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# Anti-diabetic and Hypoglycemic Activities of Onion: A review

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## Abstract:

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, action or both. Plants from the genus *Allium*, particularly onions (*Allium cepa*) have been consumed for their putative nutritional and health benefits for centuries. The studies indicated that *Allium cepa* is rich in organosulfur compounds, phenolic acids, flavonoids, thiosulfinates, and anthocyanins which were known to have hypoglycemic, hypocholesterolemic and antibacterial potentials, and antioxidant activity with beneficial effects on inflammatory conditions, diabetes mellitus and cancer prevention. In this review, we reviewed the antidiabetic and hypoglycemic properties of Onion. Several ingredients derived from these plants have chemical constituents that demonstrate anti-diabetic activity, thereby validating their importance for the management of diabetes.

**Keywords:** Onion, diabetes mellitus, Antidiabetic, hyperglycemia.

**الملخص بالعربي:**

إن داء السكري عبارة عن اضطراب أيضي يتميز بفرط جلوكوز الدم الناتج عن عيوب في إفراز الأنسولين أو فعاليته أو كليهما. يعتبر استهلاك النباتات من جنس (Allium) وخاصة البصل ( *Allium cepa* L.) يرجع لعدة قرون وذلك لفوائدها الغذائية والصحية. حيث أشارت الدراسات بأن البصل غني بمركبات الكبريت العضوي والأحماض الفينولية والفلافونويدات والثيوسولفينات والأنثوسيانين التي عرفت بقدرتها على خفض نسبة السكر في الدم، ونقص كوليسترول الدم، وكمضادات للجراثيم، وأيضاً كمضادات للأكسدة التي لها تأثيرات مفيدة على حالات الالتهاب وداء السكري، والوقاية من السرطان. في هذه المقالة، استعرضنا خصائص البصل المضادة لداء السكر وفرط جلوكوز الدم. أيضاً، تم التطرق إلى العديد من المكونات الكيميائية المشتقة من هذه النباتات التي تظهر نشاطاً مضاداً لمرض السكري، مما يؤكد أهميتها في التعامل مع هذا المرض.

**الكلمات المفتاحية:** البصل، داء السكري، المضاد للسكري، فرط جلوكوز الدم.

## 1. Introduction:

Diabetes mellitus is a disease closely associated with the metabolic syndrome and in developed countries it is a major public health problem [1]. The term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia (high blood sugar) with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [2]. Based on its etiology, diabetes mellitus is

generally divided into three classifications: type 1, type 2 and gestational. Type 1 is an autoimmune disease characterized by a defect in insulin secretion such that the pancreas produces little or no insulin. It occurs most often in children and Young adults and accounts for 5-10% of cases of diabetes. Type 2 diabetes is a metabolic disorder characterized by a defect in insulin secretion and/or the tissues are resistant to its uptake. Type 2 accounts for 90-95% of cases of diabetes [3]. Diabetes mellitus (DM) affected 451 million individuals worldwide in 2017, and the number is anticipated to increase to 693 million people by 2045 [4]. The synthetic hypoglycemic agents used in clinical practices have serious side effects like hematological effects, coma, disturbs the functions of liver and kidney. In addition, they are not suitable for use during pregnancy. Compared with synthetic drugs, drugs derived from plants are frequently considered to be less toxic with fewer side effects. Therefore, the search for more effective and safer antidiabetic agent has become an area of active research [5].

The anti-hyperglycemic effects shown by these plants are due to their capability of increasing insulin synthesis, and decreasing glucose absorption from intestines or regulation of the pancreatic function. Although herbal preparations have protective effects on β-cells and help in regulating blood glucose levels, scientific understanding of the mechanism of action for these plants is lacking [6]. Recently, the World Health Organization (WHO) recommended the use medicinal plants for the management of DM and further encouraged the expansion of the frontiers of scientific evaluation of hypoglycemic properties of diverse plant species. Consequently, current estimates showed that over 70% of the global population applies resources derived from traditional medicine for the management and alleviation of DM and its complications [7]. The reported potential antidiabetic bioactive compounds Anthocyanidins, Anthocyanins, Flavones, Isoflavones, Flavanols, Isoflavonoids, Chalcones, Tannins, Xanthones, Organic acids, Cinamic acid derivatives, Sugars, Curcuminoids and Alkaloids, etc. In addition these compounds act as α-glucosidase inhibitors. All these bioactive compounds are now using in the treatment of type 2 diabetes diseases [8]. One of the plants that can be used as an alternative is onion (*Allium cepa* L).

Allium species such as onion has attracted particular attention of modern medicine because of its widespread health use around the world, and the cherished belief that it helps in maintaining good health, warding off illnesses and providing vigor. Onion is rich in flavonoids such as quercetin and sulphur compounds, such as allyl propyl disulphide that have perceived benefits to human health. These compounds possess antidiabetic, antibiotic, hypocholesterolaemic, fibrinolytic, and other various beneficial biological effects [3]. We reviewed the antidiabetic and hypoglycemic properties of Onion.

Several ingredients derived from these plants have chemical constituents that demonstrate anti-diabetic activity, thereby validating their importance for the management of diabetes.

## 2. Chemical compositions of Onion:

*Allium cepa* (*A. cepa*) is used commonly in foodstuff and as a traditional remedy in the treatment of a variety of disorders. The pharmacological evidence for the use of *A. cepa* as an anti-asthmatic, anti-hypertensive, anti-hyperglycemic, anti-hyperlipidemic and anti-tumor agent has been reported [9]. *Allium cepa* L. is a perennial herb belonging to the Amaryllidaceae. The parts of the plant used are the fresh or dried bulbs, commonly known as onion, which are commercially cultivated worldwide. The main chemical constituents are sulfur-containing compounds, such as L-cysteine sulfoxides, and flavonoids, such as quercetin and its glycosides. A. *cepa* seems to exert its antidiabetic activity regardless of the form in which it is administered (i.e., extracts, juice, freeze-dried powder, essential oil [10].

