

The Role of Medicinal Plants Extras in Lowering the Level Blood Sugar Level

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Recently, some medicinal plants have been reported to be useful in diabetes worldwide and have been used empirically in antidiabetic and antihyperlipidemic remedies. Antihyperglycemic activity of the plants is mainly due to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes. More than 400 plant species having hypoglycemic activity have been available in literature, however, searching for new antidiabetic drugs from natural plants is still attractive because they contain substances which demonstrate alternative and safe effects on diabetes mellitus. Most of plants contain glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc., that are frequently implicated as having antidiabetic effect.

Keywords: medicinal plants , diabetes, Blood Sugar

Introduction

Health is dearer than wealth' so, the value of medicinal plants is more than what it is in the marketplace, i.e. it can be said to be essentially infinite. Human beings have been utilizing plants for basic preventive and curative health care since time immemorial. As many as 35,000 – 70,000 species of plant have been used at one time or another for medicinal purposes (Shahidullah, 2007).

From historical records, the human use of plants or floral parts to enhance physical and spiritual well-being goes back thousands of years and is difficult to date precisely. However, from those records, it is apparent that most of the early people, such as the Assyrians, Babylonians, Egyptians and ancient Hebrews, were familiar with the properties 8 and use of many medicinal plants (Shahidullah, 2007).

The practice of medicine using medicinal plants flourished most during the Greek civilization, when historical personalities like Hippocrates (born 460 BC) and Theophrastus (born 370 BC) practiced herbal medicine. The materia medica by Hippocrates listed around 400 medicinal plants and later the encyclopaedic work of Discordies, _De materia medica' (published in 78 AD), which featured about 600 medicinal plants, have been regarded as the forerunners of all modern pharmacopeias and authoritative texts on botanical medicine. In the Middle Ages, the great Greek Pharmacistphysician, Galen (131-200 AD), wrote about 500 volumes describing hundreds of recipes and formulations containing a large number of medicinal plants. He was the first person to describe the procedures and methods of preparingtherapeutic recipes, including the ingredients of both plant and animal origins (Shahidullah, 2007).

Throughout the ages, humans have relied on nature for their basic needs, for the production of food, shelter, clothing, transportation, fertilizers, flavours and fragrances, and medicines (Cragg and Newman, 2005). Plants have formed the basis of sophisticated traditional medicine systems that have been in existence for thousands of years and continue to provide mankind with new remedies. Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and probably thousands of years of use. The first records, written on clay tablets in cuneiform, are from Mesopotamia and date from about 2 600 BC (Heinrich et al., 2004). Among the substances that were used are oils of Cedrus species (cedar) and Cupressus sempervirens (cypress), Glycyrrhiza glabra (licorice), Commiphora species (myrrh) and Papaver somniferum (poppy juice), all of which are still in use today for the treatment of ailments ranging from coughs and colds to parasitic infections and inflammation. In ancient Egypt, bishop's weed (Ammi majus) was reported to be used to treat vitiligo, a skin condition characterized by a loss of pigmentation (Staniszewska, et al., 2003; Beissert and Schwarz, 2002). More recently, a drug (β-methoxypsoralen) has been produced from this plant to treat psoriasis and other skin disorders, as well as T-cell lymphoma (Beissert and Schwarz, 2002).

1.1. Aim of the study

Diabetes mellitus is one of the common metabolic disorders acquiring around 2.8% of the world's population and is anticipated to cross 5.4% by the year 2025. Since long back herbal medicines have been the highly esteemed source of medicine therefore, they have become a growing part of modern, high-tech medicine. In view of the above aspects the present study provides profiles of plants with hypoglycaemic properties, available through literature source from various database with proper categorization according to the parts used, mode of reduction in blood glucose (insulinomimetic or insulin secretagogues activity) and active phytoconstituents having insulin mimetics activity.

