Relevance of Traditional Antidiabetic Plants in the Covid-19 Pandemic Era

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Abstract

Diabetes mellitus is a major endocrine disorder characterized by chronic hyperglycaemia with associated severe complications like diabetic nephropathy, retinopathy, peripheral neuropathy, atherosclerosis and increased susceptibility to infections. Covid-19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) has been particularly more severe to people with co-morbidities like diabetes, cardiovascular diseases and other metabolic disorders. Diabetes and obesity appear to be strong risk factors for mortality in Covid-19. The prevalence of uncontrolled blood sugar levels and immunosuppressive treatments like corticosteroids have resulted in a surge of secondary bacterial as well as fungal infections like Mucormycosis in Covid patients, particularly in India. There are increasing reports of new-onset diabetes after Covid-19 infection. Prevention of diabetes and management of blood sugar levels, therefore is extremely significant in the current scenario. Medication for diabetes includes insulin injections and oral drugs like metformin that may have adverse side-effects. Many medicinal plants and polyherbal formulations used in the Indian Traditional systems of medicine can provide prophylactic and curative treatment as natural and safer alternatives for control of diabetes and insulin resistance. The article is intended to give an update of plants like *Berberis*

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aristata, Gymnema sylvestre, Tinospora cordifolia, Phyllanthus emblica, Curcuma longa and *Momordica charantia* that are potent antioxidants, anti-inflammatory, immunomodulators, hypoglycaemic, hypolipidaemic and have exhibited significant therapeutic potential for maintenance of glucose homeostasis in the body by various mechanisms including increase in insulin secretion, enhancing glucose uptake by adipose and muscle cells, inhibiting intestinal glucose absorption, regeneration of beta cells of pancreas, thus reducing the risk of infections and increasing longevity.

Keywords

Diabetes Mellitus, Covid-19 pandemic, Mortality, Insulin resistance, Antidiabetic plants, Antioxidant, Anti-inflammatory, Hypoglycaemic, Hypolipidaemic, Immunomodulator

1. Introduction

Diabetes mellitus is a chronic, metabolic disorder characterized by elevated levels of blood sugar (hyperglycaemia) and is usually associated with severe complications like diabetic nephropathy, retinopathy, peripheral neuropathy, atherosclerosis and increased susceptibility to infections. Type 1 Diabetes, called as insulin-dependent diabetes is an autoimmune disorder where the insulin-secreting beta cells of the pancreatic islet cells of Langerhans are destroyed and do not make insulin. Type 2 diabetes or noninsulin-dependent diabetes is the most prevalent form of diabetes associated with insulin resistance and a progressive loss of beta cell insulin secretion (Liu et al. 2021). Insulin resistance refers to a condition in which the adipose, muscle and liver cells do not respond to insulin and cannot take up glucose from the blood. Insulin and Glucagon are the two key hormones produced by pancreas that maintain glucose homeostasis. The insulin secreted by beta cells of the pancreas stimulates cells to absorb glucose for energy, reducing sugar levels in the blood. When blood sugar levels are too low (hypoglycaemia), the alpha cells of pancreas release Glucagon that instructs the liver to release stored glucose (glycogenolysis) which causes blood sugar to rise. In Type 2 diabetes, the beta cells produce insufficient insulin and alpha cells produce excess Glucagon. Symptoms of diabetes include polydipsia (excessive thirst), polyphagia (increased appetite), polyuria (frequent urination), impaired vision and body weight. Medication for diabetes includes sub-cutaneous insulin injections

and/or oral drugs like metformin that may have adverse side-effects including gastrointestinal disturbances, vitamin B_{12} deficiency, haemolytic anaemia and less frequently metabolic acidosis (Wang and Hoyte 2019). The global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), likely to rise to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 (Saeedi et al. 2019).

