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Antidiabetic Molecular Mechanisms of Active Compounds from Several Orchids

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Abstract: Hyperglycemia condition that leads to diabetes causes various complications. Various active compounds from plants have been studied for their antidiabetic abilities. One of them is the orchid plant. Besides being used as decoration, orchids contain several active compounds that have been proven to be used in medicine, including diabetes. This article discusses the antidiabetic mechanism of several active compounds obtained from orchids. Publication regarding orchid plant for diabetes were found in databases such as PubMed, Google Scholar, Wiley, Science Direct, Medline, Scopus, and Springer. Keywords used in this study were "orchid", "diabetes", "hyperglycemia", "compound" and "herbal". Out of the 447 collected articles (published in the period between 2011 and 2022), 416 were excluded due to non-relevant studies. There were 31 eligible studies included in this article. In conclusion, the antidiabetic mechanisms of the orchid extracts were as antioxidant, anti-inflammatory and anti-glycation agents, increasing insulin action, influencing lipid metabolism, and inhibiting α-amylase and α-glucosidase activity.

Keywords: Active compound; Antidiabetic; Mechanism; Orchid

Introduction

Hyperglycemia in diabetics can increase the generation of Advanced Glycation End Products (AGEs), a glycated protein molecule whose interaction with its receptor, RAGE, can induce the formation of Reactive Oxygen Species (ROS) through NADPH oxidase activation. One example of AGEs is H_2O_2, of which its excessive production can activate nuclear factor kappa B (NFκB) and further causes diabetes complications (Yulianti et al., 2021, 2022). There are some studies of medicinal plants that were traditionally used to treat diabetes. Their antidiabetic activities such as improved insulin sensitivity and hypoglycemic activities. These abilities are believed due to their phenolic, flavonoids, terpenoids, alkaloids, and glycosides compounds (Salleh et al., 2021). Some plants have antioxidant abilities and are used as effective herbal medicines. While their antidiabetic compounds increase insulin secretion of pancreatic tissues or decrease the intestinal absorption of glucose (Kooti et al., 2016).

Orchids are member of Angiosperm group and belong to Orchidaceae family (Tsering et al., 2017). There are 4000 species of orchids found in Indonesia (Martha & Rahayu, 2022). Orchidaceae is a flowering plant comprises of 25,000 to 35,000 species from 750 to 850 genera (Musharof Hossain, 2011). Orchids are usually used preferably for decorative flower rather than for its medicinal use. Chemical compounds from this species include polysaccharides, revesteral, stilbenoids, while the polyphenol compounds are alkaloids, flavonoids, terpenoids, bibenzyl derivatives and phenanthrenes (Ashu Rajeshbhai & Ingalhalli, 2022; Joshi et al., 2020; Martha Pérez Gutiérrez, 2010; Singh et al., 2012). Orchids has the ability of antidiabetics, anti-inflammation, antioxidant, antimicrobes, anticancer, neuroprotection, and antiallergy (Ashu Rajeshbhai &

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Ingalhalli, 2022; Minh et al., 2016). Minh et al. (2016) found that some compounds, from hybrid *Phalaenopsis* spp. namely phenolic, vanillic acid, protocatechuic acid, caffeic acid, p-hydroxybenzoic acid, syringic acid, ferulic acid, vanillin, p-coumaric acid, sinapic acid, benzoic acid, and ellagic acid have potentials as antioxidants. Orchidaceae, as a big plant family, is well known as a source of bioactive compounds, which has been studied for its new bioactive natural products (Kuo et al., 2022). This article reviews some orchids with their medicinal properties, which can be used as antidiabetics along with their particular mechanisms, using the most recent investigations available on literatures. Many studies have been carried out on the benefits of orchids for the treatment of diabetes, but have not discussed all the possible mechanisms that can be carried out by the active compounds contained in these orchids.

Method

Scientific databases such as Science Direct, PubMed, Google Scholar, Medline, Wiley, Scopus, and Springer were utilized to find publication regarding orchid plant for diabetes. The keywords used in this study included ”orchid”, “diabetes”, “hyperglycemia”, “compound” and “herbal”. Out of the 447 collected articles (published in the period between 2011 and 2022), 416 were excluded due to non-relevance studies.

