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- Review -

Natural Quercetin Derivatives: Structures and Biological Activities Based on Enzyme Inhibition

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Enzymes, as proteins that regulate various metabolic processes within the human body, play a crucial role in maintaining health. However, the overexpression of certain enzymes can disrupt metabolic balance, leading to various diseases. Enzyme inhibitors are vital in treating these diseases or conditions by inhibiting the action of these enzymes, making them indispensable in the development of effective therapies for a wide array of diseases. Quercetin, a natural product derived from plants, is a type of flavonoid that belongs to the polyphenol family. Quercetin, a natural flavonoid from the polyphenol family, has emerged as a potent enzyme inhibitor. This low-molecular-weight secondary metabolite is known for its inhibitory effects on enzymes such as α-glucosidase, acetylcholinesterase, bacterial neuraminidase, and xanthine oxidase due to its structural advantages. Quercetin is isolated from biomaterials and can be classified into glycosylated, methoxylated, and alkylated derivatives based on its structural variations. These natural quercetin derivatives possess unique substituents that enable specific binding patterns with catalytic residues in enzyme active sites. Therefore, quercetin derivatives can be expected to have better enzyme inhibitory activity than basic quercetin. Due to their specificity and enhanced activity, quercetin and its derivatives hold promise as candidates for developing potent enzyme inhibitors to treat diseases resulting from enzyme imbalances.

Key words : Catalytic site, enzyme inhibition, natural products, quercetin derivatives

Introduction

Enzymes play a crucial role in regulating various metabolic processes within the human body [15, 31, 42]. They are proteins that help speed up chemical reactions in our bodies, facilitating functions such as digestion [9, 53], liver function [11, 55], muscle and nerve function [4], and more. Enzyme activity is tightly regulated to ensure the proper functioning of metabolic pathways. For example, the end products of a metabolic pathway often inhibit the pathway's first enzymes, helping regulate how much end product is produced [57]. Additionally, cells can use inhibitors to make enzymes inactive, thereby slowing down or halting a metabolic pathway in response to changes in metabolite concentrations [8]. The catalytic site of an enzyme, also known as the active site, is where substrate molecules bind and undergo a chemical reaction [44]. This region of the enzyme consists of amino acid residues that form temporary bonds with the substrate (the binding site) and residues that catalyze a reaction of that substrate (the catalytic site). The active site is crucial for the enzyme's function as it directly catalyzes the chemical reaction, and it is evolved to be optimized to bind a particular substrate and catalyze a specific reaction, resulting in high specificity [24]. However, the overexpression enzyme causes metabolic imbalance, which can lead to health problems and diseases [29].

At this time, enzyme inhibitors play a crucial role in treating certain diseases or conditions by inhibiting the action of specific enzymes. They are essential tools in the development of effective treatments for a wide range of diseases and conditions [5]. Enzyme inhibitors act with enzymes by binding to the catalytic sites of enzyme. According to the binding type between enzyme and inhibitors, it is classified into competitive, noncompetitive, and uncompetitive inhibition modes [12, 50]. Competitive inhibitors possess a similar shape to that of the substrate molecule and compete with the substrate

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for the active site of the enzyme. This prevents the formation of enzyme-substrate complexes, leading to a decrease in the reaction rate. The level of inhibition depends on the relative concentration of substrate and inhibitor. This type of inhibition is reversible, as it involves temporary binding to the active site [38]. In noncompetitive inhibition, the inhibitor doesn't block the substrate from binding to the active site. Instead, it attaches at another site on the enzyme and blocks the enzyme from functioning properly. This type of inhibition is also reversible and allows both the inhibitor and substrate to be bound at the same time [27]. Some enzyme inhibitors can provide a mixture of competitive and noncompetitive inhibition. They may significantly reduce enzymatic activity without affecting substrate recognition or binding, leading to a combination of competitive and noncompetitive effects [21].