2. Diabetes and Covid-19

Diabetes mellitus is associated with adverse clinical outcomes and high mortality in patients with Covid-19 caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2), independent of other co-morbidities (Shrestha et al. 2021). Beta cells in the pancreas which produce insulin, may be particularly vulnerable to damage by the virus as they express an abundance of Angiotensin-converting enzyme-2 (ACE2) receptors. Angiotensin-converting enzyme-2 is a transmembrane protein that serves as the main entry point for SARS CoV-2. Impairment of Beta cells of pancreas and inflammatory cytokine storm in Covid-19 cause acute metabolic complications and premature mortality. Besides, there are reports of trigger of new-onset diabetes as a result of Covid-19 infection (Mallapaty 2020) and higher mortality rates seen in patients with new-onset diabetes and hyperglycaemia than in non-diabetic patients (Shrestha et al. 2021). It is now known that the relationship between diabetes and Covid-19 is bidirectional.

Coronavirus infection by emerging mutants, uncontrolled blood sugar levels, immunosuppressive treatments like corticosteroids have resulted in a surge of secondary bacterial as well as rare, invasive fungal infection, Mucormycosis in Covid patients. Several cases of Rhino-orbital-cerebral Mucormycosis have been reported in India. Infection by fungal species of Mucorales occurs by inhalation or ingestion of spores followed by angioinvasion, thrombosis and tissue necrosis. Immunocompromised people with uncontrolled diabetes have been found to be more susceptible to Mucormycosis and those with corticosteroids induced hyperglycaemia. Patients with dysregulated blood sugar levels continue to remain vulnerable, and therefore, prevention and control of diabetes is extremely significant in the current scenario.

3. Antidiabetic Potential of Medicinal Plants

Plants have been used in the traditional systems of medicine since millennia and there is a resurgence of global interest in herbal medicines due to their long traditional

usage, minimal side-effects, holistic treatment and cost-effectiveness. The discovery of metformin (dimethylbiguanide) is also linked to *Galega officinalis* (Fabaceae), a traditional herbal medicine in Europe, rich in alkaloids guanidine and galegine which lower blood glucose.

Medicinal plants are natural, safer, preventive, restorative alternatives to synthetic medicines. The traditional uses of many medicinal plants have been scientifically authenticated by several experimental studies on animal models, cell lines as well as clinical trials. Streptozotocin and alloxan are diabetogenic chemicals that are toxic glucose analogues, damage beta cells of pancreas and have been used extensively to induce experimental diabetic models of rats and mice (Lenzen 2008). The efficacy of many plant-based medicines in treating a broad spectrum of diseases is usually due to the presence of synergistic interactions of several secondary metabolites resulting in pleiotropic effects. Unlike conventional medicine with a single active ingredient, medicinal plants regulate the functions of body through multiple targets and multiple mechanisms (Pang et al. 2015). The article intends to give an update of selected Indian traditional plants that have exhibited enormous therapeutic potential for control of diabetes and insulin resistance.

3.1. Berberis aristata DC. (Family: Berberidaceae)

The genus *Berberis* comprises about 500 species distributed in temperate and sub-tropical regions of Asia, Europe, and America. *Berberis* is well known for its pharmacological importance in the Indian traditional systems of medicine. *Berberis aristata*, known as Indian barberry, Tree turmeric, Daruhaldi or Daruharidra is a shrub native to the Himalayas in India. The fruits are edible and rich in vitamin C. The root, stem and bark have been traditionally used for diarrhoea, diabetes, osteoporosis, eye and ear infections, jaundice, skin diseases and gynaecological disorders (Potdar et al. 2012).

