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ANTIDIABETIC PROPERTY OF MEDICINAL PLANTS IN MALAYSIA

NUR AKMAL, I[1,3]*, MUHAJIR, H[2] AND NUR ATHIRAH, Z[3]

[1]Unit of Biology, Centre of Foundation Studies for Agricultural Science, Universiti Putra Malaysia (UPM), 43400 Serdang, Selangor, Malaysia. [2]Department of Microbiology, Faculty of Biotechnology and Molecular Science, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia. [3]Natural Medicine and Products Research Laboratory, Institute of Bioscience, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor Darul Ehsan, Malaysia.

**Corresponding author: nur_akmal@upm.edu.my*
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Abstract: Medicinal plants, natural products, and phytochemicals are widely used globally as alternative medicines in the management and treatment of various diseases, including diabetes. Diabetes is a complex metabolic disorder caused by reduced insulin secretion, insulin resistance, or a combination of both. The fast-rising prevalence of diabetes indicated that the optimum control of the diabetic epidemic is still not achieved. Uncontrolled diabetes can lead to a myriad of complications such as kidney problems, loss of vision, amputation, and death. Furthermore, diabetic patients are more predisposed to the infection of COVID-19 infection, thus making them more vulnerable during the current pandemic. Therefore, it is vital to provide effective treatment for diabetic patients to reduce the complications of diabetes. The potential of medicinal plants and their phytochemicals as antidiabetic agents have been reported by many previous researchers. Every part of the plants including the leaves, roots, fruits, seeds, and stems have been associated with significant outcomes in diabetes treatment. This review aimed to provide an update on the review of the roles and mechanisms of medicinal plants in the treatment of diabetes. A literature search was performed on different scientific search engines using the keywords "antidiabetic", "medicinal plants", "phytochemicals", "mechanism of actions", "extraction", "glucose uptake", and "insulin secretion". The data obtained indicated that phytochemicals such as phenolics, flavonoids, glycosides, tannins, and alkaloids extracted from the leaves, fruits, seeds and stems exhibited antidiabetic properties. This review also suggested that phytochemicals from medicinal plants exhibited antidiabetic properties via various mechanisms in the treatment of diabetes. In short, these findings will provide important insights into the future development of antidiabetic drugs.

Keywords: Antidiabetic, Diabetes, Glucose uptake, Insulin resistance, Medicinal plants, Natural products, Phytochemicals.

Introduction

Diabetes mellitus (DM) is a metabolic disorder that has grown to become a major global health epidemic. In general, DM is characterised by hyperglycaemia in which a fasting plasma glucose level of ≥7.0mmol/L is detected in the presence or absence of insulin resistance. Diabetic patients commonly manifest symptoms such as excessive thirst (polydipsia), excessive hunger (polyphagia), and an unusually large volume of urine (polyuria) (WHO, 2013). Based on the World Health Organization (WHO) (2013), DM can be classified into type 1, type 2, and gestational diabetes according to the clinical stages and aetiological types. Type 1 DM is a result of deficient insulin production from β-cell destruction. Thus, it is also known as insulin-dependent DM (Tuomi, 2005). Meanwhile, Monnier *et al.* (2008) specifically defined type 2 DM (T2DM) as β-cell dysfunction and insulin resistance. Insulin resistance is referred to impaired clearance of insulin-mediated glucose into the peripheral tissues. Disease progression will lead to tissue damage and various complications such as cardiovascular diseases, nephropathy, retinopathy, and neuropathy (Vaiseh *et al.,* 2015; Litwak *et al.,* 2013). As for the third type of DM, gestational DM is characterised by elevated blood glucose levels during pregnancy. However, the condition can sometimes resolve after pregnancy (Olmos *et al.,* 2020).

