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Phytochemicals and their potential in anti-diabetic medicinal plants

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Abstract

The treatment of diabetes with synthetic drugs is costly and can cause side effects in some patients. Since ancient times phytomedicines have been used in various parts of the world where access to modern medicine is limited. This article thus, aimed to carry out an extensive literature review to explore the potential of phytochemicals that are reportedly present in medicinal plants which are used as anti-diabetic treatment. The patient with diabetes many inventions are used to cure and/or treat the disease, most of the inventions are cost effective and can improve the health of the patient. Beneficial glycemic control can be measured as the cornerstone management in the avoidance of diabetic complications. The findings of the reviewed articles revealed that the medicinal plants and their extracts have anti-diabetic potentials which are due to the presence of various bioactive compounds.

Key words: Anti-diabetic, medicinal plants, phytochemicals

INTRODUCTION

Phytochemicals

Are also known as phytonutrients, are naturally bioactive components contains huge number of foods like, fruits, legumes, nuts, seeds, vegetables, whole grain products etc. Although huge number of phytochemicals present in all kinds of foods, only a least amount is discovered and have been isolated and recognized from the plants source (Cao *et al*., 2017). Phytochemicals are not important nutrients and are not essential for the human body for supporting life, but it contains essential properties to prevent and fight against some common diseases. Use of the phytochemicals consists of antifungal, antimicrobial, anticancer antihypertensive and antioxidant activities (Anulika, Ignatius, Raymond, Osasere & Abiola, 2016). Phytochemicals can be divided into two

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different classes depends upon nature synthesized in the plants like: primary and secondary metabolites.

Primary metabolites

Essential metabolites, the biomolecules such as chlorophylls, sugars, starches, proteins, fats, originate in all plants are also known as primary metabolites (Malik, Ahmed & Khan, 2017).

Secondary metabolites

More prevalent group of compounds considered as phytochemicals, belonging to secondary metabolites of plants ranged diverse chemical entities for example, flavonoids, polyphenols, organosulphur compounds, steroidal saponins, and vitamins. Phytochemicals plays a major role in the development of plants i.e., symbiotic association, reproduction, and collaborations with other organisms and the environment (Akula & Ravishankar, 2011). However, more than 13,000 secondary metabolites have been insulated from the medicinal plants and identified from plants. The secondary metabolites act as a defensive molecule and accomplish specified functions in plants. These secondary metabolites retain medicinal properties which include antidiabetic activity (Singh, Arif, Khan & Sharma, 2014). These photochemical are useful in pharmaceutical applications, cosmetics, dietary supplements, and nutrition. Plants are always considered as the source of food and/or as carrier of medical compounds (Hidalgo *et al*., 2018).

Total phenolic compounds

Plants used as foods comprising phenolic as bioactive compounds and are considered good for human health. The protective functions such as combating disease through diet and maintaining the healthy lifestyle also influenced on chronic diseases, such as type 2 diabetes (T2D). Dietary phenolic bioactive compounds and their molecular features permit antioxidant property which is used for the neutralizing chronic oxidative stress that could be stimulated by the process of metabolic breakdown commonly linked with T2D. The antioxidant properties, diversity in phenolic compounds present in plant foods have therapeutic functional activities like, improving the insulin sensitivity, reducing hepatic glucose output, inhibiting activity of key digestive enzymes for carbohydrate, and modifying the absorption of glucose into the bloodstream, by this means improving post-prandial glycemic control. The above-mentioned therapeutic properties contain health effects and benefits in the dietary organization of T2D. Consequently, plant-based foods that are rich source of phenolics and are excellent dietary sources of therapeutic targets to increase overall glycemic control by handling chronic hyperglycemia and chronic oxidative stress, which are main contributing factors to T2D pathogenesis (Sarkar, Christopher & Shetty, 2021). Anti-diabetic related to anti-hyperglycemic phenolics properties is due to their capability to control the action of enzymes that are involved during glucose metabolism, along with their capability to recover beta cell function (the production and secretion of insulin), decrease hepatic glucose productivity, and change the efficacy of glucose transporters and insulin receptors. Plant foods that contain phenolic compounds such plants have potential to regulate anti-hyperglycemic properties in liver, muscle, small intestine, pancreatic and adipose tissue (Burton-Freeman *et al.,* 2019).