The aim of this research is to make focus on the important of medicinal plants in lowering the level of sugar in the blood also to study their role in prevent accruing the diabetes , additinal to study and understand the mechanism action of it's active chemical compounds.

roseus); laxative agents from Cassia sp. and a cardiotonic agent to treat heart failure from Digitalis species (Newman et al., 2000).

Approximately half (125 000) of the world's flowering plant species are found in the tropical forests. Tropical rain forests continue to support a vast reservoir of potential drug species. They continue to provide natural product chemists with invaluable compounds as starting points for the development of new drugs. The potential for finding more compounds is enormous as to date only about 1% of tropical species have been studied for their pharmaceutical potential (Cragg and Newman, 2005). This proportion is even lower for species confined to the tropical rain forests. To date about 50 drugs have come from tropical plants. The probable undiscovered pharmaceuticals for modern medicine has often been cited as one of the most important reasons for protecting tropical forests. Therefore the high annual extinction rate is a matter for concern.

Although discovered through serendipitous laboratory observation, three of the major sources of anti-cancer drugs on the market or completing clinical trials are derived from North American plants used medicinally by native Americans: the papaw (Asimina spp); the western yew tree (Taxus brevifolia), effective against ovarian cancer and the mayapple (Podophyllum peltatum) used to combat leukaemia, lymphoma lung and testicular cancer (GuribFakim, 2006).

2.1. Medicinal plants used to treat diabetes

Plants have always been a very good source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The

ethnobotanical information suggests that about 800 plants may possess antidiabetic potential, among all of them Momordica charantia,

Pterocarpus marsupium, and Trigonella foenum greacum have been reported to be beneficial for treatment of type 2 diabetes (Ponnusamy and et., al, 2011) Several such herbs have shown antidiabetic activity when evaluated using different type of experimental techniques. Wide arrays of plant derived active principles representing different type of biological activity, among these alkaloids, glycosides, galactomannan gun, polysaccharides, peptidoglycans, hypoglycans, guanidine, steroids, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions have demonstrated activity including treatment of diabetes (Grover and et., al, 2002) List of the medicinal plants having antidiabetic potential acording to the different part used and mode of action were presented in Table (2.1).

Table (2.1) List of plants having antidiabetic activity[53]

S. No.	Plant part	Name of plants		
1	Aerial parts	Artemisia pallens, Bidens pilosa, Bixa orellana, Teramnus labialis		
2	Bark	Cinnamomum zeylanicum, Croton cajucara		
3	Bulb	Allium cepa, Allium sativum		
4	Flower	Cassia auriculata, Gentiana olivier, Musa sapientum		
5	Fruit	Carum carvi, Coriandrum sativum, Embellica officinalis, Juniperus communis, Momordica charantia, Xanthium strumarium		
6	Leaves	Aloe barbadensis, Annona squamosa, Averrhoa bilimbi, Azadirachta indica, Beta vulgaris, Camellia sinensis, Cassia alata, Eclipta alba, Eucalyptus globulus , Euphrasia officinale, Ficus carica, Gymnema sylvestre, Gynura procumbens, Ipomoea		

		aquatica, Mangifera indica, Myrtus communis, Memecylon umbellatum, Morus indica, Ocimum sanctum				
7	Rhizome	Nelumbo nucifera				
8	Roots	Clausena anisata, Glycerrhiza glabra, Helicteres isora, Pandanus odorus				
9	Seed	Acacia arabica, Agrimony eupatoria, Lupinus albus, Luffa aegyptiaca, Lepidium sativum, Mucuna pruriens, Punica granatum				
10	Stem	Amaranthus spinosus, Coscinium fenestratum				
11	Tubers	Ipomoea batata				
12	Whole plant	Abies pindrow, Achyranthus aspera, Ajauga iva, Aloe vera, Anacardium occidentale, Andrographis paniculata, Capsicum frutescens, Cryptolepis sanguinolenta, Enicostemma littorale, Ficus religiosa				

