

A Polyherbal formulation Katakakhadiradi kashayam in treatment of Diabetes – Review

Abstract

Diabetes is a common non-transmittable disease in the world today. It is the fourth leading cause of mortality in most developed nations and there is significant proof that it is widespread in many developing and newly developed nations. Diabetes patients are at risk of developing ischemic heart disease, cerebrovascular disease, and peripheral vascular disease, all of which can result in severe morbidity and death. The most widely used alternative therapy for glycaemic control is herbal medication. The effectiveness of botanicals in lowering sugar levels has been confirmed scientifically for a variety of Indian plant species. Numerous plants have been shown to be effective in treating a variety of systemic illnesses in traditional medical systems. Although many traditional/indigenous medical systems are more effective than modern medications, one of the biggest problems facing traditional medicine is the absence of comprehensive standardisation. The antioxidant, anti-inflammatory, and hepatoprotective qualities of Katakakhadiradi kashayam may be responsible for its antidiabetic effects, but further research is needed to fully comprehend this kashayam's protective effects against a variety of ailments.

Keywords: Antidiabetic, Polyherbal formulation, Katakakhadiradi kashayam.

Introduction

Diabetes is a disorder that has the potential to cause long-term problems (Bush et al., 2016). People who are overweight or obese, 45 or older, have a family history of diabetes, high blood pressure, a low level of HDL cholesterol, or a high level of triglycerides, have a history of gestational diabetes or have given birth to a baby weighing 9 pounds or more, have a history of heart disease or stroke, depression, or polycystic ovary syndrome are more likely to develop diabetes (Gaulton, 2017). Diabetes can be avoided or delayed in persons at high risk of diabetes with a combination of dietary, lifestyle, and modest weight loss, according to research (Fahaver et al., 2019).

Diabetes can induce chronic kidney disease, permanent blindness, and non-traumatic lower limb amputations by causing kidney disease (nephropathy), vision impairment (retinopathy), and neurological damage (neuropathies) at the macrovascular level. This demonstrates the risk of diabetes, as the stated problems impact numerous systems in the body, and the consequences can seriously impair people's quality of life. Type 2 Diabetes Mellitus T2DM is a chronic condition that has a bigger impact on the public health system. Diabetes' metabolic control and the consequences connected with its treatment are both expensive to treat, in addition to producing a high level of morbidity and death. (Papetheodorou et al., 2017). Instead of using a single medication, the plants' combination extracts and formulations have been

employed as an anti-diabetic. Because of this, research to create more effective and cutting-edge antidiabetic formulations is urgently needed, according to the anti-diabetic activity of polyherbal formulations. The different clinical studies showed that polyherbal formulations significantly reduced blood sugar levels in humans (Kheria & Bhatia., 2014)

We used the Mesh words "polyherbal formulation," "Ayurvedic formulation," "herbal formulation," and "type 2 diabetic mellitus" to search PubMed, Scopus, and CINAHL completely up to December 2021. In addition, we carefully browsed Google Scholar and the citations of important articles. Each article that was obtained had its title and perhaps its abstract scanned. The complete report was acquired.

Therapy for Diabetes

Although pharmacological medicines are becoming more sophisticated and have more therapeutic potential, particularly in T2DM, changes in patients' lifestyles are essential to their treatment plans and are required to achieve therapeutic objectives. The co-morbidities that might coexist in a diabetes patient must also be taken into account when dietary intervention is being explored. Dietary recommendations can assist people in achieving their ideal weight, lipid profile, hypertension, insulin resistance, sleep disturbances, and blood pressure, while also reduce depression and increase quality of life altogether. Overweight and obesity may benefit the development of diabetes and its symptoms. Weight loss will primarily increase insulin sensitivity, which will help to enhance the glycemic control parameters. Consuming enough dietary fibre, particularly fibre derived from natural resources, has been linked to better glycemic and cardiovascular risk factor management, which results in a decreased risk of cardiovascular mortality in diabetics. In general, encouraging exercise within a specified plan offers a number of advantages: improved glycaemic management, lipid profile and blood pressure alterations, weight maintenance or reduction, cardiovascular advantages, improved quality of life, and psychological wellbeing.