In plants metabolites phenolic compounds are the major and most abundant groups. They contain biological properties such as anticarcinogen, antiapoptotic,

antiinflammation, cardiovascular protection, antiaging, antiatherosclerosis, and enhancement the role of endothelial cells, as well as inhibition of cell proliferation activities and angiogenesis (Ali *et al.,* 2008). Plant food sources of phenolic compounds have widespread consideration in nutritive and therapeutic involvements because of their function in contradicting the chronic oxidative stress, dyslipidemia, hyperglycemia and enhanced digestive condition, that inhibit the T2D progression and pathogenesis (Salau, Erukainure & Islam, 2020). Phenolic compounds found in plant foods such as coffee, nuts, fruits, vegetables, spices, wine, tea, berries and medicinal herbs show anti-hyperglycemic properties through different mechanisms, specially through inhibition of enzymes.

Total Flavonoids compounds

Flavonoids are naturally found and exist as secondary metabolites in plants, fruits, tea, vegetables, nuts, cocoa, grain seeds, herbs and fungi. They help in health benefits such as antioxidant activities, anti-inflammatory and naturally existing flavonoids contribute to antidiabetic properties (Sok Yen *et al*., 2021). They are classified into different groups such as flavones, flavanols and flavanones, and have several medicinal properties including antidiabetes. Flavonoids recover the diabetes pathogenesis and its complications through insulin secretion, insulin signaling glucose uptake, carbohydrate digestion and enzymes activity (Vinayagam & Xu, 2015). Moreover 5000 flavonoids have shown several positive properties, which have been recognized and isolated from different plants (Kawser *et al*., 2016).

It is reported that free radicals like reactive oxygen and nitrogen species, that are byproducts of cell metabolism in human beings, can cause numerous severe disorders such as T2DM, obesity, cancers and coronary heart diseases. Therefore, neutralizing the effect of nitrogen species and reactive oxygen flavonoids act as antioxidants against many disorders (Kawser *et al*., 2016). It is biologically acceptable that the risk of diabetes may be decreased by ingestion of flavonoids or flavonoid-rich diets (Bahadoran, Mirmiran & Azizi, 2013).

Antioxidant

In living organism antioxidants are the components responsible to inhibit and to balance the damage which could be caused by free radicals through providing electrons to damaged cells from antioxidants. Antioxidants also changes the free radicals into waste by-products which is removed from the body. Intake of vegetables and fruits rich in antioxidant reduce the danger of numerous disorders affected by free radicals (Rahman, Islam, Biswas & Alam, 2015). Free radical is a molecule that contains one or more single pair of electrons that can quickly respond with the constituents such as nucleic acid, lipids and proteins. Due to different metabolic reactions in the body free radicals are generated. These free radicals are produced by both from ordinary cell metabolisms in situ or from exterior sources such as smoke, medication, pollution, radiation, cigarette, etc. Furthermore, reactive oxygen species (ROS) which is also known as a by-product of oxidative phosphorylation. The accumulation of ROS that results of various chronic and degenerative disorders such as aging, cancer, rheumatoid arthritis, autoimmune disorders, neurodegenerative and cardiovascular diseases (Swargiary, Nath, Basumatary & Brahma 2017).