2.2. Literature Review

The study of (Przeor, 2022) was about Diabetes is a metabolic disease that affected 9.3% of adults worldwide in 2019. Its cooccurrence is suspected to increase mortality from COVID-19. The treatment of diabetes is mainly based on the long-term use of pharmacological agents, often expensive and causing unpleasant side effects. There is an alarming increase in the number of pharmaceuticals taken in Europe. The aim of this study is to concisely collect information concerning the few antidiabetic or hypoglycaemic raw plant materials that are present in the consciousness of Europeans and relatively easily accessible to them on the market and sometimes even grown on European plantations. The following raw materials are discussed in this mini-review: Morus alba L.,

Cinnamomum zeylanicum J.Presl, Trigonella foenum-graecum L., Phaseolus vulgaris L., Zingiber officinale Rosc., and Panax ginseng C.A.Meyer in terms of scientifically tested antidiabetic activity and the presence of characteristic biologically active compounds and their specific properties, including antioxidant properties. The characteristics of these raw materials are based on in vitro as well as in vivo studies: on animals and in clinical studies. In addition, for each plant, the possibility to use certain morphological elements in the light of EFSA legislation is given.

The main purpose of the study of (Zou, 2014) was to evaluate the potential of two Malian medicinal plants and one Chinese cultivated medicinal plant in the treatment of immune related diseases. This thesis also aimed to promote the sustainable use of medicinal plant resources. Seven purified pectic polysaccharides fractions were isolated from Parkia biglobosa bark. All of the fractions exhibited potent complement fixation activity, and fractions PBEII-I, PEBII-III and PBEII-IV also showed potent macrophage stimulating activity. The common structural features of these seven fractions are rhamnogalacturonan I (RG-I) backbone highly branched with arabinogalactan type I and/or type II (AG-I and/or AG-II) side chains. The homogalacturonan region may not present in fractions PBEII-III, PBEII-IV and PB100I-I due to the high ratio of rhamnose (Rha) to galacturonic acid (GalA). The higher yield and biological activities of fractions obtained from the 50% ethanol-water extract suggests that this extract could be more related to the medicinal activity than the 500 C and 1000 C water extracts.

The study of (Patel and et., al, 2012) provides profiles of plants (65 species) with hypoglycaemic properties, available through literature source from various database with proper categorization according to the parts used, mode of reduction in blood glucose (insulinomimetic or insulin secretagogues activity) and active phytoconstituents having insulin mimetics activity. From the review it was suggested that, plant showing hypoglycemic potential mainly belongs to the family Leguminoseae, Lamiaceae, Liliaceae, Cucurbitaceae, Asteraceae, Moraceae, Rosaceae and Araliaceae. The most active plants are Allium sativum, Gymnema sylvestre, Citrullus colocynthis, Trigonella foenum greacum, Momordica charantia and Ficus bengalensis. The review describes some new bioactive drugs and isolated compounds from plants such as roseoside, epigallocatechin gallate, betapyrazol-1-ylalanine, cinchonain leucocyandin 3-0-beta-d-galactosyl Ib, cellobioside, leucopelargonidin-3- O-alpha-L rhamnoside, glycyrrhetinic acid, dehydrotrametenolic acid, strictinin, isostrictinin, pedunculagin, epicatechin and christinin-A showing significant insulinomimetic and antidiabetic activity with more efficacy than conventional hypoglycaemic agents. Thus, from the review majorly, the antidiabetic activity of medicinal plants is attributed to the presence of polyphenols, flavonoids, terpenoids, coumarins and other constituents which show reduction in blood glucose levels. The review also discusses the management aspect of diabetes mellitus using these plants and their active principles.

The study of (Alaa and Wamidh, 2021) compiled and summarized all the in vivo and in vitro studies conducted for plants with potential antidiabetic activity in the Middle East region. Plants of the Asteraceae and Lamiaceae families are the most investigated. It is hoped that this review will contribute scientifically to evidence the ethnobotanical use of medicinal plants as antidiabetic agents. Work has to be done to define tagetes, mechanism of action and the compound responsible for activity.