Oral hypoglycemic drugs like metformin are considered the agent of first line for treatment of T2DM, in the absence of contraindications. Sulfonylureas and insulin secretagogues are two various types of oral hypoglycaemic medicines but they have a similar action mechanism, and they excite pancreatic beta cells to secrete insulin. Acarbose has been shown to have favorable effects by decreasing the risk of cardiovascular illness and delaying the development of diabetes in people with glucose intolerance. The use of these agents including Dipeptidyl peptidase-4 inhibitors, sodium glucose co-transporter-2 inhibitor and various injectable agents for diabetes is often restricted by their potential to induce significant side effects. For instance, metformin may induce nausea, diarrhoea, and in rare cases, lactic acidosis, whereas sulphonylureas or insulin may result in hypoglycemia and weight gain. Oedema and weight gain are also linked to thiazolidinedione usage. Modern medications, such as incretion mimics, can cause nausea, diarrhoea, and vomiting. Even with a combination of many oral medications and the addition of insulin, glycemic control might be difficult to achieve.

Therefore, efforts to develop novel action mechanisms for therapeutic medicines that do not have these adverse effects are ongoing.

Alternative treatment of diabetes

Patients with diabetes are increasingly seeking alternative therapies with antihyperglycemic properties. Given that chronic diseases, that will only be substantially relieved by conventional treatment, have been the conditions for which alternative remedies have been most extensively adopted, this is not unexpected. The most widely used alternative therapy for glycaemic control is herbal medication. The effectiveness of botanicals in lowering sugar levels has been confirmed scientifically for a variety of Indian plant species. But because several non-standardized versions of the herbs have been used as the testing material and the results have been challenging to duplicate, its efficacy and tolerability should be further evaluated by well-designed study, controlled clinically. As a result, the demand for standardised medicinal herb formulations in treatments is urgent, and a number of functional ingredients have indeed been proven to be helpful for diabetics either because of their potential or because of their favourable effects on glucose homeostasis (Saputhra et al., 2019).

The most important nutritional supplements include vanadium, nicotinamide, chromium magnesium, and vitamin E. Yoga, chiropractic, relaxation techniques, chromotherapy, and hydrotherapy are further potential complementary treatments for diabetes (Shende and Patel, 2019). The inadequacy of currently available oral antidiabetic medications in terms of safety or effectiveness, along with the emergence of other diseases that have become epidemics worldwide, Therefore, given the present circumstances, we should promote alternative therapies that may manage diabetes more effectively and safely (Ahmeda and Essaa, 2019).

Ayurveda is an antiquated medical system that is becoming more and more popular around the world as an alternate and supplementary therapy for chronic illness. T2DM is a lifelong illness that has serious long-term effects on both the individuals who have it and the healthcare system itself. The traditional Indian medical system of Ayurveda combines changes in nutrition, exercise, and lifestyle as important components of the efficient treatment of T2DM. In Ayurvedic medicine, the aetiology, causes, and illness treatment of diabetes are well known.

Synergistic effect:

Synergistic outcomes occur when two or even more medications combine to achieve a combined efficacy that is larger than the sum of the effects of the individual treatments. Pharmacodynamic and pharmacokinetic synergy are the two subcategories under which the synergistic properties of drugs are classified by pharmaceutical science. The term "pharmacodynamic synergistic" refers to the interaction of two or more medications on the same receptors that results in greater therapeutic benefits. The interaction of two or more medications results in better absorption, distribution, metabolism, and excretion of the drug, increasing the drug's concentration in the body and enhancing its therapeutic qualities (Zohu et al., 2016 & van Vuuren and Vijoen., 2011).

According to reports, combining medicinal plants to create complex polyherbal formulations has complicated synergistic effects that increase the bioavailability of active ingredients, promote therapeutic benefits, and lower toxicity. As a result, mixtures of two or more herbs that have antidiabetic properties demonstrate the potential for synergistic antidiabetic action (Williamsom., 2001).

Through underlying mechanisms including the control of similar or dissimilar targets in various pathways, polyherbal formulations' synergistic therapeutic effects are made possible. As a result, combination increase effectiveness, regulate enzymes, and enhance the absorption of oral medications and counteract overcoming medication resistance mechanisms and negative consequences. Synergism occurs when several chemical components are combined. present in either a single herb or a group of herbs (Amin et al., 2015a), which are potential treatments for certain diseases targets. Polyherbal therapy are based on this (Ma et al., 2009; Aziz et al., 2013) and therefore is regarded as more reasonable effective in illnesses with several targets (Zimmermann et al., 2007). The effects-improving and side-effect-reducing capabilities of various herbal mixtures (Gilani and Rahman, 2005)

Polyherbal formulations in the management of diabetes

The ancient literature has a clear framework for how polyherbal formulation is perceived. The herbal extracts formulation has better and longer therapeutic activity compared to the single herb. The well-known herbs *Tridax procumbens*, *Glycosmis pentaphylla*, and *Mangifera indica* are widely available in India and are frequently used to treat a variety of ailments, including diabetes mellitus. Animals were administered a polyherbal formulation that lessened the degree of the histological alterations brought on by STZ (Shah et al., 2019).