Onion (*Allium cepa*) is an important source of dietary phytochemicals with proven antioxidant properties, such as organosulfur compounds, phenolic acids, flavonoids, thiosulfinates, and anthocyanins. 30 compounds from volatiles compounds of black onion were identified, which accounted for 52.63% of all compounds and 81.69% of the total peak areas; these components included 19 sulfur-containing volatiles compounds, such as diallyl sulfide, methyl allyl sulfide, 3-hydroxysulfolane, 2,4-dimethylthiophene, 2-methoxythiophene, 1,4-dithiane, and 1,3-dithiane. A total of 49 types of volatile compounds were identified from onion, which were mainly sulfur compounds, alcohols, aldehyde, ester, and other chemical groups, but there was significant difference in volatile compound pattern and their relative contents from fresh and dried onion. The diabetic rats supplemented with either onion or with single components (alliin, allitride, and *S*-methylcysteine sulfoxide) possess lowering plasma glucose concentrations and body weight and preventive cardiovascular diseases [11].

Flavonoids are from the group of natural substances with varying phenolic structures. They are found in roots, stems, bark, flowers, fruits, vegetables and grains, and. Quercetin is a major member of flavonoid family isolated from onions, apples, grapes and tea. This flavanol is mostly well-known for its antioxidant and anti-inflammatory properties. It has been indicated that Quercetin can be beneficial for preventing hyperglycemia in experimental version of Diabetes Mellitus. Oral administration of 100mg/kg Quercetin could weaken fasting and postprandial levels of glucose in experimental Diabetes Mellitus, at least in part by inhibiting α-glucosidase activity [12].

The bulb and leaves, which are used for cooking, possess nutritional and medicinal benefits. It serves as a rich source of protein, fibre, fat, folic acid, sodium, vitamin C, vitamin B6, and many other micronutrients. The health benefits of onion include management of a number of diseases including diabetes mellitus [13]. Active ingredients in *A. cepa* include phenolic compounds (flavonoids, antocyanins, phenolic acids and flavonols), organosulphur compounds, vitamins and some minerals. These compounds may mediate the pharmacological effects of *A. cepa*. Thus, phenolic acids, such as caffeic, chlorogenic, ferulic, sinapic, p-coumaric acids, vanillic, syringic and p-hydroxybenzoic appear to be active antioxidants. Its vitamins, especially vitamin C have a protective function against oxidative damage and a powerful quencher of singlet oxygen ($O_2$), hydroxyl (OH) and peroxyl ($RO_2$) radicals [9]. Flavonols are the most abundant in onions, present as their glycosides, that is, quercetin and kaempferol, in higher concentration (280 - 400 mg/kg) than other vegetables (i.e., 100 mg/kg in broccoli, 50 mg/kg in apple). Anthocyanins, belonging to anthocyanidins, are mainly present in red onions (250 mg/kg), besides having a composition rich in flavonols as yellow onions. Fructooligosaccharides (FOS) represent another source of phytochemicals in onions bulbs. They are mainly inulin, kestose, nystose, and fructofuranosylnystose. The health benefits of these carbohydrates have been widely reported in the past years due to their prebiotic effect[14].

Onion bulbs have been recognized as the richest source of dietary flavonoids. At least 25 different flavonoids have been characterized and quercetin and its glycosides are the most important ones. Especially higher concentrations of quercetin occur in the outer dry layers of onion bulb [15]. Onion contains about 0.2% (dry matter conversion) cysteine sulfoxides (isoalliin, methyiin, and cycloalliin) as characteristic amino acids, which brings about the pungent aroma and taste of onions. Cysteine sulfoxides are cleaved by cysteine sulfoxidelyase, when onions are cut or crushed, to produce alkyl sulfenic acid which is converted to thiosulfinates and other volatile compound. It has been reported that intake of onion powder improved depression and anxiety behavior due to stress in animal study. Cysteine sulfoxides are known to have various physiological functions [16]. The active ingredient in *A. cepa* is allyl propyl disulfide (APDS), though other active sulphurous compounds are present. The use of herbal products for medicinal benefits has played an important role in nearly every culture on earth and for many years, the search for anti-diabetic products will continue to focus on plants and other natural resources [2].

**3. A review of effects of Onion on hyperglycemia and diabetes mellitus:**

Though pathophysiology of diabetes remains to be fully understood, experimental evidences suggest the involvement of free radicals in the pathogenesis of diabetes and more importantly in the development of diabetic complications. Free radicals are capable of damaging cellular molecules, DNA, proteins and lipids leading to altered cellular functions.

Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experimentally induced diabetes in animal models as well as reducing the severity of diabetic complications[17]. However, recently in the developed countries, there has been the resurgence of interest in medicinal plants that exhibit hypoglycemic property. The renewed interest in herbal anti-diabetic remedies in developed countries is believed to be motivated by several factors that include: adverse reactions, high secondary failure rates and cost of conventional synthetic anti-diabetic remedies [7].

Obviously, the significant efficacy of hypoglycaemic herbs, obtainable, via functioning as pancreatic insulin secretagogues and extrapancreatic insulin mimetics, enhancing glucose uptake by adipose and muscle tissues, or via inhibiting hepatic gluconeogenesis and intestinal carbohydrate digestibility and absorption, is comparable to conventional diabetes pharmacotherapeutics. Literature surveys of botanicals with traditional uses, critically withstanding pharmacological appraisal, indicated that local target-based and mechanistic reports on diabetes interventional phytotherapies are primarily limited and inadequate [18].

