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ANTIDIABETIC ACTIVITY OF SOME INDIAN MEDICINAL PLANTS USED FOR DIABETES MELLITUS : A REVIEW

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Abstract: The current study's objective is to assess several medicines herbs' potential as antidiabetic agents. One of the most prevalent non-communicable illnesses in the world is diabetes mellitus. People with diabetes mellitus are afflicted with this frequent and very prevalent illness in both industrialized and developing nations. This illness is thought to afflict 25% of the global population. The improper metabolism of carbohydrates, which is connected with decreased blood insulin levels or targeting organ response to insulin, is what causes diabetes mellitus. Herbal medicine has seen exponential development in the past several years and is becoming more and more popular in both developed and developing nations due to its natural origins and low negative effects. To gather data about herbal remedies used in the treatment of diabetes mellitus, a thorough review was carried out. One chronic metabolic disease with several origins is diabetes mellitus, which raises blood sugar levels. Systematic studies of herbal remedies for diabetes provide invaluable insights for the development of complementary and alternative medicine. A collection of herbal medications utilized for managing diabetes as well as medicinal herbs with shown antidiabetic properties and associated health benefits is compiled. These consist of Azadiracha indica, Fenugreek, Allium sativum, Aloe barbadensis Miller, and Allium cepa.

Index Terms - Diabetes mellitus, Antidiabetic drugs, Medicinal plants, Natural products.

I. INTRODUCTION :

The metabolic condition known as diabetes mellitus (DM), which is characterized by hyperglycemia and abnormal proteins, carb, and lipid metabolism, is the fastest-growing in the world. In addition to cancer and cardiovascular illnesses, diabetes mellitus (DM) is the third leading cause of death worldwide and a hazard to public health. By 2030, there will be 438 million persons aged 20 to 70 who will have it, up from 285 million in 2010. Over 60% of people with diabetes worldwide are from Asian nations, China and India bearing the lion's share of the burden.5. Ninety million Chinese individuals are estimated to have diabetes at

this time, and 1.3 million of them lost their lives to the illness in 2011.[1,4] Due to its significant lasting medical implications, mellitus is a metabolic illness that has become a major issue in modern society. Over eighty percent of all instances of diabetes are type 2 diabetes mellitus (T2DM), which is the most common kind of the disease. One of the main causes for this disease is abnormalities in the breakdown of glucose. A hormone called insulin is secreted by the pancreatic β-cells and is in charge of maintaining glucose homeostasis. Insulin resistance, which is defined as cells' incapacity to react to typical amounts of circulate insulin, is caused by the improper use of insulin and ultimately results in the development of the illness.[3,7] Herbal plants as well as minerals and naturally occurring substances are the source of many commonly used traditional medications. 21,000 plants are

listed by the World Health Organization (WHO) and are utilized for various purposes globally. Of these 2500 different species, 150 are employed on a reasonably considerable scale in businesses in India. India is known as a global natural paradise and is the world's greatest grower of medicinal plants. Indian Herbal Medicines for Type 2 Diabetes India is home to 45,000 formally recognized plant varieties, with an additional 7500 species thought to be medicinally significant. Diabetes has long been treated in India with a variety of potent plants and natural compounds. Several Indian herbs have been the subject of studies and publications in academic journals about their potential benefits for various forms of mellitus.[3,5,4,9]

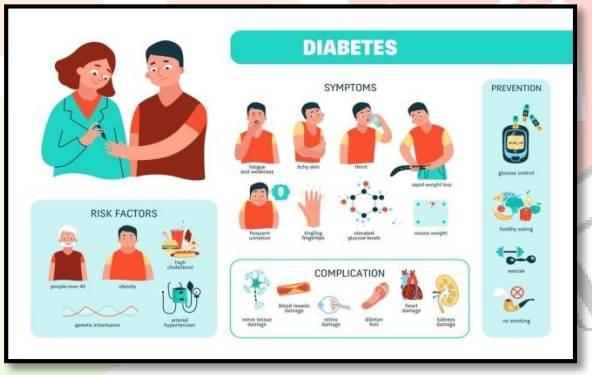

Figure.1. Diabets

adverse reactions are additionally a part of sulphonylurea and biguanide therapies. Nonetheless, alternative health care has become a growing trend in recent years for a variety of factors. It has been discovered that a number of locally grown medicinal plants can assist manage mellitus; some of them have even undergone testing to determine their active components. There is a wealth of evidence supporting the therapeutic use of herbal remedies in many countries' classical medical systems. Several plants have been utilized with any understanding of their correct ingredients or activities as nutritious adjuvants for a variety of ailments. The effectiveness of plant treatments has also been validated by several recent research studies; however, only a small number of these are really effective.[5,7]

