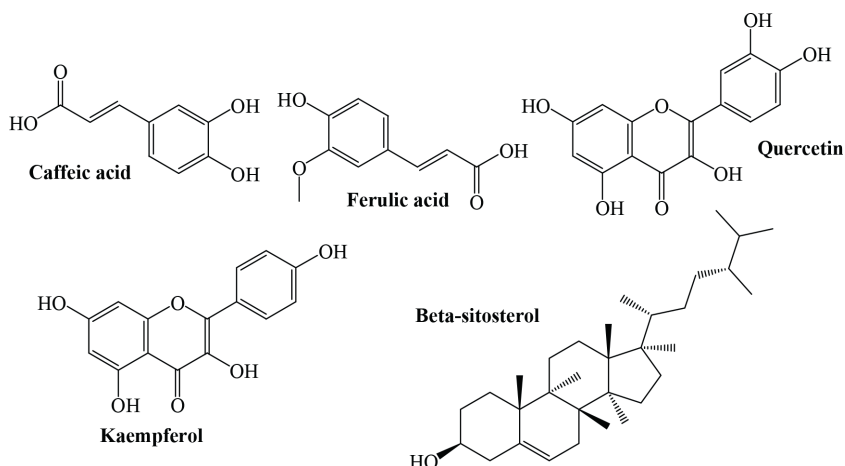


Figure 3.
Some of MO and UD common compounds. These compounds' illustrations give a concise overview of the compounds common to Moringa and Urtica. Phenolic acids and polyphenols are the predominant products in both plants, demonstrating their importance in terms of bioactive constituents. However, it should be noted that these compounds exist in varying concentrations in each plant species. This variation in concentration suggests that while Moringa and Urtica share common compounds, their compositions may differ, which could influence their individual therapeutic properties and applications.

2.2.2 Diabetes pathogenesis

According to the World Health Organization (WHO), in 1999, diabetes mellitus was defined as “multiple aetiology’s metabolic disorder which is caused by chronic hyperglycaemia accompanied by disorders of carbohydrate, lipid and protein metabolism resulting from abnormalities in insulin secretion, insulin action or both of them,” Nevertheless, insulin, a hormone produced by the islet cells of the pancreas, and glucagon, another hormone produced by the α cells of the pancreas, together regulate blood sugar levels [14]. Besides, high blood sugar levels trigger the release of insulin, which activates carbohydrates’ absorption, particularly glucose, via specific receptors in the muscles, adipose tissue, and liver. Additionally, two main pathogenic pathways contribute to chronic hyperglycaemia in diabetes: (i) destruction of β -cells leading to insufficient insulin production, and (ii) insufficient insulin action due to deficient insulin secretion and/or defects in insulin reactivity. Moreover, prolonged elevation of blood glucose levels can cause damage to various organs, including the eyes, kidneys, nerves, heart, and blood vessels.

2.2.3 Diabetes’s types

The World Health Organization (WHO) has first delineated diabetes into the following clinical categories [15]:

2.2.3.1 Type 1 diabetes

The first one or type 1 diabetes, results from the destruction of β -cells, usually leading to absolute insulin deficiency. The latter is an immune-mediated process (referred to as type 1A). Although a small subset of cases present with an idiopathic form of the disease (identified as type 1B). Its main clinical features include a sudden

onset at a young age (before 35), a normal body mass index (BMI), the introduction of insulin within 12 months of diagnosis, and an increased risk of diabetic ketoacidosis [16]. This form accounts for 5–10% of cases of diabetes.

2.2.3.2 Type 2 diabetes

Til 95% of diabetes cases belong to type 2, which arises owing to cell dysfunction, leading to a progressive insulin secretion loss amidst insulin resistance [15]. This diabetes's category onset is gradual and typically occurs at a later age which is notably distinct point from type 1. In addition, most individuals with this kind of diabetes are overweight or obese. Besides, they are less likely to require insulin treatment within 12 months of diagnosis, and they do not present ketoacidosis [16].

