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Shallot (*Allium ascalonicum*): An overview of antidiabetic activity by α-glucosidase inhibition

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Abstract
Allium ascalonicum (shallot) is a medicinal plant with promising potential in the management of type 2 diabetes mellitus (T2DM). This review summarizes the phytochemical constituents, mechanisms of action, and existing research gaps that warrant further exploration for targeted drug development. A systematic literature search was performed using PubMed, ScienceDirect, and Google Scholar to identify relevant studies published between 2013 and 2023. Only full-text original research articles in English were included, while reviews and incomplete studies were excluded. The search strategy employed the keywords: "*Allium ascalonicum* OR shallot AND α-glucosidase." The findings indicate that *A. ascalonicum* demonstrates significant antidiabetic activity across in vitro, in vivo, and limited human studies, primarily through inhibition of the α-glucosidase enzyme. This activity is largely attributed to quercetin and other flavonoid compounds, which play an essential role in reducing blood glucose levels and mitigating oxidative stress. Collectively, the evidence highlights the therapeutic potential of *A. ascalonicum* as a natural α-glucosidase inhibitor. However, further clinical investigations and comprehensive toxicity assessments are required to establish its efficacy and safety as a standardized herbal medicine and future phytopharmaceutical candidate for diabetes management.

Keywords: *Allium ascalonicum*, antidiabetic, phytochemicals, shallot, α-glucosidase inhibition

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Abstrak
Allium ascalonicum (bawang merah) merupakan tanaman obat yang memiliki potensi menjanjikan dalam pengelolaan diabetes melitus tipe 2 (DMT2). Artikel tinjauan ini merangkum kandungan fitokimia, mekanisme kerja, serta celah penelitian yang masih ada dan perlu dieksplorasi lebih lanjut untuk pengembangan obat yang lebih terarah. Pencarian literatur dilakukan melalui basis data PubMed, ScienceDirect, dan *Google Scholar* untuk mengidentifikasi penelitian relevan yang diterbitkan pada periode 2013 hingga 2023. Hanya artikel penelitian asli berteks lengkap dalam bahasa Inggris yang disertakan, sementara artikel tinjauan dan penelitian yang tidak lengkap dikecualikan. Strategi pencarian menggunakan kata kunci: "*Allium ascalonicum* OR shallot AND α-glucosidase." Hasil kajian menunjukkan bahwa *A. ascalonicum* memiliki aktivitas antidiabetes yang signifikan pada uji in vitro, in vivo, dan terbatas pada penelitian manusia, terutama melalui mekanisme penghambatan enzim α-glukosidase. Aktivitas ini terutama dikaitkan dengan kandungan quercetin dan senyawa flavonoid lainnya yang berperan penting dalam menurunkan kadar glukosa darah serta mengurangi stres oksidatif. Secara keseluruhan, bukti yang ada menegaskan potensi terapeutik *A. ascalonicum* sebagai inhibitor α-glukosidase alami. Namun demikian, penelitian klinis lebih lanjut dan evaluasi toksisitas yang komprehensif masih diperlukan untuk memastikan efektivitas dan keamanannya sebagai obat herbal terstandar maupun kandidat fitofarmaka di masa depan untuk pengelolaan diabetes.

Kata Kunci: *Allium ascalonicum*, antidiabetes, bawang merah, fitokimia, penghambatan α-glukosidase