II. DIABETES MELLITUS TYPES :

IDDM, NIDDM, and gestural diabetes (occur during pregnancy) are the three primary kinds of diabetes mellitus that the World Health Organization's (WHO) recognizes. While their causes and demographic distributions vary, all three types of diabetes have the same symptoms, indicators, and outcomes. All of this eventually happens because the pancreatic β-cells are unable to produce enough insulin to stop hyperglycemia.

1. IDDM (INSULIN DEPENDENT DIABETES MELLITUS TYPE 1): is usually caused by inflammatory injury to the β-cells within the pancreas, which are responsible for producing glucose. It is brought on by an immune system response in which the body's self-defense system kills the β cells that produce insulin. The production of insulin is either very low or absent in people with diabetes who have type 1 diabetes. The illness often strikes while a person is younger. Patients' ability to control blood glucose levels is entirely dependent on external insulin. It is thought that genetic factors have a vital role in it.

2. NIDDM (NON-INSULIN DEPENDENT DIABETES MELLITUS TYPE 2): is demonstrated by tissue-wide glucose resistance, but its expansion requires the breakdown of β cell activity. This group accounts for around 90% of all patients with diabetes. Diabetes insufficiency and sensitivity are its defining characteristics. The reason for this is the degeneration of viable β cells. There are extremely significant consequences with type 2 diabetes that can end one's life.

3. GESTATIONAL DIABETES GDM TYPE 3: is comparable to type-2 diabetes as it is characterized by elevated levels of sugar in the blood during pregnancy and insulin resistance, which is brought on by the predisposal of estrogen during pregnancy. In the second or third trimester of a pregnancy, it happens in 4% of cases. [7,9]

SIGNS AND SYMPTOMS:

Unexpected reduction in body weight, polyuria, polydipsia and polyphagia are the hallmark signs of diabetes that is uncontrolled. In type 1 diabetes, indications might appear for several weeks or months before they appear, while in type 2 diabetes, signs typically appear much later and can even be nonexistent. Even though they are not unique to diabetes, a number of other symptoms and indications might indicate the start of the condition. These include, besides to the well-known ones mentioned above, headaches, tiredness, delayed recovery from wounds, and dermatitis. Long-term elevated blood glucose levels can result in glucose absorption in the lens of the eye, changing its structure and eyesight. Retinal damage caused by diabetes can potentially result in long-term visual loss. Diabetic dermadromes are a group of irritations of the skin that can arise in people with mellitus.[2,13,14]

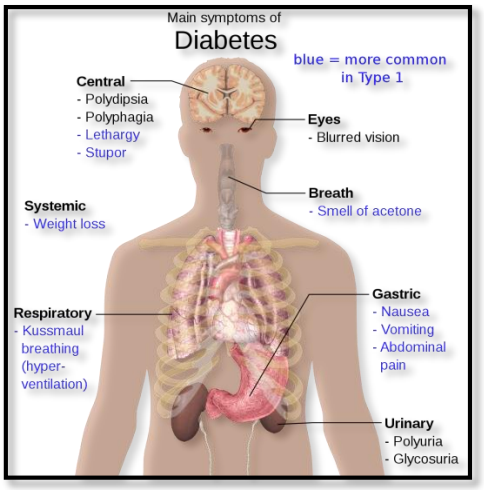

Figure.2. Sign and symptoms

III. CLASSIFICATION OF ANTIDIABETICS DRUGS:

1. PRANDIAL INSULIN RELEASERS WITH RAPID ACTION:

A reduced reaction of the initial phase of glucose-stimulated insulin secretion has been found in the typical course of type 2 diabetes. In the perioperative interval, liver gluconeogenesis must be suppressed by an early insulin spike. The levels of HbA1C are negatively impacted and postprandial hyperglycemia is exacerbated if this process malfunctions. To solve this issue, meglitinides were created.These medications' brief half-lives enhance the effects of insulin secretion during the initial stage, but not during its later.[11]

