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MEDICINAL PLANTS AND THEIR ACTIVE CONSTITUENTS FOR THE TREATMENT OF METABOLIC SYNDROME

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Abstract

To increase the risk of cardiovascular disease, stroke, and type 2 diabetes, a group of metabolic diseases known as "metabolic syndrome" must be present. Metabolic syndrome may be treated with the help of medicinal plants' plethora of bioactive components, such as phytochemicals, which have a wide range of effects on the metabolism. There is some indication that these plants have been used medicinally for quite some time. The other side of the coin is that in order for botanical preparations to be standardized and described before they can be utilized successfully against metabolic syndrome, controlled clinical studies with well-defined outcomes are required. During this procedure, the active chemicals and the mechanisms by which they exert their effects are identified. In this research, which reviews examples of botanicals that are both well-known and incompletely explored, considerations for the phytochemical, preclinical, and clinical characterization of botanicals connected to metabolic syndrome are discussed. These considerations concern the botanicals' potential effects on metabolic syndrome.

Keywords: - *Diabetes, Hypertension, Cardiovascular illness, Medicinal Plants and Botany.*

Introduction

Metabolic disorders are very common and impact a large portion of the global population. Some examples of these diseases include cancer, obesity, NAFLD, and type 2 diabetes mellitus (T2DM). Chronic illnesses may develop when these irregularities disrupt the body's metabolic rate and energy balance. The treatment of metabolic illnesses is seeing a resurgence of the use of chemicals and plant extracts as medicinal agents. These methods have a long history of use, and their efficacy in treating various diseases has been well-documented. Pharmacological approaches are the only ones that can be utilized to create remedies for specific illnesses. Using computational methods, one may determine the pharmacological activity of a metabolite or extract and also provide early theories about likely targets and processes. Potential novel treatment targets and approaches for metabolic illnesses may be better understood if we had a better grasp of the molecular processes underlying these conditions and the potential advantages of herbal medications, particularly herbal medicinal products. [9](Lu, *et al.* 2019)

There is a long history of using herbal medicines for a wide range of diseases, and the use

of herbal medicines in the treatment of metabolic disorders is consistent with this tradition. The use of pharmacological techniques is very necessary for the identification and assessment of herbal treatments for a wide variety of illnesses. In the event that an individual's metabolic profiles shift as a consequence of the routines they engage in on a daily basis, we refer to this as a lifestyle disorder. Lifestyle issues such as casual eating habits, ignored exercise routines, and other similar factors have been linked to a significant number of lifestyle-related diseases. [14](Singh, *et al.* 2020). The rise in the prevalence of metabolic syndrome may be attributed to the epidemic of obesity. The World Health Organization defines metabolic syndrome as a collection of health problems that include insulin resistance, hypertension, abnormal lipid profiles, and abdominal obesity. Additionally, excess fat around the waistline is a hallmark of metabolic syndrome. One of its many names is insulin resistance, and it is this disease that explains syndrome X. Co-occurring disorders include, but are not limited to, prothrombotic disorders, proinflammatory disorders, nonalcoholic fatty liver disease, and reproductive problems. The socioeconomic status of an individual has a substantial influence on their prognosis for long-term metabolic conditions like diabetes. Diabetic prevalence has been on the rise in several developed nations throughout the past few decades. This trend has been slow but steady. If current treatment strategies do not change, the International Diabetes Federation projects that the number of people living with diabetes would grow by 693 million by 2045. [6](Jarouliya, *et al.* 2019)

Due to the fact that diabetes has been increasingly prevalent over the last several decades, it is anticipated that this rising trend will continue. These specific issues, together with cancer, respiratory disorders, and cardiovascular effects, account for 80% of the fatalities caused by preventable noncommunicable diseases (NCDs). According to data from the International Diabetes Federation, the prevalence of diabetes in India is increasing. [3](Chawla, *et al.* 2013). Diabetes affects around 8.7 percent of the world's population at some time in their lives, mostly between the ages of 20 and 70. A characteristic feature of type 2 diabetes is difficulties in the metabolism of glucose, lipids, and proteins. Following this point, insulin resistance or insufficiency will begin to develop. Type 2 diabetes mellitus is characterized by a number of signs and symptoms, including thirst, polyuria, poor vision, and weight loss. Over eight decades have passed since the discovery of metabolic syndrome. The prevalence of metabolic syndrome has significantly increased around the globe over the course of the last two decades. The epidemic of obesity and diabetes that is sweeping the globe is one of the factors that is contributing to this rise. It is imperative that there be treatments available in order to put a halt to the imminent global pandemic of metabolic syndrome, which serves to raise the risk of both diabetes and cardiovascular disease. (Keservani,*et al.* 2017)