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1. Introduction

Indonesia is recognized as one of the world's largest producers of shallots. According to data from the Central Bureau of Statistics (BPS, 2022), the country produced approximately 1.97 million tons of shallots, with Central Java being the leading contributor, yielding 556,058 thousand tons. Within this province, Brebes accounted for the highest share at 62.86%, followed by Demak (9.56%) and Pati (8.23%).[1] Shallots (*Allium ascalonicum* L.) are widely cultivated horticultural crops in Indonesia and are commonly used both as flavoring agents in traditional cuisine and as herbal remedies. Around 80% of the Indonesian population relies on medicinal plants for disease treatment due to strong empirical beliefs in their efficacy, including for managing blood glucose levels, rather than depending solely on conventional therapies. Diabetes mellitus (DM) is a metabolic disease characterized by chronic hyperglycemia, where blood glucose levels remain above normal thresholds.[2] Standard fasting blood glucose (FBG) concentrations range between 70–100 mg/dL, while postprandial glucose (PPG) levels should not exceed 140 mg/dL, and random blood glucose (RBG) levels should remain below 200 mg/dL. By contrast, diabetic conditions are defined by FBG ≥ 126 mg/dL, PPG ≥ 200 mg/dL, or RBG ≥ 200 mg/dL. Approximately 90% of diabetes cases in Indonesia were classified as type 2 diabetes mellitus (T2DM) in 2021, a year when the country ranked fifth among the ten nations with the highest diabetes prevalence worldwide.[3]

The management of T2DM is strongly associated with postprandial glucose regulation, which reflects blood glucose levels measured two hours after a meal.[4–6] During digestion, starch is hydrolyzed into monosaccharides, a process in which two key enzymes—α-amylase and α-glucosidase—play crucial roles.[7–9] Inhibiting these enzymes has become an important therapeutic strategy, with acarbose being one of the most widely prescribed α-glucosidase inhibitors. Adverse gastrointestinal effects—such as flatulence, nausea, and abdominal discomfort—often limit its therapeutic use in clinical settings.[10,11] This has prompted increasing interest in exploring plant-derived alternatives, such as shallots, which are expected to offer hypoglycemic benefits with fewer side effects.

Allium ascalonicum is a perennial herb characterized by multi-layered bulbs formed from leaf sheaths. Taxonomically, it belongs to the genus *Allium*, formerly classified under Alliaceae but now placed within the Amaryllidaceae family.[12,13] Although morphologically similar to *Allium cepa* (common onion), shallots differ in several aspects: they are smaller in size, possess an elongated shape, and exhibit a stronger aroma, largely due to their higher sulfur content.[14] In addition to its sulfur constituents, the volatile compound 2-methyl-2-pentenal also serves as a key marker that differentiates onions from shallots.[15] This plant has many benefits for the wider community that have been proven, including antidiabetic,[9,16–18] antimicrobial,[19–24] antioxidant,[14,19,25–30] antifungal,[29,31–33] and anti-inflammation.[33,34] In addition, other activities have been reported, including cytotoxic[35], antiandrogen[34], antiallergic[36], analgesic[33], and anoctamin-1 inhibitor.[37]

Although various pharmacological investigations on natural products such as shallots have been conducted, studies specifically evaluating the antidiabetic potential of *A. ascalonicum*—whether *in vitro, in vivo*, or through clinical trials—remain scarce. This gap underlies the present review, which aims to highlight the bioactive metabolites contained in *A. ascalonicum* and assess their potential role in the development of standardized herbal medicines for glycemic control. By compiling current findings, this article seeks to provide a stronger empirical basis for the antidiabetic applications of shallots and encourage future research toward their therapeutic utilization.

2. Materials and Methods

The literature review was carried out through a systematic search of several electronic databases, including PubMed, ScienceDirect, and Google Scholar, to identify relevant publications concerning the use of *Allium ascalonicum* in the prevention and management of diabetes. The search was restricted to articles published between 2013 and 2023, with inclusion criteria limited to full-text research papers available in English. Review articles and incomplete studies were excluded from consideration.

The search strategy employed the keywords: "*Allium ascalonicum* OR shallot AND α-glucosidase." Titles and abstracts retrieved through this process were screened to ensure their relevance to the focus of the present study. Moreover, further relevant studies were retrieved through a review of the reference lists of the included articles. A detailed flow diagram outlining the search process and the number of articles obtained is presented in Figure 1.

3. Result and Discussion

Of the 912 articles identified, 17 studies included eligibility criteria for analysis. The results of phytochemical, *in vitro, in vivo,* and human studies are tabulated in Table 1-4.