2.2.3.3 Gestational diabetes mellitus (GDM)

GDM is diagnosed during pregnancy, especially in the second or third trimester. Typically, it disappears after delivery, but some type 2 diabetes cases may be identified during pregnancy [15]. Overweight status, older age, family history of diabetes, or a personal history of GDM are the main risk factors. Nevertheless, lifestyle interventions and insulin injections may mitigate adverse pregnancy outcomes such as macrocosmic infants and preeclampsia.

2.2.3.4 Specific diabetes type (SDT)

This diabetes class may arise from a tremendous condition not encompassed within the previous ones. Nevertheless, included in this category are as follows:

- ailments affecting the exocrine pancreas,
- endocrine disorders,
- chemically induced diabetes (resulting from the administration of glucocorticoids or antifungals, e.g., pentamidine),
- infections,
- single-gene abnormalities impacting β -cell function,
- monogenic defects in insulin action,
- various genetic syndromes associated with diabetes such as Down syndrome or Klinefelter syndrome [16].

2.2.3.5 Diabetes's hybrid forms

This last one was considered by the World Health Organization (WHO) as a “Hybrid Forms of Diabetes,” which incorporates clinical presentations that amalgamate characteristics from both type 1 and type 2 diabetes [15]. Besides, it accommodates conditions such as slowly progressive immune-mediated diabetes, previously referred to as latent autoimmune diabetes in adults (LADA), where clinical features mirror those of type 2

diabetes, yet individuals display pancreatic autoantibodies. Additionally, ketosis-prone type 2 diabetes might be considered as “example for this diabetes type.”

2.2.4 Diagnostic profile

Globally, the diabetes's classic symptoms include polyuria, polydipsia, fatigue, and weakness. In type 1 diabetes, these symptoms may also be accompanied by weight loss despite an increased appetite and occasional blurred vision. Notably, type 1 diabetes symptoms tend to manifest rapidly within days or weeks, making it less likely that they will be detected during routine medical screenings [16].

Conversely, the onset of diabetes's type 2 onset often transpires without overt clinical manifestations, necessitating diagnoses during routine examinations. Beyond the conventional symptoms of diabetes, type 2 cases may manifest additional conditions such as skin infections or impaired wound healing. An estimated one-third of patients diagnosed with type 2 diabetes already present chronic complications at the diagnosis point.

2.2.4.1 Blood test for diabetes diagnosis (DD)

According to the diabetes diagnosis of WHO [17], the distinct advantages and insights related to the four prevalent blood tests employed for diagnosing diabetes and prediabetes are illustrated in **Table 1**.

2.2.5 Treatment

2.2.5.1 Lifestyle management

Firstly, embracing a health-conscious lifestyle serves as a cornerstone for both preventing diabetes and mitigating its potential complications [16]. Secondly, every meal should contain a carbohydrate, while adhering to principles of moderation regarding fat intake.

Nevertheless, by incorporating complex carbohydrates strategically across meals while factoring in the glycaemic index, diabetic individuals can ensure sustained energy levels while minimizing blood sugar spikes [21].

Owing to the increasing role of physical activity, the World Health Organization (WHO) generally recommends 150 minutes of moderate-intensity physical activity or 75 minutes per week of vigorous activity, which is recommended per week, tailored to the individual's age and capabilities. It might also help control blood sugar, reduce cardiovascular risk factors, and enhance overall well-being and mental health [20].

Because cardiovascular disease, premature mortality, and microvascular complications are major risk factors for smokers, individuals with diabetes are strongly encouraged to abstain from tobacco use [21].

2.2.5.2 Pharmacological treatment

2.2.5.2.1 Pharmacological type 1 diabetes treatment

Besides, the last one might result from combinations of intermediate or long action with rapid action. Moreover, people with type 1 diabetes need insulin treatment to survive (**Table 2**) [22].