Quercetin is one of the well-known natural flavonols, belonging to the polyphenols especially. Quercetin is widely distributed in plant sources such as vegetables, fruits, and flowers [49]. Many studies have shown that quercetin is isolated and characterized from onion peel, capers, whortleberry, broccoli, and cabbages [19, 25, 39, 49]. The quercetin derivatives have the diverse chemical structure types including glycosylated, methoxylated, prenylated, and geranylated quercetins. Moreover, the natural quercetins are one of the famous chemicals to have distinctive biological properties including antioxidants, anti-inflammation, anti-cancer, and other chronic diseases [2, 3, 10, 14]. These outstanding and various biological activities may occur based on the chemical structure of quercetin. Quercetin derivatives can affect different targeted bioactive functions in enzyme inhibition because of diverse substituents in their chemical skeleton. Thus, in recent years, quercetin has gained considerable attention as a natural product. Ongoing research and studies are actively exploring its potential applications, further emphasizing its growing significance in various scientific fields.

Natural Quercetin Derivatives

Quercetin biosynthetic pathway in plants

Quercetin is a natural flavonoid with three rings and five hydroxyl groups (-OH). Quercetin is known to synthesis from phenylpropanoid pathway in plants [13] (Fig. 1). Initially, *p*-coumaric acid is synthesized from L-tyrosine catalyzed by tyrosine ammonia lyase (TAL). *p*-Coumaric acid with a carboxylic group undergoes ligation with CoA and produces *p*-coumaroyl-CoA via 4-coumaroyl-CoA lyase (4CL). The generated *p*-coumaroyl CoA was biosynthesized into naringenin chalcone with a C6-C3-C6 skeleton by chalcone synthase (CHS). Afterwards, it is converted into naringenin, a flavonoid skeleton with three rings of C6-C3-C6, by chalcone isomerase (CHI). This particular reaction is a key step in the biosynthesis of quercetin, a bioactive natural compound built upon the flavone structure: C6 (A-ring)-C3 (C-ring)-C6 (B-ring). Moreover, flavonoid 3-hydroxylase (F3H) is involved in the conversion of naringenin into dihydrokaempferol by attaching the hydroxyl group to the C3 position. flavonoid 3′-hydroxylase (F3′H) also acts to add a hydroxy group on the C3′ position of the B-ring to be dihydrokampferol. The final transformation into quercetin is facilitated by the action of flavonol synthase (FLS). One double bond is formed between the C2 and C3 positions to convert dihydroquercetin to the flavonol compound (quercetin). This conversion is catalyzed by the enzyme flavonol synthase (FLS) [45, 54]. As the biosynthetic process, the characterized chemical structure is the resorcinol moiety in C-ring, the catechol moiety in B-ring, and one distinctive hydroxy group on C3 in A-ring. It has the resorcinol moiety, characterized by attaching two hydroxyl groups on C6 and C8. Moreover, the catechol structure also can be found from two hydroxyl groups on C3' and 4' in the independent B-ring [32, 51] as shown in Fig. 2.

Natural quercetin derivatives in plants

As shown in Fig. 2, quercetin derivatives in plants are formed by modifying the quercetin, a naturally occurring flavonoid. In the plant metabolite biosynthetic pathways, glycosylation, methylation, and alkylation predominantly occur in the hydroxy group of quercetin. These transformations yield O-methylated quercetin, O-alkylated quercetin, quercetin glucuronide, and quercetin glycoside. Alkylation occurs at the carbon site where the hydroxy group is not attached in the quercetin skeleton, forming C-alkylated quercetin [2, 3, 10, 28].