In the past decade, the incidence of T2DM has escalated into a worldwide epidemic. The International Diabetes Federation (IDF) (2019) reported that approximately 463 million adults suffered from T2DM in 2019. It is projected that the global prevalence could reach 578 million by 2030 and 700 million by 2045 if no urgent action is taken. Internationally, the highest prevalence of diabetes is found in China with 116.4 million, followed by India with 77 million, and the United States of America 31 million (IDF, 2019). Similarly, the diabetes prevalence in Malaysia has also been showing an upward trend. According to the third National Health and Mobility Survey in 2019, there were a total of 3.9 million adults aged 18 years and above diagnosed with T2DM in Malaysia in 2019 (National Health and Morbidity Survey, 2019). The diabetes prevalence was the highest among people aged 60 and above (41.5%). Meanwhile, the prevalence of diabetes across different states in Malaysia showed the highest rate in Negeri Sembilan (33.2%), followed by Perlis (32.6%), and Pahang (25.7%).

DM is associated with reduced productivity and negative economic growth of countries. In 2019, health expenditure related to DM amounted to at least USD 760 billion worldwide (IDF, 2019). Furthermore, it is predicted that the global epidemiological burden of DM will continue to increase along with its long-term life- threatening complications and possible side effects from synthetic antidiabetic drugs. Previous studies have established that hyperglycaemia is associated with an increased number of mortalities among diabetic patients with stroke, heart attack, pneumonia, and surgical history. Worse still, diabetic patients have been shown to be more severely affected by the current COVID-19 pandemic. They are predisposed to twice the risk of death and an increased risk of severe complications compared to the healthy population (Gupta *et al.,* 2020).

Lifestyle, dietary composition, and genetic predisposition are major risk factors that affect both the development of diabetes and its complications (Chan *et al.,* 2007; Weber & Narayan, 2008; Kontogianni *et al.,* 2012). The shift from traditional to urban lifestyle has changed the pattern and activities of mankind. According to Leahy (2005), sedentary lifestyles such as watching too much television, consuming high calorie foods, not performing sufficient physical activity, and relying on automobile transportations such as cars are common in modern living. High calorie foods such as fatty foods can induce the development of diabetes as it influences glucose metabolism via several mechanisms such as defective cell membrane function, insulin signalling, enzyme activity, and gene expression (Risérus *et al.,* 2009).

In the past few decades, Malaysia has been slowly transitioning from an agricultural country to an urbanised industrial country. Parallel with this transition, the Malaysian people also experience certain impacts from the perspective of socioeconomic status and lifestyle changes. With the shift from agricultural activity to industrial activity, the local population becomes less involved in physical activity. Furthermore, there is also a change in the dietary pattern whereby the consumption of food with high fat content gains more popularity. All these modifications can exert undesirable effects on health as evidenced by the rising prevalence of various non-communicable diseases such as diabetes and obesity among the Malaysian population (Jamal *et al.,* 2014). In view of the worsening situation, Malaysia has taken vigorous actions to control this problem. For instance, the Ministry of Health Malaysia conducted a nationwide programme to promote healthy lifestyles in terms of dietary intake and physical activity. Based on the Malaysian Medical Nutritional Therapy Guidelines for T2DM (Malaysian Dietitians' Association, 2013), diabetic patients are recommended to consume a high fibre diet (20 – 30 g fibre/day) consisting of vegetables, fruits, legumes, and whole grain cereals. Meanwhile, their cholesterol intake must be limited to less than 200 mg/day. In terms of physical activity, Malaysians are encouraged to perform at least 30 minute of exercise three times per week. Based on a published study, this programme has successfully increased the awareness of a healthy lifestyle among the Malaysian population (Hussein *et al.,* 2015).