According to a research by Begun et al. (2019), the study participants showed a notable reduction in weight, indicating that the polyherbal formulation protects the hyperglycemia-induced loss of muscle. Enhanced plasma insulin levels or elevated blood sugar transport into peripheral tissue may be to blame for the drop in glucose levels. The research provides evidence that the herbal extracts formulation raises plasma insulin sensitivity and has a beneficial antidiabetic impact. Increases in serum concentrations , SGOT, SGPT, urea, and creatinine—remarkable indicators of compromised liver and renal function—were caused by the STZ-induced diabetes hyperglycemia. The impact of STZ on the kidney and liver markers was reversed in the patients treated with the polyherbal formulation. This might be as a result of the formulation's individual herbs' hepatoprotective properties. The STZ-induced hyperglycemia in the treated rats was prevented by the polyherbal formulation, which may have been due to the different herbs' unique free radical scavenging properties (Shah et al., 2019).

Katakakhadiradi kashayam

The use of conventional drugs to treat diabetes has a bright future. Several medicinal plants are used to treat clinical disorders related to diabetes, and certain medicinal herbs have indeed been believed to be helpful in diabetes globally with little to no scientific support for their hypoglycemic and diabetic effects. Several medications have been discussed in relation to conditions resembling diabetes in the Ayurvedic classics, and numerous concoctions have been utilised in actual practise by various schools of practitioners for thousands of years. The Ayurvedic remedy "Katakakhadiradi kashayam" is used to cure diabetes, urinary tract infections, and skin conditions. Twelve different plant species make up the kashayam, which is used to treat illnesses linked to the vata and kapha doshas. Once or once a day, five to ten ml of this medication should be given before eating, or as directed by a doctor. Regular mild exercise and abstaining from sweets are encouraged. Swetha gunjadigulika, Niruryadigulika, and Mehasaharigulika are used as adjuvants along with this medication (Jessica et al., 2016).

A herbal remedy called katakakhadiradi kashayam contains 10 gram of twelve different plants. The following herbs are employed in the preparation of the kashayam: Kataka (Strychnos potatorum), Khadira (Acacia catechu), Dhatri/Amla (Embelica officinalis), Darvi (Daruharidra (Berberis aristata)), Samanga (Biophytumsensitivum), Vidula (Barringtonia actuangula), Abda (Cyperus rotundus (Cyclepeltata)).

The anti-inflammatory, anti-diabetic, anti - ulcerogenic, hepato protective, anti - nociceptive, antipyretic, antiatherogenic, antidiarrheal, diuretic, and antibacterial properties of kataka have now been demonstrated. Khadira is used medicinally for its anti-inflammatory, antioxidant, and chemoprotective effects (Dhasarathan and Therippan, 2011; Ekambaran et al., 2010). Amla is used as a skin care product, an antioxidant, painkiller, and an antipyretic, as well as a treatment for gonorrhoea, nausea, vomiting, indigestion, and nasal bleed (Bhide and Nitave, 2014). Daruharida's hepatoprotective, hypoglycemic, anticancer, antibacterial, anti-inflammatory, and antioxidant properties have been demonstrated. There are significant medical benefits of the samanga plant, including antiangiogenic, antimicrobial, antiulcer, and antibacterial activities (Sharma et al., 2011).

According to reports, vidula contains anti-tumor, antioxidant, hypoglycemic, Anti - convulsant, hepatoprotective, anti-fungal, antinociceptive and anti-inflammatory, anthelmintic, and anti-diarrheal qualities (Lakshmi et al., 2013). Anti-inflammatory, antipyretic, analgesic, sedative, antiemetic, hepatoprotective, antiarthritic, anticancer, antidiabetic, hypolipidemic, cytotoxic, and apoptotic properties are all possessed by abda (Sundaram et al., 2008). Antihypertriglyceridemic, anti-diabetic, and antioxidant properties are all present in vairi (Medagama, 2015). The Rajani plant has anti-inflammation, anti-microbial, anti-fungal, anti-cancer, cardio-protective, hypoglycemic, and antidiabetic properties (Shikha et al., 2015).

