

Review Article

Diabetes and Phytomedicine

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Abstract

Phytomedicines have been in use against various diseases since time immemorial. The primitive man used herbs as therapeutic agents and medicament, which they were able to procure easily. The nature has provided abundant plant wealth for all living creatures, which possess medicinal virtues. Despite considerable progress in the management of diabetes mellitus by synthetic drugs, the search for natural anti-diabetic plant products for controlling diabetes is going on. There are many antidiabetic plants known through the folklore but their introduction into the modern therapy system awaits the discovery of animal test system that closely parallels to the pathological course of diabetes in human beings. The present review article provides an outlook about the present scenario of the developments made in the field of herbal medicine research worldwide for diabetes. The latest approaches and the related challenges have also been discussed.

Keywords: Phytomedicine, Diabetes, antidiabetic plants

Introduction

Herbalism is the use of plants for medicinal purposes. The use of plants as medicines dates as far back as the origin of humankind. Plants have been the basis for medical treatments through much of human history, and such traditional medicine is still widely practiced today. Natural products from plant, animal and minerals have been the basis of the treatment of human disease. Today about 80 % of people in developing countries still rely on traditional medicine, based largely on species of plants and animals, for their primary health care. In recent years, there has been growing interest in alternative therapies and the therapeutic use of natural products, especially those derived from plants. [1] This interest in drugs of plant origin is due to several reasons, namely, conventional medicine can be inefficient (e.g. side effects and ineffective therapy), abusive and/or incorrect use of synthetic drugs results in side effects and other problems, a large percentage of the world's population does not have access to conventional pharmacological treatment, and folk medicine and ecological awareness suggest that natural products are harmless. About 25% of the drugs prescribed worldwide come from plants, 121 such active compounds being in current use. Of the 252 drugs considered as basic and essential by the World Health Organisation (WHO), 11% are exclusively of plant origin and a significant number are synthetic drugs obtained from natural precursors. Examples of important drugs obtained from plants are digoxin from *Digitalis* spp., quinine and quinidine from *Cinchona* spp., vincristine and vinblastine from *Catharanthus roseus*, atropine from *Atropa belladonna* and morphine and codeine from *Papaver somniferum*. [2]

Medicinal plants helped to secure survival of our ancestors in a non-civilized world, which was not dominated by the technological achievements of the 20th and 21st centuries. Medicinal plants were the only indispensable for basic health care of indigenous tribes in former ages as modern medicine was not in place. Even nowadays, phytotherapy is still used by a majority of the world's population. Over 50,000 plants would possess therapeutic virtues in the world and about 80% of human use herbal medicines at least once in their life. [3,4] The pharmacological screening of plants is an important mean for the discovery of new, safe, and effective drugs in classical pharmacology.[5] Hence, it comes as no surprise that research on medicinal plants and natural products derived from them experiences a thriving revival in the past years.

There are many traditional systems of medicine in the world, each with different associated philosophies and cultural origins. Some of these, such as Tibetan traditional medicine, remain relatively localized in their country of origin; while others such as Ayurvedic and Chinese traditional medicines are increasingly used in many different areas of the world. Ayurveda is the most widely practiced of the Indian traditional medicine systems, but there are others such as Siddha and Unani which are also used in the Indian subcontinent. [6]

The literal meaning of Ayurveda is "science of life" because ancient Indian system of health care focused on views of man and his illness. It has been pointed out that the positive health means metabolically well-balanced human beings. Ayurveda is also called the "science of longevity" because it offers a complete system to live a long healthy life. It offers programs to rejuvenate the body through diet and nutrition. It offers treatment methods to cure many common diseases such as food allergies, which have few modern treatments. However, one should be aware that Ayurvedic nutrition is not a "magic bullet" system but requires the full participation of

the patient to succeed. It is an interactive system that is user-friendly and educational. It teaches the patient to become responsible and self-empowered. Ayurveda is not a nutritional system for those seeking an escape or excuse to further abuse their body or mind. It is a system for empowerment, a system of freedom, and long life. [7]