3.1. Phytochemical content

Table 1. Phytochemical of *Allium ascalonicum*

Part of use	Main chemical compound	Ref
Bulbs/flesh	Quercetin	56
Peel/skin	Quercetin, anthocyanin	16
Bulbs/flesh	Quercetin 3,4'-diglucoside, quercetin 4'-glucoside, and quercetin	74
Bulbs/flesh	Quercetin, quercetin-4'-O-glucoside and quercetin-3,4'-O-diglucoside	38
Peel and bulbs	Quercetin, quercetin aglycone, quercetin monoglycoside, quercetin-di-glucoside, methylated-quercetin-hexose(-glucoside)	40
Bulbs	Quercetin, rosmarinic, p-coumaric acids	75
Bulbs	Flavonoids, volatile oil, saponins, tannins, and terpenoid	76
Bulbs	3,24-acetonideclethric acid, ursolic acid, randiasaponin IV, ilekudinoside W, and (25S)- 1β,3β,24β-trihydroxyspirost-5-en 1-O-α-L-rhamnopyranosyl-(1→2)- α-L-arabinopyranoside	20
Rhizome	Triterpenoid	37
Peel/skin	Phenolic acid, flavonoid and anthocyanin	19
Peel/skin	Alkaloids, polyphenols, flavonoids, anthocyanin, and tannins	30
Oil	2-methyl-2-pentenal	15

A large number of secondary metabolites has been reported from *A. ascalonicum* and each part contains a different content. Identification with thin layer chromatography (TLC) of shallot bulbs exhibited quercetin, quercetin-4'-O-glucoside and quercetin-3,4'-O-diglucoside compound,[36,38–40] alkaloids, glycosides, tannins, saponins, flavonoid, anthraquinones, phlobatannins, rosmarinic, p-coumaric acids, dipropyl disulphide, and allyl propyl disulphide.[34,41,42] Besides, identification with HR-ESI-MS, NMR spectral data showed five compounds detected in dichloromethane, ethyl acetate, and water fraction bulb of *A. ascalonicum*, 3,24-acetonideclethric acid (1), ursolic acid (2), randiasaponin IV (3), ilekudinoside W (4), and (25S)- 1β,3β,24β-trihydroxyspirost-5-en 1-O-α-L-rhamnopyranosyl-(1→2)- α-L-arabinopyranoside.[20] Another part, such as rhizome contains triterpenoid,[43] skin contains flavonoid, phenolic acid, anthocyanin, alkaloids, polyphenols, and tannins[19,30], and oil contains diallyl sulphides and 2-methyl-2-pentenal.[44,45]

The bulb part is the most commonly used and one of the most common compounds sfound is quercetin which belongs to the group of flavonols, flavonoids.[36] Quercetin is one of the component that is also responsible for color pigments in shallot.[46] Moreover, as the principal α-glucosidase inhibitor in *A. ascalonicum,* quercetin plays an important role in diabetes mellitus management and is associated with multiple pharmacological effects.[41,47]

Quercetin might be a future potential for drug development. Research by Zubair *et.al*. 2021 showed quercetin content was 65.46±0.0002mg/kg, total flavonoids content of the ethanol extract *A. ascalonicum* bulb was 0.3634 ± 0.018 mg QE/100 mg while the total phenolics content was 0.4834 ± 0.003 mg GAE/100 mg.[29] Another study shown the total flavonoid content of ethanol extract (bulb) was 13.484 mg QE/g and the n-hexane, ethyl acetate, and water fractions are 5.436+_0.001, 96.776+_0.015, and 7.200+_0.001 mg QE/g, respectively.[48]