Managing Diabetes

A clear understanding of the pathogenesis of T2DM has enabled scientists to find a better approach in preventing and treating diabetes. The modification from a sedentary lifestyle to the uptake of mild exercise is a pre-treatment requirement for diabetic patients. Excessive body weight can be reduced by increasing the energy expenditure during exercise. Subsequently, insulin sensitivity and glucose tolerance will improve (DeFronzo & Abdul Ghani, 2011). Meanwhile, consumption of healthy diet consisting of low fat, high fibre, and the necessary micronutrients is recommended for the prevention and treatment of T2DM (Schwingshackl & Hoffman, 2013). In addition to physical exercise and dietary management, a pharmaceutical approach can also be used to treat T2DM. Currently, there are five major classes of therapeutic drugs for the treatment of T2DM, namely sulfonylureas, biguanides, thiazolidinediones, meglitinides, and α-glucosidase inhibitors. They are classified based on the mechanism of action on multiple target sites, either through reduction of glucose absorption in the intestines, an increase of insulin secretion, or the stimulation of PPAR (Patel *et al.,* 2012). According to Bastaki (2005), the combination of two drugs such as metformin and sulfonylurea can increase the hypoglycaemic activity via the dual mode of action. Despite the effectiveness of antidiabetic drugs, their prolonged usage can potentially cause adverse effects due to the increased risk of lactic acidosis, hypoglycaemia (Fatima *et al*., 2018), congestive heart failure, rapid weight gain, bones fractures, and stroke (Sharma *et al*., 2017; Ahn & Lim, 2019). Thus, natural products especially plant-based materials have been increasingly explored as an alternative form of antidiabetic medicine.

In the past, many traditional medicines were developed from plants. With the advancement of modern technology, many plant-based therapeutic agents have undergone a substantial evolutionary process to improve their benefits. Nowadays, ethnopharmacotherapy is widely accepted among individuals and communities as a type of alternative medicine. Ethnopharmacology is a study of biologically active agents that are traditionally applied or observed by individuals in the local communities (Baars & Hamre, 2017). Therefore, the description of the use and effect of traditional remedies, identification of bioactive compounds, phytochemicals, and the relevant pharmacological studies are all under the scope of ethnopharmacology (Chugh *et al.,* 2018). Many of the findings regarding ethnopharmacology are based on folklore resources. Thus, they need to be further examined by modern technologies and properly documented for future application.

In order to improve the utilisation of herbal products, any medicinal products that contain parts of plants need to be evaluated from the perspective of side effects, effectiveness, dosage, and active ingredients (Patwardhan, 2005) to establish their scientific basis. For example, *Momordica charantia* has been used as a folk medicine all over the world to treat different types of diseases including diabetes (Polito *et al.,* 2016). Examination by modern scientific technology showed that *M. charantia* possesses antidiabetic properties (Saad *et al*., 2017). With the establishment of proper scientific evidence, several *M. charantia* products are now commercialised and made available in the market. Type equation here.

The Use of Medicinal Plants in Diabetes Management

High demand for alternative treatment in diabetes has led scientists to investigate potential plant-based antidiabetic agents because of the minimal side effects compared to other synthetic medications (Bharti *et al*., 2018, Moradi *et al*., 2018, Singh *et al.,* 2007). The plant-based antidiabetic drugs currently available in the market nowadays have different modes of action in the amelioration of diabetic problems.

They can act by 1) improving activation of 5' iadenosine monophosphate-activated protein kinase (AMPK) and peroxisome proliferator-activated receptors (PPARs) (Ren *et al.,* 2019), 2) inhibiting α-amylase and α-glucosidase levels (Jhong *et al.,* 2015), 3) increasing activation of insulin receptor (Kasuga, 2019), 4) increasing the levels of hormone or cytokine (Achari & Jain, 2017), and 5) inducing a hypolipidaemic effect (Wu & Xu, 2018). Although these modes of action are similar to antidiabetic drugs such as metformin and thiazolidinediones (TZD), plant-based antidiabetic drugs contain a diverse range of phytochemicals that displays a variety of mechanisms that are likely to be involved in the prevention and treatment of T2DM. Thus, it is vital to obtain a proper understanding of the mechanism of actions of these plant- and herb-based drugs on ameliorating the diabetes problem to maximise their potentials in diabetic treatment.