Inclusion and Exclusion Criteria

The search was restricted to only articles written in English language. All studies found during the search were evaluated by three different authors independently. After compliance with inclusion criteria, the eligibility screening was done by reading title and abstract of all articles to remove irrelevant studies. Most of the unselected journals were due to the plants studied do not belong to the Orchidaceae, or even though they are known as orchid trees or orchid, but they have no antidiabetic activities. Some of the journals were the same journal, or not in English. There were ultimately 31 eligible studies that included in this article. The data extraction was performed by classifying the articles to answer the research questions. Research design and method should be clearly defined**.**

Result and Discussion

Inclusion Studies on Antidiabetics Mechanism of Orchids Extract

There are several types of orchids that have been found to demonstrate antidiabetic abilities. The antidiabetic ability shown by these orchids are through various mechanisms (Table 1 Antidiabetes properties of some orchids and heir mechanisms). The antidiabetic activity of orchids were found using different extraction methods, plant parts and research methods (*in vitro* and *in vivo*).

Table 1 shows various antidiabetic activities possessed by the compounds found from the extraction of various plant parts from orchids. Almost all parts of the plant can be used and have antidiabetic activity. The parts of the orchid plants used in these studies included flower parts, leaves, stems, roots, and even some studies used all parts of the plant. The active compounds were obtained using various solvents, namely chloroform, ethanol, methanol, hexane, ethyl acetate and water. This shows that the active compounds produced in these studies have different polarities, from polar to non-polar. Solvent polarity affected phytochemical substances obtained from the isolation and purification steps of plant material. Phytochemicals are extracted in solvents of different polarity as no single solvent (Nawaz et al., 2020). There are several antidiabetic mechanisms carried out by active compounds extracted from orchids, which are as follows:

Antioxidant Activity

The extract of some orchids, *Dendrobium huoshanense*, *D. officinale*, *D. nobile, D.chrysotoxum*, *P. karwinskii*, *Prosthechea* michuacana (Lex.) W.E. Higgins, *Dendrobium crepidatum*, *Dendrobium aqueum* Lindl, *Dactylorhiza romana* subsp. Georgica, *Dendrobium officinale, Anacamptis pyramidalis* (L.) Rich, *Bauhinia variegate, Gastrodia elata* Blume, *Maxillaria tenuifolia, Eulophia ochreata* L, *Gymnadenia orchidis* Lindl and *Grammatophyllum speciosum* Blume have an activity as antioxidant. The antioxidant activities were done by controlling and scavenging free radicals to offer cell protection against oxidative stress (Gutierrez, 2013; Hunyadi, 2019) as well as acting as antioxidant via their hydrogen-donating ability (Paudel et al., 2019). They are capable of donating hydrogen to a free radical in order to remove odd electron, which is responsible for the radical’s reactivity (Mukherjee et al., 2012; Nimse & Pal, 2015). Many of compounds have antioxidant properties which act through either enzymatic or non-enzymatic pathways (Safari et al., 2018). Table 1 shows several species of orchids containing flavonoids. Flavonoids as antidiabetic compounds act as antioxidants because they have three benzene rings and one hydroxyl group (Ahmed et al., 2020; Yeh et al., 2017). The antioxidant activity of phenolic compounds varies, their biological activity depends on the structure of these compounds, their combination with other compounds, their solubility, absorption and metabolism (Francenia Santos-Sánchez et al., 2019; Ji et al., 2020).