Quercetin is the most abundant flavonoid in the diet, and it is estimated that the average person consumes 10–100 mg of it daily through various food sources. Foods that commonly contain quercetin include onions, apples, grapes, berries, broccoli, citrus fruits, cherries, green tea, coffee, red wine, and capers [19, 25, 39]. Quercetin glycosides are a group of naturally occurring compounds where the flavonoid quercetin is bound to one or more sugar molecules. Glucose, rhamnose, arabinoside, and galactose are mainly found in the form of oxygen substituted at C3 and C7: quercetin-3-O-glucoside (isoquercitrin), quercetin 7-O-glucoside (quercimeritrin), quer-

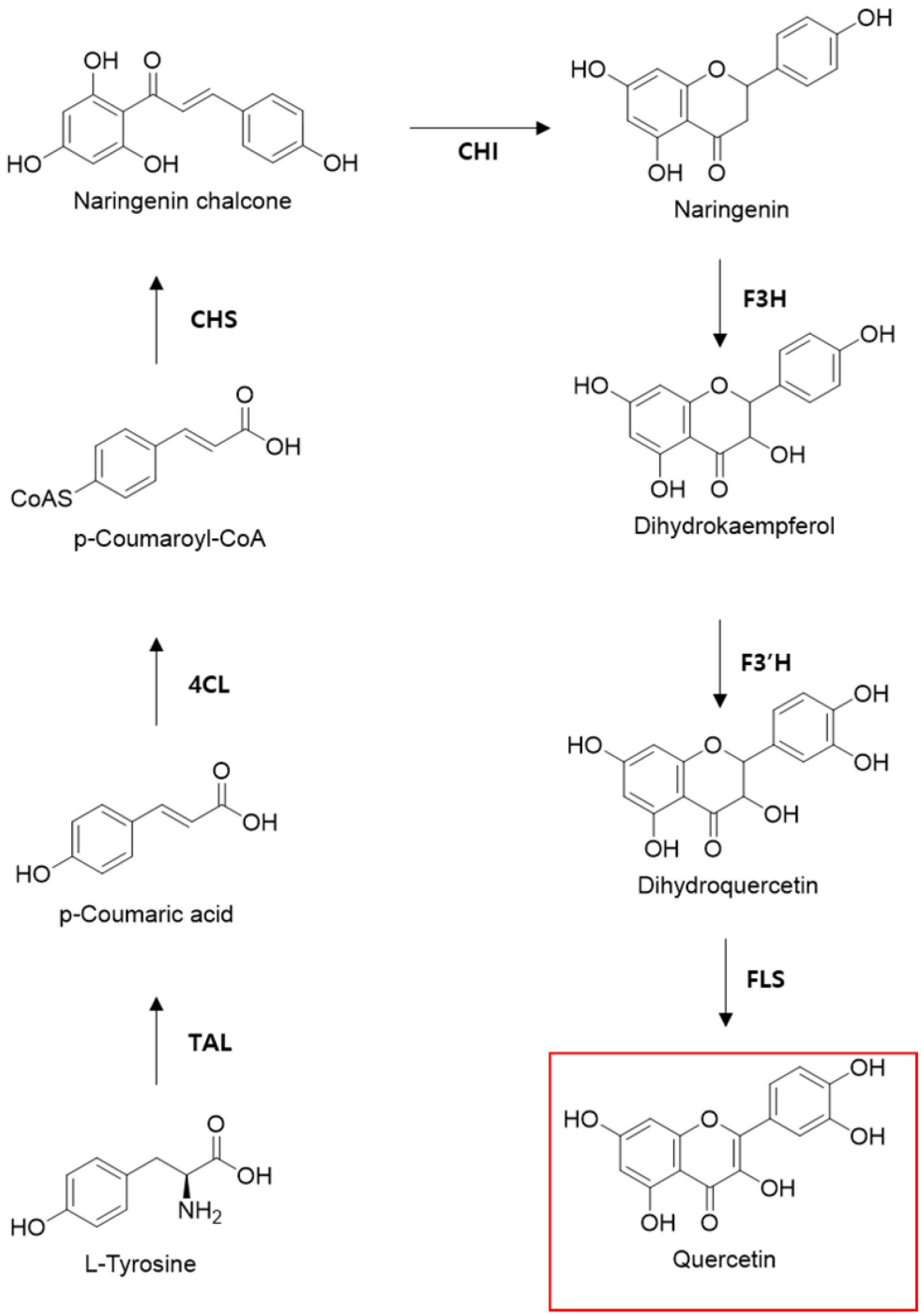

Fig. 1. Biosynthetic pathway of quercetin in plant metabolism. TAL, tyrosine ammonia-lyase; 4CL, 4-coumaroyl-CoA lyase; CHS, chalcone synthase; CHI, chalcone isomerase; F3H, flavanone 3-hydroxylase; F3′H, flavanone 3′-hydrolase; FLS, flavonol synthase.