Overproduction of free radicals or ROS contributes to oxidative stress, which can result to destruct the cell membranes and macromolecules like as proteins, lipids and nucleic acids which leads to cell death or causing mutations. If the cellular

antioxidant system is disturbed and becomes deficient the oxidative stress arises and promoting numerous disorders such as cancer, diabetes, cardiovascular diseases, etc. (Engwa, 2018). For plants unfavorable environments, such as heavy metals, extreme temperature, nutrient deficiencies, drought and high salinity, cause high concentrations of ROS, which is source of oxidative stress (Barua, 2014). Various research has been carried out that most of the plants are rich source of antioxidant. For instance, phenolic compounds like tannins, flavonoids and lignins and vitamins A, C, E, found in plants that all are act as antioxidant. (Khan, Khan, Ahmad & Mushtaq, 2015).

Medicinal plants

Since ancient time, many modern medicines have been developed through the medicinal plants for the treatment of different disease (Figure. 1). Many of the rural areas uses medicinal plants medicines for healing different disease but it is not common in many of the other communities. Medicinal herbs are not as important as the primary healthcare. Many of the people prefer natural products as these are inexpensive and are natural having least side effects and widely available all around the world (Roglic & Norris, 2018). For the health benefits of living things such as human and animal, natural products considered as plants, animals or microorganisms plays an important role. It has been estimated by World Health Organization that 80% of the total population living in developing countries depends upon the traditional medicines prepared through plants for the purpose of curing different diseases. (Tran, Pham & Le, 2020).

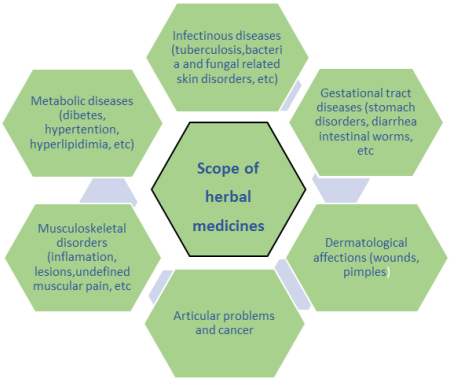

Figure 1. Scope of medicinal plants

Different diseases such as memory Alzheimer, diabetic wounds, immune disorder, memory loss, liver disorders, osteoporosis etc., are not properly curable through modern medicines but can be cured through medicines derived from medicinal plants (Watanabe, 2001). A lots of research studies has been carried out on medicinal plants and it has been reported that they contain therapeutic potential for the treatment or management of nervous, circulatory, respiratory, digestive, and urinary disorders; as well as disfunction of the sexual organs, skin diseases, vision disorders, hearing and taste related diseases (Rashid *et al.*, 2014).

Parts of the plants consists of leaf, stem, root, fruit, seed, bark, arial part and whole plant can be use of the establishment of medicines. Drugs were made up of commonly out of decoction and maceration. Other methods like: poultice and smoke, powder, infusion, and paste, sticky paste and dessert are also used. Many remedies

were prepared and prescribed in different ways including nasally, orally or anally. Many medicines can be made from a single plant (61.5%) as well as through the combination of two or more than two plants (38.5%). The maximum number of the species are widely used in traditional medicine for curing infections, inflammation, diabetes, bleeding, malaria, diarrhea and digestive disorder (Karar & Kuhnert, 2017). The decoction was the major element for the preparation of herbal medicines counted as 48% followed by powder (14%), vegetable (14%), juice (9%), infusion (9%), roast (4%) and ash (2%). In ethnobotanical practice decoction is the main form of preparation because it is an easy method to prepare by mixing with water, tea, or soup (Figure. 2). (Hussain *et al*., 2018).

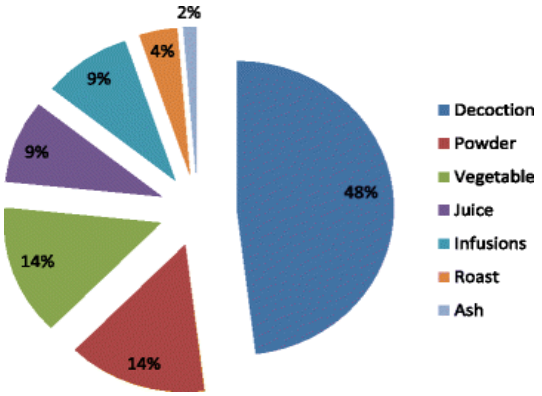

Figure 2. Different modes of preparation of herbal medicines.