*Allium cepa* belongs to the family Liliaceae and is probably native of south west Asia and is widely cultivated throughout the world. *Allium cepa* (onion) dried powder shown anti hyperglycemic activity in diabetic rat. *Allium cepa* is also know to have antioxidant and hypolipidaemic activity [19]. Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. *Allium cepa* is also known to have antioxidant and hypolipidaemic activity. Administration of a sulfur containing amino acid from *Allium cepa*, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels [17]. A preliminary study evaluated the hypoglycemic effects of the oral administration of small slices of A. *cepa* (100 g/day) in type 1 and type 2 diabetic patients. Onion exhibited significant antidiabetic effects, reducing fasting blood glucose by about 89

mg/dL in type 1 diabetes patients and by 40 mg/dL in type 2 diabetes patients. A reduction of the induced hyperglycemia by 120 mg/dL in the diabetes 1 group and by 159 mg/dL in the type 2 diabetes was also observed [10].

In this review, several studies reported anti-diabetic activities of Onion are discussed. Research work carried out by Ojieh *et. al*., (2015)[20] assessed the antidiabetic activities of *Allium cepa* (onions) in streptozotocin-induced diabetic male Wistar rats. Adult male Wistar rats were randomly divided into eight (8) groups of five rats each (n=5). Groups 1a and 2a served as the control groups. The normoglycaemic groups (1b, 1c and 1d) and the streptozotocin-induced diabetic groups (2b, 2c and 2d) were treated with graded doses of *A. cepa* extract (0.4g/100gbw, and 0.6g/100gbw) and metformin (0.5g/100gbw) respectively 28 days. The results show that fasting blood glucose levels of diabetic rats was reduced by 50.00% and 35.05% on administration of 0.4g/100gbw and 0.6g/100gbw of *Allium cepa* respectively. These study concluded that *Allium Cepa* (Extract) demonstrated significant antidiabetic activities in diabetic rat [20]. In another study by Mohamed *et. al*., (2016) [21] aimed to investigate the antidiabetic, antihyperlipidemia and antioxidant activities of methanolic extract of *Allium porrum* leaves at 200 and 400 mg/kg bw in streptozotocin-induced diabetic rats. The extract exhibited antidiabetic, antihyperlipidemia and antioxidant activities and consequently may alleviate liver and renal damage caused by STZ -induced diabetes this might be attributed to the presence of flavonoides, phenolics and sulphur compounds which may be acting as free radical scavenging effect, inhibiting lipid peroxidation and increasing antioxidant activities. *Allium porrum* has a potential and helpful to the prevention of diabetic and its complications [21].

Also, Airaodion *et. al*., (2020) [14] aimed to evaluate the antidiabetic potency of *Allium cepa* bulb in alloxan-induced diabetic rats. Thirty-six male albino rats were induced intraperitoneally with alloxan. The rats were grouped into six groups of six animals per group: Group A was not induced with alloxan and untreated, group B animals were induced but not treated, group C animals were treated with glibenclaimide, group D, E and F animals were induced and treated with 1, 2 and 3 mL/100g body weight of *A. cepa* juice respectively. The administration was via oral route for 14 days. The animal's blood sugar levels were determined using glucometer. The animals administered with 1, 2 and 3 mL/100g bodyweight of *A. cepa* showed significant decrease ($P < 0.05$) in blood sugar level compared to the untreated animals. The decrease in the blood glucose level of the animals following the administration of the juice suggested that the plant possesses antidiabetic effects [14]. In addition, Taj Eldin *et. al*., (2009) [3] conducted to investigate the hypoglycemic effects of *Allium cepa* in

patients with type 2 diabetes mellitus. In type 2 diabetes patients (n=21) the administration of crude *Allium cepa* (100g) markedly reduced fasting blood glucose levels by 40 mg/dl 4 hours later, compared to glibenclamide (81 mg/dl). This study concluded that crude *Allium cepa* produced hypoglycemic effects, thus it could be used as a dietary supplement in management of diabetes [3].

Additionally, study by Ozougwu., (2011) [2] investigated the hypoglycaemic and hypolipidaemic effects of the increasing dosages of *Allium cepa* aqueous extracts on alloxan - induced diabetic *Rattus novergicus* for possible use in the management of diabetes mellitus. Diabetes mellitus was induced in 54 out of a total of 63 adult *R.novergicus* using 150 mg/kg of alloxan monohydrate. Increasing dosages (200, 250 and 300 mg/kg) of *A. cepa* aqueous extracts were given to the diabetic rats for six weeks while the control rats got either normal saline (1 ml) or increasing dosages of glibenclamide (2.5, 3.8 and 5.0 mg/kg) during the same period. Increasing dosages of *A. cepa* aqueous extracts produced a dose-dependent significant ($P < 0.05$) reductions in the blood glucose levels, total serum lipid and total serum cholesterol when compared with that of the control rats. The most effective percentage reduction in blood glucose level, total serum lipids and cholesterol were observed at 300 mg/kg. This study concluded that *A. cepa* studied exhibited promising hypoglycaemic and hypolipidaemic activity in alloxan-induced diabetic rats. It's hypoglycaemic and hypolipidaemic effects could represent a protective mechanism against the development of hyperglycaemia and hyperlipidaemia characteristic of diabetes mellitus [2]. Also, Ülger and Çakiroglu., (2019) [22] evaluated the effects of onion (*Allium cepa* L.) against hyperglycaemia and determine possible changes in these effects due to different heat treatments applied to onion. 32 male Wistar-albino rats were divided into 4 groups as follows: the groups C and DC were fed with standard rat diet; the DLO group was fed with rat diet including 5% onion powder dried at -76°C in a lyophilizator, and the DFO group was fed with rat diet including 5% onion powder dried at 80°C in a furnace. The results observed a decreasing tendency in fasting blood glucose (FBG) values of DLO group during the experiment period and it was found that the 6th and 8th weeks values were significantly lower than the 1st and 2nd weeks values ($p<0.05$). On the other hand, no statistical difference was observed in the FBG values measured at different weeks in the DFO group. This study concluded that lyophilized onion powder may be protective against hyperglycaemia arising from diabetes [22].