Table 1. Antidiabetes Properties of Some Orchids and Heir Mechanisms

Orchid	Part of the plant	Model description	Major finding	Control	Isolated Bioactive compound	Reference
Dendrobium huoshanense (DHP), *D. officinale* (DOP), *D. nobile* (DNP) and *D.chrysotoxum* (DCP)	freeze-dried stems	alloxan induced diabetic Male Kunming mice	hypoglycemic and antioxidative activities between four Dendrobium polysaccharides	metformin	polysaccharides	(Pan et al., 2014)
Prosthechea karwinskii	leaves extract (100, 200, and 300 mg/kg p.o.)	Metabolic syndrome was induced in Wistar rats through administration of a 40% sucrose diet for 20 weeks	decreasing weight gain, abdominal and pericardial fat deposits, insulin resistance, triglycerides, TNF-α, HS-CRP, and adiponectin	metformin (200 mg/kg p.o.)	quinic acid, neochlorogenic acid, chlorogenic acid, rutin, kaempferol-3-o-β-rutinoside, and embelin	(Barragán-Zarate et al., 2021)
Prosthechea karwinskii (Mart.) J.M.H. Shaw	leaves	inhibition of ROS using peripheral blood mononuclear cells (PBMC). Inflammation using Female Wistar rats induced 100 μL of carrageenan 1% (w/v)	inhibiting reactive oxygen species and exerted an anti-inflammatory effect	naproxen	quinic acid, malic acid, neochlorogenic acid, chlorogenic acid, rutin, embelin, pinellic acid, and azelaic acid	(Barragán-Zarate et al., 2020)
Prosthechea michuacana (Lex.) W.E. Higgins (PM)	bulbs hexane extract	streptozotocin (STZ) and nicotinamide-induced type 2 diabetic male CD1 mice	anti-diabetic effect by stimulating insulin -dependent and by protecting pancreatic β-cells from oxidative stress and also an anti-obese, anti-insulin resistance and antihyperglycemic pro-drug.	glibenclamide	triterpenes (tetracyclic triterpenoids: 24-methyl, 24-hydroxy-5α-lanosta-9(11), 25-dien-3α-acetate and 24-methyl-24-hydroxy-5-lanosta 9 (11)-en-3α acetate)	(Gutierrez, 2013)
Dendrobium crepidatum	Ethanol and acetone stem's extracts	DPPH (2,2-diphenyl-1-picrylhydrazyl), in vitro	inhibiting DPPH free radicals	ascorbic acid	tetracosane, triacontane, stigmasterol, and some phenol derivatives (2-methoxy-4-vinylphenol, 2-methoxy-5-(1-propenyl)-phenol, p-mesyloxyphenol, and 2,6-dimethoxy-4-(2-propenyl)-phenol)	(Paudel et al., 2019)
Malaxis rheedei SW	whole plant methanol extract	α-amylase and α-glucosidase activities with	inhibiting the enzymes like salivary, amylase and glucosidase and shows potential		flavonoid, tannin, glycoside, resin, steroids,	(Haridas et al., 2017)

Orchid	Part of the plant	Model description	Major finding	Control	Isolated Bioactive compound	Reference
		half-maximal inhibitory concentration (IC50), in vitro	activities against diabetes mellitus disease		terpenoids, cardiac glycosides and triterpenoids etc	
Dendrobium aqueum Lindl	aqueous extracts of pseudoobulbs	Antioxidant activity using DPPH, the protein glycation inhibitory using albumin/fructose glycation model	DPPH free-radical scavenging potential and antiglycation potential			(Mukherjee et al., 2012)
Dactylorhiza romana subsp. Georgica	tubers chloroform, ethyl acetate, methanol, ethanol and hexane extract	phosphomolybdate test method, DPPH scavenging activity, α-amylase and α-glucosidase activity	antioxidant and antimicrobial agent, or enzyme inhibitor		Gallic acid, protocatechuic acid, catechin, p-hydroxybenzoic acid, chlorogenic acid, caffeic acid, epicatechin, syringic acid, vanillin, p-coumaric acid, o-coumaric acid, ferulic acid, sinapic acid, benzoic acid, routine, rosmarinic acid, cinnamic acid, quercetin, kaempferol and luteolin	(Kotiloğlu et al., 2020)
Prosthechea karwinskii	pseudobulbs, leaves and flowers	40% sucrose induced MS male Wistar rats	reducing glucose level, reducing cholesterol and triglycerides levels		flavonoid	(Rojas-Olivos et al., 2017)
Dendrobium officinale	stem	type 2 diabetic rats	ameliorate the symptoms of oxidative stress, inflammation, and hepatic lipid accumulation of liver	metformin	polysaccharide	(Yang et al., 2020)
Dactylorhiza hatagirea (*D. hatagirea*)	hydroalcoholic extract of root	alloxan monohydrate induced wistar albino rats.	reducing blood glucose, lipid parameters and significantly increasing body weight.	glibenclamide	flavonoids (quercetin), carbohydrate and saponins	(Choukarya et al., 2019)
Orchis anatolica	roots ethanol extraction	Alloxan induced diabetic rat	antihyperglycemic effect, correct some biochemical markers induced by diabetes	glibenclamide	flavonoids, triallate, theobromade, and tannins	(Khouri & Daradka, 2013)
Dendrobium gibsonii	whole-plant	α-glucosidase inhibition assay	α-glucosidase inhibitory activity as a noncompetitive inhibitor of α-glucosidase	acarbose	dihydrodengibsinin, dendrogibsol, ephemeranthol A, dengibsinin, nobilone, aloifol I, lusianthridin, denchrysan A and 4-methoxy-9H-fluorene-2,5,9-triol	(Thant et al., 2020)
Dendrobium formosum	whole plant	rat L6 myoblasts	Compounds 1 and 12 showed higher -glucosidase inhibitory activity. Lusianthridin (6) and	acarbose and orlistat	confusarin (1), hircinol (2), erianthridin (3),	(Inthongkaew et al., 2017)

