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Role of bitter melon, turmeric and fennel in lowering blood sugar levels

Ruaa. Ali. Abdul. Al-asadi

Medicinal and Aromatic Plants Research Unit, College of Agricultural Engineering Sciences
University of Baghdad, Iraq

Corresponding author: E-mail: ruaa.abd1005@coagri.uobaghdad.edu.iq *

ABSTRACT

Diabetes is a group of metabolic conditions that has become a global epidemic. It occurs when the pancreas fails to produce enough insulin or when the insulin produced is ineffective in helping the body's cells absorb glucose, leading to high blood glucose levels. There is growing evidence that herbal supplements can be effective in preventing and managing diabetes. Therefore, it is essential to raise awareness about the use of medicinal plants that can help control blood sugar levels and keep them within normal limits rather than aiming to cure diabetes completely. Among the herbal plants known to contain antioxidants that help control diabetes are bitter melon, turmeric, and fennel, as they contain flavonoids, saponins, glycosides, and terpenoids that have a blood sugar-lowering effect by inhibiting alpha-glucosidase. They can play a role in preventing oxidative stress associated with diabetes. Some people around the world have used herbal extracts as a treatment for diabetes, and they have been of great benefit, especially in the early stages of the disease.

KEY WORDS:

Medicinal plants, glycoside, phenols, Diabetes

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دور القرع المر والكرم والشمر في خفض مستوى السكر في الدم

رؤى عبد الحسين علي الاسدي

وحدة بحوث النباتات الطبية - كلية علوم الهندسة الزراعية - جامعة بغداد

الخلاصة

داء السكري هو مجموعة من الحالات الأيضية التي وصلت إلى أبعاد وبائية في جميع أنحاء العالم. هناك أدلة متزايدة حول فعالية استخدام المكملات العشبية في الوقاية من مرض السكري والسيطرة عليه. و يحدث عندما تتجاوز مستويات الجلوكوز في الدم الحدود الطبيعية بسبب عدم إنتاج البنكرياس ما يكفي من الأنسولين أو لأن الأنسولين المنتج غير فعال في المساعدة على امتصاص الجلوكوز في خلايا الجسم. لذلك لابد من التوعية باستخدام بعض النباتات الطبية والتي لا تهدف الى علاج مرض السكري بشكل كامل بل يهدف إلى التحكم في مستويات السكر في الدم بحيث تكون ضمن الحدود الطبيعية. من النباتات العشبية المعروفة باحتوائها على مضادات الأكسدة والتي تساعد على السيطرة على مرض السكري هي نباتات القرع المر والكرم والشمر فاكهة الشمر إذ تحتوي على مركبات الفلافونويد والصابونين والجليكوسيدات والتيربينويدات التي لها تأثير خافض

لسكر الدم عن طريق تثبيط ألفا جلوكوزيداز. و يمكن أن تلعب دورًا في منع الإجهاد التأكسدي المرتبط ببدء السكري. استخدم بعض الأشخاص المستخلصات العشبية كعلاج لمرض السكري في جميع أنحاء العالم وكانت لها فائدة كبيرة خاصة في المراحل المبكرة من المرض.

الكلمات المفتاحية: نباتات طبية، الكلايكوسيد، الفينول، مرض السكر

Introduction

Medicinal and aromatic plants are non-traditional crops used by humans throughout the ages for various purposes, sometimes as spices for cooking foods or medicine. In the Middle and Modern Ages, it became clear how vital medicinal and aromatic plants are in treating many human diseases. Additionally, these plants were helpful in many food industries, such as preservatives, flavorings, and appetite stimulants. They were also consumed as tonic or soothing drinks. Diabetes mellitus is a disturbed metabolism syndrome usually due to genetic and environmental causes, resulting in abnormally high blood sugar levels (Leu and Zonszein, 2010; Joseph and Jin, 2011; Taher et al., 2021). It is a major global health issue, with its prevalence expected to increase from 171 million in 2000 to 366 million in 2030, causing concern worldwide (Shaw et al., 2010). This disease is found all over the world and has become the third most common human disease that is rapidly increasing. It affects 16 million individuals in the United States and up to 200 million worldwide (WHO, 2019). It is also widely spread not only in developed countries but also in developing ones (Hossain et al., 2007).