Study by Masood *et. al*., (2021) [23] evaluated the anti-hyperglycemic and antioxidant effects of wheat bread supplemented with onion peel extract (OPE) or onion powder (OP) on diabetic rats. Ethanolic extract of onion peel and onion

bulb were prepared separately. Male Sprague Dawley rats were divided into 6 groups (n = 7). Different regimens of supplemented wheat bread (OPE (1% and 3%) and OP (5% and 7%)) were given to diabetic rats for eight weeks, plain bread was used as the control. The results demonstrated that bread supplemented with 1% and 3% onion peel extract and 7% onion powder significantly reduced blood glucose levels in the treated rats compared with the control group diabetic rats. These findings suggested that onion supplementation is effective in lowering blood glucose and could potentially aid in protecting organs from oxidative stress [23]. Also, study by Jung *et. al*., (2011) [15] concluded Onion peel extract (OPE) might improve glucose response and insulin resistance associated with type 2 diabetes by alleviating metabolic dysregulation of free fatty acids, suppressing oxidative stress, up-regulating glucose uptake at peripheral tissues, and/or down-regulating inflammatory gene expression in liver. Moreover, in most cases, OPE showed greater potency than pure quercetin equivalent. These findings provide a basis for the use of onion peel to improve insulin insensitivity in type 2 diabetes [15].

In 2009, an *in vivo* study demonstrated that A. *cepa* (7% freeze-dried onion powder added into control diet) may represent an interesting anti-hyperglycaemic dietary adjunct for diabetic therapy, since it decreases serum cholesterol, triacylglycerol and LDL-cholesterol in streptozocin-induced diabetics rats, without alterations in the cholesterol and HDL-cholesterol levels. Hyperglycemia causes glucose autoxidation, impaired mitochondrial bioenergetics and induces reactive oxygen species (ROS) production, leading to an impairment of intracellular pathways (i.e., JAK/STAT, JNK, p38, ERK/MAPK) and to insulin resistance. Onion (400 mg/day) possesses a significant free radical-scavenging property and exerts a regulation on lipid metabolism, decreasing superoxide dismutase activity and lowering lipid hydroperoxide and lipoperoxide concentrations in diabetic rats [10].

Several studies have established insulinotropic, and insulin-sensitizing effects of onion either in diabetic or hypercholesterolemic animal models or human-based studies. Some researchers indicated the hypoglycemic and insulin sensitizing capacity of onion peel extract containing high quercetin (QR) in high-fat diet/ diabetic rats. Additionally, in a cross-over clinical trial on 20 well-controlled diabetic patients, consumption of 20 g of fresh onion (three times daily) for one week could significantly reduce fasting blood sugar (FBS). While it was previously reported that onion does not reduce blood sugar levels in healthy non-diabetic people [24]. The presence of quercetin, allyl propyl disulphide oxide (dipropyl disulphide oxide), S-methylcysteine sulphoxide, and S-allyl cysteine sulphoxide in onion is reported to be responsible for the drop in

glucose level and lipid profile. Allyl propyl disulphide oxide also aids in insulin secretion. S-allyl cysteine sulphoxide from onion also markedly decreased blood glucose level of diabetic rats. Daily oral administration of about 200 mg of S-methylcysteine sulphoxide for 45 days to alloxan diabetic rats controlled their blood glucose and lipid levels. The same study also reports improvement in the activities of liver glucose-6-phosphatase, hexokinase, and HMG CoA reductase. The observed effect of S-methylcysteine sulphoxide was analogous to that of insulin and glibenclamide. Oral administration of S-methyl cysteine sulphoxide to alloxan diabetic rats for one-month period ameliorated hyperglycaemia and was similar to animals treated with glibenclamide and insulin [13].

The above studies investigates the hypoglycemic property of onion and its protective effects in diabetes mellitus and hyperglycemia. These studies were supported the effectiveness of Onion in reducing blood glucose in streptozotocin induced, as well as alloxan-induced diabetes mellitus in experimental animals.

**4. Possible mechanism of action of Onion in hyperglycemia and diabetes mellitus:**

The antidiabetic effects of many phytochemicals including polyphenols, terpenes, alkaloids, saponins, and quinones have been well-documented. Furthermore, clinical trials with medicinal plants and natural products have been conducted, whereas some of them have been used for the development of herbal formulations controlling DM. Regarding the mechanism of action of natural products, (i) the inhibition of α-glucosidase and α-amylase in the digestive tract, (ii) the boost of insulin secretion and pancreatic β cell proliferation, (iii) the regulation of glucose uptake and glucose transporters, (iv) the inhibition of protein tyrosine phosphatase 1B activity, and (v) the reduction in the generation of oxidative stress are the main modes of action of pure phytochemicals and crude extracts [25].