Orchid	Part of the plant	Model description	Major finding	Control	Isolated Bioactive compound	Reference
Roxb. ex Lindl			moscatilin (11) had higher activity than insulin.		gigantol (4), nudol (5), lusianthridin (6), coelonin (7), dihydroconiferyl dihydro-p-coumarate (8), batatasin III (9), 2,5,7-trihydroxy-4-methoxy-9,10-dihydrophenanthrene (10), moscatilin (11), and 5-methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone (12)	
Anacamptis pyramidalis (L.) Rich		The antioxidant potential was evaluated by DPPH, ABTS, CUPRAC and FRAP assays. Enzymes inhibition activity against ACh, BChE, tyrosinase, α-glucosidase, and α-amylase			Disaccharide, Citric acid, Parishin G, Roseoside, Gastrodin derivative, Parishin B, Parishin C, Dihydroxybenzoic acid derivative, Caffeic acid derivative, Acacetin derivative, Oxo-dihydroxy-octadecenoic acid, Trihydroxy-octadecenoic acid	(Mahomoodally et al., 2020)
Prosthechea michuacana (Lex.) WE Higgins	bulbs Hexane, chloroform and methanol extracts of P. michuacana	STZ induced diabetic Wistar albino rats	anti-hyperglycemic and antihyperlipemic activity, improving the hyperinsulinemia and produces a significant change on AGEs formation	AGEs formation in vitro with aminoguanidine, antihyperglycemia in vivo with glibenclamide and tolbutamide		(Gutierrez & Hoyo-Vadillo, 2011)
Bauhinia variegata	Young B. variegata L. (var. Candida) leaves	STZ induced diabetic rats	antidiabetic effect through restoring the normal architecture of pancreatic β-cells in addition to the antioxidant and hypolipidemic effect		Polyphenol	(Abdel-Halim et al., 2020)
Gastrodia elata Blume (GE)	GE, fermented by Saccharomyces cerevisiae	High Glucose induced human umbilical vein endothelial cells (HUVECs)	protect against the oxidative stress, and inflammatory conditions in endothelial cells, caused by HG		Phenolic compounds (gastrodin, p-hydroxybenzyl alcohol (HBA), p-	(Kwon et al., 2012)