Blood test	Features	Conditions and %
Hemoglobin A1c (HbA1c)	- Simply performed. - Diabetes and prediabetes diagnosis. - Linked to the glucose percentage which is attached to hemoglobin.	- No prior fasting required. - Blood sugar indicator. - Not affected by stress [18]. 6.5 and between 5.7 and 6.4 are, respectively, related to diabetes and prediabetes [19].
The plasma glucose (PG) value at any time	Similar diabetes symptoms	- No prior fasting required 11.1 mmol/l (200 mg/dl)
The oral glucose tolerance test (OGTT)	- DD - PG measurement	2 hours after taking syrup containing 75 grams of glucose. 7.8 and 11 mmol/l (140–199 mg/dl) for PG = [glucose intolerance] [19].
The fasting glucose test (FAG)	DD	- Measuring venous PG levels after 8 hours fasting. - DD measurements (twice) test is 7 mmol/l (≥ 126 mg/dl). 6.1 and 6.9 mmol/l (110–125 mg/dl) according to WHO. 5.6 and 6.9 mmol/l (100–125 mg/dl) according to American Diabetes Association (ADA) [20].

Table 1 explains that hemoglobin A1c (HbA1c) is a simple test used to diagnose diabetes and prediabetes. It measures the percentage of glucose bound to hemoglobin in the blood over time. Unlike other tests, it does not require fasting. HbA1c serves as an indicator of blood glucose levels and is not affected by stress. A result of 6.5 or more indicates diabetes, while a result between 5.7 and 6.4 indicates pre-diabetes. Besides, the plasma glucose (PG) value at any given time is a measure of glucose concentration in the blood. It presents symptoms like those of diabetes and does not require fasting before testing. A plasma glucose level of 11.1 mmol/l (200 mg/dl) or more indicates diabetes. The oral glucose tolerance test (OGTT) is a diagnostic test for diabetes. It involves measuring plasma glucose levels 2 hours after consuming a syrup containing 75 grams of glucose. If plasma glucose levels are between 7.8 and 11 mmol/l (140–199 mg/dl), this indicates glucose intolerance, which is a precursor to diabetes. The fasting plasma glucose test is a diagnostic test for diabetes. It involves measuring the glucose level in venous plasma after an 8-hour fasting period. A diagnosis of diabetes is made if the plasma glucose level is equal to or greater than 7 mmol/l (≥ 126 mg/dl) on two separate occasions. According to the World Health Organization (WHO), a fasting blood glucose level between 6.1 and 6.9 mmol/l (110–125 mg/dl) indicates impaired fasting glucose, while the American Diabetes Association (ADA) defines this range as between 5.6 and 6.9 mmol/l (100–125 mg/dl) [20].

Table 1.
Blood glucose tests features.

2.2.5.2.2 Pharmacological type 2 diabetes treatment

Managing diabetes type 2 primarily involves both dietary and lifestyle modifications.

Pharmacological intervention becomes necessary when glycaemic targets remain unattained, typically commencing with metformin, an oral hypoglycaemic agent belonging to the biguanide class [20]. According to French recommendations outlined

Insulin type	Features	Conditions
Fast-acting insulin	Action begins approximately 15 minutes after injection	Peaking at 1 hour and having effects for 2–4 hours
Intermediate-acting insulin	Its action begins between 2 and 4 hours after injection	Its peak is reached in 4–12 hours, and it is effective for 12–18 hours
Long-acting insulin	It reaches the bloodstream within a few hours of injection	Its action lasts 24 hours or more, without peak

Table 2 explains that the fast-acting insulin starts to work around 15 minutes after injection, with a peak at 1 hour and effects for 2–4 hours. Intermediate-acting insulin begins to act between 2 and 4 hours after injection, with a peak reached between 4 and 12 hours, and remains effective for 12–18 hours. Long-acting insulin reaches the bloodstream a few hours after injection, and its action lasts 24 hours or more, with no pronounced peak.

Table 2.
Insulin's categories.

by the High Authority of Health (HAS), this initial stage is defined as “monotherapy” [23]. In contrast, when glycaemic goals are not met, practitioners must introduce another medication, which allows “dual therapy by metformin and sulfonylurea combination.”

A third hypoglycaemic agent medication, either oral (such as alpha-glucosidase inhibitors, gliptins, or gliflozin's) or injectable (either insulin or glucagon-like peptide-1 [GLP-1] analogs) could be added when blood sugar levels could not decrease. Besides, patients with advanced stage, may combine “intermediate- or long-acting insulin” along with rapid-acting insulin.