Ayurveda, the oldest medicinal system in the world, provides leads to find therapeutically useful compounds from plants. Therefore, ayurvedic knowledge supported by modern science is necessary to isolate, characterize, and standardize the active constituents from herbal source. This combination of traditional and modern knowledge can produce better drugs with fewer side effects. Herbs are widely available in India and other countries. The wide spectrum makes them attractive candidates for further research.[8]

Herbal medicines in India

India is a vast repository of medicinal plants that are used in traditional medical treatments.[9] The various indigenous systems such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different ailments. [10] The use of herbal medicine is becoming popular due to toxicity and side effects of allopathic medicines. This has led to sudden increase in the number of herbal drug manufactures. [11] Herbal medicines as the major remedy in traditional system of medicine have been used in medical practices since antiquity. The practices continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of world especially in India.

India has one of the richest plants medical traditions in the world. There are estimated to be around 25,000 effective plant-based formulations, used in folk medicine and known to rural communities in India. There are over 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications. It is estimated that there are over 7800 medicinal drug-manufacturing units in India, which consume about 2000 tonnes of herbs annually.

Worldwide & Indian scenario of Diabetes

Diabetes mellitus (DM) is a menace that haunts around 366 million people, thriving every single moment (International Diabetes Federation). The time is not far when it emerges as a pernicious giant, seizing the world in its deadly clutches and challenging health problems in the 21st century. In 2007, 246 million people (roughly 6%) were affected worldwide and it is estimated that this will increase to 380 million, or 7.3% by 2030. [12,13] During last 30 years the status of diabetes, once considered as a mild disorder of the elderly, has changed to one of the major causes of morbidity and mortality affecting the youth and middle aged people. [14] Although there is an increase in the prevalence of type 1 diabetes also, but it is type 2 diabetes mellitus (T2DM), which reports for more than 90 per cent of all diabetes cases. [15] According to a recent estimate published by the International Diabetes Federation in 2006, the number of people with diabetes in India is currently around 40.9 million that is expected to rise to 69.9

million by 2025. [16] More of reasons have been attributed to trend of urbanization and rapid changes in lifestyle resulting from socio-economic advances, perhaps most importantly a "Western-style" diet. However, there is very little understanding of the causal mechanism(s) at present, more of it involves intricate speculations derived from multi-variate statistical comparisons. [17, 14]

Based on available data, increased occurrence of diabetes in Asian population can be attributed to high incidence of increased body weight, sedentary life style or other environmental factors. [18,19] Certain unique clinical and biochemical abnormalities in Asian Indians which include increased insulin resistance (IR), [20] greater abdominal adiposity i.e., higher waist circumference despite lower body mass index, [21] lower adiponectin and higher high sensitive C-reactive protein levels have now been referred as "Asian Indian Phenotype". [22,23,15]

Herbs used to treat Diabetes

The rapidly increasing diabetes mellitus is becoming a serious threat to mankind health in all parts of the world. The control and treatment of diabetes and its complications mainly depend on the chemical or biochemical agents, but the fact is that it has never been reported that someone had recovered totally from diabetes. Diabetes mellitus is a clinical syndrome characterized by inappropriate hyperglycemia caused by a relative or absolute deficiency of insulin or by a resistance to the action of insulin at the cellular level. Plant materials which are being used as traditional medicine for the treatment of diabetes are considered one of the good sources for a new drug or a lead to make a new drug. Plant extract or different folk plant preparations are being prescribed by the traditional practitioners and also accepted by the users for diabetes like for any other diseases in many countries.

The NAPRALERT database lists over 1200 species of plants representing 725 genera in 183 families extending from the marine algae and fungi with antidiabetic activity. Over half of these have been used ethnopharmacologically in traditional medicine as antidiabetics, and some 50% of these traditional remedies have been studied experimentally. [24] The use of traditional medicine and medicinal plants in most developing countries, as a normative basis for the maintenance of good health, has been widely observed. Furthermore, an increasing reliance on the use of medicinal plants in the industrialized societies has been traced to the extraction and development of several drugs and chemotherapeutics from these plants as well as from traditionally used herbal remedies.