Orchid	Part of the plant	Model description	Major finding	Control	Isolated Bioactive compound	Reference
					hydroxybenzaldehyde (HBZ))	
Maxillaria tenuifolia	EtOAc extract of the flower	Anti-oxidant activity were determined in ferric thiocyanate method. α-glucosidase inhibitory activity compared with synthetic inhibitor	suppressing carbohydrate disintegration and could prevent damage to organisms by oxidative stress	acarbose	3,4-dihydroxy benzoic acid methyl ester (1), flavanthridin (2), vanillic acid (3) and mangiferin (4)	(C. Li, 2021)
Diaphananthe bidens (D. bidens) (AFZEL. EX SW) SCHLTR	methanol leaf extract	STZ induced hyperglycemic rats	reducing blood glucose	tolbutamide	saponins, steroids, tannins and terpernoids	(Ottah et al., 2012)
Bletilla striata	polysaccharides of B. striata	high fat diet (HFD)-fed mice	reducing obesity and metabolic disorders in HFD-fed mice		polysaccharides of B. striata	(Hu et al., 2020)
Dendrobium ofcinale	leaves hot water extraction, alcohol sedimentation and chromatographic separation	infammatory cell model by LPS acting THP-1 cells	protecting THP-1 cells from LPS-stimulated cytotoxicity, inhibiting reactive oxygen species formation, suppressed toll-like receptor-4 (TLR-4), myeloid diferentiation factor (MyD88) and tumour necrosis factor receptor-associated factor-6 (TRAF-6) mRNA and protein expression		polysaccharides	(Zhang et al., 2018)
Dendrobium candidum	dry dendrobium	human corneal epithelial cells (HCEC)	improving the proliferative activity of HCEC cells under the high glucose environment and reduce the apoptosis of cells by regulating the expression of bax and bcl-2. Protecting and repairing corneal epithelial cells damage in high glucose.		polysaccharide	(Q. Li et al., 2017)
Aerides multiflora	dried powder from the whole plants macerated with MeOH	The liberation of pnitrophenol from the substrate p-nitrophenol-α-D-glucopyranoside (PNPG).	compound revealed a non-competitive inhibition and suggested as a candidate structure for α-glucosidase inhibitor		Aerimultin, Dihydrosinapyl dihydroferulate, 6-Methoxy coelonin, Gigantol, Imbricatin, Agrostonin, Dihydroconiferyl dihydro-p-coumarate, 5-Methoxy-9,10-dihydrophenanthrene-2,3,7-triol, Acarbose	(Thant et al., 2021)

Orchid	Part of the plant	Model description	Major finding	Control	Isolated Bioactive compound	Reference
Eulophia ochreata L	Tubers extracted with methanol and distilled water	antioxidant activity using DPPH radical scavenging activity, total antioxidant capacity using phosphomolybdenum method, amylase inhibition assay using the chromogenic DNSA method, antiglycation activity using BSA-fructose assay, Nitrobluetetrazolium assay was used to determine the fructosamine	antioxidant activuty and favorable α amylase inhibitory activity	ascorbic acid	Phenolic and flavonoids compounds	(Jagtap et al., 2012)
Gymnadenia orchidis Lindl	fibrous root	STZ induced adult female albino mice of BALB C	inhibiting glycation of the hemoglobin, normalizing the lipid profile of diabetic animals, improving antioxidant status and reducing lipid peroxidation, recovering DNA stand breakage		Terpenoids	(Arzoo et al., 2018)
Grammatophyllum speciosum Blume	ethanol extracts prepared from leaf, rhizome+root and pseudobulbs	antioxidant activity using DPPH assay, α-glucosidase inhibition assay was undertaken according to a modified Lebowitz (1998).	DPPH free radical scavenging activity and α-Glucosidase inhibitory activity	Trolox (6-hydroxy-2, 5, 7, 8-tetramethylchroman-2-carboxylic acid) and Acarbose		(Rungruchkanont & Chatsuwan, 2019)
Dendrobium christyanum Rchb.f	A methanolic extract from the dried root	in vitro α-glucosidase inhibitory and glucose uptake stimulatory activities	Compounds 4 and 6 appear to be potential hypoglycemic agents since they possess both α-glucosidase inhibitory and glucose uptake stimulatory activities.	acarbose	Methyl haematommate (1), methyl 2,4-dihydroxy-3,6-dimethylbenzoate (3), ndocosyl 4-hydroxy-trans-cinnamate (4), vanillin (5), coniferyl aldehyde (6), 4,5-dihydroxy-2-methoxy-9,10-dihydrophenanthrene (7), gigantol (10), and diorcinolic acid (13) .	(San et al., 2020)
Dactylorhiza hatagirea	methanolic leaf extract	α-amylase and α-glucosidase inhibition	inhibiting α-Amylase and α-Glucosidase enzymes, elevating relative expression	Acarbose and Metformin		(Alsawalha et al., 2019)