Besides, controlling glucose levels remains essential for the human body balance owing to the pancreas's beta cells generating the hypoglycaemic hormone. Besides, this glucose metabolism steadiness could be reestablished by exploring its homeostasis regulation ways and consequences upon the pathological paths [24].

3. Insulin resistance and diabetes

Insulin resistance is a key pathophysiological and a powerful predictor of future type 2 diabetes mellitus, and metabolic syndrome is the foremost therapeutic target in the treatment of hyperglycaemia (**Figure 4**) [25]. Current research has shown that natural products including *Moringa oleifera* (commonly known as drumstick tree) and *Urtica dioica* (commonly known as stinging nettle) have promising beneficial effects on insulin resistance.

3.1 *Moringa oleifera*'s impacts upon insulin resistance and diabetes

3.1.1 *Moringa oleifera*'s effect upon insulin resistance

Moringa oleifera has gained a lot of attention in recent years due to its potential health benefits in managing insulin resistance, a condition associated with metabolic disorders and type 2 diabetes [26]. Various scientific research and studies have investigated the impact of *Moringa oleifera* on insulin resistance and have shown promising results.

Amelia et al. carried out the impact of *Moringa oleifera* on insulin levels and folliculogenesis in a polycystic ovary syndrome model rats with insulin resistance.

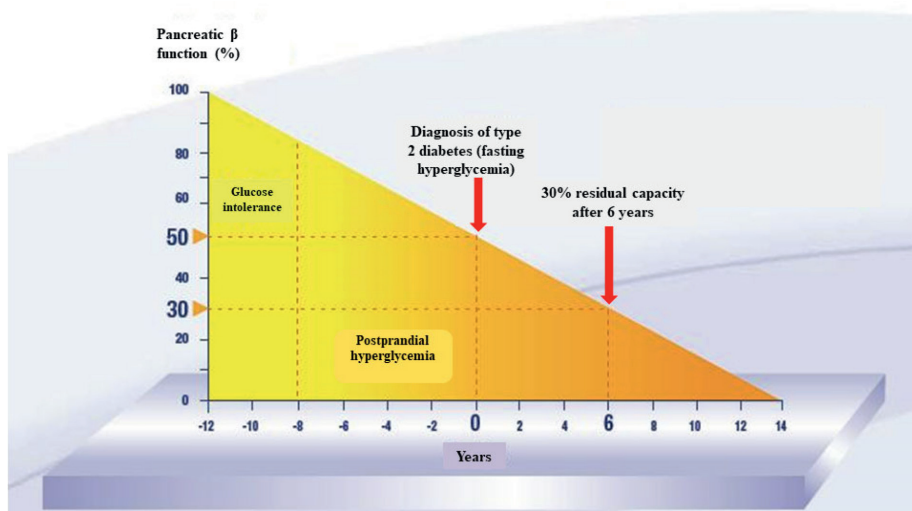


Figure 4.

Correlation between β -cell function and diabetes evolution: insulin resistance and impaired insulin secretion are two key factors in the development of type 2 diabetes (T2D). These factors often manifest themselves in people with pre-diabetes and progressively worsen over time. At the time of diagnosis, pancreatic beta-cell function is generally around 50% of normal, with an annual decline of around 5%. Research suggests that the decline in beta-cell function begins around 10–12 years before diagnosis, and by 6 years after diagnosis, it can fall to less than 25% of normal function. This highlights the progressive nature of β -cell dysfunction in the development and progression of T2DM.

The results showed that rats fed with *Moringa oleifera* extract showed an improvement in insulin sensitivity through increasing insulin signaling, leading to better glucose uptake and regulating folliculogenesis, thus managing insulin resistance associated with polycystic ovary syndrome [27]. Similarly, Divi et al. [28] investigate the potential therapeutic effects on diabetes and hyperlipidemia in insulin resistance rats. The study compares the effects of *Moringa oleifera* extract in streptozotocin-induced diabetes rats and insulin resistance in rats fed with a high-fructose diet. The results demonstrate that the aqueous extract of *Moringa oleifera* improves insulin sensitivity and regulates glucose levels, which could be crucial for treating polycystic ovary syndrome. Also, it ameliorates serum lipid profiles and corrects abdominal fat content [28]. Additionally, Siahaan et al. explore the effect of *Moringa oleifera* leaves on insulin and glucose levels in *Rattus norvegicus* polycystic ovary syndrome model. The study shows an enhancement in insulin levels, insulin sensitivity improvement, and regulation of glucose homeostasis in *Moringa oleifera* leaves treated rats (Table 3) [31].