For treating different disease, the use of different parts of plant, medicinal plants as a whole were used generally (28%), fruit (27%), leaves (21%), stem (13%) and flowers (11%). In many cases (45%), underground parts such as roots were used for treating ailment, were as leaves and aerial parts; stem and flowers were the least used parts of plant (Uniyal, Singh, Jamwal & Lal, 2006). Medicinal plants are said to be safe and efficient but some of the products or medicines prepared through these medicinal plants are unlicensed and can lack in the safety and efficiency. These may result in allergic or toxic reactions, drug interactions or contamination and mistaken plant (Tabuti, 2008).

Medicinal Plants for Diabetes Management

World Health Organization has suggested to use the traditional plant for the treatment for diabetes as these plants are effective, non-toxic, having least side effects and are discovered as exceptional aspirants for oral therapy (Shokeen, Anand, Murali & Tandon, 2008). Medicinal plants contain medicinal value of herbs, and these plants contain naturally biological active ingredients having drug making properties. (Keskin, 2018). Almost 50,000 angiosperm plants are used as medicines, in which more than 600 species are used in Pakistan for the treatment of several diseases (Waris, Iqbal, Hussain, Khan, Ali & Khan, 2018). Some of the medicinal plants are used as anti-diabetes remedy due to their antidiabetic properties such as insulin sensitivity hypoglycemic activities. These plants contain high level of phenolic compounds, alkaloids, flavonoids, glycosides and terpenoids which results in the improvement of insulin secretions and controls blood sugar (Kooti, Farokhipour, Asadzadeh, Ashtary-Larky & Asadi-Samani, 2016).

Mechanism of Action of Anti-Diabetic Plants

Medicinal plants which effects in lowering the blood glucose have the capability to modulate the pathways which control insulin resistance, *β*-cell function, GLP-1 homeostasis, and glucose re-absorption (Chang *et al*., 2013). Various proposed mechanisms for the reaction of anti-diabetic plants include:

1. Inhibition of the pathological conversion of starch to glucose and stimulation of glycogenesis and hepatic glycolysis (Chawla et al., 2013).
2. inhibition of insulin degradative processes, Stimulation of insulin secretion, and reduction of insulin resistance (Mukherjee, Venkatesh & Ponnusankar, 2010).
3. Increasing the number and size of cells in the islets of langerhans, protecting the destruction of the ß- cells and regenerating or repairing pancreatic ß - cells (Oh, 2015).
4. Providing certain essential elements like calcium, zinc, magnesium, manganese and copper for the ß - cells (Dwivedi & Daspaul, 2013).
5. Inhibition of α-amylase and α–glucosidase enzymes (Kazeem, Adamson & Ogunwande, 2013).
6. Preventing oxidative stress in pancreatic ß- cell dysfunction (Hosseini, Shafiee-Nick, & Ghorbani, 2015).

CONCLUSION

Numerous research has established that the presence of phytochemicals confers pharmacological and physiological qualities such as antioxidants (AA), antibacterial, and anti-diabetic capabilities. The existence of phytochemical elements in these medicinal plants demonstrates that humans can use them. Additionally, plant extracts can now be used with regular medications to treat various conditions. Each plant has unique active components that help manage blood sugar levels and diabetic problems. Generally, medicinal plants are extracted using a variety of solvents, including ethanolic, methanolic, chloroform, and aqueous. While most studies favored methanolic and ethanolic extracts, the current review demonstrated that nonalcoholic extractions such as n-hexane, acetone, and distilled water also inhibited bacterial growth. One may argue that plants contain various bioactive chemicals, making them a valuable medicinal commodity. However, further research is required to fully characterize its toxicological profile, bioactivity, environmental influence, and agricultural outputs.

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