Orchid	Part of the plant	Model description	Major finding	Control	Isolated Bioactive compound	Reference
		assays and in vitro cellular assays such as glucose uptake assay and glucose transporter type 4 (GLUT4) expression studies in 3T3-L1 cell line	rates of GLUT4 receptor and amount of 2-(N-(7-Nitrobenz-2-oxa-1,3-diazol-4-yl) Amino)-2-Deoxyglucose taken up by 3T3-L1 cells			
Calanthe fimbriata Franch.	roots of C. fimbriata methanol extract	oral glucose tolerance test (OGTT) mice and in streptozotocin (STZ)-induced diabetic mice	decreasing ALT, AST and TG levels, improving hepatomegaly, and increasing hepatic glycogen content	Gliclazide and metformin	more than 40 constituents were determined including organic acids, ester, and sterols, etc.	(Peng et al., 2019)
Dendrobium delacourii	dried powder of whole plant macerated with MeOH and partitioned with ethyl acetate (EtOAc)	α-glucosidase enzyme assay using p-nitrophenyl-α-D-glucoside (PNPG) and anti-adipogenic activity using Mouse embryonic preadipocyte 3T3-L1 cell	α-glucosidase inhibitory activity and anti-adipogenic properties	oxyresveratrol	Phoyunnanin E, phoyunnanin C, densifloral B	(Thant et al., 2022)

Antiglycation Potential

Four orchids of this study, *Gymnadenia orchidis* Lindl, *Eulophia ochreata* L, *Dendrobium aqueum* Lindl, and *Prosthechea* michuacana (Lex.) WE Higgins have antiglycation activity. Protein glycation is a biomarker for diagnosis of diabetes. Glucose is a directed glycating agent of amino group in proteins, which modifies N-terminal and sidechain amino groups. Afterwards, at later stage, AGEs, are formed by the degradation of fructosamines and by the reaction of reactive dicarbonyl metabolites, such as methylglyoxal (MGO) (Rabbani & Thornalley, 2021). Inhibition of MGO formation is known as one of the antiglyclation mechanisms to inhibit AGE formation. In addition to inhibiting its formation, the antiglycation mechanism can also be carried out by acting as a scavenger for this molecule (Jung et al., 2019). Protein glycation and oxidative stress caused by chronic hyperglycemia are the major factors in diabetic complication. Some substances prevent the formation of AGEs by acting as an antioxidant, inhibiting sugar autoxidation, binding to amino groups, early degradation of Maillard Reaction Products (MRP), and by reducing sugars, so that these sugars cannot bind to the amino groups of a protein (Yulianti et al., 2021). Another mechanism of action of antiglycation compounds is by binding to their receptors, this can cause cellular mechanisms due to the interaction of AGEs with their receptors to be inhibited (Sindhuja et al., 2021). Orchids also contain polyphenols, such as *Bauhinia variegate* (Abdel-Halim et al., 2020). Polyphenols are one of the antiglycation compounds that increase the work of peroxisome proliferator-activated receptors (PPAR), which controls carbohydrate and lipid metabolism, and has been shown to reduce RAGE expression (Di Sotto et al., 2019).

Stimulating Insulin, Anti-insulin Resistance and Elevating GLUT4 Receptor

Insulin is a peptide hormone that binds plasma membrane-bound receptors in target cells. This hormone promotes glucose utilization and storage by increasing glucose transport and glycogen synthesis in skeletal muscle, activating glycogen synthesis, increasing lipogenesis and decreasing gluconeogenic gene expression in liver, as well as suppressing lipolysis and increasing glucose transport and lipogenesis in white adipocyte tissue (Petersen & Shulman, 2018). There are some orchids from this study that improve the insulin signaling namely *Dactylorhiza hatagirea, Prosthechea michuacana* (Lex.) W.E. Higgins and *Prosthechea karwinskii*. Targets of these compounds that affect insulin signaling include insulin receptor substrate, phosphatidylinositol 3-kinase, glucose transporter, activated protein kinase (AMPK), glycogen synthase kinase 3, MAPKs, *JNK*, NF-κB, protein tyrosine phosphatase 1B, nuclear factor-E2-related factor 2, and peroxisome proliferator-activated receptors (J. Li et al., 2019). Maintenance and enhancement of β-cell function has the potential to improve diabetes. Specific growth factors, cell cycle mediators, and nuclear factors have been proposed to regulate β-cell homeostasis (Chang et al., 2013).

