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UNANI DRUGS WITH ANTIDIABETIC ACTIVITY IN THE LIGHT OF SCIENTIFIC INVESTIGATION

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ABSTRACT

Diabetes is one of the most common ailments that create great impacts on humankind. The increasing rate of the disease day by day reveals that even the recent remarkable advancement in medical sciences does not have a justifiable answer to tackle their side effects and its ever-increasing load; therefore, there is a need of time to rethink about the preventive strategies, line of treatment, management and all aspects of diabetes. According to the World Health Organization, up to 90% of population in developing countries use plants and its products as traditional medicine for primary health care. Over the recent years, there has been a tremendous development in the field of Unani system of medicine all over the world as a result of their high efficacy and no side effects. In this article, detailed information about anti-diabetic drugs used in Unani system of medicine is compiled including their Unani name; scientific name, parts used, active chemical constituents and data regarding their hypoglycaemic activities are described. The paper emphasizes anti-diabetic activity of Unani drugs.

KEYWORDS: Diabetes, Anti-Diabetic drugs, Unani System of Medicine.

1. INTRODUCTION

Unani system of medicine plays a key role for ameliorating ailments of humankind. There have been very strong traditional systems of medicine such as Chinese, Ayurvedic, and the Unani, born and practiced, more in the eastern continent over the last 2500 years. These traditions are still growing, since; approximately 90% of the people in the developing countries rely on these systems of medicine for their primary health care needs.[1] These Unani drugs contain substances that can be used for therapeutic purposes, of which are

precursors for the synthesis of drugs.[2] Diabetes is characterized by metabolic deregulation primarily of carbohydrate metabolism, manifested by hyper-glycemia resulting from defects in insulin secretion, impaired insulin action, or both.[3]. It is made up of two types: Type I and Type II. Type I diabetes often referred to as juvenile diabetes, is insulin dependent and known to affect only 5% of the diabetic population. The Type II, which is non-insulin dependent, usually develops in adults over the age of 40. It has already been established that chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and eventually the failure of organs, especially the eyes, kidneys, nerves, heart and blood vessels.[4] It has an adverse effect on carbohydrate, lipid and protein metabolism resulting in chronic hyperglycemia and abnormality of lipid profile. These lead to series of secondary complications including polyurea, polyphasia, ketosis, retinopathy as well as cardiovascular disorder.[5] In spite of the introduction and extensive utilization of hypoglycemic agents, diabetes and the related complications continue to be a major health problem worldwide, which is affecting nearly 10% of the population all over the world[6] and considered as a major cause of high economic loss which can in turn impede the development of nations.[7] It is projected to become one of the world's main disablers and killers within the next 25 years. Many factors contribute to the on-set of diabetes and these are termed as predisposing or risk factors. Environmental factors such as diet, obesity and sedentary life style increase the risk of diabetes. Other important risk factors include high family aggregation, insulin resistance, nutritional status, age and lifestyle change due to urbanization.[8] The management of diabetes is a global problem until now and successful treatment is not yet discovered.[9]

Currently available therapy for diabetes includes insulin and various oral hypoglycemic agents such as sulfonylureas, metformin, glucosidase inhibitors, troglitazone, etc. But these are reported to produce serious adverse side effects such as liver problems, lactic acidosis and diarrhoea.[10] It is currently affecting around 143 million people[11] and the number of those affected is increasing day by day, by 2030 it is predicted to reach 366 million populations worldwide.[12] A number of Unani drugs have been reported to possess antidiabetic properties. Biological actions of the plants are related to chemical composition that are rich in phenolics, alkaloids, flavonoids, terpenoids, coumarins, and glycosides usually show positive effects. On the other hand, many conventional drugs for treatment of diabetes, such as metformin are secretagogues which have a plant origin.[14] According to the World Health Organization (WHO), up to 90% of the population in developing countries uses plants and its products as traditional medicine for primary health care.[38] The WHO has listed 21,000

plants, which are used for medicinal purposes around the world. Among these, 2500 species are in India.[39] There are about 800 plants which have been reported to show antidiabetic potential.[40] A wide collection of plant-derived active principles representing numerous bioactive compounds have established their role for possible use in the treatment of diabetes.[40]