*Allium cepa* comonly known as onions are among the most common vegetables used every day in the kitchen. It is a spice plant that belongs to the Amaryllidaceae family. *Allium cepa* also helps to regulate the hypoglycemic activity associated with diabetes mellitus. This is due to presence of flavonoids (quercetin) and sulphur compounds (S-methyl cysteine) which helps to reduce the level of blood glucose, lipid peroxidation, serum lipids as well as oxidative stress. These compounds also aid in insulin secretion as well as boost the antioxidant enzyme activities taking place in the body. Onion extracts also aid in hypolipidemic activities. The hypolipidemic and hypoglycemic effects of onion is due to its ability to normalize the activities of HMG coenzyme-A reductase, liver hexokinase and glucose 6-phosphatase. Some preliminary clinical trials

carried out reveal that glucose levels can be reduced by taking *Allium cepa* aqueous extracts. Onion and onion by products and its extracts did not show any toxicity including geno-toxicity in rodents, the only side effect observed was anemia. Thus onion can be a safe treatment option for diabetes [26]. A. *cepa* exerts its antidiabetic activity through multiple pharmacologic actions attributed to the presence of many active constituents: for example, quercetin is responsible for α-glucosidase inhibition and, along with rutin, for the increase of GLUT-4 translocation, glucose uptake and insulin action. Differently, L-cysteine sulfoxides and allyl propyl disulphide can act directly as free radicals scavengers. In fact, they take part in the redox process of glutathione and cysteine, and can also increase the activity of superoxide dismutase and catalase, independently or through the stimulation of insulin secretion [10].

Flavonoids have multiple positive health effects on metabolic disorders, such as cardiovascular disease, cancer, obesity, and diabetes. Research and clinical studies have postulated the function of flavonoids in preventing and treating certain viral diseases like influenza. They also serve as antioxidants which modulate oxidative stress in the body by neutralizing the effect of nitrogen and oxygen species, thus preventing the disease. The antidiabetic activity of flavonoids supports the regulation of carbohydrate digestion, insulin signaling, insulin secretion, glucose uptake, and adipose deposition. They target multiple molecules that are involved in the regulation of several pathways, like improving β-cell proliferation, promoting insulin secretion, reducing apoptosis, and improving hyperglycemia by regulating glucose metabolism in the liver[27].

Hypoglycemic activity of *Allium cepa* Linn. extracts have been reported. The bulb part contains S-methyl cysteine sulfoxide, S-allyl cysteine sulfoxide has been proven anti-diabetic activity. These compounds can lower blood glucose levels and has a potent antioxidant activity which may account for hypoglycemic potential. S-methylcysteine sulfoxide exerts antidiabetic action in 3 different ways: (1) stimulate the production of insulin in the body and enhance the secretion of the pancreas; (20) interfere with dietary glucose absorption; and (3) use insulin effectively [28].

Previous studies have related polyphenols, which include quercetin, to anti-α-amylase effects. Diabetes mellitus type II is a chronic metabolic disorder caused by increased cell resistance to insulin. Benefits of pharmaceutical factors to treat this disease aggressively in its early stages were indicated, but such medications can have unwanted side effects[29]. Quercetin is involved in several biological actions such as: glucose homeostasis; insulin sensitizing and secreting; glucose utilization in peripheral tissues; the inhibition of intestinal glucose absorption. Quercetin intake is inversely associated with the prevalence

of T2DM in the Chinese population which suggests its preventive activity against T2DM. A recent systematic review and meta-analysis of animal studies showed that quercetin decreases serum levels of glucose at doses of 10, 25, and 50 mg/kg of body weight. Quercetin extracted from berries induced an insulin independent 5' adenosine monophosphate-activated protein kinase (AMPK) pathway which slows the oxygen consumption of
adenosine diphosphate by stimulating GLUT 4 translocation and expression in isolated mitochondria [27]. This mechanism has a similar activity as metformin (medication used to treat type 2 diabetes). The antidiabetic action of quercetin involves the reduction of lipid peroxidation, glucose absorption by GLUT2, and the inhibition of insulin dependent activation of phosphoinositide 3-kinases (PI3K). In addition to this, quercetin and its derivatives stimulate a glucose uptake in muscle cells, and activate AMPK. Treating streptozotocin (STZ)-induced diabetic rats with quercetin decreases the activity of glucokinase, hyperglycemia stimulating GLUT 4, hepatic gluconeogenesis, and glycogenolysis while it increases glucose liver uptake. Quercetin supplementation for two weeks lowered the blood glucose level, upregulated the expression of genes involved in cell survival and proliferation in a liver, and enhanced the serum insulin in STZ- induced diabetic mice. An injection of quercetin intraperitoneally into STZ- induced diabetic rats, reported a decrease in hyperglycemia, plasma cholesterol and triglycerides, and an improve glucose tolerance and hepatic glucokinase activity. The co-treatment of quercetin and sitagliptin (a selective dipeptidyl peptidase-IV inhibitor) demonstrated an improvement in its oxidative and inflammatory status, metabolic profile,
glycemic control, β-cells function, and islet structure in STZ- induced DM in rats. Quercetin blocks the activities of a tyrosine kinase inhibitor, which has shown an effect against diabetes. The regulatory effect of quercetin to nuclear factor kappa-light-chain-enhancer of the activated B cells (NF-κB) also helps in improving glucose stimulated insulin secretion [27].

Numerous studies have found increased lipid peroxides or ROS and oxidative stress (or both) in different animal models of diabetes. Oxidative stress has been shown to be responsible, at least in part, for the β-cell dysfunction caused by glucose toxicity. Under hyperglycemia, production of various reducing sugars such as glucose-6-phosphate and fructose increases through glycolysis and the polyol pathway. During this process, ROS are produced and cause tissue damage. In vitro and in vivo studies have suggested the implication of oxidative stress in the progression of β -cell dysfunction in type 2 diabetes. Z has a β -cell cytotoxic and it is not fully understood, it is thought to be mediated by the inhibition of free radical scavenger-enzymes thereby enhancing the

production of the superoxide radical. Eventually, STZ causes diabetes and it is associated with the generation of ROS causing oxidative damage[21].

