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Review

Comparative study of molecular mechanism of action of allopathic drugs and herbal drugs: A mini review

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Abstract. Different kinds of allopathic medications are already accessible that operate admirably in managing sugar levels through their distinct action mechanisms; nonetheless, the point of worry is that they cause our body organs to overwork, or, in other words, they overstress our bodies. Quite a few allopathic medicines are known to cause adverse reactions. None of these however provide a cure for diabetes, although they do assist in successful diabetic control. Polyherbal formulations are a concept unique to Ayurveda. Natural compounds commonly known as phytochemicals originating from plants have played a significant part in medication development efforts and still do. Given the toxicity and myriad negative consequences of allopathic medications, it is possible to greatly expand the number of herbal drug manufacturing enterprises, which is related to the current growth in interest and demand for herbal medicines. Additionally, plant-based phytochemical medications offer a plentiful supply of physiologically active substances with pharmacological action and little side effects. Since various preparations function by distinct mechanisms, theoretically alternative combinations of these extracts may be more successful in lowering blood glucose levels. In this study, we sought to elucidate the mechanism of plant phytochemical anti-diabetic properties in polyherbal formulations.

Key words: Type 2 Diabetes; Herbal drugs; Phytochemicals, Molecular mechanism

Introduction

Type 2 diabetes is a group of metabolic diseases characterized by hyperglycemia caused by insulin generation or insulin action. Aside from chronic hyperglycaemia in diabetes mellitus, chronic hyperglycemia eventually damages several organs, including the eyes, kidneys, nerves, heart, and blood vessels (1). A person suffering from diabetes mellitus can experience thirst, polyuria, blurred vision, and weight loss (2).

In the management of diabetes mellitus, several treatment agents are available, but even though all of these chemical drugs can control blood sugar levels, they may also have adverse effects. For instance, sulfonylurea cause hypoglycemia, but promote weight gain. A major role of biguanides in altering lipid profiles includes lowering low density lipoprotein (LDL), triglyceride (TG), total cholesterol (TC), and very low density cholesterol (VLDL) levels while raising high density lipoprotein (HDL) levels (3). Insulin treatment, likewise, might be a risk factor for cardiovascular

disease (4). Sulfonylurea, Alpha glucosidase inhibitor, thiazolidinediones and metformin are the common anti-diabetic drugs used in allopathic treatment(5,6). The action of these drugs and their target organs are represented in figure 1 while comparative study of this allopathic medicine with their mechanism of action, advantages and disadvantages is discussed in table 1.

Ayurveda, on the other hand, is a science that uses supplements, which are herbal extracts. The research on the herbal plants used in Ayurveda show that herbs might provide better management with very few or no negative effects (13). As a result, Ayurveda takes a comprehensive approach to diabetes mellitus care and may provide superior choices for type 2 diabetes mellitus prevention (both primary and secondary) and maintenance. Traditional medicine for treating diabetes with plant components are thought to be a good source of a novel drug or a lead in the development of a new therapy(14,15). Plant extracts or various folk plant medicines are given by traditional practitioners and accepted by consumers in many nations, particularly in third-world countries, for diabetes and other disorders(16,17).

Plant medications can help people with diabetes improve their glucose metabolism and general health by enhancing their lipid metabolism, antioxidant status, and capillary function, in addition to hypoglycemic benefits (18). Plant medicines are generally thought to be less harmful and have fewer negative effects than

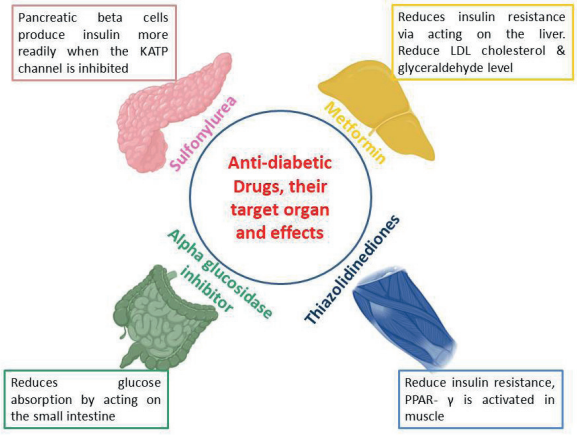

Figure 1. Mechanism of action of allopathic drug at different organs of body as anti-diabetic drug.