Objective

1. List medicinal plants with positive effects on metabolic syndrome components, both traditionally and scientifically.

2. Conduct a comprehensive examination of ethnobotanical and pharmacological literature to find interesting candidates.

Management of Metabolic Syndrome with Herbal Medicine

The metabolic disease known as type 2 diabetes, or diabetes mellitus (DM), affects millions of individuals globally. Internal variables that contribute to the onset of diabetes include inadequate insulin production and inadequate pancreatic insulin synthesis. Although several synthetic medications have been developed, none of them provide a long-term solution. We still need nontoxic, reasonably priced medications, even if there may be serious side effects from using some synthetic compounds over a long period of time. Almost every culture that has ever existed has had a great deal of regard for traditional medicine. Because of their widespread use, it is evident that herbs constitute an integral part of cutting-edge, modern medicine. Out of the 21,000 plants used for medicinal reasons worldwide, at least 400 might be used to treat diabetes, according to the World Health Organization (WHO). [16](Suryawanshi, *et al.* 2020)

It is possible that plant extracts or bioactive components might heal a wide variety of plants. This encompasses pharmaceutical formulations that include metabolic syndrome and are created by nanotechnology. Researchers and medical professionals are now investigating new, complementary and alternative therapy approaches that are both safe and effective in order to tackle this pervasive problem. New herbal remedies have emerged in recent years, and they may aid in weight loss and fat reduction. Several of the possible medicinal uses of herbs have been investigated in human and animal clinical trials [1](Cao, *et al.* 2022). Among them is the prospect that they may alleviate inflammation, reduce free radical damage, and cure diabetes and obesity. Despite being simple, inexpensive, and entirely natural, medicinal herbs have advantages when used as a substitute for conventional medicine in the treatment of metabolic disorders. There is evidence that some herbal remedies may improve insulin secretion, cardiovascular health, inflammation, gluconeogenesis, and oxidative stress. Multiple investigations have confirmed these advantages. Diabetes and its complications have prompted the development of many plant extracts as possible therapies. A possible way to improve the anti-diabetic effects of herbal extracts in nanostructured formulations is by controlling their pharmacokinetics and increasing their body availability. [10](Nanjappan, *et al* 2018)

Even though the use of some synthetic chemicals for an extended period of time may result in major adverse consequences, there is still a continued need for medications that are widely accessible and safe. For a considerable amount of time, people were under the impression that conventional treatments were the most successful. These are utilized extensively all around the world, which demonstrates how herbs are becoming an increasingly significant component of contemporary and cutting-edge therapy. One of the most significant advantages of herbal medicines is that they have a minimal risk of adverse effects. This is one of the reasons why several researchers have been inspired to create novel molecules for the treatment of diabetes. A

wide variety of herbal medications are now being investigated in various phases of clinical trials, and all of them have the potential to treat diabetes and avoid the problems that are associated with it. [11](Parasuraman, et al. 2018).

Several herbal medicines, including capsicum annum, which belongs to the capsicum family, have been demonstrated to have the potential to enhance glucose tolerance, lower insulin levels, and raise peripheral insulin sensitivity. These are all factors that contribute to the anti-diabetic advantages experienced by individuals with diabetes. Capsaicin, the active component of capsicums, stimulates the body to create GLP-1, which in turn elevates blood glucagon levels and reduces ghrelin levels, which is an orexigenic hormone. Capsicums are associated with a multitude of health benefits. The activity of amylase and glucosease has been proven to be decreased, according to investigations conducted prior to clinical trials. [15](Singh, *et al.* 2021)

Relationship Between Ayurveda and Modern Medicine

Ayurveda is a well-known ancient medical system that originated in India. It has made a substantial contribution to the development of contemporary therapies for chronic ailments. It is possible that the building of structural activity libraries might be improved by integrating the remarkable capabilities of combinatorial sciences and high throughput screening with the extensive knowledge base of ancient systems such as ayurveda. Medicine development has a number of significant hurdles, some of the most significant of which include time limits, economic constraints, and considerations linked to toxicity. Utilizing Ayurvedic knowledge in conjunction with experience databases may result in the discovery of novel functional leads that may be used to address these challenges. Due to the fact that these medications have been examined in great detail on human subjects for a considerable amount of time and have a lengthy history of use, this knowledge is very important. There is currently a lack of comprehensive pharmacoepidemiologic evidence on the efficacy and safety of ayurvedic medicines. Standardized herbal formulations are now the center of attention at the New Millennium Indian Technology Leadership Initiative (NMITLI), which is overseen by the Scientific and Industrial Research Organization [8](CSIR). (Li, *et al.* 2017)