The Unani drugs are used to treat diabetes by improving insulin sensitivity, increasing insulin production and decreasing the amount of glucose in blood. The adverse effect of drug treatment are not always satisfactory in maintaining normal levels of blood glucose and this view many Unani medicinal plants have been provided a potential source of antidiabetic principle which are widely used for the treatment of diabetes mellitus in various traditional system of medicine worldwide and many of them are known to be effective against diabetes. The hypoglycemic effect of pharmacologically active component of plant decreases the effect on α-amylase and various direct and indirect effects of different blood parameters responsible for development of diabetes.[15] A large number of antidiabetic medicines are available in the pharmaceutical market for diabetes and its related complications; however, currently no effective therapy is available to cure the disease. However, due to unwanted side effects the efficacies of these compounds are debatable and there is a demand for new compounds for the treatment of diabetes.[16, 17] In the last few years, there has been a growing interest in the herbal medicine in care and management of diabetes both in developing and developed countries, due to their natural origin and less side effects.[19, 20]

The present review elaborates the antidiabetic effect of some important plants used in Unani system of medicine in India for the management of type 2 diabetes mellitus. An attempt has been made to compile the reported hypoglycemic Unani drugs available in different scientific journals and may be useful to the health professionals, scientists and scholars working in the field of pharmacology and therapeutics to develop evidence based alternative medicine to cure different kinds of diabetes in man and animals. This review shows the importance of Unani medicinal plants to demonstrate their antidiabetic effects and the responsible bioactive agents. The review also covers the Unani name of a plant, the parts that are commonly used as a remedy sources, extracts, doses, and a test model.

Table 1: Scientific investigation of different plant parts for diabetes mellitus use in Unani System of Medicine.

S.No	Unani Name	Family	Botanical name	Parts used	Extracts	Active chemical constituents	Dose mg./Kg.	Test model	Result	References
1.	**Bael**	Rutaceae	*Aegle marmelos*	Leaf Seed Fruit	Ethanolic, Aqueous	Aegeline 2, Coumari, Flavonoid Tannin Alkaloid	I.p., 14d; p.o., 14d; 1.0 g/kg	STZ rat	↓Glucose, ↓glycosylated Hemoglobin, ↑C-Peptide ↑glucose, Tolerance, ↑glycogen,	[19, 20,21, 22, 23,24, 1,2]
2.	**Elwa**	Asphodelaceae	*Aloe barbadensis*	Leaf	-	Lophenol, 24-methyl-lophenol, 24-ethyllophenol	-	-	-	[31,2]
3.	**Neem**	Meliaceae	*Azadirachta indica*	Leaf, Seed	-	Nimbidin	-	-	-	[32,1,2]
4.	**Zanjbeel**	Zingiberaceae	*Zingiber officinale*	Bulb	-	Gingerol, Ethanol	-	-	-	[3,4,2]
5.	**Gurmar booti**	Asclepiadaceae	*Gymnema sylvestre*	Leaf	-	Gymnemic acid, Gymnema, Saponin	-	-	-	[9,2]
6.	**Amla**	Euphorbiaceae	*Emblica officinalis*	Fruit	-	Tannoid	-	-	-	[10,1,2]
7.	**Maghze Kanwal Gutta**	Nymphaeaceae	*Nelumbo nucifera*	Flower	-	Tolbutamide	-	-	-	[13,2]
8.	**Tamar hindi**	Fabaceae	*Tamarindus indica*	Seed, Fruit	Methanolic	Flavonoid, Polysaccharide	200	STZ rat	-	[33,34, 35,36, 1,2]
9.	**Seer/Lehsun**	Alliaceae	*Allium sativum*	Root	Ethanolic	Diallyl disulphide oxide, Ajoene, Allyl	P.o., 14d, 21-112 d	STZ rat	↑Insulin,↓Glucose, ↓Lipid, ↓Oxidative stress	[25,26, 27,28, 29, 30,2]