One of the common pharmacological effects of antidiabetic plants is the retardation of the absorption of glucose in the digestive tract via the inhibition of α-amylase and α-glucosidase (Jhong *et al.,* 2015). These enzymes delay carbohydrate digestion and decrease the postprandial hyperglycaemia in diabetic patients (Zhu *et al.,* 2020). An *in-vitro* study by Zabidi *et al.* (2021) showed that *Curculigo latifolia* extract could inhibit α-glucosidase activity. This finding has been supported by molecular docking data. The results revealed that phlorizin, a compound found in the *C. latifolia,* bound strongly with α-glucosidase. Therefore, *C. latifolia* is a potential α-glucosidase inhibitor in lowering post-prandial hyperglycaemia.

Apart from that, some antidiabetic plants also possess insulin-mimetics and/or insulin-sensitising effects on the insulin receptor, thus influencing the blood glucose level (Salehi *et al.,* 2019). *Abies pindrow* (morinda), *Acacia arabica* (babool), and *Aloe barbadensis* (Gheequar) are examples of plants that exert these effects. They enhance the insulin signalling by triggering the insulin receptors on the cells and then increase the regulation of glucose uptake by the translocation of GLUT4 (Patel *et al.,* 2012, Hedge *et al.,* 2014). Moreover, insulin sensitiser can also act through the nuclear receptor, i.e., PPARγ as antidiabetic activity of plant has been correlated with PPARγ transactivation potency in a recent study (Shao *et al.,* 2016).

Furthermore, another property of the antidiabetic plant is the stimulation of hormone secretion such as adiponectin, leptin, and resistin. These hormones are derived from the adipose tissues and play a role in modulating metabolic processes such as glucose uptake, gluconeogenesis, and fatty acid oxidation (Mirza *et al.,* 2019). Besides, these hormones are also involved in food intake, energy expenditure, and body weight maintenance (Robertson, 2016, Guerre-Millo, 2008). *Monolluma quadrangular* is a succulent bush plant traditionally used to treat diabetes. A recent study revealed that *M. quadrangular* ameliorates the metabolic disturbances in rats with T2DM by increasing the serum adiponectin level and the gene expression of hepatic adiponectin (Bin-Jumah, 2019). Another plant, *Mangifera indica* L., or more commonly known as mango, showed a high concentration of phytochemical compounds (mangiferin, myo-inositol, and γ-oryzanol) with antidiabetic activity (Kozuka *et al.,* 2013). Thus, it is involved in the secretion of adiponectin and regulation of adipogenesis in 3T3-L1 adipocyte cells (Sferrazzo *et al.,* 2019).

Additionally, recent findings showed that bioactive compounds in antidiabetic plants have a synergistic effect as they can ameliorate diabetic problems by improving both the blood glucose level and lipid profiles of the patients (Salehi *et al.,* 2019). Moreover, PPARs and AMPK have become the main pharmacological targets in the treatment of insulin resistance (Janani & Ranjitha Kumari, 2015). Improvement in the activation of AMPK and PPARs results in increased transportation of glucose transporter to the plasma membrane through the classical insulin-signalling pathway. Moreover, it also increases insulin sensitivity in the peripheral tissues (Ren *et al.,* 2019). An *in-vitro* study showed that the extracts from ethanolic chamomile (*Matricaria recutita*) flowers could trigger PPARγ in human primary adipocytes. This finding complemented and supported the evidence that plant-based agents help to manage diabetic problems via reduced insulin resistance and glucose intolerance, as well as improved lipid profiles (Weidner *et al.,* 2013).