USES : In addition to a nutritious diet and regular physical activity, nateglinide is administered alone or in combination using other drugs to treat excessive glucose levels. Individuals with type 2 diabetes use it. Keeping your sugar levels under control can help avoid kidney disease, lack of vision, nerve harm, missing limbs, and issues with intimacy. Keeping your diabetes under management can decrease your chance of having a coronary artery disease or attack. It functions by encouraging the body to make more insulin.[16,17]

SIDE EFFECTS:

- Sudden changes in behavior or mood.
- Shakiness.
- Sweating.
- Dizziness or lightheadedness.
- Nervousness or irritability.

DRUG INTERACTIONS:

Numerous medications might alter blood sugar levels, making management more difficult. The drugs (like prednisone), psychiatric drugs (like olanzapine), and fluoroquinolone-based antibiotics (like ciprofloxacin) are a few examples. sugar on a regular schedule as instructed, and let your physician know the outcome. [16,17]

2. SULFONYLUREA'S:

Since their invention in the early 1920s, sulphonylureas have proven to be essential in the treatment of type 2 diabetes. A immediate secreted impact on the islets of the pancreas beta-cells is part of the process of action. The beta-cells' adenosine triphosphate-sensitive potassium channels, which are made up of a pore and an inhibitor unit, are crucial for the absorption of glucose.[11]

USES:

The primary purpose of sulfonylureas is the management of diabetes of type 2. When a patient has a complete lack of insulin generation, as in type 1 diabetes or after a pancreatectomy, sulfonylureas are useless. Certain forms of pediatric diabetes can be treated with sulfonylureas. Although type I diabetes was once thought to be the usual diagnosis for adults with hyperglycemia along with low blood glucose levels, it has been shown that patients who acquire the condition before reaching the age of six months are frequently suited for sulfonylureas as opposed to glucose during their lives.[15]

SIDE EFFECTS:

- Signs of low blood sugar, such as sweating, confusion, dizziness or nervousness.
- Skin reactions.
- Dark-colored urine.
- Upset stomach.
- Weight gain.
- Hunger.

DRUG INTERACTION:

The following medications may have an impact on how well sulfonylurea works: Certain antimicrobial agents, such as sulfonamide, ciprofloxacin, , clarithromycin, rifampin, chloramphenicol and ketoconazole and isoniazid, fluconazole, have antifungal properties. [15]

3. INSULIN SENSITIZERS:

Metformin is a biguanide. Since the year 1950, metformin has been accessible. Its historical provenance and source are linked to the guanidine-rich Galega officinalis, often known as French lilac or goat's rue, which has long been utilized as a diabetic remedy in Europe. Beyond only reducing blood sugar, metformin has a number of other beneficial therapeutic benefits, including weight loss, lipid profile improvement, improved endothelial function in the vascular system, and a reduction in PAI-1 levels.4. As of now, biological mechanisms of action remain unclear.

USES:

Glucose levels are managed with the use of metformin. It improves sensitivity to insulin without changing your body's insulin production capacity. As a result, your bloodstream's level of glucose drops, the amount of glucose produced in the liver is decreased, and your cells are better able to absorb glucose for power. The intestines consume glucose to make lactic acid, which is produced by the liver processes but can have the unintended consequence of causing lactic acidosis. [21,11]

SIDE EFFECTS:

- Gas.
- Little appetite.
- Bloating.
- Diarrhea.

DRUG INTERACTIONS:

Metformin must be given with food in order to reduce gastric adverse effects, even if this isn't due to a pharmacological combination. Vitamin B12 absorption brought on by metformin may lead to a B12 shortage and consequent anemic. Although the specific process by which metformin promotes B12 malabsorption is unknown, rectification may be achieved with calcium supplements or B12 either orally or intravenously. Metformin is excreted from the body by the process of glomerular filtration and tubular secretion; it does not go through conversion. [22]

DIABETES AND SIGNIFICANCE:

A complicated metabolism condition called diabetes mellitus is brought on by either insufficient or malfunctioning insulin. Because there are insufficient beta cells in the body, insulin becomes insufficient, leading to type I diabetes (insulin dependent). Patients with Type II diabetes, who are insulin reliant and cannot respond to insulin, receive treatment with diet modifications, physical activity, and medical care. Patients with this condition are consequently entirely dependent on external sources of insulin. Ninety percent of people with diabetes have type II diabetes, which is the most prevalent kind of the disease. For both types of diabetes, symptoms might include: Glucose levels that are abnormally higher; excessive thirsty; constant urinating; severe hunger and decreased weight; impaired eyesight; vomiting and dizziness; severe weakness and exhaustion; irritation and fluctuating emotions etc. [1]

IV. TREATMENT OF DIABETES MELLITUS:

1. INSULIN AND ORAL HYPOGLYCEMIC DRUG:

The goal of treatment with insulin should be to emulate their nature, which limits postprandial hyperglycemia and avoids hypoglycemia during between diets with remarkable efficacy. There are several forms of insulin available, including human, cow, and hog insulin. There are drawbacks and dangers to insulin treatment. The two most significant side effects of taking an incorrect

dose of insulin and timing food and insulin injections are increased body weight and hypoglycemia. They attach to ß-cell plasma membrane sulfonylurea receptors, closing ATP-sensitive potassium channels and depolarizing the cell layer in the process. [23]

2. HERBAL TREATMENT OF DIABETES:

Many are a number of evaluations of the scientific literature about natural treatments for diabetes, but Atta Ar Rahman's review which lists over 300 kinds of herbs recognized to have hypoglycemic qualities is the most enlightening. The plants used in this study have been categorized based on their scientific name, location of source, components utilized, and kind of active substance. Momordica charantia, a member of the Cucurbitaceae group of plants, is one interesting plant. According to the WHO, 21,000 plants are utilized globally for medical reasons.[3]

V. ANTIDIABETIC PHYTOCHEMICALS:

1. ALKALOIDS:

Spontaneous nitrogenous chemical compounds called alkaloids have medicinal effects on individuals and other animals. Because of their diverse chemical structure and range of biochemical actions, alkaloids are acknowledged as a significant class of phytonutrients. Morphine was the first alkaloid to be found therapeutically; it was extracted from the papaver somniferum Linn poppy species. There have been reports of using alkaloid compounds from plants to treat diabetes. In the pancreatic islets of rats, beberine, unlike sulphonylureas, increased glucose-stimulated insulin production in a dose-related way, most likely through a mechanism implicating hepatic nuclear factor 4α. [6]

2. PHENOLICS:

It has been proven that phenolic chemicals interact with molecules to prevent enzyme function.Meal-grade phenols derived from nutritional extracts of plants that impede α-amylase activity may be a safer substitute for controlling the glycemic index of food items and regulating the digestion of carbohydrates.[6]

3. TRITERPENES:

Numerous investigations on the anti diabetic effects of terpenoids derived from plants were conducted. An ethanol extraction of Larix laricina K. Koch (Pinaceae) bark yielded a novel cycloartane triterpene (23-oxo-3α-hydroxycycloart-24-en-26-oic acid), which was shown to have potential diabetic medications action due to its substantial enhancement of adipogenesis in 3T3-L1 cells, with an EC50 of 7.7 μM. [6]

4. FLAVONOIDS:

The compounds known as flavonoids are polyphenolic chemicals with two benzene rings connected by a linear three-carbon chain, totaling fifteen carbon atoms. Flavonoids exhibit a multitude of properties, one of which is its ability to prevent hyperglycemia. There have been a lot of research published on the

possible antidiabetic effects of plant-based flavonoids. In streptozotocin (STZ)-induced diabetic rats, quercetin enhanced insulin production and restored the islets of the pancreas.[6]

VI. INDIAN MEDICINAL PLANTS WITH ANTIDIABETIC ACTIVITY:

1. ALOVERA (*Aloe barbadensis Miller*): [1, 4, 12,18,19]

Plant name: Aloevera.

Synonyms: Aloe, Ghritkumari, Aliyo**.**

Figure.3. Aloevera plant

Biological source: Aloe is the dried juice collected by incision from the bases of the leaves of various species of aloe.

Family: Liliaceae.

Geographical source: Among of the approximately 160 varieties of aloe, the ones that follow are significant and used to prepare aloe.