In addition, safety and pharmacokinetic parameters should be investigated.

In the study of (Singh and et., al, 2011). Herbal treatments for diabetes have been used in patients with insulindependent and non-insulin-dependant diabetes, diabetic retinopathy, diabetic peripheral neuropathy, etc. Several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level. So all these plant materials help to control diabetes.

3.1. White Mulberry (*Morus alba L.*)

Mulberry is a fast-growing, deciduous plant from the Moraceae family that is found at various geographical latitudes, i.e., in climates from tropical to moderate (Kumari et al, 2009).

White mulberry originates from China, Japan, and India, and historical sources have revealed that all its parts, i.e., fruits, leaves, and bark, were already used in medicine in 3000 B.C. It was brought to Europe in the 11th century with silkworm caterpillars. It is also very common in other countries of Asia, Europe, and America. White mulberry is also grown in Europe due to low agrotechnical requirements, relatively easy and cheap cultivation, and the possibility of using it in the food industry (Przeor et al, 2016).

Mulberry leaves contain nutrients such as proteins, lipids, carbohydrates, fiber, β carotene, xanthophylls, vitamin C, and complex vitamins, including folic acid, vitamins D and E, β -sitosterol, and minerals. Mulberry leaves are also rich in valuable compounds of pharmacological activity, including polyphenolic compounds such as quercetin 3-(6-malonyl-glucoside), kaempferol 3-(6-malonyl-glucoside), rutin, morcetin, isoquercetin, astragalin, and other glycosides, tannins, and coumarins, as well as phenolic acids. The most common biologically active compounds present in white mulberry and defined as probably antidiabetic are shown in Table (3.1).

Table (3.1) The most common biologically active compounds identified as probably antidiabetic in medicinal plants.

Medicinal Plant	Biologically Probably Res Antidiabetic Act	Main Antidiabetic Mechanism of Action on Organism	
White mulberry <i>Morus alba</i> L.	1.5-dideoxy- 1.5- imino- D-sorbitol (DNJ)	HO OH	inhibition of α-amylase; inhibition of α- glucosidase; hypolipidemic;
	morin	он о он	antioxidant
	galactomannans	-	
	4- hydroxyisoleucine	H ₃ C CH ₃ O OH OH NH ₂	
Fenugreek Trigonella foenum graecum L.	saponins	-	decrease blood glucose concentration
	trigonelline + nicotinic acid	он он + Он	

Numerous scientific reports have proven that chemical substances, including polyphenolic compounds, contained in white mulberry leaves demonstrate antiradical activity as well as chelating and reducing properties. Thus, extracts of mulberry fruits may prevent liver cancer, and leaf extracts lower postprandial glucose or are used in antidiabetic treatment and show antibacterial activity; white mulberry can inhibit atherosclerosis due to its antioxidant activity. In Chinese medicine, the brews are used in the treatment of colds, sore throats, and toothache and also in liver protection and for the purposes of lowering blood pressure. Moreover, white mulberry extracts are used in the treatment of skin discoloration and its regeneration (Akhtar et al, 2012).

Antidiabetic activity is strongly related to the anti-obesity effect of Morus alba. There are preclinical studies that present the mechanisms responsible for the anti-obesity effects of white mulberry. They include:

- Inhibition of digestive enzymes, i.e., pancreatic lipase, cholesterol esterase, pancreatic α -amylase (weak effect) (Akhtar et al, 2012), intestinal α -glucosidase;
- Adipocyte differentiation;
- Influence on the appetite;
- Regulation of lipid metabolism: improvement of lipid profile;
- Improving the oxidative status of the organism.

At the same time, it is difficult to find clinical studies that undertake the issue of this relationship.