Treatment of Diabetes with All-Natural Methods

Alternative remedies are quickly becoming more popular, and they are following in the footsteps of the long-standing practice of using natural ingredients as a kind of therapy. The results of a telephone study conducted in the United States in 2002 revealed that 18.8 percent of individuals routinely include natural products such as herbs into their diet. Because of the potential for harmful effects, such as severe hypoglycemia, and the lack of safety associated with synthetic anti-diabetic medications, it is essential to research alternative pharmacological choices when it comes to the treatment of diabetes. There are several instances in which alternative medications ought should be simpler to get, less costly, and far safer. [5](Fang, *et al.* 2018). According to the globe Health Organization, countries with low and intermediate incomes are home to around 65–80 percent of the total population of the globe. This group need access to

traditional treatments since there are not enough modern medical services available to them. At first glance, it would seem that the perspectives and values of patients are more in line with the various alternative therapeutic approaches. As part of their diabetic treatment plans, Eastern and some Western countries, such as the United States of America, Germany, France, and Italy, make use of herbal therapy. [4](Dutra, *et al.* 2016). It is one of the alternative medications that is used the most often. Plants' therapeutic qualities ensure their continued prominence in the medical and pharmaceutical industries, even in the face of the fast development of modern medicine in recent years. [2](Castro,*et al.* 2016)

It is abundantly obvious that natural goods continue to be an excellent source for discovering possible new pharmaceuticals, since there are now a vast number of substances that originate from natural products that are being tested in clinical studies. Due to the fact that the evidence that is currently available is inadequate, more meta-analyses and systematic reviews are required in order to validate the effectiveness and safety of herbal medicines. [13](Sharma, *et al.2020*)

Polyphenols

Aromatic compounds make up the great bulk of phenolic chemicals found in plants. Also included in this category are anthocyanins and flavonoids. The five main classes of flavonoids—flavones, and isoflavones—will be covered in this article. Among the many useful characteristics of plants in this genus, the chelating of metals, activation of antioxidant enzymes, and capture of free radicals are among the most recognized. Their potential benefits include protecting cells from oxidative stress and lessening the impact of ROS and ARN emissions. A comprehensive review of randomized controlled trials including resveratrol in conjunction with other treatments for type 2 diabetes was published not long ago. Recent years have seen the conduct of several trials. Systolic blood pressure, hemoglobin A1C, and creatinine all shown statistically significant benefits with resveratrol as compared to the control or placebo. When it came to insulin, fasting glucose, diastolic blood pressure, HOMA index, and lipid profiles, however, none of those things improved. [18](Yan, et al. 2020)

Glycetein, genistein, and daidzein are the three main isoflavones that people consume. Soybean is the primary source for most of these isoflavones. Soybeans have more genistein than any other isoflavone. Glucose absorption by peripheral tissues and pancreatic insulin release might both be enhanced by genistein. Curcumin, a polyphenol present as diferuloylmethane, is the principal ingredient of turmeric, a spice used in cooking. Ayurvedic medicine in India has a long history of using this ingredient, which is derived from the Curcuma longa plant. Among its many antioxidant characteristics are the following: scavenging free radicals, decreasing adhesion molecules and antiapoptotic proteins, halting lipid peroxidation, and inhibiting pro-inflammatory cytokines.

Nrf2 activators

As a consequence of oxidative stress, a number of Nrf2 activators have been discovered

as potential treatments for illnesses that are associated with it. Activators that are currently being studied in clinical trials include the synthetic triterpenoid bardoxolone methyl and the natural isothiocyanate sulforaphane, which may be found in broccoli sprouts. Researchers must proceed with caution when modifying this mode of administration, according to the early results of a phase 3 clinical study of bardoxolone methyl in patients with type 2 diabetes and chronic renal impairment.

Herbal phosphodiesterase inhibitors

PDEIs have the potential to inhibit phosphodiesterase (PDE) via increasing levels of cAMP and cGMP. PDEIs were shown to have both anti-inflammatory and antioxidant properties during the course of the investigation. There was a correlation between these benefits and a reduction in the levels of oxidative stress and lipid peroxidation, as well as an increase in the capacities of antioxidants, and an improvement in the performance of cultured islet cells.