cetin-3-O-rhamnoside (quercitrin), quercetin-3-O-arabinofuranoside (guaijaverin), quercetin-3-O-galactopyranoside (hyperoside), quercetin 3-O-rutinoside (rutin), and quercetin 3-O-rhamnoside-7-O-glucoside [7, 30, 48]. Quercetin glucuronide is a glucuronide conjugate of quercetin, where a glucuronic acid molecule is attached to the oxygen C3 position of the quercetin skeleton. Quercetin 3-O-glucuronide, also known as miquelianin, is a significant metabolite of quercetin and a naturally occurring flavonol glucuronide [23]. O-Methylated quercetin refers to derivatives of quercetin where one or more

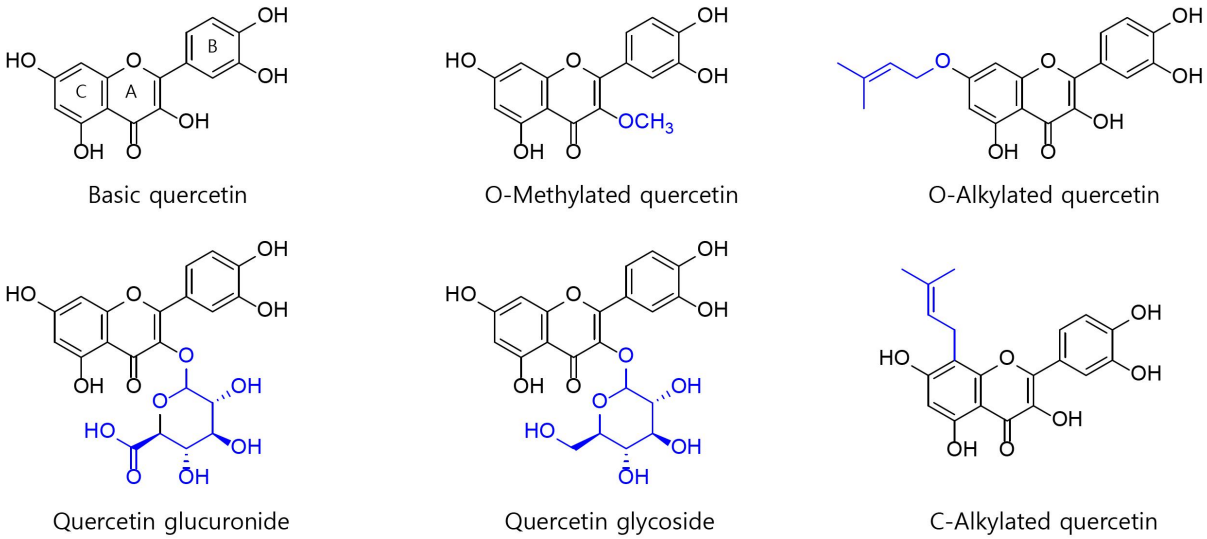

Fig. 2. Chemical skeleton of natural quercetin derivatives: basic quercetin, O-methylated quercetin, O-alkylated quercetin, quercetin glucuronide, quercetin glycoside, C-alkylated quercetin.