Mulberry leaves are considered an important raw material, having antidiabetic and hypoglycaemic activity (Cai et al ,2016). This is related to the presence of alkaloids, including 1.5-dideoxy-1.5-imino-D-sorbitol (DNJ), terpenes, and steroids. Morus alba has a natural flavonoid— morin—that is an activator and sensitizer of the insulin receptor stimulating the metabolic pathways (Salehi, and et.al, 2019). Morin can

also reduce endoplasmic reticulum stress (this factor, combined with hyperglycaemia, largely contributes to the pathogenesis of type 2 diabetes) in diabetic rats.

3.2. Fenugreek (*Trigonella foenum-graecum L.*)

Fenugreek is an annual herbal plant with fine seeds from the Leguminosae family. In its natural state, fenugreek is found in the Mediterranean area as well as in India and China. It is cultivated mainly as a forage plant. Both the seeds and leaves of fenugreek appear in literature as an ingredient of food and as medicine.

The high levels of protein, vitamins, and mineral compounds mean that germinated fenugreek seeds are a valuable component of a so-called healthy diet. The seeds of fenugreek contain mucous polysaccharides— galactomannans (25–45%), proteins (43.8%; mainly tryptophan and lysine), free amino acids (mainly 4-hydroxyisoleucine and histidine) [106], fats (7.9%), steroid saponins, alkaloid—trigonelline, coumarins, flavonoids, sterols, lecithin, and choline as well as nicotinic acid (formed from the breakdown of trigonelline during roasting) and minerals. Fenugreek leaves are a source of β -carotene (0.019%), ascorbate

(0.22%), iron, calcium, and zinc. In the group of fenugreek polyphenol compounds, rhaponticin and isovitexin are believed to be the most bioactive.

The presence of these compounds and their interaction have a positive effect on the course of many diseases and help to protect against their occurrence. Both in vitro and in vivo studies have been conducted on the therapeutic or prophylactic role of fenugreek

Nutraceutical properties of fenugreek include, i.a., blood purification; sweat-inducing effects, supporting the removal of toxins; cleaning the lymphatic system; maintaining mu- Pharmaceuticals 2022, 15, 65 8 of 25 cous membranes in good condition; removing excess mucus from the throat; relieving colds, bronchial problems, flu, asthma, rhinitis, constipation, sinusitis, pneumonia, and laryngitis (Wani et al, 2018). The use of fenugreek seeds in supporting the treatment of neurodegenerative diseases such as Parkinson's disease has also been analyzed.

With respect to the gastrointestinal tract, it was observed that dried or germinated fenugreek seeds, or a pap made of them, stimulate appetite and digestion and are used in alimentary tract disorders: dyspepsia, tympanites, gastritis, and liver diseases. They are also used as a raw material with expectorant activity in upper respiratory tract diseases. In traditional medicine, hot compresses made from fenugreek seeds (cataplasms) are used in the treatment of local inflammatory conditions of the skin and subcutaneous tissue, e.g., furuncles, abscesses, and ulcerations (Król-Kogus et al, 2011).

Trigonella foenum-graecum is a valuable raw material in the regulation of the lipid profile. In studies (Kumar et al, 2014) with Wistar rats with obesity induced by a high-fat diet, reduction in body weight gain, body mass index, blood glucose, white adipose tissue weights, and serum insulin were observed. In clinical studies, a 30-day administration of 25 mg of fenugreek seed powder solution significantly helped in the area of dyslipidemia in newly diagnosed type 2 diabetic patients.

Fenugreek has antioxidant properties, resulting from the presence of, i.a., gallic acid, protocatechuic acid, catechin, gentisic acid, chlorogenic acid, and vanillic acid [106]. In a DPPH radical test, the value of IC50 for

a Trigonella foenum-graecum seed methanol extract was determined at 350 μ g/mL, while in a ABTS IC50 cation radical test, it was 117 μ g/mL.