Bitter melon

Bitter melon *Momordica charantia* is an important medicinal plant of the family Cucurbitaceae. It has many names, including bitter melon, karela balsam pear, and bitter gourd. The name of the genus *Momordica* comes from the Latin word “Mordeo” (Momordi), referring to the serrated edges of the bitter gourd leaves. The plant is a monoecious in which male and female flowers are found separately on the same plant (Cefalu et al., 2008; Anilakumar et al., 2015). Bitter melon is widely grown as food and medicine in China, Malaysia, India, Africa, Southeast Asia, and South America (Rai Pandey, 2007; Kumar et al., 2010). It is an annual or perennial climbing plant with a thin, branched stem that grows up to five meters. Its leaves are alternate, 5-12 cm wide, containing 5-7 lobes. The tendrils are simple and thin, the flowers are yellow to orange, and its green fruits are elongated and ribbed with protrusions. Bitter gourd seeds are brown, compressed, and 12-16 mm wide. They are planted at a distance of half a meter from each other and irrigated once or twice a week. Plants begin inflorescence 30-35 days or more after planting the seeds, and the fruits become ready for reaping 15-20 days after setting (Nadkarni, 1993; Kumar et al., 2011a).

Active ingredients in bitter melon

Several proteins that function similarly to human insulin in the body have been isolated from bitter melon seeds and can be used as an insulin substitute for patients with type 1 diabetes (Paul and Raychaudhuri, 2010). Wehash et al. (2012) found that oral intake of bitter melon seed extract affects declining diabetes type 1 that could be treated with streptozotocin (STZ), indicating that compounds found in bitter melon seeds other than P-insulin may also be effective in treating type 1 disease. One of the most critical essential components in bitter melon is charantin (Al-asadi and Al-jebory, 2020 and 2021), which has properties similar to insulin, as various pharmacological studies have proven that it is more effective than tolbutamide, taken orally, in lowering glycemia (Krawinkel and Keding, 2006; Cousens, 2008; Patel et al., 2010).

Bitter melon use in alternative medicine

The texts of Ayurveda (ancient Indian medicine) mentioned that bitter melon appeared in India from 2000 to 200 BC. It was recommended to treat many diseases, including cholera, bronchitis, anemia, ulcers, diarrhea, and dysentery, and used as an aphrodisiac (Decker-Walters, 1999). Some Indian tribes also used it for abortion, birth control, increasing the flow of milk in breastfeeding women, menstrual disorders, vaginal discharge, constipation, jaundice, gout, eczema, hemorrhoids, and skin diseases, especially leprosy and psoriasis, to treat diabetes, and to expel gases. It is also used topically to treat sores, wounds, and infections (Jagessar et al. (2008). Bitter melon was used by local people in the Amazon region who grew it in their gardens as food and medicine (Singh et al., 2004b). They add acid and salt before boiling it to remove some of the bitter taste (Basch et al., 2003; Abhishek et al., 2004; Wang et al., 2011). When Africans immigrated to America, they also transported many medicinal plants, including bitter melon, which was determined to be effective in treating fever, bacteria, viruses, fungal infections, stomach problems, and miscarriages. It was then used to treat diabetes and malaria without knowing what medicinal components could be the reason for these beneficial properties (Grover and Yadav, 2004). Currently, thanks to technical development, the effective components of bitter melon, which are used in the treatment of many diseases, have been identified (Hussain, 2001). Mahomoodally et al. (2012) and Tabata (2012) discovered some effective components in bitter melon, including substances acting similarly to insulin in controlling diabetes.

Nutritional and medical importance of bitter melon

Despite the bitter taste of its fruits, bitter melon has been used in many Asian vegetable dishes for a long time due to its nutritional importance for the high content of iron, potassium, beta-carotene, and other nutrients. Bitter melon fruits are characterized by low calories, giving 17 calories per 100 grams of fruits (Klomann et al., 2010). The fruit contains 83.2% water, 2.9% protein, 1% fat, 1.4% minerals, and 1.7% fiber. It is an excellent source of vitamins such as B1, B2, and B3, in addition to containing magnesium, folic acid, zinc, phosphorus, and manganese (Jiratchariyakul et al., 2001; Keding and Krawinkel, 2006). Immature fruits are eaten as vegetables as they are rich in nutrients; however, the bitter taste is due to the alkaloid Momordin produced in the fruits and leaves (Ali et al., 2008; Paul et al., 2009). Balasubramanian et al. (2007) concluded that fresh bitter melon is an excellent source of vitamin C (which is a powerful natural antioxidant that helps the body get rid of harmful free radicals and plays a role in building the immune system and maintaining healthy tissues, skin, gums, and blood vessels). It contains another essential antioxidant, vitamin A, which supports vitamin C to rid the body of free radicals derived from oxygen and reactive oxygen species (ROS), which have a role against aging, cancers, and various diseases, in addition to its role in strengthening sighting and treatment of eye problems. Bitter melon is an excellent source of flavonoids, including β -carotene, α -carotene, lutein, and zeaxanthin (Sathishsekar and Subramanian, 2005). Studies have shown that consuming bitter melon juice can aid weight loss by reducing fat accumulation and increasing its decomposition, ultimately eliminating obesity (Chen et al., 2008; Huang et al., 2008; Nerurkar et al., 2005). It occupies an important place among people with diabetes due to its anti-diabetic properties. Traditional treatment with the bitter melon plant is boiling the leaves and fruits for a few minutes and then drinking them as tea (Senanayake et al., 2004; Li, 201). Plants contain various secondary compounds, including alkaloids, saponins, tannins, glycosides, antibiotics, antioxidants, and antivirals. These compounds contribute to the medicinal value of plants (Grover and Yadav, 2004; Ahmed and Beigh, 2009; Aboa and Jaiyesimi, 2008; Wu