Umashankar et al in 2011, discovered the effects of herbal remedies including the most widely sold herbal medicinal products, like liquorice, garlic, ginger, green tea, onion, methi and chilli pepper etc., against the diabetes and reinforce the safety aspect of herbal products, which are considered to be relatively safe by common people.[6]

In India, plants like *Abroma augusta* (L.) L.f., *Abutilum indicum* (L.) Sw., *Aconitum palmatum* D. Don., *Aloe barbadensis* Mill., *Asparagus racemosus* Willd., *Berberis aristata* DC., *Calamus rotang* (L.), *Cannabis sativa* (L.), *Catharanthus roseus* (L.) G. Don.,

Cinnamomum tamala (Buch.-Ham.) Nees, *Coccinea grandis* (L.) Voigt., *Costus speciosus* (Koenig) Sm., *Ficus racemosa* (L.), *Ipomoea batatas* (L.) Lamk., *Momordica charantia* (L.), *Nardostachys jatamansi* DC., *Picrorhiza kurrooa* Royle ex Benth., *Quercus lanata* Sm., *Swertia chirayita* (Roxb. ex Flem.) Karst., *Syzygium cumini* (L.) Skeels, *Trigonella foenum-graecum* (L.), *Urtica dioica* (L.), *Zingiber officinale* Rosc., *Allium cepa* L., *Allium sativum* L., *Aloe vera* (L.) Burm.f., *Cajanus cajan* (L.) Millsp., *Coccinia indica* Wight & Arn., *Caesalpinia bonducella* (L.) Roxb., *Ficus bengalensis* L., *Gymnema sylvestre* R. Br., *Momordica charantia* L., *Ocimum sanctum* L., *Pterocarpus marsupium* Roxb., *Tinospor cordifolia* (Willd.) Hook.f. & Thomson, etc., are most commonly used species in traditional medicine as antidiabetic agents. [25,26]

Al-Rowais in 2002, determined the prevalence of the use of herbs among diabetics and study was conducted on diabetic patients attending the outpatient clinics in 4 major hospitals in Riyadh, Kingdom of Saudi Arabia. He observed that 296 diabetic patients out of 300 were interviewed giving a response rate of 98.6%. Fifty-one subjects (17.4%) reported using some form of herbs. The commonest herbs used were myrrh, black seed, helteet, fenugreek and aloes.[27]

Otoom et al in 2006 observed in his cross-sectional study that was conducted by interviewing 310 diabetic patients visiting two medical centers in Jordan: Jordan University of Science & Technology Medical Center and Sarih Medical Center between December 2003 and August 2004. They found that 31% of interviewed patients have used herbal products (96 patients). The results revealed that the most commonly used herbs by diabetic patients in Jordan were *Trigonella foenum-graecum* (22.9%), *Lupinus albus* (14.6%), *Allium sativum* (11.5%), *Allium cepa* (5.2%), *Nigella sativa* (7.3%), *Zea mays* L. (6.3%), *Urtica dioica* L. (8.3%), *Eucalyptus globules* LA (9.4%), *Olea europea* L. (3.1%), *Cuminum cyminum* (9.4%), *Coriandrum sativum* (10.4%), *Salvia officinalis* L. (3.1%), and *Tilia cordata* (1%). Furthermore, it was found that 47.9% of the patients used herbs according to advice from their friends on a daily basis. [28]

Li et al in 2004 reported that from large number of chemical and pharmacological research work, numerous bioactive compounds have been found in Chinese medicinal plants for diabetes. They reviewed 86 natural medicines with regards to their origin, anti-diabetic active principles and/or pharmacological test results, which are commonly used in the traditional Chinese medical system and have demonstrated experimental or/and clinical anti-diabetic effectiveness. Among these natural medicines, 82 originate from plants and 4 from animals or insects, which covers 45 families. It is strongly significant to pay close attention to traditional Chinese medical therapeutics and natural medicines for treatment of diabetes mellitus and its complications.[29]

Malviya et al in 2010 reviewed natural medicines with their mechanism of action and their pharmacological test results. Also collected available data on plants with anti-diabetic activity reported in the pharmaceutical journals. In their study, they reviewed that most of plants contain glycosides, alkaloids, terpenoids, flavonoids,

cartenoids, etc. that are frequently implicated as having antidiabetic effect. They were *Anacardium occidentale* Linn., *Annona squamosa* Linn., *Annona muricata* Linn., *Boerhaavia diffusa* Linn., *Bougainvillea spectabilis* Linn., *Bridelia ndellensis* Beille., *Canavalia ensiformis* DC., *Cassia kleinii* Wight & Arn, *Cocculus hirsutus* Linn., *Dioscorea dumetorum* Pax, *Ficus hispida* Linn, *Murraya koenigii* Linn., *Syzygium cumini* Linn., *Terminalia chebula* Retz., *Terminalia catappa* Linn. Etc[30]