Quercetin (3,5,7-trihydroxy-2-(3,4-dihydroxyphenyl)-4Hchromen-4-one) is a flavonoid naturally occurring in plants and natural foods such as fruit and vegetables [30]. The biological activities of quercetin are anticancer, antidiabetic, antiobesity, neuroprotective, antimicrobial, antiviral, hepatoprotective, and anti-inflammatory activity [31]. It reduces the formation of reactive oxygen species (ROS), inhibits lipid peroxidation, increases plasma levels of adiponectin and HDL cholesterol. In addition, it has strong antidiabetic properties. It can enhance glucose uptake by a MAPK insulin-dependent mechanism and increase the phosphorylation of PI3K/Akt signalling pathways. This condition leads to the translocation of the glucose transporter 4 and downregulation of the activity of gluconeogenesis enzymes in the liver. Quercetin also interacts with the PPAR receptor. Its consumption improves the action of β-cells and proliferation, and inhibits alpha-glucosidase and alpha-amylase activities. Quercetin may improve diabetic bone disorder in patients with T2DM[30].

The effect of onion supplementation in reducing blood glucose level was also reported in some recent studies. Phytochemicals such as quercetin and allyl-propyl disulfides found in onion peel and bulb might be responsible for the beneficial effect on blood glucose level by up-regulating the expression of insulin receptors and glucose transporters, improving insulin sensitivity and promoting glucose metabolism in peripheral tissues in diabetic rats [23].

In the human body, *α*-amylase first reduces starch to three different oligosaccharides - maltose, maltotriose, and dextrin. While *α*-glucosidase ultimately hydrolysis oligosaccharides into glucose monomers, the glucoses are then transported into the enterocytes in the small intestine. Onion displayed the inhibitory activity against *α*-glucosidase, and thus even it activates *α*-amylase, the final overall effects could be inhibitory activity in terms of conversion starch to glucose. This verified previous studies in which onion exhibited *in vitro* and *in vivo* pharmacological activities, which might benefit to diabetes [32]. About 85% of the selected plant material have α-glucosidase and/or α-amylase inhibitory activity. Both enzymes are considered as carbohydrate-hydrolyzing enzymes and are linked with postprandial hyperglycaemia as they regulate the absorption of glucose. Studies also demonstrated the stimulation of insulin secretion using different pancreatic β-cells [33]. The most abundant types of antioxidative compounds in plants are phenolic compounds. This suggests that the phenolic compounds may play important roles in inhibitory effect on digestive enzymes. Actually, phenolic compounds have been reported to possess

inhibitory activities on *α*-glucosidase or *α*-amylase in several cases. One study reported that flavonoids, such as quercetin and anthocyanins from the *Allium cepa* (white and red onion), had inhibitory activity on *α*-amylase [32].

In this context, polyphenols (and thus quercetin) may be effective for the treatment of patients with diabetes mellitus type II due to their many hypoglycemic effects, including inhibition of α-glucosidase and α-amylase, which are key enzymes in the digestion of dietary carbohydrates into glucose. Through inhibition of these enzymes, polyphenols can delay carbohydrate digestion, which results in decreased glucose absorption, thereby reducing the postprandial plasma glucose rise [29]. Flavonoids and other polyphenols show BG-lowering activities by enhancing GLUT-2 expression in pancreatic *β*-cells, enhancing insulin release, and increasing expression and promoting translocation of GLUT-4, which can increase glucose uptake by the muscle, liver, and adipose tissue. Flavonoids also regenerate pancreatic beta cells, reduce aldose reductase, increase calcium ion uptake, retard the gastric emptying rate, and inhibit *α*-glycosidase and *α*-amylase. In addition, they have antiapoptotic activities [34]. Alkaloids, in recent years, have received extra attention due to their potential role in the treatment of diabetes through inhibition of *α*-glucosidase, *α*-amylase, dipeptidyl peptidase-4 (DPP-4), and AGEs and by possessing potent protein tyrosine phosphatase 1B (PTP1B) inhibitory effects. They activate 50 adenosine monophosphate-activated protein kinases (AMPK) and GLUT- 4 translocation. Alkaloids are effective for pancreatic regeneration and insulin release. They also show protective effects on oxidative tissue damage [34].

The Dayak onion bulb contains naphthoquinone compounds and their derivatives, such as eleutherine, elecanacine, eleuthernone, and eleutherol. The ethanol extract of Dayak onion bulbs also contains tannin, alkaloids, saponins, phenolics, steroids, flavonoids and triterpenoids. Naphthoquinone is an antioxidant that can reduce excessive levels of xanthine oxidase enzymes; xanthine oxidase enzymes play a role in the formation of free radicals. The decrease in this enzyme will reduce free radicals and thus inhibit the damage of pancreatic beta cells, then the synthesis and secretion of insulin will increase. Increased synthesis and secretion of insulin will increase the work of lipid-breaking enzymes so that lipid absorption is reduced. The broken lipid will be transported and metabolized in the liver, and then excessive lipid is released through bile secretion [35].

Phytochemicals such as quercetin, isorhamnetin and kaempferol which possess strong antidiabetic potential are much more abundant in the outer dry scales and fleshy peels than the inner layers and this might be the reason behind more

potent antihyperglycemic and antioxidant activity of the onion peel as compared to the bulb [23]. Consumption of these bioactive compounds together in the form of natural products is beneficial and safe, as cofactors or other present biomolecules negate the each other's adverse effects and are therefore considered to be safe [36].

## 5. Conclusion:

In this review we discussed about Onion for treatment of Diabetes mellitus. It showed that these plants have hypoglycaemic effects. Numerous new bioactive compounds isolated from these plants having anti-diabetic effects exist anti-diabetic activity. At the same time, this review study has shown various mechanisms of action and active components in plants which have greatly enhanced our understanding on the rationale underpinning popular usage for these plants for the prevention and treatment of diabetic complications in order to develop effective medicines for the prevention and treatment of diabetic complications. It may be extremely useful to the health professionals, researchers who are doing research in this field for the development of anti-diabetic drugs.