and Ng, 2008). Recent studies have shown that antioxidants of plant origin can be of great importance as therapeutic agents in delaying signs of aging (Zhang et al., 2009a). Fruits and seeds of bitter melon are used to treat blood hyperglycemia, as antifungal and bacterial agents, and to combat viruses, especially HIV (Grover and Yadav, 2004). Sathishsekar and Subramanian (2005) and Aminah and Anna (2011) also found that bitter melon has a vital role in treating diabetes, as estimates report that up to a third of patients who have diabetes used some form of complementary or alternative medicine, including bitter melon, which received great interest in this field (Braca et al., 2008; Emanuel et al., 2018). Bitter melon is a treatment for blood diabetes because it contains charantin, which increases insulin secretion in the pancreas, reduces intestinal glucose absorption and increases glucose absorption and utilization in peripheral tissues (Habicht et al., 2014). In an experiment to assess the effectiveness of bitter melon in treating diabetes, a group of five individuals who have diabetes were given dried fruit powder three times a day. Additionally, another group consumed an aqueous extract made from 100 grams of fruit per 100 ml of water. After three weeks of use, individuals who consumed the fruit powder reported a 25% decrease in blood sugar levels, while those who used the aqueous extract experienced a reduction of 54% in blood sugar levels (Soundararajan et al., 2012). It also delays complications in diabetic patients (such as nephropathy, neuropathy, and atherosclerosis); moreover, bitter melon fruits are cheap, easy, and available in tropical countries (Scartezzini and Speroni, 2000).

Figure 1. The plant and some of the medications used to treat diabetes

Turmeric

Turmeric is a perennial herb that grows 3-5 feet with cylindrical orange or yellow rhizomes. Its leaves are large, oblong, and tapered, with serrated edges resembling a lily, and it has a length of 102 cm. The flowers are cone-shaped and pale in yellow, and their length ranges between 10 to 15 cm. They blossom from late spring until mid-summer, and the most commonly used parts are rhizomes. Turmeric has many names, and in some regions it is known as “alwars”, “hard” (which is a Persian name), “karkub”, “Aqid al-Hind”, “Indian saffron”, “jadwar”, “Zarnab”, and “Uroq al-Dabagheen” (Faraha, 1995). Turmeric was initially used as a food seasoning and a natural dye for clothing until it was recently discovered as an essential source of many new medicines for treating various diseases (Mutasher et al., 2016). *Curcuma longa* is used as a spice or seasoning, food preservative, and coloring agent in India, China, and Southeast Asia. It is used in traditional medicine as a home remedy for many diseases, including biliary disorder, cough, diabetes, liver disorder, rheumatism, and sinusitis. Curcumin (diferuloylmethane) is the yellow bioactive ingredient in turmeric. It has a broad spectrum of activities such as anti-inflammatory, anti-oxidant, anti-cancer, anti-mutagenic, anti-thrombotic, anti-diabetic, anti-bacterial, anti-fungal, as well as anti-viral and anti-protozoal (Chattopadhyay et al., 2004 and Akram et al., 2010).

Active ingredients in turmeric

Turmeric contains many phytochemicals (11, 12), as it comprises water (80-90%), followed by carbohydrates (about 13%), proteins (2%), minerals (2%), and fats (1%) (13). Among the minor components of turmeric are curcuminoids, which play a central role and may constitute up to 10% of dry turmeric powder. This category mainly includes curcumin, dimethoxy-curcumin, and bisdemethoxycurcumin, which can account for 62-90, 9-23, and 0.3-14 mg/g of commercial turmeric products (extracts and powders), respectively. Curcuminoid is the most important active

substance in the turmeric plant, to which most of turmeric's therapeutic properties are attributed. It was first extracted in 1815, and its molecular formula $C_{21}H_{20}O_6$ was discovered in 1910. This molecule is hydrophobic and does not dissolve in water but in substances such as dimethyl sulfoxide, acetone, ethanol, and oil (Beyene et al., 2021). Moreover, more than 50 curcuminoids (such as bisapocurcumin, curcumalongin, cyclocurcumin, and terbicormin) have been recognized in turmeric (Meng et al., 2018 and Thangavel and Dhivya, 2019), which give the yellow color of turmeric.