Anti-Adipogenic Properties

Lipid metabolism, such as increased lipogenesis and decreased lipolysis in adipose tissue occurs largely as a response of glucose homeostasis to insulin stimulation (M. Li et al., 2022). Orchids *Prosthechea karwinskii, Prosthechea michuacana* (Lex.) W.E. Higgins, *Dendrobium officinale, Dactylorhiza hatagirea, Prosthechea michuacana* (Lex.) WE Higgins, *Bauhinia variegate, Bletilla striata, Gymnadenia orchidis* Lindl, *Calanthe fimbriata* Franch, *Dendrobium delacourii* have the properties to improve lipid metabolism in diabetes. Polyphenols, besides functioning as antioxidants also have antiadipogenic abilities. Reduction of adipose tissue is carried out through the mechanism of inhibiting cell proliferation, increasing cell apoptosis, inhibiting differentiation from pre-adipose to adipose, inhibiting cellular lipid accumulation and increasing lipolysis (Nam et al., 2019).

Inhibiting a-Amylase

α-Amylase catalyzes the hydrolysis of starch which will produce glucose as the final product. The catalytic activity of this enzyme can be controlled to reduce glucose production at the postprandial stage, which could be of therapeutic benefit to diabetics (Khadayat et al., 2020). Some α-Amylase inhibiotor show their mechanisms by interacting with the key active site residues through an array of hydrophobic interactions and hydrogen bonds (Ogunyemi et al., 2022). *Malaxis rheedei* SW, *Anacamptis pyramidalis* (L.) Rich, *Eulophia ochreata* L, *Dactylorhiza hatagirea* are some orchids with antidiabetic property as an α-Amylase inhibitor. Based on table 1, the orchid *Dactylorhiza romana* subsp. Georgica (Kotiloğlu et al., 2020) and *Dactylorhiza hatagirea* (Choukarya et al., 2019) contain quercetin compounds. Quercetin is a compound that has been shown to act as an inhibitor for α amylase. The inhibition mechanism carried out by this compound is by forming molecular interactions with the enzyme binding sites (Oso & Olaoye, 2020).

Inhibiting a-Glucosidase

Glucosidases are required for starch digestion. Hence, α-glucosidase inhibitor is one of the methods for treating diabetes by *suppressing* the digestion of carbohydrates, thus slowing down the process of glucose assimilation which will lead to a significant reduction of plasma glucose and postprandial insulin levels (Choudhury et al., 2018). Some orchids in this study which have this property are *Malaxis rheedei* SW, *Dendrobium gibsonii, Dendrobium formosum* Roxb. ex Lindl, *Anacamptis pyramidalis* (L.) Rich, *Maxillaria tenuifolia, Aerides multiflora, Grammatophyllum speciosum* Blume, *Dendrobium christyanum* Rchb.f, *Dactylorhiza hatagirea, Dendrobium delacourii*. Previous study has showed competitive mode of inhibition mechanism of α-Glucosidase inhibitor from some plant substances (Lianza et al., 2022).

Antiinflammation

Metabolic inflammation is involved in diabetes and its complications (such as diabetic nephropathy, retinopathy and neuropathy). Systemic inflammation occurs as a result of an increase in proinflammatory cytokines (IL-6, IL-1β, TNF-α), which are elicited by chemokines. Increased recruitment of inflammatory cells in metabolic networks, and activation of inflammatory responses occur due to NF-κB activation and signaling of AMPK and PPAR-γ (Kong et al., 2021). *Prosthechea karwinskii, Dendrobium officinale, Gastrodia elata* Blume have the antiinflammation activity. Bioactive compounds from plants that can regulate AKT, mTOR, adenosine monophosphate, AMPK, AGEs, growth factors, proinflammatory cytokines (IL-1β and TNF-α), oxygen species, and various other signaling mechanisms related to diabetes can be projected as an effective therapy (Kaabi, 2022).

Conclusion

In conclusion, orchid has been widely used in traditional medicine. All parts of these plants can be extracted and contain some active substances. Several studies have reported some antidiabetic mechanisms of several species of orchids. These anti-diabetic mechanisms include being antioxidants, anti-glycation and anti-inflammation, increasing insulin action, influencing lipid metabolism, and inhibiting α-amylase and α-glucosidase.

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Author Contributions

EY, ISM and LS constructed the idea for this manuscript and planned the methods. EY, ISM and LS had responsibility in extracting the data from the journals, data management and reporting. EY and TCH analyzed and interpreted the extracting datas. EY had responsibility in the construction of the manuscript. All authors read and approved the final manuscript.

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Conflicts of Interest

There is no conflict of interest.

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