Moreover, accumulating studies explore the impact of isothiocyanate-rich extract from *Moringa oleifera* extract on hepatic glucogenesis, weight gain, and insulin resistance in mice. Those results show that isothiocyanate-rich extract from *Moringa oleifera* inhibits hepatic glucogenesis, which is important in managing blood glucose levels, especially for those with insulin resistance. Furthermore, the extract has a significant effect on alleviating insulin resistance in HepG2 cells via enhancing glucose uptake modulation insulin signaling pathways and improving insulin sensitivity and glucose metabolism through activation of the AMPK pathway, a key player in regulating cellular energy balance [30, 32, 33]. Similarly, Gu et al. found that crud polysaccharides from *Moringa oleifera* improve insulin resistance in HepG2

Parameter	<i>Moringa oleifera</i>	<i>Urtica dioica</i>
Insulin sensitivity (IS)	Improves IS through increasing glucose uptake and insulin signaling pathways	Enhances IS via several molecular mechanisms, such as inhibition of inflammatory pathways and decreasing adiposity
Glucose homeostasis	Control blood glucose levels (BGL) through utilization and stimulation glucose uptake	Participate in the regulation of BGL by reducing insulin resistance-related metabolic and improving pancreatic β -cell function
Oxidative stress (OS)	Mitigates OS associated with insulin resistance	Decreasing OS, preserve and restore β -cell function
Inflammation (IM)	Decreases systemic IM and inhibits inflammatory pathways associated to insulin resistance	Improves insulin sensitivity by suppressing IM processes linked to insulin resistance.
Adiposity (AD)	Impairment of insulin resistance through AD reduction	Improves insulin sensitivity via decreasing AD and adipose tissue inflammation
Pancreatic function	Enhances pancreatic β -cell function and insulin production	Ameliorates insulin secretion, enhances glucose homeostasis, and improves β -cell function and glucose tolerance
Lipid metabolism (LM)	Reduces dyslipidemia, improves LM and regulates lipid metabolism profiles	Improves metabolism, decrease lipid levels and exhibits hypolipidemic activities

From this table, it demonstrates that *Moringa oleifera* and *Urtica dioica* both have beneficial effects on diabetes-related parameters. *Moringa oleifera* improves insulin sensitivity by enhancing glucose uptake and insulin signaling pathways, while *Urtica dioica* improves insulin sensitivity by inhibiting inflammatory pathways and reducing adiposity. Both plants contribute to glucose homeostasis, with *Moringa oleifera* promoting glucose utilization and absorption and *Urtica dioica* regulating blood sugar levels by reducing problems associated with insulin resistance and improving pancreatic β -cell function. In addition, they both alleviate the oxidative stress associated with insulin resistance, reduce inflammation, improve pancreatic function, and regulate lipid metabolism. *Moringa oleifera* reduces dyslipidaemia and improves lipid metabolism profiles, while *Urtica dioica* decreases lipid levels and exhibits hypolipidemic activities.

Table 3.
Effect of *Moringa oleifera* and *Urtica dioica* on insulin resistance [29, 30].

cells [34]. Additionally, another study conducted by Afifah et al. demonstrates that *Moringa oleifera* extract alleviates insulin resistance through increasing insulin and GLUT-2 expression in pancreatic islet cells, showing its potential therapeutic effects on improving insulin sensitivity and enhancing pancreatic β -cell function, ensuring an appropriate amount of insulin production, and improving pancreatic glucose sensing [35]. Moreover, molecular docking studies revealed that *Moringa oleifera* compounds interacted effectively with insulin tyrosine kinase receptors, showing its potential therapeutic effects on modulating insulin signaling pathways and managing diabetes [36].