The concern is the content of flavonoids that are found in plants. Flavonoids have many bioactivities such as antidiabetic, antioxidant, lower risk of fatal cardiovascular, and are always present in plants.[49] Based on the relation between structure and activity, polyhydroxy groups in flavonoids have an important role in inhibiting the activity of α-glucosidase enzymes.[50] According to a review by Dhanya *et al.* (2022), quercetin demonstrates potential as an antidiabetic agent by acting on multiple physiological targets, including the pancreas, small intestine, liver, and skeletal muscle. Over the long term, quercetin is considered a valuable natural compound for managing diabetes and its complications, largely through its ability to modulate key metabolic and signaling pathways.[51]

Flavonoids and phenolic compounds, known for their

Table 2. *In vitro*

Part of use	Reference drug/ Standard	Object of research	Mechanism	Result	Ref
Peel (Ethyl acetate and methanol extract)	Acarbose	*Saccharomyces cerevisiae*	α-glucosidase inhibition	IC_{50} extract = 0.012±0.002 mg/mL and 0.047±0.04 mg/mL	16

Table 3. In vivo.

Animal	Exposure and/ standard drugs	Mechanism	Treatment (part of use, dose, period, extract)	Result	Ref
Male Wistar rats	•Alloxan monohydrate 18 mg/150g BW (i.p) •Metformin 45mg/kg BW (p.o)	Improve histopathology liver.	*A. ascalonicum* at a dose 0.25, 0.5, and 0.75 g/kg BW (bulbs, i.p, 14 days, extract)	↑ histopathological feature of liver	57
Male Wistar rats	•Alloxan monohydrate 100 mg/kg BW (s.c) •Glibenclamide 5mg/kg BW (p.o), metformin 100mg/kg BW (p.o), acarbose 20mg/kg BW (p.o)	Inhibit α-glucosidase.	*A. ascalonicum* at a dose 0.25 and 0.5 g/kg BW (bulbs, i.p, eight weeks, methanolic extract)	Blood glucose ↓	56

Administration: per oral (p.o), intraperitoneally (i.p), intravenously (i.v), subcutan (s.c), intragastric (i.g).

strong association with antidiabetic properties, were identified through phytochemical evaluation of *A. ascalonicum* extracts. These bioactive constituents are believed to contribute significantly to the plant's hypoglycemic effects, highlighting their potential as functional ingredients for the development of supplements or standardized herbal formulations aimed at glycemic control.

3.2. In vitro

The α-glucosidase inhibitory activity of *A. ascalonicum* peel extracts has been evaluated *in vitro* using different solvents. The ethyl acetate extract demonstrated a half-maximal inhibitory concentration (IC_{50}) of 0.012 ± 0.002 mg/mL, whereas the methanol extract exhibited an IC_{50} of 0.047 ± 0.04 mg/mL. In comparison, the reference standard acarbose displayed a markedly higher IC_{50} value of 0.47 ± 0.02 mg/mL. These results indicate that A. ascalonicum, particularly the ethyl acetate extract, exhibits stronger inhibitory activity against α-glucosidase than acarbose, thereby suggesting its potential in lowering blood glucose levels.[16]

The enzymatic reaction involves α-glucosidase, the chromogenic substrate *p*-nitrophenyl-α-D-glucopyranoside, and phosphate buffer. This reaction generates yellow *p*-nitrophenol and glucose. The concentration of glucose released was quantified using the glucose oxidase method with a commercially available kit, and the percentage inhibition was calculated relative to the standard drug control.[4,52,53]

Acarbose, a well-known oral antidiabetic drug, serves as a competitive inhibitor of the α-glucosidase enzyme. By mimicking the natural substrate of α-glucosidase, acarbose binds competitively to the enzyme's active site, forming a stable enzyme–inhibitor complex. This mechanism underlies its function as an oral antidiabetic drug, inhibiting the hydrolysis of dietary starch and consequently limiting the production of *p*-nitrophenol and glucose. Consequently, the suppression of carbohydrate breakdown contributes to the reduction of postprandial blood glucose levels.[52,54,55]