The therapeutic properties of *Berberis aristata* including antidiabetic, febrifuge, antimicrobial, hypotensive, antioxidant, immunostimulator, hypolipidaemic, anti-arrhythmia, hepatoprotective, cardioprotective and anticancer are largely attributed to berberine, a quarternary benzylisoquinoline alkaloid (also found in other *Berberis* species like *Berberis asiatica, Berberis vulgaris, Berberis lycium,* and *Coptis chinensis*). Various pharmacological experiments in animal models as well as clinical trials validating the therapeutic effects of *Berberis* extracts and berberine in metabolic disorders including Type 2 diabetes mellitus, obesity, non-alcoholic

fatty liver disease and hyperlipidaemia have been documented (Belwal et al. 2020; Xu et al. 2021). *Berberis aristata* root extract administered in alloxan-induced diabetic rats has been reported to decrease blood glucose, restore antioxidant status, reduce oxidative stress and regulate glucose homeostasis through decreased gluconeogenesis (Singh and Kakkar 2009). The main constituents of the root were identified as berberine, berbamine and palmatine through HPTLC. In a clinical study involving 90 diabetic patients, the effect of *Berberis aristata* stem as an add on therapy with conventional antidiabetic and antihyperlipidaemic treatment, exhibited significant reduction in fasting blood glucose, total cholesterol, and triglycerides (Sharma et al. 2017). *Berberis* fruit extracts have also shown significant reduction in serum glucose and glycated haemoglobin (HbA1c) in patients with type 2 diabetes (Moazeri and Qujeq 2014).

Berberine has been reported to promote insulin secretion, attenuate insulin resistance, regenerate beta cells, protect islet areas, inhibit hepatic gluconeogenesis, promote glucose uptake by peripheral tissues, downregulate inflammation, inhibit lipogenesis, alleviate adipose tissue fibrosis, reduce hepatic steatosis, and improve gut microbiota dysbiosis (Pang et al. 2015; Han et al. 2021). Berberine is a versatile potential drug for regulation of glucose and lipid homeostasis comparable to metformin as well as obesity by downregulation of adipogenesis and lipogenesis (Wang et al. 2018). Berberine exhibits significant potential for the treatment of diabetic nephropathy, neuropathy, diabetic cardiopathy due to its potent antioxidant and anti-inflammatory activities (Pang et al. 2015). Berberine has also been reported to protect against metformin-associated lactic acidosis in streptozocin-induced diabetic rat models (Almani et al. 2017).

3.2. Gymnema sylvestre (Retz.) R. Br. ex Sm. (Family: Apocynaceae)

Gymnema sylvestre (commonly called as Gymnema, Periploca of the wood, Australian cowplant) is a perennial woody climber growing in the tropical forests of India. The plant is popularly known as 'Gurmar' which means 'sugar killer' or sugar destroyer, that neutralizes excess sugar in the body (Kanetkar et al. 2007). The main plant parts used are the leaves, flowers, roots, and bark. The major phytoconstituents are triterpene saponins; including gymnemic acids and gymnemasaponins, that are members of oleanane type of saponins and gymnemasides, that are dammarane saponins. Other constituents include anthraquinones, flavones, tartaric acid, polypeptide gurmarin, lupeol, and

stigmasterol. *Gymnema sylvestre* is known to have antidiabetic, antioxidant, anti-inflammatory, antiviral, hepatoprotective, anticancer and hypolipidaemic activities. *Gymnema* leaves are used as an ingredient of antidiabetic formulations in Indian Ayurveda, Unani and Siddha systems of medicine, as an effective natural remedy for diabetes mellitus. The plant extract has also been used for treating arthritis, osteoporosis, hyperlipidaemia, obesity, cardiopathy, tachycardia, asthma, bronchitis, microbial infections, skin problems, indigestion, piles, liver diseases, eye diseases, cataract, urino-genital infections and dental caries (Kanetkar et al. 2007; Tiwari et al. 2014).