Bioactive Compounds of Antidiabetic Plants

Polyphenols

Plants are rich in phytochemicals. The most widely distributed phytochemical in plant-based diets such as vegetables, fruits, cereals, and beverages are polyphenols. It can be divided into five subgroups, i.e., flavonoids, phenolic acids, lignans, stilbenes, and others. These phenolic compounds are known to produce the colour and sensory characteristics of the plant. Besides, it also plays an important role in the growth and development of the plants (Balasundram *et al.,* 2006). From another point of view, the phenolic compounds in plants have been associated with a reduced risk of human diseases. It exhibits a wide range of health benefits such as antidiabetic, antimicrobial, anticancer, antioxidant, and anti-inflammatory properties (Manach *et al.,* 2004; Kim *et al.,* 2016; Guasch-Ferre *et al.,* 2017). Evidence also suggests that the antioxidant properties of the phenolic compounds reduce the risk of diabetes, cancer, and cardiovascular diseases (Raghavan *et al.,* 2008). Several studies also reported on the association between dietary intake of polyphenols such as flavonoids with T2DM. It influences glucose metabolism through the inhibition of glucose absorption in the intestine and/or inhibition of glucose uptake in the peripheral tissues (Salehi *et al.,* 2019, Chen *et al.,* 2018, Kozuka et al., 2013). Besides, these polyphenols also improve insulin resistance by activating the insulin action (Esfandiar *et al.,* 2020).

A recent study by Gulcin et al. (2020) showed that kaempferol-3-O-rutinoside (Figure 1) in the methanol extract of *Mentha pulegium* significantly inhibited the action of α-glycosidase and α-amylase. It was reported that quercetin, myricetin, and resveratrol (Figure 1) in red grapes possess antihyperglycaemic properties and can retard the development of diabetic complications (Pandey & Rizvi, 2014). Furthermore, the polyphenols from aqueous cinnamon extract (CE) also display antihyperglycemic activity, most probably via the inhibition of hepatic glucose production. Another study highlighted that water soluble polyphenols from CE decreased the gene expression of two major regulators of hepatic gluconeogenesis, i.e., phosphoenolpyruvate carboxykinase and glucose-6-phosphatase (Cheng *et al.,* 2012). Therefore, polyphenols could be a promising therapy in the treatment of T2DM and its complications.

Polysaccharides

Polysaccharides are the most abundantly available natural biopolymer. The properties of polysaccharides are based on the type of chain branching, the type of monosaccharides in the polymer backbone, and the type of linkage between residues (Chen *et al.,* 2016). In plants, starch and cellulose (Figure 1) are the most common polysaccharides. Starch is digestible storage of polysaccharides while cellulose is a prime structural component of plant cell walls. In addition, some polysaccharides are proven to have nutritional and health benefits (Zeng *et al.,* 2019). The antidiabetic function of polysaccharides has been reported in several studies. According to Bai *et al.* (2020), polysaccharides derived from six legumes (soybean, white kidney bean, red kidney bean, small black soybean, field bean, and lentil) exerted antidiabetic properties in high-fat diet and streptozotocin (STZ)-induced T2DM mice. The results also showed that polysaccharides from red kidney beans (RK) decreased the levels of fasting blood glucose, total cholesterol, triglycerides, and insulin resistance (Bai *et al.,* 2020).

Additionally, it was reported that polysaccharides from *Momordica charantia* L. (*M. charantia*) showed antihyperglycaemic activities in a high fat diet and STZ-induced T2DM mice by repairing the damage that