3.3. In vivo

A significant reduction in postprandial blood glucose (PBG) of 13% and 22% was observed in alloxan-induced diabetic rats after administration of *A. ascalonicum* methanolic bulb extract at doses of 250 and 500 mg/kg body weight (BW), respectively, thereby demonstrating its antidiabetic activity *in vivo*. In addition, intestinal α-glucosidase activity was markedly inhibited, with sucrase and maltase reduced by 17.41% and 14.62%, respectively.[56] Alloxan induction is known to induce hyperglycemia accompanied by oxidative stress in multiple organs, including the liver, which may ultimately result in hepatocellular damage and necrosis.[57]

Additional research indicated that *A. ascalonicum*

Table 4. In humans

Object of research	Treatment	Result	Ref
48 participant women ages 45-70 years, not being on insulin treatment.	Divided to two groups: •Group 1 (n=22): 150 ml of low-fat yogurt (1.5% fat) •Group 2 (n=26): 150 ml of low-fat yogurt (1.5% fat) + shallot (2g/100g yogurt) •Respondent receive the treatment for 10 weeks.	LDL-C ↓ TG ↓ TC ↓ Fasting blood glucose ↓ In group 2.	70

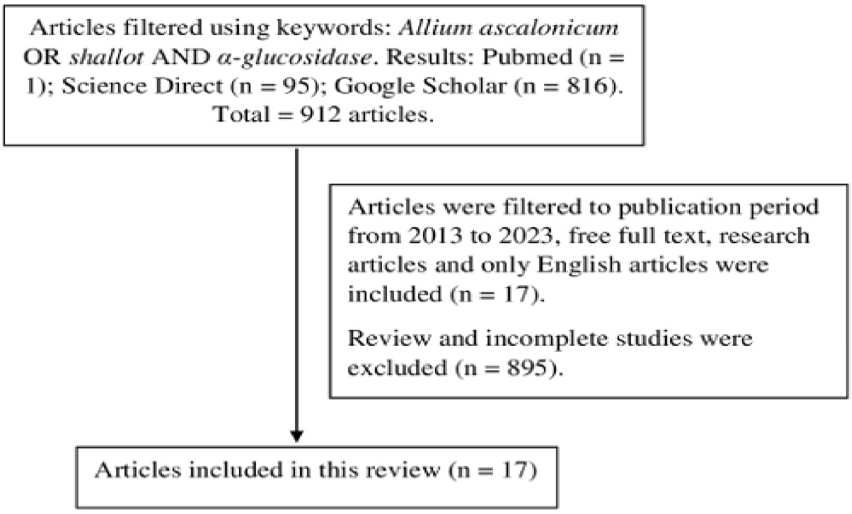

Figure 1. Flow chart diagram of the review process

extract at a dose of 750 mg/kg BW ameliorated liver histopathological damage in alloxan-induced diabetic rats. This protective effect on the liver is associated with the phenolic fraction of the extract, supporting previous evidence that phenolics and diallyl disulfide in shallots markedly reduce fasting blood glucose and improve glucose tolerance in insulin-resistant rats 57,58. Administration of aqueous bulb extract (500 mg/kg BW) in fructose-induced insulin-resistant rats produced marked metabolic benefits, including a 24.2% reduction in fasting glucose, a 32% increase in glucose tolerance, and a 34% improvement in fasting insulin resistance index (FIRI).[59]

Alloxan selectively targets pancreatic β-cells, leading to impaired insulin secretion. Due to its structural similarity to glucose, alloxan is transported via GLUT2 into β-cells, where it triggers cytotoxicity and oxidative stress. β-cell damage is closely associated with DNA injury caused by free radicals, which in turn affects multiple organs. Oxidative stress, a major contributor to diabetes-associated complications, arises from an imbalance between elevated levels of reactive oxygen species (ROS) and insufficient antioxidant protection.[60–63]