Tag et al in 2012 studied herbal medicines used in the treatment of diabetes mellitus in Arunachal Himalaya, northeast, India and identified forty-six plant species to treat diabetes mellitus by the Khamptis "Chau ya" traditional healers. These plant species are *Begonia roxburghii*, *Calamus tenuis*, *Callicarpa arborea*, *Cuscuta reflexa*, *Dillenia indica*, *Diplazium esculentum*, *Lectuca gracilis*, *Millingtonia hortensis*, *Oxalis griffithii*, *Saccharum spontaneum*, and *Solanum viarum*. Some of the plants reported in this study have an antidiabetic effect on rodent models but none have sufficient clinical evidence of effectiveness. [31]

Pharmaco-genomic approaches for Diabetes Mellitus and the Related Challenges

Genomics is now playing a major role in identifying information from the human body and applying it to current drug therapy. It has produced a new era of individualized drug therapy for patients to achieve higher efficacy and safety. Due to the enhanced development of today's technologies, the long-term benefits of pharma- cotherapy management are becoming closer to implement in clinical practice. [32]

The concept of pharmacotherapy has been influenced through previous research of associating populations with respect to their geographical, ethnic, or racial back- ground in regards to their disease disposition or intelligence. In return, pharmacotherapy research has taken this association to correlate genetic response to medications. [32,33]

The search for new medicinal products has been extrapolated from plants, animals, and micro-organisms, with historical evidence suggesting the use and benefits of natural products. [34] It has led the pharmaceutical industry to several plant-derived medications through modern analytical and structural analysis of plant-based compounds. [35]

Long before the birth of orthodox Western medicine, medicinal herbs were applied to treat a wide range of disease categories. [36] Due to emphasis on scientism and other complicated reasons, Western medicine now prevails over "traditional" forms of medicine including herbal medicine systems. Although herbal medicine systems are sometimes misinterpreted as being unscientific and anachronistic, their long-term existence proves they are able to compete with Western drugs at some level. The use of a medicinal herb, alone or in combination with other herbs, can be thought of as a type of combination therapy because of the complexity of the phytochemicals and bioactivities in the plant. Thus, a single antidiabetic herb with thousands of phytochemicals may have multiple benefits by targeting several metabolic pathways.



Medicinal herbs have never become obsolete and still play a prominent role in human health care. Among them, over 1200 plants have been claimed to be remedies for diabetes. [37, 38] Over 400 plants as well as 700 recipes and compounds have been scientifically evaluated for type 2 diabetes (T2D) treatment. [39] Metformin was developed based on a biguanide compound from the antidiabetic herb, French lilac, and is now a first-line drug for T2D. [40] Medicinal herbs contain diverse bioactive compounds and can have multiple actions on insulin action, insulin production, or both.

Conclusion

Medicinal herbs, long used in alternative and complementary medicine systems, are an extremely rich source of diabetes remedies. Currently, understanding of the mechanisms through which herbal therapies mediate diabetes is evolving, and they are generally being viewed as modulating of multiple metabolic pathways. Based on safety and their multiple targeting actions, herbal therapies are potent therapeutic means in diabetes. The chemistry and biology of nearly 40 extracts and compounds of plant origin have been demonstrated to prevent and treat T2D via the regulation of insulin resistance, cell function, incretin pathways,

and glucose (re)absorption. However, in addition, the actions, mechanisms and therapeutic potential of plant compounds and/or extracts, and new insights into the advantage of herbal therapy, which simultaneously governs distinct metabolic pathways, immune cells and cells need to be evaluated for T2D. Systematic information about the structure, activity, and modes of action of these plants and compounds needs to be explored that will ultimately pave the way for research and development of antidiabetic drugs.

Conflict of Interest

The authors declare that there is no conflict of interest.

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