The antiglycaemic activity of fenugreek probably results from the synergistic activity of various chemical compounds. Some research explains that the presence of galactomannans means that consumption of fenugreek seeds in the form of pap delays stomach emptying, moderates carbohydrate absorption, and inhibits glucose transport. It has been proposed that the mucilage contained in the raw material covers the intestine diffusion layer and thus retards nutrient absorption, including carbohydrates. It has also been demonstrated that an effect of Trigonella

foenum-graecum extract activity involves an increase in the amount of erythrocyte insulin receptors and thus peripheral glucose consumption. Hypoglycaemic activity may be related to the normalization of gluconeogenic enzymes and a decrease in glycolytic enzyme activity. In turn, Broca et al. conducted a study on rats with induced diabetes and demonstrated that 4-hydroxyisoleucine was the active component causing the hyperglycaemia reduction. In this study, the administration of 4- hydroxyisoleucine to sick animals for 6 days resulted in a glycaemia reduction from 163.5 to 143.6 mg/dL. This amino acid has been identified as the main active component of fenugreek seeds by many other researchers. 4-Hydroxyisoleucine inhibits insulin secretion in a wide concentration range, which contributes to a decrease in blood glucose levels. Apart from lowering glucose levels, fenugreek seeds also cause a reduction in TC.

There are also some reports suggesting that the hypoglycaemic properties of Trigonella foenum-graecum result from its high content of dietary fiber (up to as much as 30%), especially its insoluble fraction. Steroid saponins from Trigonella are also indicated as bioactive

compounds responsible for the antidiabetic effect of this spice, and their amount shows wide variability among the fenugreek genotypes (Arivalagan, et al, 2011).

In rats with induced diabetes, it was observed that consumption of ethanolic fenugreek seed extract (0.25 and 0.5 g per kg of body weight) for 14 days significantly reduced serum glucose compared to the control group. The level of changes was very similar to that caused by glibenclamide—a drug used for the purposes of attenuation of serum parameters in diabetics (Eidi et al, 2007).

The antidiabetic potential of fenugreek seeds extract was analyzed in a 4-week study with streptozocin-induced diabetic Sprague-Dawley rats. The dose of 100 mg per kg of body weight significantly reduced blood glucose, reduced levels of liver enzymes (aspartate aminotransferase and alanine aminotransferase), and reduced triglycerides. Moreover, mild protection of hepatic, renal, and pancreatic tissues after fenugreek administration was observed.

In terms of inhibition of pancreatic lipase, the ethanol extracts of fenugreek compared to the ethanol extracts of quinoa showed 10-fold higher inhibitory activity. In turn, the levels of α -amylase inhibition by these two raw materials were significantly lower than those obtained in tests with pancreatic lipase and were similar to each other—mild inhibition (24.8% for quinoa and 27.3% for fenugreek concentrated extracts).

They can be administered to people in a variety of forms: basic, crushed, slightly processed, or as an ingredient of functional food. The status of these plants is described as non-toxic to the average patient, allowing them to be used as a substitute for conventional pharmacology. The antidiabetic properties of the analyzed plants have been confirmed by numerous in vitro tests and many

preclinical in vivo studies published. Even though the results of the published papers are very favorable, the number of clinical trials is still disappointing. Increasing clinical trials, with the use of larger populations, is recommended. Moreover, there is a small number of trials considering mixed therapies (drugs and plant pharmaceuticals of natural origin). Plant-based diets are becoming more popular with the next generation of Europeans, also due to the ecological aspects. For this reason, future outcomes of clinical trials should indicate the optimal methods of introducing medicinal plants into the pharmacological treatment of diabetes mellitus and the optimization of doses and forms of plants in mixed therapies in order to avoid undesirable side effects. Simultaneously, the safety of the proposed therapies should be analyzed. The literature data also highlight many other activities of these plants, and the impact of bioactive compounds contained in them can be described as multi-fold.

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