Turmeric contains about 3-8% curcumin (depending on the growing season). One spoonful of turmeric powder (3 grams) contains an average of 30-90 mg of curcumin (Fabianowska et al., 2021). It is considered an antiseptic, anti-inflammatory, and antioxidant substance and is used to treat Alzheimer's, diabetes, asthma, stomach ulcers, and others (Guo et al., 2018; Esmaeili et al., 2021; Al-Salman et al., 2022). It is also used to treat some types of cancer due to its anti-cancer effects as well as its influential role in protecting the heart (Trigo-Gutierrez et al., 2021; Wang et al., 2021; Abd Wahab et al., 2020; El-Hadary and Sitohy, 2021). The benefits of turmeric are also for humans and animals because it increases their weight when added to feed and improves the food conversion process (Abd Al-Jaleel, 2012).

Benefits of turmeric for diabetics

The health of people with diabetes depends greatly on lifestyle and diet. Curcumin helps prevent fatty deposits in the blood vessels and reduces fatty tissue growth in the organs. It improves the function of beta cells in the pancreas, which helps produce insulin. It also secretes cytokines, helping maintain a healthy weight and reducing the risk of diabetes. Curcuminoids reduce insulin resistance, glucose, and insulin levels; increase adiponectin release; and reduce levels of leptin, resistin, interleukin (IL)-6 IL-1 β , and tumor necrosis factor α in patients with type 2 (Hajavi et al., 2017). Some findings suggest that these compounds can influence glucose homeostasis, diabetes complications, and vascular risk in patients (Katsuki et al., 2018). Some studies have shown that curcuminoid supplementation improves the lipid level and increases total antioxidant capacity in patients (Altobelli et al., 2021), thus supporting other available evidence on the role of curcuminoids in mitigating heart disease risk (Cicero et al., 2017; Ward et al., 2017).

Daily permissible amount of turmeric per day

The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) have provided some guidelines for turmeric consumption. A person can consume between 1.5 and 3 grams of turmeric per day, or approximately 1.4 mg of turmeric per pound of body weight, several times daily.

Fennel

Fennel is a perennial plant of the family Apiaceae that grows in barren lands and dry hills. Its height is 1 to 2 meters, its green stem has many branches, and its leaves are green to blue, dark, and shiny. Its flowers are yellow, and its fruits are dark grey, grooved and spindle-shaped. (Diaaz-Maroto et al., 2006).

Fennel uses in alternative medicine

It has long been used as a medicinal herb and spice. Wild fennel has been found to exhibit radical scavenging activity and lower total phenolic and flavonoid content (Choi and Hwang, 2004). Fennel

is mainly used medicinally with laxatives to relieve their side effects. It is used to treat flatulence in infants. Fennel tea is also used as a carminative and is made by pouring boiling water over a teaspoon of ground fennel seeds. In the Indian subcontinent, fennel seeds are eaten raw, sometimes with some sweetener, to improve eyesight. Studies conducted on animals have shown fennel benefits in treating diabetes, as a diuretic, and high blood pressure. It has been used to improve milk production in breastfeeding mothers. (Agarwal et al., 2008).

Active ingredients in fennel

Fennel plants contain aromatic oil at a percentage between 2-1.3%, and its main components are anethole and fenchone, whose percentage varies according to the growth stage. Fennel contains water by 6.3%, protein concentration 9.5%, fat 10%, minerals 13.4%, fiber 18.5%. % and carbohydrates 42.3%. Mineral content involves calcium, phosphorus, iron, sodium, and potassium; vitamins are thiamin, riboflavin, niacin, and vitamin C. The main components of FV are transanethol (50-70%) and estrogen-dianthol. Flavonoids and organic acids (Kaur and Arora, 2010; Kazemi et al., 2012).

Fennel benefits in treating diabetes

Fennel is rich in dietary fiber, which improves the health of people with diabetes. Vitamin C in the fennel plant is essential in enhancing diabetics' immunity. Antioxidants in fennel help diabetics control blood sugar. The amino acids in fennel help people with diabetes regulate blood sugar and protect the eyes from diabetic complications. It is rich in potassium, which reduces high blood pressure associated with diabetes. Fennel improves blood circulation due to its richness in potassium, which benefits the health of diabetics. It is considered a disinfectant for the intestines and stomach and reduces the effect of diabetes medications on the digestive system. Eating fresh fennel reduces high blood glucose levels. Fennel is one of the best types of plants that increase the protection rate against diabetes complications (Telugu et al., 2019).

Fennel usage method for diabetes treatment

Eat green fennel in salads or cooking, or use fennel seasoning with foods and salads. Alternatively, drink boiled fennel tea with water. It is recommended to take four ground seeds once daily for two months (Shabbir et al., 2020).

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