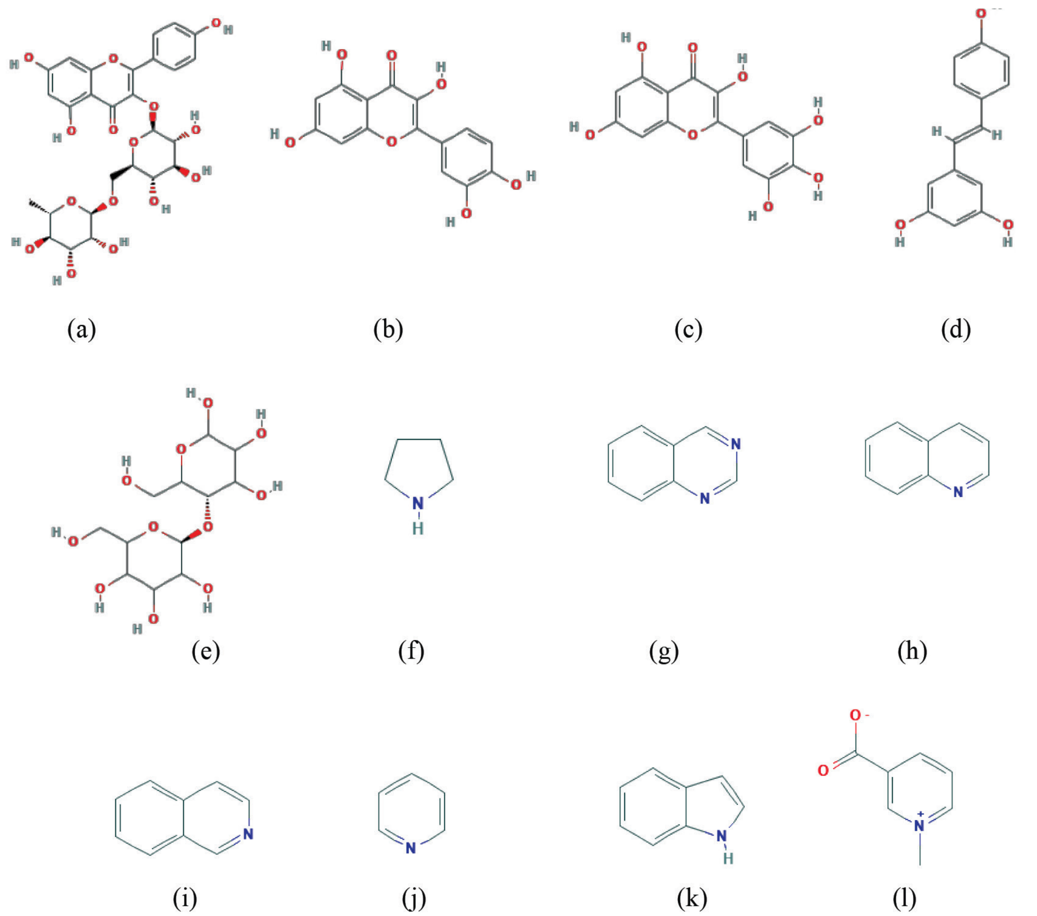

Figure 1: Chemical structures of selected phytochemicals found in antidiabetic plants; a) kaempferol-3-O-rutinoside, b) quercetin, c) myricetin, d) resveratrol, e) cellulose, f) pyrrolidine, g) quinazoline, h) quinoline, i) isoquinoline, j) pyridine, k) indole, and l) trigonelline

was caused by STZ on pancreatic β cells. Subsequently, such activities by polysaccharides may prevent the development of further diabetic complications in pancreatic cells (Wang *et al.,* 2019). In another study, polysaccharides-rich extract from *Apocynum venetum* leaves showed significant antihypoglycaemic effects by decreasing the levels of fasting blood glucose, serum insulin, glycated serum protein, as well as improving serum lipids profiles including lowering the levels of total cholesterol, triacylglycerols, low-density lipoprotein cholesterol, and non-esterified fatty acid (Zhou *et al.,* 2020; Yuan *et al.,* 2020). Furthermore, another study also indicated that polysaccharide-rich extracts could modulate the gut microbiota in diabetic rats (Yuan *et al.,* 2020). All of these findings provided new insights that facilitated the exploitation of polysaccharides as a promising antidiabetic nutraceutical for T2DM.