Katakakhadiradi Kashayam lowers blood sugar levels by regulating the pancreas' hormonal secretions. Numerous Katakakhadiradi kashayam ingredients have been shown to have antioxidant properties. By its antioxidant characteristics, katakakhadiradikashaym has an

antidiabetic effect (Jessica et al., 2016). The antioxidant analysis of this kashayam produced favourable results, which is a step in the correct way for understanding the scientific basis for its use in the treatment of diabetes. Additional research is necessary to demonstrate the anti-diabetic effects of Katakakhadiradi Kashayam.

Diabetes-related problems including neuropathy can be helped by katakakhadiradi kashayam. It includes a lot of antioxidants because of the amla in it. This kashayam has now been utilised often in clinical practise for clinical conditions similar to diabetes and has had positive therapeutic results.

Table 1: List of plants and their common name

Scientific name	Part used	g	Common name
Strychnospotatorum	Seed	50g	Kataka
Acacia catechu	Heartwood	50g	Khadira
Emblica officinalis	Fruit rind	50g	Amla
Salacia reticulata	Root	50g	Vairi
Berberis aristata	Bark	50g	Darvi
Cassia mimosoides	Whole plant	50g	Samanga
Cycleapeltata	Root	50g	Peta
Curcuma longa	Rhizome	50g	Haldi
Barringtonia acutangula	Rhizome	50g	Vidula
Mangifera indica	Seed	50g	Chootabija
Terminalia chebula	Fruit rind	50g	Haritaki
Cyperus rotundus	Rhizome	50g	Abda

In order to declare the antihyperglycemic impact of the ingredients in the entire formulation, it is fair to indicate that the herbs that make up this kashayam function in a complementary and/or synergistic manner.

Acacia catechu Willd's Khadira The Kashayarasa, Katuvipaka, exhibits kaphashoshan property (Kappa Absorption), unclogs the channels by removing obstacles, and enhances the hypofunctioning of Agni. The characteristics of Aampachan, Angnideepana, and Srotoshodhana are shown in the tika rasa Khadra (Table 1). The primary chemical components of Acacia

catechu that have anti-diabetic properties are polyphenols, tannins, saponins, alkaloids, and glycosides. Khadira has been demonstrated to have a wide range of therapeutic qualities, including antioxidants, hypolipidemic, antidiabetic, antiobesity, wound-healing, analgesic, antifungal, and anti-inflammation actions, which aid in the glyceic management of diabetes.

The preferred treatment for diabetes (Kasinath., 2005) and skin infections is guduchi [*Tinospora cordifolia*], which could be found in Amrutha Choornam. It functions as a superb Rasayana, a Vyadhipratyneeka, and an outstanding immunomodulator (Sharma et al., 2015). Studies have revealed that *Tinospora cordifolia* has the ability to heal wounds (Kalikar et al., 2008).

Khadira was also tested for its effectiveness in treating diabetic wounds and diabetes related with obesity. Native to India, *katakastrychnosporatorum* is common in the deciduous woods of Central India and South India. The mature seeds are utilised to clean murky water (Jessica et al., 2016, 2017, 2021).

According to reports, the seeds have diuretic, antidiarrheal, hepatoprotective, antioxidant, antiulcer, anti-inflammatory, and antiarthritic properties. The seeds have historically been used to treat diabetes and gonorrhoea. Alkaloids and a new triterpenoid called isomotirol have both been found in the plant's bark. According to studies, *Berberis aristata* was found to decrease oxidative stress, minimise enzymes involved in glucose metabolism, and lower blood glucose levels in diabetic rats produced by alloxan.

Both healthy and diabetic rats induced with alloxan showed a substantial antihyperglycemic response to aqueous extracts from *C. mimosoids*. They also shown improvements in body weight, serum lipid profiles, and histological tests revealed pancreatic beta-cell regeneration, suggesting that they may be useful in the treatment of diabetes. Likewise, it has been suggested that amla can prevent or lessen hyperglycemia, cardiac problems, diabetic nephropathy, neuropathy, cataractogenesis, and protein wasting. Due in large part to the fact that curcumin, the principal component of turmeric, decreases levels of blood sugar and hyperlipidemia in rat models of diabetes while being generally safe and economical, it has received a lot of interest as a potential therapy for diabetic as well as its consequences. Numerous species of the *Salacia* genus are known to have anti-inflammatory, antilipidemic, antiperoxidative, antibacterial, antileukemic, astringent, and antimalarial properties in addition to their antidiabetic properties. A number of herbal remedies for diabetes and obesity contain *salacia*. Many researchers have asserted that *Mangifera indica* Linn, also known as the mango tree, has antidiabetic properties (Ironi et al., 2016).