Chemical Constituents: Aloin, a combination of three isomers—barbaloin, βbarbaioin, and isobarbaloin—can make up as much as 30% of aloe. All four types of barbaloin have the same slightly yellow color, unpleasant taste, and water solubility as crystalline glycosides.

Antidiabetic activity:

A recent research in Thailand suggests that aloe vera supplements may help lower fasting plasma glucose levels in individuals with preconception and enhance HbA1c levels, an indication of managing blood sugar over the previous two to three months, in persons with Type 2 diabetes. The scientists performed a meta-analysis, or an examination of data from numerous studies, on eight controlled studies including 470 participants with Type 2 diabetes as well as prediabetes in order to assess the effects of aloe vera on blood sugar levels. The experiments examined how aloe vera affected blood sugar levels in comparison to placebo, or inactive therapy, or no therapy at all.[18,19]

Uses:

1. Powerful purgatives, aloe and aloin can also have abortifacient properties at greater dosages.
2. Aloe typically works best when paired with carminatives or antispasmodics like belladonna or hyocyamus since when taken alone, it induces griping.
3. Aloe gel cream is applied to treat burns from the sun burns caused by heat, irradiation burns, abrasions, and skin irritations; it also guards against ulcers and cancer.

2. AZADIRACHTA INDICA *[1,4,20,24]*

Plant Name : Azadirachta Indica.

Synonyms: neem , *arishth, neem seed, margosa, kadulimb.*

Figure.3. Azadirachta indica plant

Biological source: Neem is made up of Azadirachta indica J. Juss's either fresh or dried leaf and seed butter (also known as Melia Indica or M. azadirachta Linn.)

Family : Meliaceae.

Geographical source:

It may be located in the tropical regions of Australia and Africa as well as in the countries of Sri Lanka, India, Malaya, Pakistan,Indonesia, and Japan. It may be found in the states of Rajasthan, Uttar Pradesh, Maharashtra, Tamil Nadu,and M.P. in India. The world's largest producer of neem seeds, India produces over 4,42,300 tons of seedlings yearly, which are converted into 3,53,800 tons of cake made from neem and 88,400 tons of neem oil.

Chemical constituents:

At doses that range from 100 to 500 ppm, limonoids such as nimocinolide and iso-nimocinolide have an effect on fertility in house flies (Musca domestica). Additionally, they have mutagenic qualities in intermediate-producing mosquitoes (Aedes aegypti).Nimbosterol and flavonoids such as kaempferol, melicitrin, and others are present in the volatile oil of the plants, which is composed of sesquiterpene derivatives.

Antidiabetic activity:

Major changes in plasma glucose, lipids, total cholesterol, urea, it and creatinine concentrations were noted in both the acute and chronic research groups following the ingestion of neem leaf extract with ethanol. In usual, glucose-fed and STZ diabetic rats, the hydroalcoholic extract of Azadirachta indica demonstrated antihyperglycemic and hypoglycemic effects. Regardless of when it is administered prior to or after the injection of alloxan the plant exhibits its pharmacological effect. The plant increases peripheral glucose consumption by inhibiting the effects of adrenaline on the utilization of glucose. In the isolated rat hemi diaphragm, it likewise enhanced the absorption of glucose and the deposition of glycogen. Every portion of the neem tree has some therapeutic value, making it a valuable commodity.

Uses: managing issues with the scalp, such as dandruff, itching, and headaches. treating skin conditions including psoriasis and itch. diagnosing and curing burning, ring-worm, bacterial infections, and wounds with infections. addressing nail fungal infection, acne, and repairing weak nails.

3. ALLIUM SATIVUM: [1,4,26]

Plant name: Allium Sativum.

Synonyms- *Allium arenarium* Sadler ex Rchb, *Allium controversum* Schrad. Ex Wild *Allium longicuspis* Rege.

Figure.4. Allium Sativum

Biological source: Garlic (*Allium sativum*) is a species in the onion genus, *Allium*. Its close relatives include the onion, shallot, leek, chive and *Chinese onion*.

Family: Liliaceae.

Geographical source: Although it is grown in the USA, Europe, Africa, India, and other places, garlic originated originally from central Asia. It's been a mainstay in Mediterranean cuisine for a very long time.

Chemical Constituents: Many different minerals, vitamins, carbs, amino acids, volatile petroleum products, and other trace components are found in the cloves of garlic.Garlic possesses the greatest sulfur concentration among all members of the Allium species. Garlic contains volatile oils in a quantity of 0.1-0.5%.