						propyl disulfide, S-allyl cysteine, S-allyl mercaptocysteine				
10.	**Jamun**	Myrtaceae	*Syzygium cumini*	Fruit	Methanolic	Anthocyanin, Citric, Malic, Gallic acid	100 ng ml-1	-	-	[5,6,7,8, 1,2]
11.	**Anba/Aam**	Anacardiaceae	*Mangifera indica*	Leaf, Stem Bark, Fruit	Aqueous, Alcoholic	Mangiferin, Phenolics, Flavonoid	i.p., AT; 100-200 mg/kg	STZ rat, Alloxan rat	↓Glucose	[11,12,1,2]
12.	**Tanbol/Paan**	Piperaceae	*Piper betle*	Leaf	Aqueous	-	p.o., 30 d	STZ rat	↓Glucose, ↓Glycosylated hemoglobin	[15,16]
13.	**Halela**	Combretaceae	*Terminalia chebula*	Seed, Fruit	chloroform, Aqueous	Shikimic, Gallic, Triacontanoic, Palmitic acid, β-sitosterol, Daucosterol	p.o., AT; 200 mg/kg	STZ rat	↓Glucose	[14,17,18,1]

AT: Acute treatment, i.p.: Intraperitoneal route, p.o.: oral route and STZ: Streptozotocin.

2. DISCUSSION

Diabetes is considered to be a metabolic disorder that mainly occurs due to defects in either insulin secretion, insulin action, or both. Diabetes is a disease that can lead to serious problems affecting human health. In the long term, effects can cause micro and macro vascular problems.[41] In addition, uncontrolled diabetes can cause many chronic complications, including blindness, heart disease, and renal failure.[42] A significant change occurs in the structure and metabolism of lipid in diabetes. Lipid peroxidation is associated with hyperlipidemia. The liver plays a critical role in glucose, lipid homeostasis, and has an important effect on diabetes. The liver and kidneys participate in the absorption, oxidation, and metabolism of free fatty acids and synthesize cholesterol, phospholipids, and triglycerides. Despite the presence of anti-diabetic drugs in the pharmaceutical market, the treatment of diabetes with medicinal plants is often successful. Herbal medicines and plant components with insignificant toxicity and no side effects are notable therapeutic options for the treatment of this disease around the world.[43] Most tests have demonstrated the benefits of medicinal plants containing hypoglycemic properties in diabetes management. The most common herbal active ingredients used in treating diabetes are flavonoids, tannins, phenolic, and alkaloids.[42] The existence of these compounds implies the importance of the anti-diabetic properties of these plants.[43] For example, tannin improves the function of pancreatic Beta-cells and increases insulin secretion. Quercetin is an antioxidant that acts in several mechanisms related with the removal of oxygen radicals, so prevents lipid peroxidation and metal ion chelation. In fact, the mechanisms of actions for hypoglycemic plants include: increasing of insulin secretion, increasing of glucoses absorption by muscle and fat tissues, prevention of glucose absorption from the intestine.

The 13 plant species belonging to different families were reviewed for treatment of diabetes in Unani system of Medicine. The majority of the experiments confirmed the benefits of medicinal plants with hypoglycemic effects in the management of diabetes mellitus. The detailed natural plants not only used for the treatment of diabetes, but also treated for other ailments also. The fruits were most commonly used plant parts and other parts (leaf, root, stem, bark, flower, and whole plant) were also useful for curing. However, the diabetic model that was most commonly used was the streptozotocin and alloxan-induced diabetic mouse or rat as diabetic models. In this study, most commonly used animal model was STZ rat. In some cases alloxan mice, glucose tolerance mice, KK-Ay diabetic mice, and diabetic patient

were used as a model. Some authors have used hereditary diabetic mice e.g. KK Ay mice as a model of type II diabetes with hyperinsulinemia.[44]

3. CONCLUSION

As per Unani System of Medicine, there exists a huge collection of plants with antidiabetic potential. Only few of them have been scientifically proven and a lot more have yet to be explored and proved. Some of these plant derived medicines, however, offer potential for cost effective management of diabetes through dietary interventions, nutrient supplementation, and combination therapies with synthetic drugs in the short term, and as the sole medication from natural sources over the long term. The antidiabetic activity of these Unani drugs is mainly due to the presences of bioactive chemicals. However, more researches are needed in order to separate the active components of plants and molecular interactions of their compounds for analysis of their curative properties.

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