hydroxyl groups have been replaced with a methyl group such as 3-O-methylquercetin, 3′-O-methylquercetin, 4′-O-methylquercetin, 3,4′-di-O-methylquercetin, 3,7-di-O-methylquercetin, 3,3′-di-O-methylquercetin, 3,7,3′-tri-O-methylquercetin, 3,7,4′-tri-O-methylquercetin. In addition, compounds such as 3,7-di-O-methylquercetin-4′-O-glucoside and 3,7-di-O-methylquercetin-3′-O-glucoside in which both methylation and glycosylation have occurred are also found [46, 58]. O-alkylated quercetin is mainly distributed to form in the prenyl or geranyl group attached to oxygen atoms at C6, C7, and C8. The representative O-alkylated quercetin has been reported as 7-O-prenyl quercetin-4′-O-glucoside (pteleifolosin C) and 7-O-prenyl quercetin-3′-O-glucoside (pteleifolosin E). The most representative C-alkylated quercetin is known to be 8-prenylquercetin, which has a prenyl group substituted at C8 [6, 16].

The role of plant metabolites as enzyme inhibitors

Enzyme inhibitors play a very important role in the development of new drugs. Enzymes are proteins used to promote or inhibit chemical reactions in living organisms. Enzyme inhibitors help treat certain diseases or conditions by inhibiting the action of these enzymes. Enzyme inhibitors can be used to treat a variety of diseases [40]. For example, Tamiflu, a flu drug, is a neuraminidase inhibitor [35], and benazepril, a high blood pressure drug, is an angiotensin-converting inhibitor [33]. Therefore, enzyme inhibitors are essential tools in the development of effective treatments for a wide range of diseases and conditions.

Plant secondary metabolites are a diverse group of compounds with various intrinsic and extrinsic functions. These compounds have been reported to have potential as enzyme inhibitors, particularly in relation to the enzymatic activity of hydrolytic enzymes. Previous research has reported that the enzymatic activity of hydrolytic enzymes is high [40]. Additionally, secondary metabolites from plants have been demonstrated to be suitable anticancer agents, leading to the development of new clinical drugs with new anticancer mechanisms of action [43]. Most hydrolytic enzymes share similar catalytic residues, typically including aspartic acid, glutamic acid, serine, and histidine. These amino acids are crucial because they can exchange protons, which is essential for the catalytic activity of the enzymes. The serine esterases, for example, have a catalytic triad composed of serine, glutamic or aspartic acid, and histidine, which is a common configuration found in many enzymes [41].

There are various types of enzymes, each depending on its specific function. Enzymes commonly used in research for developing enzyme inhibitors using natural substances include α-glucosidase, neuraminidase, xanthine oxidase (XO), tyrosinase, acetylcholinesterase (AChE), β-secretase, angiotensin converting enzyme (ACE), and neutrophil elastase. α-Glucosidase is an enzyme that plays a role in carbohydrate metabolism by breaking down complex sugars into simpler sugars such as glucose. It is involved in carbohydrate metabolism by breaking down complex sugars into simpler sugars like glucose [17]. Neuraminidase is an enzyme that cleaves sialic acid residues from glycoproteins and glycolipids. It is

known for its role in the life cycle of influenza viruses. It cleaves sialic acid residues from glycoproteins and glycolipids [52]. XO is the enzyme required to produce uric acid by the breakdown of purine nucleotides. It is also involved in the generation of reactive oxygen species during its enzymatic reaction. XO is required to produce uric acid by the breakdown of purine nucleotides. The uric acid itself, as well as the reactive oxygen species released during the enzymatic reaction, can have detrimental effects on the body [20]. Tyrosinase is an enzyme involved in the production of melanin, the pigment responsible for the color of skin, hair, and eyes in humans and other animals [34]. AChE is an enzyme that catalyzes the breakdown of the neurotransmitter acetylcholine in the nervous system. β-Secretase is an enzyme involved in the production of beta-amyloid peptide, a major component of amyloid plaques found in the brains of Alzheimer's disease patients [6]. Angiotensin-converting enzyme (ACE) is a zinc-containing metallopeptidase that plays a major part in the regulation of blood pressure and participates in several other physiological functions, including renal development and male reproduction. It converts the hormone angiotensin I to the active vasoconstrictor angiotensin II [18]. Neutrophil elastase is an enzyme released by neutrophils that regulates the formation of neutrophil extracellular traps and is involved in antibacterial innate immunity [22].