The atomic arrangement of gymnemic acid molecules is similar to that of glucose molecules and curbs sugar cravings by blocking the sugar receptors on taste buds. Gymnemic acid molecules prevent sugar absorption by the intestine by blocking the receptor site for sugar in the absorptive external layers of the intestine, thus reducing sugar levels (Sahu et al. 1996). Many experimental studies indicate that Gymnemic acids present in the leaves promote regeneration of islet cells of pancreas, increase insulin secretion, lower intestinal glucose absorption, control postprandial blood sugar levels and aid weight loss. The aqueous leaf extract of *Gymnema sylvestre* is reported to improve the altered glucose, lipid and insulin levels in dexamethasone-induced insulin resistance rats as well as improved the histopathology of liver of experimental rats (Kumar et al. 2015). *In vivo* diabetic evaluation of gymnemic acid in streptozocin-induced rats revealed dose-dependent reduction in the levels of blood glucose, total cholesterol, triglycerides, urea, creatinine and lipids. The volume of islet cells in drug treated animals was also found to be significantly more than diabetic control in histopathological studies (Dholi et al. 2014). Treatment of streptozocin-induced diabetic rats with leaf extracts of *Gymnema sylvestre,* significantly decreased plasma glucose, triglycerides, total cholesterol, LDL-cholesterol, malondialdehyde, as well as deranged liver function enzymes, alanine transaminase (ALT) and aspartate transminase (AST) with a concomitant increase in insulin, HDL-cholesterol and erythrocyte superoxide dismutase levels (Shafey et al. 2013). Administration of *Gymnema sylvestre* in patients with impaired glucose tolerance, is reported to result in decreased 2-h oral glucose tolerance test and glycated haemoglobin (HbA1c), increasing insulin sensitivity (Gaytan Martinez et al. 2021). The study has also reported improvement in anthropogenic measures and lipid profile.

3.3. Tinospora cordifolia (Willd.) Miers (Family: Menispermaceae)

Tinospora cordifolia (commonly called as Indian Tinospora, Heart leaved moonseed, Giloya, Guduchi, Amrita) is a large, glabrous, deciduous climbing shrub. The pharmaceutical effects of the stems, leaves, and roots of *Tinospora cordifolia* are attributed to the major phytoconstituents including alkaloids (Tinosporine, magnoflorine, berberine, palmatine, jatrorrhizine, tembetarine, and tetrahydropalmatine); terpenoids (tinocordin, tinosponone, tinosporaside, tinocordioside, cordioside, cordifolisides A to E, and tinocordifolioside); and steroids (ecdysterone, β-sitosterol).

Tinospora cordifolia is used as a *Rasayana* drug in Ayurveda system of medicine for its rejuvenating, immune-stimulating and adaptogen properties. It is a powerful antioxidant, immunomodulator, antidiabetic, anti-tumour, antipyretic, anti-arthritic, anti-allergic, anti-hyperlipidaemic, anti-inflammatory, antineoplastic, hepatoprotective, osteoprotective and neuroprotective. The drug is prescribed for intermittent fevers, malaria, liver damage, respiratory tract infections, tuberculosis, gout, diabetes, jaundice, dyspepsia, urinary problems, AIDS, chronic diarrhoea, dysentery and skin diseases. It is also useful in the treatment of heart diseases, leprosy, helminthiasis, osteoporosis and rheumatoid arthritis (Chaudhry 2019). The plant is also a source of essential micronutrients like copper, calcium, phosphorus, iron, zinc and manganese (Rahal et al. 2014). The analgesic, antipyretic and anti-inflammatory properties have been experimentally validated in albino mice models (Hussain et al. 2015).

Several studies validating the therapeutic potential of *Tinospora cordifolia* for treatment of endocrine and metabolic disorders have been documented (Chakraborty 2016; Dhama et al. 2017). The whole plant extract of *Tinospora cordifolia* has shown significant anti-diabetic activity by reduction of plasma glucose levels in alloxan-induced diabetic rats (Kinkar and Patel 2015) and streptozocin-induced diabetic rats (Pathak et al. 2016). A novel polysaccharide isolated from *Tinospora cordifolia* stem extract has been found to possess β-cell regenerative potential and significantly decreased plasma glucose, HBA1c, triglycerides and total cholesterol (Rajalakshmi and Anita 2016). In a clinical trial, prescription of powdered stem of *Tinospora cordifolia* for 15 days at 50 mg/ kg body weight in type 2 diabetic patients, resulted in significant decrease in the levels of fasting blood sugar as well as total cholesterol, triglycerides, lipoproteins B validating its antidiabetic and anti-dyslipidaemia potential (Kumar et al. 2016). The alkaloids magnoflorine, palmatine, and jatorrhizine