Alkaloids

Alkaloids are mainly found in coffee, cocoa beans, and tea leaves. These natural compounds are categorised into several main groups including pyrrolidine, quinazoline, quinoline, isoquinoline, pyridine, and indole (Figure 1) (Memariani *et al.,* 2020). Although certain alkaloids can be pharmacologically active to the extent of being poisonous in high doses, some alkaloids in foods are safe to be consumed daily. A study by Fernandez-Gomez *et al.* showed that coffee silver skin from the Arabica (*Coffea arabica*) extract could reduce the risk of diabetes through pancreatic protection. The substance exhibits antidiabetic activity by increasing insulin secretion and providing protection for the INS-1E cells (Fernandez-Gomez, 2016). Furthermore, trigonelline (Figure 1), a major alkaloid component of fenugreek, was reported to display hypoglycaemic and hypolipidaemic effects by attenuating the high levels of glucose and glycosylated haemoglobin. Hence, the insulin level was improved following enhancement in the hepatic and muscular glycogen content in HFD/STZ-induced T2DM rats (Subramanian & Prasath, 2014). Furthermore, the potential of alkaloids as antidiabetic agents was also found in steroidal alkaloids isolated from *Sarcococca saligna* whereby its hypoglycaemic effect was found to improve diabetic-associated complications in a recent study (Jan *et al.,* 2018).

Antidiabetic plants in Malaysia

Malaysia is rich in natural resources. It is known as one of the world's 17 mega biodiversity-rich countries (Institute for Medical Research, 2002; Ang, 2004). Hence, Malaysia is committed to conserve biological diversity and to promote sustainable use to ensure fair and equitable sharing of the benefits arising from the utilization of these biological resources. These commitments are outlined in the National Policy on Biological Diversity 2016 - 2025 (Ministry of Natural Resources and Environment, 2017). There are approximately 1300 plants with potential medicinal properties that can be used as traditional medicines (Jantan, 2004). Furthermore, every part of the plant has been examined to obtain active components that can exhibit therapeutic effects. Many of these plant species are indigenous to Malaysia, thus making them a natural asset that is truly worth conserving. Apart from that, many native communities in Malaysia still depend on traditional medicines to fulfil their healthcare needs. Moreover, plants and plant products have also been incorporated as part of the component of many modern commercial drugs, such as bitter gourd (*Momordica charanthia*), *petai belalang* (*Leucaena leucocephala*), *hempedu bumi* (*Andrographis paniculata*), *belalai gajah* (*Clinacanthus nutans*), *mas cotek* (*Ficus deltoidea*), *senduduk* (*Melastoma malabathricum*), and others. All these plants have shown potential health benefits in the prevention and treatment of diabetes (Table 1).

Table 1: Antidiabetic plants in Malaysia

Plant	Common Name	Effect and Mechanisms	References
Momordica charanthia	Bitter gourd	Phytochemicals such as proteins, polysaccharides, flavonoids, triterpenes, saponins, ascorbic acid, and steroids showed antioxidant, antibacterial, antiviral, hypoglycaemic, hypolipidaemia, hepatoprotective, anticancer, and anti-inflammatory activities	Zhang, Lin & Xie, 2016, Chen *et al.,* 2019, Wang *et al.,* 2016, Jia *et al.,* 2017, Thent *et al.,* 2018
		M. charanthia fruit extracts showed antidiabetic properties by improving glucose uptake at the isolated rat diaphragm muscles in the presence and absence of insulin.	Tan *et al.,* 2016, Wang *et al.,* 2016