3.1.2 *Moringa oleifera*'s effect upon diabetes

Of note, both phenolic and flavonoid *Moringa*'s compounds tested aqueous extract (MTAE) regenerate the pancreas's β -cells, which boosts insulin secretion [37]. In the second one's case, their oxidative activity's inhibition is due to proton donors. Also, carotenoids and phenolic compounds are among *Moringa*'s leaves' phytochemicals. Besides, lipid peroxidation is prevented by antioxidants *Moringa* plant peroxyl radicals, while the ability to trap elements such as hydroxyl radicals is attributed to phenolic compounds [38]. Considering glucose, whether

in hypoglycemia or hyperglycemia, with insulin levels which are inversely proportional, on the first hand, they are a condition where the blood glucose levels are respectively less than 60 mg/dl and more than 180 mg/dl. On the other hand, organs might be damaged when their concentration is higher than 125 mg/dl. For this, extra insulin doses decrease blood sugar levels and prevent the consequent glucose level complications fluctuations. Back to phototherapeutics implication, being considered as the best medicinal plant, *Moringa oleifera* could help combat a tremendous disease, especially diabetes mellitus [39]. Furthermore, thanks to their phytochemicals, *Moringa* leaves significantly affect pancreatic insulin. Among them, antioxidants can prevent lipid peroxidation, as mentioned above. These nutraceuticals are involved in preventing diabetes mellitus onset, progression, and complications [39].

3.2 *Urtica dioica*'s impacts upon insulin resistance and diabetes

3.2.1 *Urtica dioica* and insulin resistance

Urtica dioica, commonly known as stinging nettle, has been studied for its potential health benefits, such as insulin resistance, suggesting the potential effect of this plant in improving glucose metabolism and preventing type 2 diabetes [40, 41]. *Urtica dioica* contains a variety of bioactive compounds, including lectins, phenolic acids, triterpenes, sterols, and flavonoids, which have shown antioxidant, anti-inflammatory, and antidiabetic activities [42]. Various studies have explored the effects of *Urtica dioica* on diabetes and insulin resistance. Shahrokhi through a randomized controlled trial, showed a significant reduction in HbA1c levels in the *Urtica dioica* treated group compared to the placebo group. This study suggests that *Urtica dioica* could be used as adjunctive therapy in type 1 diabetes mellitus as it demonstrates a positive impact on preserving pancreatic β -cell function and enhancing insulin sensitivity via the reduction in HbA1c [43]. Fan also investigates the potential use of *Urtica dioica* in mitigating insulin resistance and fat accumulation using a prediabetic mouse model. The result showed an increase in insulin sensitivity and an improvement in glucose tolerance in mice fed with *Urtica dioica*, indicating its promising role in managing metabolic syndrome such as diabetes [29]. In addition, *Urtica dioica* extract exhibits a significant amelioration in insulin sensitivity in obese mice through inhibition of PP2A activity, which phosphorylates insulin receptor substrates, leading to enhanced glucose uptake and insulin signaling pathways in skeletal muscle cells [44]. Another study found that *Urtica dioica* leaf extract stimulates insulin secretion in isolated islets of Langerhans cells and improves glucose tolerance in streptozotocin-induced diabetic rats, suggesting its potential therapeutic role in treating diabetes [45].

3.2.2 *Urtica dioica* and diabetes

Nettle has several properties related to insulin, such as insulin sensitivity and secretagogue. It also has several properties related to insulin such as being insulin-sensitizing and secretagogue. In addition, the intestine is the starting line related to the nettle's action, where it acts either on the underlying tissues or glucose absorption, respectively. This glucose absorption mechanism is based upon enzyme inhibiting detailed (e.g., α -amylase), as shown in **Figure 5**, which is involved in the carbohydrate compounds digestion via the enzymatic pathway.