Studies have shown that methanolic extracts of *A. ascalonicum* can significantly increase the activity of key antioxidant enzymes—SOD, GPx, and CAT—by 65%, 43%, and 55%, respectively, in alloxan-induced rats. This effect counteracts the reduction of endogenous antioxidant defenses under hyperglycemic conditions, which otherwise leaves pancreatic β-cells vulnerable to nitric oxide- and ROS-mediated damage64. Quercetin, phenolic compounds, S-alk(en)yl-L-cysteine sulfoxides (ACSO), and saponins present in shallots are considered the primary contributors to these effects.[45,49] Significant reductions in TC, TG, LDL, and VLDL levels in diabetic rats were reported by Sani et al. (2012), who found that methanolic extracts of *A. ascalonicum* effectively improved lipid profiles.[64] The saponin content is considered the main factor underlying these hypolipidemic effects. Since lipid accumulation plays a key role in the advancement of diabetic complications, their reduction holds clinical importance. This aligns with Ahmadvand et al.'s findings showing that shallot-derived compounds possess antioxidant activity capable of inhibiting LDL oxidation in vitro.[65]

Biomarkers of liver damage, including ALT, AST, and ALP, are typically elevated in diabetic conditions. This state of chronic hyperglycemia also accelerates lipid peroxidation, as demonstrated by increased levels of thiobarbituric acid reactive substances (TBARS) in tissues. This oxidative process compromises cellular membranes by reducing fluidity, impairing deformability, and increasing stiffness, ultimately exacerbating liver damage and other diabetes-related complications.[7,44,61,66–69]

3.4. In human

Human-based investigations on the antidiabetic potential of *A. ascalonicum* remain very limited. To date, only one clinical study has been reported, in which shallots were administered in combination with yogurt to female patients with diabetes in Iran. A single clinical trial in Iran involving 26 female diabetic patients showed that consuming 150 mL of low-fat yogurt (1.5% fat) fortified with 2 g of shallot per 100 g yogurt significantly reduced FBG and lipid profiles levels.[70]

In humans, persistent hyperglycemia contributes to various diabetes-related complications, one of which is dyslipidemia. The free radical-scavenging capacity of *A. ascalonicum* plays an important role in protecting against oxidative damage and preventing lipid oxidation. An imbalance between overproduction of free radicals and insufficient antioxidant defenses—defining features of oxidative stress (OS)—plays a central role in the pathophysiology of diabetes mellitus (DM). Postprandial hyperglycemia acts as a trigger for oxidative stress, promoting vascular inflammation, endothelial dysfunction, atherosclerosis, and subsequent cardiovascular complications. The elevated production of reactive oxygen species (ROS) under diabetic conditions further exacerbates oxidative damage and contributes to the progression of secondary complications.[14,51,55,71–73]

Despite promising preclinical findings, the current evidence base regarding the antidiabetic effects of *A. ascalonicum* in humans remains insufficient. More rigorous clinical investigations are necessary to validate its efficacy and safety. Such studies should extend beyond crude extract evaluation to include standardized herbal formulations and novel dosage forms that have undergone comprehensive toxicity testing. The development of antidiabetic agents from *A. ascalonicum* presents unique challenges, particularly in isolating pure bioactive compounds with specific activity against α-glucosidase. Targeting this enzyme may influence other crucial mechanisms, including enhancement of insulin secretion, restoration of pancreatic β-cell function, and mitigation of oxidative stress, thereby broadening the therapeutic potential of this plant in diabetes management.

4. Conclusion

Although *in vitro, in vivo,* and preliminary clinical evidence points to the antidiabetic potential of *Allium ascalonicum*—primarily via α-glucosidase inhibition and the action of quercetin—current data are not yet adequate for clinical implementation. To bridge this gap, further high-quality clinical trials are necessary to substantiate its efficacy and safety profile. Such efforts will be pivotal for advancing this plant from preliminary studies toward development as a standardized herbal medicine (OHT) and, ultimately, as a phytopharmaceutical agent for diabetes management.

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Disclosure statement

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Conflict of Interest

The authors declare no conflicts of interest.

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