have been reported to exhibit insulin-releasing and insulin-mimicking effects *in vitro* and *in vivo* (Patel and Mishra 2011).

Tinospora cordifolia exhibits multiple therapeutic effects for improving pathological status of diabetes via inhibition of glycogenolysis in liver, improving glucose uptake and utilization, inhibiting gluconeogenesis, inhibiting intestinal glucose absorption, inhibiting alpha-glucosidase and alpha-amylase, mitigating oxidative stress, antioxidant properties and exhibits beneficial role in diabetic neuropathy, nephropathy, gastropathy and retinopathy (Sharma et al. 2015).

3.4. Phyllanthus emblica L. (Family: Phyllanthaceae)

Phyllanthus emblica (commonly called as Indian Gooseberry, *Emblic myrobalan*, Amla) is a small to medium-sized deciduous tree with feathery drooping foliage and spreading branches. The fruit is a fleshy, smooth, globose drupe, light greenish-yellow, with six vertical stripes or furrows. The fruits are rich in hydrolysable tannins like emblicanin A and B, punigluconin, pendunculagin; flavonoids like quercitin and kaempferol; also gallic acid, ellagic acid, chebulinic acid, chebulagic acid, citric acid and pectin. The fruit is an excellent source of vitamin C, enhances food absorption, balances stomach acid, fortifies the liver, nourishes the brain and mental functioning, supports the heart and blood circulation, strengthens the lungs, detoxifies blood, reduces macular degeneration, increases skin health, promotes healthier bones, teeth, nails, hair, enhances vitality, immunity and augments intellect (Chaudhry 2021). The plant is a powerful *Rasayana* (rejuvenator) drug in Ayurveda that delays degenerative and senescence processes and is effective for the treatment of hypertension, diabetes, neurological disorders, colitis, gastritis, scurvy, ophthalmic problems, fever, asthma, hepatic disorders and cancer (Gaire and Subed 2015; Yadav et al. 2017). It is a powerful antioxidant, antidiabetic, cardioprotective, hepatoprotective, antimicrobial, neuroprotective, anticancer and antiaging plant, used as an important ingredient of Indian Ayurvedic drug, Amalaki Rasayana, and Ayurvedic polyherbal formulations- Triphala and Chyawanprash.

The anti-diabetic effects of fruits of *Phyllanthus emblica* and/or its constituents including gallic acid, gallotannin, ellagic acid and corilagin have been well documented due to their antioxidant and free radical scavenging properties. Amla has been reported to prevent/reduce hyperglycaemia, cardiac complications, diabetic nephropathy, neuropathy, cataractogenesis and protein wasting (D'souza et al. 2014). Treatment with *Phyllanthus emblica* extract has been reported to exhibit significant reduction in fasting blood glucose, increased serum insulin, increased plasma total

antioxidants, increased beta cells numbers as well as size in diabetic rats in a dose-dependent manner (Fatima et al. 2017). In addition, the ellagic acid in *Phyllanthus emblica* promoted glucose-stimulated insulin secretion from isolated islets of pancreas and decreased glucose intolerance in diabetic rats. Administration of quercetin extracted from the fruits of *Phyllanthus emblica* in streptozotocin- induced diabetic rats daily for 28 days at 25, 50 and 75 mg/kg body weight, resulted in a significant decrease in blood glucose and urine sugar, with a considerable rise in plasma insulin and haemoglobin levels (Srinivasan et al. 2018). Quercetin also improved the profiles of triglycerides, total cholesterol, LDL, VLDL and HDL. In another study, ethyl acetate fraction of *Phyllanthus emblica* fruit flesh administered in glucose-induced rats at a concentration of 100 mg/kg body weight could reduce blood sugar levels equivalent to the administration of metformin with a concentration of 65 mg/kg body weight and was also able to repair damaged cells of kidney, pancreas and liver of the tested rats, as evident in the histopathological studies (Musman et al. 2019).