## References

1. Aleksandra Pałasz, Dariusz Cież, Bartosz Trzewik, Katarzyna Miszczak, Grzegorz Tynor, and Bartłomiej Bazan, (2019): In the Search of Glycoside-Based Molecules as Antidiabetic Agents. *Topics in Current Chemistry*, 377:19.

2. Jevas C. Ozougwu, (2011): Anti-diabetic effects of *Allium cepa* (onions) aqueous extracts on alloxan-induced diabetic *Rattus novergicus*. *Journal of Medicinal Plants Research*, 5(7):1134-1139.

3. Imad M. Taj Eldin, Elhadi M. Ahmed, and Abd Elwahab HM, (2009): Clinical hypoglycemic effects of *Allium cepa* (Red onion) in Type 1 Diabetic patients. *Sudan JMS*, 4(2): 153-156.

4. Anshul Sharma, Joo Wan Kim, Sae-Kwang Ku, Jae-Suk Choi and Hae-Jeung Lee, (2019): Anti-diabetic effects of blue honeyberry on high-fed-diet-induced type II diabetic mouse. *Nutrition Research and Practice*, 13(5):367-376.

5. Yasodha Krishna Janapti, (2015): Optimize diabetes by herbal medicine: A Review. *Journal of advances in medical and pharmaceutical sciences*, 3(3): 98-111.

6. Tahira Shamim, Hafiz Muhammad Asif, Ghazala Shaheen, Laila Sumreen, Sultan Ayaz, Tasneem Qureshi, Aymen Owais Ghauri, Tanveer Ali, Mukhtiar Ahmad, Farhan Sajid, Ijaz Khadim, Rida Tanveer, Raeesa Noor, Hina Nawaz, Jahanzaib Kaleem, (2020): Anti-diabetic Potential of Indigenous Medicinal Plants of Cholistan Desert, Pakistan: A Review. The Review of diabetic studies, 18(2): 93-99.

7. Paul C. Chikezie, Okey A. Ojiako, and Kanayo C. Nwufo, (2015): Overview of anti-Diabetic medicinal plants: The Nigerian research experience. *J Diabetes Metab*, 6:6.

8. Rama Shankar Dubey, Navneet Kumar Verma, Ajay Kumar Shukla, and M.A. Naidu, (2021): Diabetes mellitus - A Report on antidiabetic medicinal plants and their potent bioactive molecules. *Journal of Medical Pharmaceutical and Allied Sciences*, V 10-I3, 1414, P-2949-2960.

9. O.S. Ogunmodede, L.C. Saalu, B. Ogunlade, G.G. Akunna, and A.O. Oyewopo, (2012): An Evaluation of the hypoglycemic, antioxidant and hepatoprotective potentials of Onion (*Allium cepa* L.) on Alloxan-induced diabetic rabbits. *Int. J. Pharmacol*., 8(1): 21-29.

10. Paolo Governa, Giulia Baini, Vittoria Borgonetti, Giulia Cettolin, Daniela Giachetti, Anna Rosa Magnano, Elisabetta Miraldi, and Marco Biagi, (2018): Phytotherapy in the management of diabetes: A Review. *Molecules*, 23, 105.

11. Yawen Zeng, Yuping Li, Jiazhen Yang, Xiaoying Pu, Juan Du, Xiaomeng Yang, Tao Yang, and Shuming Yang, (2017): Therapeutic role of functional components in Alliums for preventive chronic disease in human Being, *Evidence-based complementary and alternative medicine*, Vol. 2017, 9402849.

12. Osama A. Shaikhomar, and Omar S. Bahattab, (2021): Physiological effect of Quercetin as a natural flavonoid to be used as hypoglycemic agent in Diabetes Mellitus Type II Rats. *Saudi J Biomed Res*, 6(1): 10-17.

13. Michael Buenor Adinortey, Rosemary Agbeko, Daniel Boison, William Ekloh, Lydia Enyonam Kuatsienu, Emmanuel Ekow Biney, Obed O. Affum, Jeffery Kwarteng, and Alexander Kwadwo Nyarko, (2019): Phytomedicines used for diabetes mellitus in Ghana: A systematic search and review of preclinical and clinical evidence. *Evidence-Based Complementary and Alternative Medicine*, Vol. 2019, 6021209.

14. Augustine I Airaodion, Ime U Akaninyene, Kenneth O Ngwogu, John A Ekenjoku, and Ada C Ngwogu, (2020): Hypolipidaemic and antidiabetic

potency of *Allium cepa* (Onions) bulb in Alloxan-induced diabetic rats. *Acta Scientific Nutritional Health*, 4(3): 73-80.

15. Ji Young Jung, Yeni Lim, Min Sun Moon, Ji Yeon Kim and Oran Kwon, (2011): Onion peel extracts ameliorate hyperglycemia and insulin resistance in high fat diet/ streptozotocin-induced diabetic rats. *Nutrition and Metabolism*, 8:18.

16. Yuya Nakayama, Miki Makita, Satomi Nozaki, and Yosuke Kikuchi, (2020): Effects of onion extract containing concentrated cysteine sulfoxides on sleep quality: a randomized, double-blind, placebocontrolled, crossover study. *Food Sci Biotechnol*, 29(12):1755-1762.

17. Manisha Modak, Priyanjali Dixit, Jayant Londhe, Saroj Ghaskadbi, and Thomas Paul A. Devasagayam, (2007): Indian herbs and herbal drugs used for the treatment of diabetes. *J. Clin. Biochem. Nutr*., 40, 163-173.

18. Fatma U. Afifi, and Violet Kasabri, (2013): Pharmacological and phytochemical appraisal of selected medicinal plants from Jordan with Claimed antidiabetic activities. *Sci Pharm*., 81: 889-932.

19. Rawat Smit, Kumar Neeraj, and Kothiyal Preeti, (2013): Traditional medicinal plants used for the treatment of diabetes. *Int. J. Pharm. Phytopharmacol. Res.*, 3(3): 171-175.