		M. charanthia fruit improved the histopathological features of the pancreatic cells due to its antioxidant activity.	Mahmoud *et al.,* 2017
		Aqueous extract of *M. charanthia* fruit stimulated insulin secretion by the β cells in pancreatic islets isolated from obese-hyperglycaemic mice.	Jia *et al.,* 2017
		M. charanthia inhibited intestinal glucose absorption and fat synthesis by the stimulation of auxiliary lipid-lowering activity.	Wang *et al.,* 2017 Fan *et al.,* 2019
*Leucaena leucocephal*a	*Petai belalang*	Kaempferol-3-O-rutinoside contained in *L. leucocephala* leaves showed lower gastrointestinal absorption due to its binding affinity on protein dipeptidyl peptidase-4 and α-glucosidase in the molecular docking study.	Nurmaylindha *et al.,* 2020
		Seed extracts significantly decreased the blood glucose level and increased the serum insulin level in diabetic-treated rats.	Chowtivannakul *et al.,* 2016
		L. leucocephala fruit aqueous extract stimulated adipogenesis, lipolysis, and glucose uptake by upregulation of Glucose Transporter 4 (GLUT4) and Hormone Sensitive Lipase (HSL).	Kuppusamy *et al.,* 2014
		The seed extracts inhibited the elevation in blood glucose and lipid levels. They also increased the number of pancreatic islets.	Syamsudin & Simanjuntak, 2010
Andrographis paniculata	*Hempedu bumi*	Hypoglycaemic properties of *A. paniculata* active compound i.e., andrographolide reduced pre- and postprandial blood glucose levels and expression of GLUT-4 protein in muscle tissues.	Komalasari & Harimurti, 2015
		A. paniculata powder reduced fasting blood glucose, oral glucose tolerance, serum insulin, lipid profile, and glucose uptake in high fat and sucrose-induced type-2 diabetic rat.	Augustine *et al.,* 2014
		Reduced number of HOMA-IR index (Homeostatic Model Assessment-Insulin Resistance).	Nugroho *et al.,* 2012

Clinacanthus nutans	*Belalai gajah*	The *n*-hexane of *C. nutans* leaves fraction exhibited the highest α-glucosidase inhibitory activity.	Murugesu *et al.,* 2019
		Aqueous extract of *C. nutans* at 50 mg/mL resulted in 88% inhibition of α-glucosidase activity.	Kamarudin *et al.,* 2017
		Oven-dried leaves of *C. nutans* (70% ethanol with sonication) moderately inhibited α-glucosidase activity.	Khoo *et al.,* 2015
Ficus deltoidea	*Mas cotek*	Methanol extracts increased insulin secretion and prevented hepatic glucose production through down-regulation of phosphoenolpyruvate carboxykinase and glucose-6-phosphatase genes expression.	Farsi *et al.,* 2014
		F. deltoidea bark, leaf, and isolated compounds ameliorated the alloxan- and STZ-induced diabetic complications in animal models.	Misbah *et al.,* 2013
		Hot aqueous and methanolic extracts alleviated basal and insulin-stimulated adiponectin secretion from adipocyte cells.	Adam *et al.,* 2012
Melastoma malabathricum	*Senduduk, Sekeduduk, Kenduduk*	Ethanol extract of *M. malabathricum* leaf decreased blood glucose, glycosylated haemoglobin, and altered serum lipid profiles in diabetic rats.	Balamurugan *et al.,* 2014
		Methanolic leaf extract decreased the levels of serum glucose, glycated haemoglobin, glucose-6-phosphatase, fructose-1-6-biphosphate, and increased the level of plasma insulin, hexokinase.	Kumar *et al.,* 2013

Conclusion

Diabetes mellitus is a complicated disease and can lead to various serious complications. In the current pandemic, diabetic patients have been shown to be associated with a high risk of contracting COVID-19. The hallmark of diabetes treatment is to reduce the risk of developing diabetic complications. The application of natural products as traditional remedies since time immemorial has enlightened the modern world to explore their potential as alternative medicines. *In vitro*, *in vivo,* and genetic studies have demonstrated the antidiabetic properties of many plants. Thus, many natural products have become alternative antidiabetic medicine due to their clinically-proven bioactive compounds that exhibited a wide spectrum of mechanisms in the treatment of diabetes. In many studies, the antidiabetic properties of plants demonstrated hypoglycaemic activities by stimulating insulin secretion, increasing glucose uptake, and inhibiting α-amylase and α-glucosidase with the aim of retarding glucose absorption. Thus, the available scientific evidence supports the use and confirms the health benefits of the application of traditional plant-based medication. Moreover, the elucidation of the modes of action of antidiabetic plants in the treatment of T2DM is important for the future development of new antidiabetic drugs. However, more research and clinical trials are warranted to obtain a better understanding of the bioactive activities of the active compounds and their mechanisms.

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