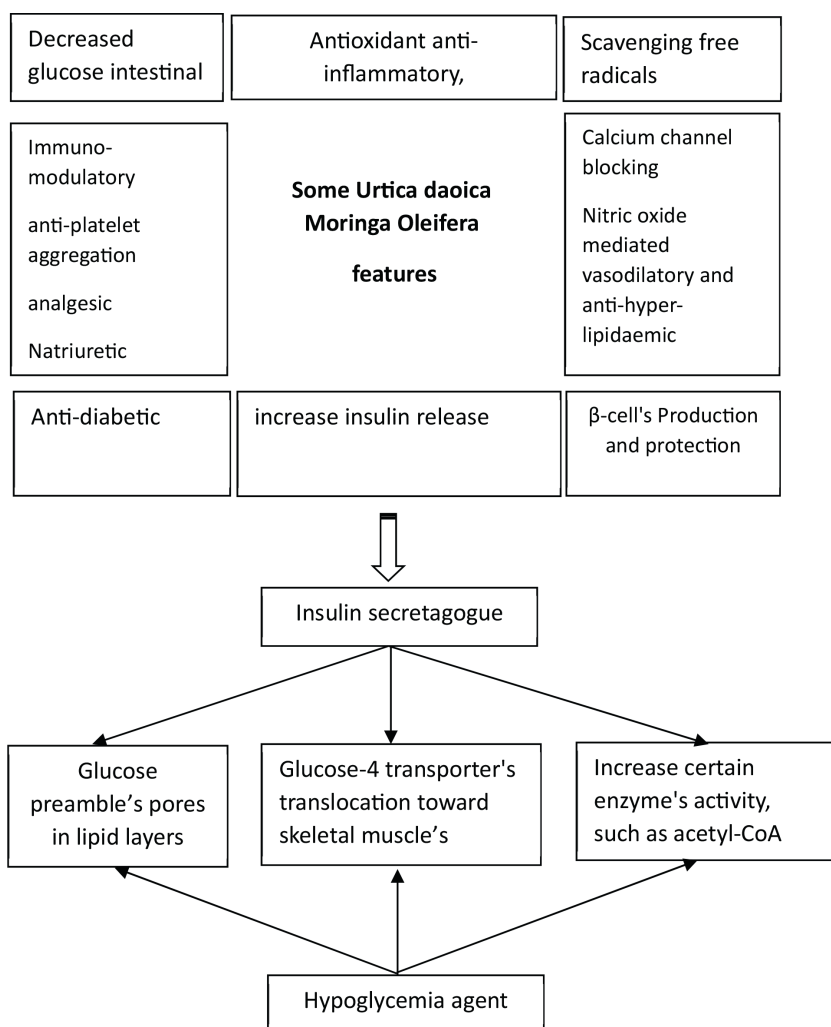


Figure 5.

Both of *Urtica dioica* and *Moringa oleifera* properties with main PAM's actions upon human antidiabetic mechanism: Anti-diabetic agents often work by increasing insulin release from the pancreatic β -cells, which are responsible for insulin production. In addition, some compounds have protective effects on β -cells, shielding them from damage and promoting their regeneration. This dual action not only helps regulate blood sugar levels but also preserves the functionality and integrity of pancreatic β -cells, thus contributing to the long-term management of diabetes. Insulin secretagogues increase insulin release from pancreatic β -cells, leading to a reduction in blood glucose levels. They also facilitate glucose transport into cells, improve glucose utilization by skeletal muscle, and increase enzymatic activity for energy production. This overall action helps manage diabetes by improving glycemic control and metabolic function.

4. Conclusion

Both *Moringa oleifera* and *Urtica dioica* present hypoglycaemic properties, giving them the ability to prevent diabetes's onset and even help treat it, owing to their bioactive phytochemicals. Their ability to improve insulin sensitivity, regulate blood glucose levels, mitigate oxidative stress, and reduce inflammation makes them valuable in addressing insulin resistance and related metabolic disorders. Further research and exploration of the mechanisms underlying their effects on diabetes are

warranted to harness their full therapeutic potential. The biochemical properties of *Moringa oleifera* and *Urtica dioica* offer valuable insights into their potential as natural remedies for diabetes prevention and treatment. Their diverse range of bioactive compounds and their impact on insulin resistance and glucose metabolism make them promising candidates for further investigation in the field of diabetes management. Nevertheless, understanding the mechanisms of glucose metabolism and homeostasis is crucial for effectively managing diabetes, and these plant models offer valuable insights into this research area. Moreover, studies are needed to explore the specific mechanisms by which *Moringa oleifera* and *Urtica dioica* regulate blood sugar levels.

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