Cycleapeltata promotes wound repair in diabetic rats and opens the door to a more thorough investigation of the phytochemical component for medicinal uses (Sivaraman et al., 2018). In STZ diabetic mice, an ethanolic extract of *Cyclearotundus* significantly lowered levels of blood glucose (Wang et al., 2019). *Acutangular Barringtonia* L. A common medicinal plant from the

family Lecythidaceae is used historically for its wide range of ailments, including diabetes, syphilis, lumbar discomfort, blennorrhoea, and febrifuge (Sahu et al., 2019). When haritaki powder is consumed, the pancreatic beta-cells' ability to produce insulin is activated. Additionally, it aids in reducing the conversion of starch to glucose, which controls the release of insulin and results in low blood sugar levels (Sharma et al., 2019).

Effects that shield the pancreas:

Katakakhadiradi kashayam exhibits antidiabetic activity combined having antioxidant activities which can be highly beneficial for diabetes Mellitus. It also protects pancreatic beta-cells and smooths out fluctuations in glucose levels (Jessica et al, 2021).

Hepatoprotective property

Multiple morphological and histological changes in the liver tissues, as shown by an increase in glycogen reduction, are linked to lipid accumulation, inflammatory cell infiltration, and Kupffer cell hyperplasia. Most tissues, including the liver, are known to experience significant alterations in intracellular metabolism as a result of diabetes (Lin et al., 2017). The inclusion of flavonoid, phenols, tannins, and other bioactive chemicals in Katakakhadiradi kashayam is likely what causes the hepatoprotective action (Jessica et al 2020).

Effect on Nephroprotection:

The renal parenchyma of STZ-induced rats experiences a variety of changes as a result of hyperglycemia. Glastras and colleagues 2019, The glomerulus, bowman's capsules, renal cell size, and renal tubules of control rats had normal histology of the kidney architecture, according to an investigation of haematoxylin and eosin staining. Diabetic rats had proximal tubule production of lipofuscin pigments, thickening of the renal artery wall and tubular basement membrane, eosinophilic deposits, and vascularization of renal cells. Because Katakakhadiradi kashayam contains a variety of medicinal herbs, it has therapeutic capabilities and protects renal tissues and kidney function (Jessica et al., 2021).

Discussion:

There has to be more research done on the signs and symptoms of diabetes mellitus, one of the most serious and dangerous complicated conditions. It is a complex metabolic disease that can lead to medical issues in the body. The pathologically elevated blood glucose level, the decline in antioxidants, and the aberrant metabolism of lipids, carbohydrates, proteins, and electrolytes are all symptoms of this illness. Diabetes mellitus continues to be a major cause of death and morbidity in the globe, despite all advancements in diabetology, diabetes mellitus biology, and treatments, including the use of hypoglycemic medications.

The importance of herbal medicines as a resource of hypoglycemic agents has begun to grow. The chemical makeup of plant items utilised as alternative diabetic treatments is related to their biological activity. The blood glucose levels are reduced by phenolic chemicals, terpenes,

polyphenols, coumarins, and other elements found in plant products. The research and popular literature **have** identified a number of plant species as having anti-diabetic properties. Herbal medications are recommended because they are thought to be helpful, have fewer adverse effects in clinical practise, and are reasonably inexpensive. Since many years ago, medicinal plant extracts and preparations have been utilised to treat diabetes mellitus.

The majority of the current products on the market have not gone through the medication approval procedure to confirm their safety, and herbal medicines do occasionally cause negative effects. As a result, a major focus will need to be placed on standardising a procedure for assessing the therapeutic risk/benefit and safety of using a polyherbal composition. The fact that many practitioners are still not entirely aware with the scientific nomenclature, pharmacodynamics, and proper dose of herbal drugs presents another challenge.

Conclusion:

Altogether, katakakhadiradi kashayam is a superb anti-inflammatory and anti-microbial. It helps heal wounds and ulcers as well as skin conditions including acne and wounds (Jessica et al., 2016). Additionally, it can be used to treat other urinary conditions including dysuria. It helps to alleviate diabetic complications like neuropathy. It is used to manage illnesses linked to Vata and Kapha (Jessica et al., 2017). The antioxidant, anti-inflammatory, and hepatoprotective qualities of Katakakhadiradi kashayam may be responsible for its antidiabetic effects, but further research is needed to fully comprehend this kashayam's protective effects against a variety of ailments. **Due to the paucity of high-quality randomised trials, the effectiveness of polyherbal formulations has not yet been proven. To ascertain the greater therapeutic efficacy of herbal extracts formulations in controlling blood sugar and cholesterol levels in diabetes patients, advanced well-designed randomized clinical trials with a larger number of participants are needed.**

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