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Antidiabetic activity: It is currently shown that garlic lowers the levels of glucose in the blood in diabetic rats and mice that have been induced by alloxan or STZ. Garlic has been shown in the majority of trials to lower blood glucose levels in rats with diabetes, mice, and rabbit. Augusti and Sheela repeatedly demonstrated that garlic's S-allyl cysteine sulphoxide, or allicin, a sulfur-containing amino acid, has the ability to nearly completely reverse the diabetic state in rats (200 mg/kg body weight) when compared to glibenclamide.

Uses: Garlic is reported to reduce cholesterol in people with hypercholesterolemia. The diallyl disulphides and diallyl trisulphides found in garlic oil are thought to cause interference with the enzymes that are typically in charge of lipid synthesis, which is the suggested explanation for this. Garlic has the ability to lessen the body's enzymes' thiol collective activity.

4. FENUGREEK [1,10,27,]

Plant name : Fenugreek.

Family : Fabaceae.

Synonym :Methi.

Figure.5. Fenugreek

Biological Source: His is made up of mature, dehydrated seeds and drying leaves of Trigonella foenum graecum Linn (Fabaceae family) cultivars. On a dry-based basis, it must include at least 0.1% w/w of trigonelline. The plant grows annually from seedlings that reach a maximum height of thirty centimeters.

Chemical Constitution *:*

Methi is seeds have around 3.0% mucilage, 5.0% fixed oil, 0.5-2.5% steroidal saponin, and 20% protein. The seed also contains alkaloid compounds such as trigonelline and choline. Trigofoenoside saponnin.

Anti-diabetic activity :

Studies conducted over the last 20 years have demonstrated that fenugreek seeds can assist diabetic people reduce their blood sugar levels. The soluble fiber from diet fraction has been shown to have diabetic medications properties, as evidenced by reduced blood sugar levels during fasting and improved ability to tolerate glucose among test subjects. The hypolipidemic action of this fraction may be attributed to the agent's bioactive fiber, which retards the absorption of fat and carbohydrates. According to our research, diabetics had higher blood levels of urea, creatinine, and uric acid.

Uses : hypoglycemic, anti-inflammatory, anti-cholesterolemic, and galactogogue. It is used as an demulcent laxative and expectorant.

5. ALLIUM CEPA: [1,2,4]

Synonyms: wild onion, allium fistulosum, tree onion.

Plant name : allium cepa.

Family: Alliaceae.

Biological source: The onion (Allium cepa L., from Latin cepa "onion"), also known as the bulb onion or common onion, is avegetablethat is the most widely cultivated species of the

genusAllium. Its close relatives include thegarlic,leek,chive,andChinese onion. It is commonly obtained from root of onion plant.

Figure.6. Allium cepa.

Geographical source:

A few species are indigenous to Central America, South America, and Africa. Allium dregeanum, the only known instance, is found in South Africa in the Southern Hemisphere. There are two primary centers of variation: one is located in the Mediterranean Basin and extends to Central Asia, Pakistan while the other is located in western North America.

Chemical Constituents*:* Bulb Analysis of the onion (big) gave the following values: The huge onion's bulb testing yielded a number of values: An Indian onion specimen's basic amino acid content was as follows. methionine, 1.12; phenylalanine, 2.88; threonine, 1.44; isoleucine, 1.44; leucine, 2.72; valine, 2.24; histidine, 1.12; lysine, 4.64; arginine, 2.72; tryptophan, 1.44., trihydroxylase Acid, Octadec-10-enoic acid, Abscisic Acetic acid, acetal adenosine, from Allium cepa.

Antidiabetic activity: Mice were given 0.5 milliliters of the fresh bulb intravenously, and the decoction proved to be effective. When 25% pure extract was employed instead of alloxan-induced hyperglycemia, the maximum change in blood sugar was 28.2%. At a dosage of 250.0 mg/kg, the bulb's 95 percent ethanol extract was effective in preventing alloxan-induced hyperglycemia in rabbits. Two hours after therapy, there was an 18.57% decrease in blood glucose. Dried bulb extracts in ethanol and ether (95%) var. be hairy and given to rats at a dosage of 50.0 gm/kg by stomach intubation.

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