Table 1. Comparative study of allopathic drugs and their mechanism of action.

Comparative study of anti-diabetic drugs

Drugs	Mechanism	Advantages	Disadvantages
Sulfonylurea (glyburide, glimepiride, glipizide)	Pancreatic beta cells produce insulin more readily when the KATP channel is inhibited(7)	• Immediately effective • Blood pressure is not affected • Low-density lipoproteins are not affected • An affordable price	• Hypoglycemia is more likely to occur • Compared to metformin, this drug has a higher death rate
Metformin (glucophage)	Reduces insulin resistance via acting on the liver (8)	• Comparatively low risk of hypoglycemia • LDL cholesterol is reduced in a positive manner • Reduces triglyceride levels	• increased risk of gastrointestinal problems • less convenient dosing
Alpha glucosidase inhibitor (Acarbose, miglitol)	Reduces glucose absorption by acting on the small intestine, causing a reduction in the development of enzymes required for carbohydrate digestion (9, 10)	• Comparatively lower hypoglycemia risk than sulfonylurea • Reduces triglycerides. • The cholesterol level remains unchanged	• Reduces glycated haemoglobin in less effective ways than other diabetes drugs • Other diabetes drugs except metformin have a higher risk of GI problems • Distasteful dosing
Thiazolidinediones (Actos, Avandia)	In order to reduce insulin resistance, PPAR- γis activated in fat and muscle (11, 12).	• The chances of hypoglycemia are lower • An increase in high density lipoprotein is observed • Reduce triglyceride levels • Convenient dosing	• A rise in low-density lipoprotein • It is associated with elevated triglycerides and a higher risk of heart attacks • requires monitoring for hepatotoxicity

manmade medicines. These plants' hypoglycemic impact comes from their capacity to restore pancreatic tissue function by increasing insulin secretion, inhibiting glucose absorption in the intestine, and facilitating metabolites in insulin-dependent activities(19). Herbs are employed as decoctions, infusions, tinctures, and powders in Ayurveda's major formulations(20). Ayurvedic drug formulation is based on two principles (as stated in Ayurvedic treatises such as Charaka Samhita and Sushruta Samhita): (a). Use as a single medication, and (b). More than two medications are being used. The term "polyherbal formulation" refers to a formulation that contains two or more herbs. Polyherbalism is a notion unique to Ayurveda(21,22). Since various preparations function by distinct mechanisms, it is theoretically plausible that alternative combinations of these extracts will perform a better job in lowering blood glucose (23,24).

Comparative study of the herbal medicine with their action mechanism

The medicinal properties of herbal formulations, according to Soetan et al., (2008), are related to the presence of phytochemicals, which are created by plants for own defense (25). It is now thought to have therapeutic promise in the treatment of diabetes. The Phytochemicals present in the different herbal plants used to prepare diabetic formulations and their therapeutic properties are discussed in the table 2:

Diabecon, a product of 'Himalaya,' is said to improve glucose consumption in the peripheral circulation, boost hepatic and muscle glucagon levels, enhance B cell repair through reducing oxidative stress and enhancing antioxidant effects. It modulates lipid profile, reduces haemoglobin glycation, and normalizes microalbuminuria. Diabetic complications are reduced as a result of it(47). Epicatechin, a benzopyran, is the active component of Epinsulin, which is marketed by Swastik formulations. Epicatechin raises the islet cAMP concentration, which is linked to enhanced insulin release. It increases cathepsin activity, which aids in the conversion of proinsulin to insulin. In addition to reducing osmotic fragility of human erythrocytes, it inhibits Na/K ATPase activity, and can help treat neurological conditions, retinopathy, diabetes, and lipid metabolism disorders. There is a claim that this medication will cure non-insulin-dependent diabetes mellitus (NIDDM), as well as treat insulin-dependent diabetes mellitus (IDDM) by lowering the quantity of insulin required. Pancreatic Tonic 180 cp is an ayurvedic blend of herbal formulations that is sold as a nutritional supplement to the diabetic patients (48, 49). According to Admark Herbals Ltd., Dia-Care cures Type 1 and Type 2 diabetes within 18 months and is effective within 90 days of treatment(50). Insulin users will finally be free from their drug dependency. The treatment is divided into six phases, each lasting 90 days. Approximately five grams (1 tea spoon) of powder are mixed with half a glass of water, thoroughly mixed, and stored in a refrigerator for overnight use. In the morning, consume only the water, not the sediment. The remaining medication is dissolved in fresh water, preserved for the entire day and swallowed before dinner. There are no side effects associated with this natural formulation. A product manufactured by Garry and Sun Pharma, Gurmar powder reduces blood sugar levels by inhibiting sacharide absorption. When administered on the tongue, it suppresses sweet taste receptors, which helps to eliminate glycosuria increases insulin secretion and lowers blood sugar. Gurmar powder is also a heart stimulant and diuretics, as well as anamendment of metabolic activities in the liver, kidneys, and muscles. In capsule form, Diabeta contains anti-diabetic herbal formulations enriched with effective immunomodulators, antihyperlipidemics, anti-stress, and hepatoprotective activities(51). Diabeta's formulation is supported by modern research and clinical tests and is based on ancient Ayurvedic principles. Diabeta controls variables and pathways that lead to diabetes mellitus by acting on different sites in diverse ways. It targets the numerous causes that produce diabetes and corrects the degenerative consequences that arise as a result of the disease. When administered as an adjuvant to cases of uncontrolled diabetes, Diabeta helps overcome resistance to oral hypoglycemic medications. Diabeta provides patients with a sense of well-being and promotes symptomatic alleviation of problems such as weakness, giddiness, leg pain, body discomfort, polyuria, and pruritus (49).

Diasulin is the herbal formulations marketed in the form of capsules, which lowers blood glucose levels(52). The putative mechanism of action of the

Table 2. Phytochemicals found in the various constituents of herbal formulations as well as their potential therapeutic mode of action.

S. No	Name	Phytochemicals	Mode of action	References
1.	*Gymnema sylvestre*	• Gymnemic acids, saponins,stigmasterol, quercitol, and the amino acid derivatives betaine, choline and trimethylamine	• Induces the uptake and utilization of glucose by activating the enzymes required for glucose uptake • Corticotrophin and somatotrophin are inhibited by this plant drugs, reduces peripheral glucose utilization. • Epidephrine-induced hyperglycemia can be inhibited	(26-28)
2.	*Pterocarpus marsupiumm,*	• 7-O-γ-L-rhamnopyranosyl oxy-4'-methoxy-5-hydroxy isoflavone	• Affects GLUT -4 • Affects PPARγ, PI3 Kinase	(29)
3.	*Glycyrrhiza glabra*	• Glycyrrhizin	• Activates pancreatic islet cells	(30)
4.	*Casearia esculenta*	• Epicatechin	• Conversion of pro insulin to insulin	(31)
5.	*Syzygium cumini*	• Polyphenolic compounds	• Quercetin and rutin stimulate the secretion of insulin through blockage of L-type calcium channels on pancreatic beta cells • Quercetin and phenolic acids (ellagic andgallic acids) inhibit (HMG)-CoA reductase in the liver,helps in antihyperlipidemic properties.	(32)
6.	*Asparagus racemosus*	• steroidal saponins	• Stimulate γ-cells for insulin secretion. • Insulin secretion and intracellular Ca2+.	(33)
7.	*Boerhavia diffusa*	• Alkaloids	• Action of Hexokinase activity increased and glucose-6 phosphatase, fructose1,6 bisphosphatase activity significantly decrease. • increase plasma insulin level	(34)
8.	*Sphaeranthus indicus*	• Spaeranthine	• Acceleration of lipolysis, • Inhibition of adipogenesis, • Inhibition of alpha-amylase • Increasing insulin sensitivity.	(35)
9.	*Tinospora cardifolia*	• Isoquinoline alkaloid • Berberine	• Insulin releasing effect. • Inhibits FOXO1, which integrates insulin signaling	(36, 37)
10	*Swertia chirata*	• Mangiferin • Amarogentin • Amaroswerin • Sweroside • Swertiamarin	• β*cells to release insulin* • Promotes liver glycogenesis by increasing glycolytic enzymes. • Glucosidase is suppressed as well as other enzymes like maltase, sucrase, isomaltase, and aldose reductase. • Glucose is more readily utilized by peripheral tissues. • Increases GLP-1 by inhibiting dipeptidyl peptidase IV degradation	(16, 38, 39)
11	*Tribulus terrestris*	• Steroidal saponins • Flavonoids	• Reduce in blood sugar level by induction of beta cells of pancreas	(40, 41)
12.	*Phyllanthus amarus*	• Tannins • Lignans • Ellagitannins • Tritepene	• Reduction in total cholesterol, urea, total protein, uric acid.	(42)
13.	*Gmelina arborea*	• Flavanoids,	• It has been reported to reduce production of proinflammatory mediators in LPS-stimulated macrophages, fibroblasts, and intestinal epithelial cells.	(43)
14.	*Syzygium cumini*	• Mycaminose	• remarkable reduce the blood glucose level	(44)
15.	*Trigonella foenum-graecum L.*	• Trigonelline • Nicotinic acid • Coumarin	• Seeds of this plant helps to increase the hepatic and muscle glycogen content, stimulated hexokinase, glucokinase, pyruvate kinase, and others that helps to help in the glucose metabolism	(19, 45)
16.	*Nelumbo nucifera Gaertn.*	• Alkaloid (Nuciferine)	• It was reported that it helps to increase the insulin secretion in both isolated islets.	(46)