20. Anthony E. Ojieh, Ese C. Adegor, Anthony C. Okolo, Ewhre O. Lawrence, Ikenna P. Njoku, and Christopher U. Onyekpe, (2015): Hypoglycemic and hypolipidaemic effect of *Allium Cepa* in streptozotocin-induced diabetes. *International Journal of Scientific and Engineering Research*, 6(10):23-29.

21. Samy M. Mohamed, Gehad A. Abdel Jaleel, Heba M.I. Abdallah, Samir A.E. Bashandy, Adel B. Salama, and Ahlam H. mahmoud, (2016): Hypoglycemic, hypolipidemic and antioxidant activities of Allium porrum leaves extract in streptozotocin-induced diabetic rats. International Journal of PharmTech Research, 9(11): 187-200.

22. Taha Gökmen Ülger, and Funda Pınar Çakiroglu, (2020): The effects of onion (*Allium cepa* L.) dried by different heat treatments on plasma lipid profile and fasting blood glucose level in diabetic rats. *AJP*, 10(4): 325-333.

23. Sara Masood, Attiq ur Rehman, Shahid Bashir, Mohamed El Shazly, Muhammad Imran, Palwasha Khalil, Faiza Ifthikar, Hafiza Madiha Jaffar, and Tara Khursheed, (2021): Investigation of the anti-hyperglycemic and antioxidant

effects of wheat bread supplemented with onion peel extract and onion powder in diabetic rats. *Journal of Diabetes and Metabolic Disorders*, 20:485-495.

24. Mehranghiz Ebrahimi-Mamaghani, Maryam Saghafi-Asl, Mitra Niafarc, Mohamma Asghari-Jafarabadi, Mehran Mesgari-Abbasi, (2017): Raw red onion intake and insulin resistance markers in overweight or obese patients with polycystic ovary syndrome: a randomized controlled-clinical trial. *Progress in Nutrition*, Vol. 10, Supplement 1: 199-208.

25. Vlasios Goulas, Antonio J. Banegas-Luna, Athena Constantinou, Horacio Pérez-Sánchez, and Alexandra Barbouti, (2022): Computation screening of multi-target antidiabetic properties of phytochemicals in common Edible Mediterranean plants. *Plants*, 11, 1637.

26. Sinha Suhani, and Khatua Soubhik, (2018): Effects and safety profile of commonly used herbal anti-diabetic preparations. *GSC Biological and Pharmaceutical Sciences*, 04(02), 066–079.

27. Raghad Khalid AL-Ishaq, Mariam Abotaleb, Peter Kubatka, Karol Kajo, and Dietrich Büsselberg, (2019): Flavonoids and their anti-diabetic effects: Cellular mechanisms and effects to improve blood sugar Levels. *Biomolecules*, 9, 430.

28. Ngan Tran, Bao Pham, and Ly Le, (2020): Bioactive compounds in anti-Diabetic plants: From herbal medicine to modern drug discovery. *Biology*, 9, 252.

29. Mariana Gois Ruivo da Silva, Mihaela Skrt, Draženka Komes, Nataša Poklar Ulrih, and Lea Pogacnik, (2020): Enhanced yield of bioactivities from Onion (Allium cepa L.) skin and their antioxidant and anti-α-amylase activities. *Int. J. Mol. Sci*., 21, 2909.

30. Jana Blahova, Monika Martiniakova, Martina Babikova, Veronika Kovacova, Vladimira Mondockova, and Radoslav Omelka, (2021): Pharmaceutical drugs and natural therapeutic products for the treatment of Type 2 Diabetes Mellitus. *Pharmaceuticals*, 14, 806.

31. Wamidh H. Talib, Asma Ismail Mahmod, Sara Feras. Abuarab, Eliza Hasen, Amer A. Munaim, Shatha Khaled Haif, Amani Marwan Ayyash, Samar Khater, Intisar Hadi AL-Yasari and Lina T. Al Kury, (2021): Diabetes and Cancer: Metabolic association, Therapeutic Challenges, and the role of natural products. *Molecules*, 26, 2179.

32. Hairong Wu and Baojun Xu, (2014): Inhibitory effects of Onion against α-Glucosidase activity and its correlation with phenolic antioxidants. *International Journal of Food Properties*, 17:599-609.

33. Vlasios Goulas, Antonio J. Banegas-Luna, Athena Constantinou, Horacio Pérez-Sánchez, and Alexandra Barbouti, (2022): Computation screening of Multi-Target antidiabetic properties of phytochemicals in common Edible Mediterranean plants. *Plants*, 11, 1637.

34. Berhan Begashaw Yikna and Awgichew Shewasinad Yehualashet, (2021): Medicinal Plant Extracts Evaluated *In Vitro* and *In Vivo* for Antidiabetic Activities in Ethiopia: Bases for Future Clinical Trials and Related Investigations. *Evidence-Based Complementary and Alternative Medicine*, Vol.2021, 9108499.

35. I Gusti Agung Ayu Kusuma Wardani, Fitria Megawati, and Ni Made Dharma Shantini Suena, (2019): The Effect of Dayak Onion Bulb Ethanol Extract (*Sisyrinchium palmifolium* L.) on Triglyceride Level and Aorta Histopathology in Diabetes Melitus White Rat Induced by Alloxan. *Trad. Med. J.*, 24(2): 77-84.

36. Lan Bai, Xiaofang Li, Li He, Yu Zheng, Haiying Lu, Jinqi Li, Lei Zhong, Rongsheng Tong, Zhongliang Jiang, Jianyou Shi, and Jian Li, (2019): Antidiabetic potential of flavonoids from traditional chinese medicine: A review. The American journal of chinese medicine, 47(5): 933-957.

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