3.5. Curcuma longa L. (Zingiberaceae)

Curcuma longa, commonly known as Turmeric in English and Haldi in Hindi, is a rhizomatous perennial herb, native to tropical South Asia. The thickened rhizomes of the plant are medicinally important. The active phytochemicals include curcuminoids such as Curcumin (diferuloylmethane), demethoxycurcumin, monodemethoxycurcumin, bisdemethoxycurcumin, dihydrocurcumin and cyclocurcumin. The essential oil obtained by steam distillation of rhizome has phellandrene, sabinene, borneol, zingiberenes and sesquiterpenes. Curcumin is the most active constituent responsible for the bright yellow colour of turmeric.

Curcuma longa has been extensively used in the Ayurveda, Siddha and Unani Systems of Medicine. It is a powerful anti-inflammatory, cardioprotective, neuroprotective, hepatoprotective plant, traditionally used for the treatment of biliary disorders, anorexia, cough, sinusitis, asthma, rheumatism, diabetic wounds, hepatic disorders, healing and disinfection of wounds, jaundice, flatulence, dyspepsia, intermittent fever, eczema, sprains, bruises, inflammatory troubles of joints, conjunctivitis and purulent ophthalmia.

The therapeutic effects of curcumin against metabolic syndrome, neurodegenerative disorders, cardiovascular diseases, pulmonary diseases, autoimmune and neoplastic diseases are largely attributed to its antioxidant and anti-inflammatory mechanisms

(Aggarwal and Harikumar 2009; Wickenberg et al. 2010; Labban et al. 2014; Panahi et al. 2016; Hewlings and Kalman 2017). Numerous *in vitro* and *in vivo* studies have supported the efficacy of curcumin against type 2 diabetes mellitus (Nabavi et al. 2015; Pivari et al. 2019; Oliveira et al. 2020) and its therapeutic potential in attenuation of diabetic nephropathy, retinopathy and neuropathy (Parsamanesh et al. 2018). Significant blood glucose lowering effects have been reported with bio-enhanced preparation of turmeric in streptozocin-nicotinamide induced type-2 diabetic Wistar rats resulting in improved beta-cell function, insulin sensitivity and decreased insulin resistance (Sayeli and Shenoy 2021). Treatment of diabetic rats with curcumin combined with metformin is reported to show synergistic activity, decreasing glycaemia, dyslipidaemia, glycoxidative stress and increasing paraoxonase activity, suggesting a promising strategy for combating diabetic complications (Roxo et al. 2019). In animal models, curcumin extract delays diabetes development, improves beta cell function, prevents beta cell death and decreases insulin resistance (Pivari et al. 2019) and that doses of upto 12 gm per day of curcumin are safe, tolerable and non-toxic.

A randomized, double-blind clinical trial in type 2 diabetic patients reports that daily administration of 1500 mg curcumin for 10 weeks resulted in reduction of fasting blood glucose, body weight and hip circumference but no effect on serum insulin, insulin resistance and HbA1c (Hodaei et al. 2019). A meta-analysis study concluded that curcumin supplementation is effective in reduction of alanine transaminase (ALT), aspartate transaminase (AST), serum total cholesterol (TC), low–density lipoprotein (LDL), fasting blood sugar, serum insulin and waist circumference in patients with non-alcoholic fatty disease (Jalali et al. 2020).