One of the dithiol molecules called lipoic acid is formed from octanoic acid. Among its many antioxidant characteristics include the ability to bind metal ions, scavenge free radicals, and recycle antioxidants. Successful replication of diabetic complications in animal models of the illness includes retinopathy, neuropathy, altered nerve transmission, and reduced blood flow. Melatonin, also known as 5-methoxy-nacetyltryptamine, is produced by the pineal gland. Melatonin may reduce oxidative stress and stop cancers from growing. It protects DNA, proteins, and membranes from harm thanks to its antioxidant properties. reduced lipid peroxidation and increased catalase (CAT) activity are the results of reduced hepatic glutathione peroxidase (GSH-Px) activity. The results of the reduced activity level are these. [19](Zhang, *et al.* 2018)

Anti-obesity effects of natural treatments

Results from clinical examinations on herbal remedies for obesity have shown that these remedies are beneficial in reducing body weight, fat mass, waist and hip circumferences, and calorie consumption, in addition to displaying antihyperglycemic, antihyperlipidemic, and antioxidant characteristics. The following plants may be useful in the battle against obesity, according to studies.

A few of these features include a rise in energy expenditure and a fall in the rates of lipid absorption, energy intake, pre-adipocyte differentiation and proliferation, lipogenesis, and lipolysis. Chemicals that can affect food intake include caffeine, ephedra, Caralluma fimbriata, hydroxycitric acid, fenugreek fiber, epigallocatechin (found in green tea), and a complex that occurs naturally and contains capsicum and various lipotropic components. Some chemicals that might impact hormonal balance include Agave tequilana, Dasylirion spp., Pomegranate leaf, Tree peony root, and Gyeong Shang angjeehwan. In large enough doses, these drugs may also reduce appetite and cholesterol in the blood.

The phytochemicals that may be found in food can be broken down into four primary categories: polyphenols, terpenoids, organosulfur, and phytosterols. The fact that they are able to suppress the formation of adipose tissue, pre-adipocyte differentiation, lipolysis activation, and

apoptosis induction makes them powerful anti-obesity drugs.

Among the polyphenols are: There is a subclass of polyphenols known as stilbenes, which resveratrol is inside. Resveratrol (grapes, blue berries, peanut) is a substance that has been shown to have weight-loss and antioxidant benefits. The fact that it protects against oxidative stress is more likely to be attributed to the influence that it has on redox enzymes than to the moderate amount of ROS that it is able to scavenge. Resveratrol inhibits eNOS uncoupling, increases antioxidant enzyme activity, and boosts eNOS expression, among its many essential effects. It does this via altering apoptotic activation, lipolysis, calorie-regulating enzyme activity, and fat mass. It prevents mature preadipocytes from surviving and also stops the process of adipogenesis. Beyond this, it may inhibit TNF-activated NF-B signaling, alter adipokine expression, increase insulin sensitivity, decrease lipid synthesis, and slow cell proliferation. [12](Rane, *et al.* 2020)

Additionally, curcumin is a polyphenol that belongs to the group of chemicals known as curcuminoid. Among curcumin's many medicinal uses include lowering blood sugar levels, protecting the liver, and increasing adiponectin. Production, the reduction of body weight gain, and the regulation of the expression of genes such as PPAR that are involved in the metabolism of energy, the storage of fat, and the process of lipogenesis. Additionally, it has the potential to reduce inflammation, angiogenesis, and metabolic problems such as insulin resistance, hyperglycemia, that are often associated with obesity. (Tabatabaei *et al*. 2015)

Conclusion

Patients who have worries about their lifestyle individuals at an increased risk for developing a range of diseases, including aortic stenosis, stroke, thromboembolic sickness, atrial fibrillation, and heart disease. The findings suggest that those who have metabolic syndrome may be at a much higher risk of experiencing an ischemic stroke than was previously believed. Metabolic syndrome is related with a higher chance of developing malignancies of the gallbladder, colon, and kidneys, which is one of the additional consequences that are connected with the condition. The risk of cognitive impairment is also increased in those who have metabolic syndrome. Finally, those who have polypharmacy is more often used to describe metabolic syndrome than the general population. Because of this, medical expenses go up, the likelihood of falling into poverty goes up, and there are more obstacles to overcome in order to have access to care of a high standard. It is anticipated that basic medications would decrease the symptoms of metabolic syndrome, and these treatments are risk-free. It is anticipated that complementary and alternative medicine will prove to be a viable treatment option in the future. In this scenario, patients have faith in alternative medicines such as plant-based drugs since they are reliable, non-toxic, and cost-effective. This enables them to avoid the financial constraints and hazardous side effects that are connected with pharmaceuticals.

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