extract could be linked to the effect of hypoglycemic sulphonylureas, which enhance insulin secretion by closing K^+-ATP channels, depolarizing the membrane, and stimulating Ca^{2+} influx, an early important step in insulin production(53).

Discussion

Despite significant advancements in the knowledge and management of diabetes, the illness and its complications continue to grow unchecked. Despite the availability of proven antidiabetic medications on the market, medicinal plant treatments are successfully utilised to treat diabetes. Many traditional plant-based diabetes therapies are utilised all over the world. Plant medications and herbal formulations are often thought to be less harmful and free of adverse effects than manufactured drugs. According to WHO standards, hyperglycaemic drugs derived from plants are significant in traditional medicine. In addition to providing antihyperglycemic benefits, these plants increase insulin secretion, inhibit glucose absorption in the intestine or facilitate insulin dependent functions by restoring pancreatic tissue function. The herbal medicine treatment therefore, protects cells and at the same time smooths out the fluctuations in glucose level. Although the exact mechanisms involved in the treatment of diabetes are not widely understood, the majority of plants contain compounds such as glycosides, alkaloids, terpenoids, flavonoids, and other compounds that are often implicated as being diabetic control. Plant formulations and mixed extracts of plants are employed as drugs of choice in the traditional Indian medical system, rather than individual plants. Plants have been utilized by humans for food, clothing, and even medicine since the dawn of time. Plant-based goods have been popular for millennia all throughout the world. Some herbs have the ability to stimulate the regeneration of beta cells. In addition to altering blood sugar levels, certain herbs also have antioxidant properties, cholesterol-lowering properties, and liver glycogen repair abilities. Herbs are employed as decoctions, infusions, tinctures, and powders in Ayurveda's major formulations. The term "Polyherbal formulation" refers to a formulation that contains two or more herbs. Since various preparations function by distinct mechanisms, it is theoretically plausible that alternative combinations of these extracts would lower blood sugar more effectively. In the traditional system of plant medicine, formulas and extracts from plants are more effective than isolated drugs.

A healthy diet and lifestyle promotion should be a fundamental component of diabetes care because it is complex and multidisciplinary disease. Exercise and dietary management are critical treatment pillars for T2DM, and both may be sufficient to achieve and maintain the therapeutic targets of normolipidemia and normoglycemia (54).

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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