3.6. Momordica charantia L. (Cucurbitaceae)

Momordica charantia (commonly called as Bitter melon, Bitter gourd in English and Karela in Hindi) is an annual vine, native to East India. All parts of the plant are bitter including the fruit which has a warty surface and is rich in phytochemicals. The fruit has been used for the treatment of type 2 diabetes, hypertension, obesity, cancer, bacterial and viral infections. It is a nutrient-dense vegetable rich in vital vitamins C, A, E, B_1, B_2, B_3 and B_9 as well as minerals like potassium, calcium, zinc and magnesium. It exhibits numerous therapeutic properties like antioxidant, hypoglycaemic, anti-inflammatory, hypolipidaemic, immunomodulator, antiviral, anti-obesity and hepatoprotective. The main hypoglycaemic phytoconstituent of

Momordica charantia has charantin, a triterpenoid with insulin like activity that can ameliorate insulin resistance.

Abundant studies conducted in animal models have demonstrated the hypoglycaemic potential of *Momordica charantia* (Liu et al. 2021). It can regenerate beta cells in pancreatic islets, increase pancreatic islet size, total beta cell area and the number of beta cells in rat models. It enhances glucose uptake by adipose and muscle tissue, inhibits glucose absorption from intestine, inhibits glucose production from liver, plays a role in suppression of key gluconeogenic enzymes, as well as protection of pancreatic beta cells and their functions.

Oral administration of *Momordica charantia* fruit juice at 10 ml/kg/day in streptozocin-induced diabetic rats, resulted in significant reduction of serum glucose, fructosamine, total cholesterol, triglycerides level, insulin resistance index and pancreatic malondialdehyde content as well as significant increase of serum insulin, HDL-cholesterol, total antioxidant, beta cells function percent and improved histopathological changes of the pancreas, thus exhibiting excellent hypoglycaemic, hypolipidaemic, and strong antioxidant properties (Mahmoud et al. 2017). In a randomized, placebo-controlled clinical trial of 90 patients, significant hypoglycaemic efficiency of *Momordica charantia* used as an adjuvant therapy has been reported with no serious adverse effects (Kim et al. 2020). Administration of *Momordica charantia* at 2000 mg/day in another clinical trial on 24 type 2 diabetic patients, resulted in insulin secretion and/or insulin sensitivity, reduced glycated haemoglobin, 2-h serum glucose, as well as anthropometric variables like weight, body mass index and fat percentage (Cortez-Navarrate et al. 2021).

4. Conclusion and Perspective

The increased prevalence of diabetes mellitus over the past few decades, bidirectional link with Covid-19 and adverse effects of conventional drugs has rekindled interest in natural products and herbal supplements. Good glycaemic control can not only reduce the risk of microvascular complications of diabetes like nephropathy, retinopathy, neuropathy and macrovascular complications like coronary heart disease, but also lower susceptibility to bacterial, viral and fungal infections. Traditional plants like Indian Barberry, *Gymnema*, Indian Gooseberry, Indian Tinospora, Turmeric and Bitter Gourd, that are easily available and affordable, can restore healthy function of vital organs by reversing dysregulated inflammatory reactions in the body, maintain glucose homeostasis and provide prophylactic and curative treatment

against diabetes. As an alternative to synthetic medicines, they exhibit significant potential in alleviation of diabetes, insulin resistance and other metabolic disorders like dyslipidaemia, owing to their powerful antioxidant, anti-inflammatory, immunomodulator, hypoglycaemic and hypolipidemic activities. As an adjuvant therapy, they may lower the dose of conventional medicine or lower the frequency of administration of drug, thus mitigating the adverse effects. Healthy nutrition is an essential component of diabetes management and varied, balanced diet must be practiced to keep blood glucose levels stable. Food with low glycaemic index including whole grains, pseudocereals, millets, fruits, green leafy vegetables, nuts, probiotics to maintain healthy gut, avoidance of packaged, processed food, saturated fats, white sugar and salt, as well as moderate physical exercise, are lifestyle interventions that must be adopted.

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