Quercetin Derivatives as an Enzyme Inhibitor

Basic quercetin

Quercetin is a powerful antioxidant found in a variety of fruits, vegetables, leaves, seeds, and grains. Red onions are particularly high in quercetin, and other good sources include kale, spinach, red leaf lettuce, broccoli, capers, shallots, scallions, cabbage, red and yellow apples, berries such as blueberries, cranberries, and cherries, as well as citrus fruits like oranges and grapefruits. Green tea is also a good source of quercetin, containing an average of 15 mg. In addition, quercetin is the most basic and powerful compound distributed in traditional medicines containing flavonoids [19, 25, 39, 49].

Many studies have been reported to exhibit biological activities of quercetin based on enzyme inhibition. Quercetin isolated from *Croton menyharthii* leaves displays AChE and α-glucosidase inhibition. Quercetin inhibits AChE and α-glucosidase activities with 43.7 and 30.9 μg/ml of IC_{50} values. It shows more active than AChE (galanthamine, IC_{50}=88.3 μg/ml) and α-glucosidase (acarbose, IC_{50}=83.6 μg/ml) positive control, respectively [1]. Other studies demonstrate that quercetin inhibits XO with IC_{50} values of 10.5 μg/ml in onion (*Allium cepa* L.) solid waste [36]. Moreover, quercetin isolated from the dried flower of *Heterotheca inuloides* inhibits the oxidation from L-tyrosine to L-DOPA by suppressing tyrosinase activities. Quercetin as a tyrosinase inhibitor behaves competitive inhibition mode with 0.07 mM of IC_{50} values. It also acts as a cofactor by elongating the lag time of L-DOPA production [26]. The inhibition of these specific enzymes by quercetin suggests its potential use in treating conditions like Alzheimer's disease, diabetes, skin hyperpigmentation, and certain oxidative stress-related diseases via AChE, α-glucosidase, tyrosinase, and XO inhibition. This broad spectrum of quercetin against particular enzyme inhibition underscores its potential in pharmaceutical and therapeutic fields.

Quercetin glycoside

Glycosylated quercetin derivatives are among the most common forms of quercetin found in nature. These derivatives offer several advantages over the basic quercetin skeleton, primarily due to the addition of sugar moieties. Quercetin-3-O-galactopyranoside and quercetin-3-O-arabinopyranoside isolated from *Limonium michelsonii* have been reported to exhibit ACE inhibition. Quercetin-3-O-galactopyranoside and quercetin-3-O-arabinopyranoside show the inhibitory effects having IC_{50} values at 10.2 and 14.8 μM, respectively. The inhibitory potencies of quercetin glycoside are 2–3 folds active than quercetin (IC_{50}=35.3 μM). The quercetin derivatives with a sugar moiety exhibits enhanced ACE activity, although their enzyme inhibition mechanism remains consistent with the competitive mode observed in quercetin and its glycoside [18]. Rutin is a disaccharide derivatives with glucose and rhamnose sugar group attaching on C3 position. In one study, rutin demonstrates stronger inhibitory activity against carbohydrate-hydrolyzing enzymes associated with type 2 diabetes compared to quercetin. The α-glucosidase inhibitory activity of quercetin and rutin exhibits similar IC_{50} values at 38 and 37 nM, respectively, but rutin (IC_{50}=43 nM) elucidates better α-amylase inhibitory activity than quercetin (IC_{50}=61 nM) [37] (Table 1). Overall, the addition of sugar moieties to quercetin enhances its bioavailability and therapeutic potential, making glycosylated derivatives valuable in pharmacological applications.

Table 1. Representative natural quercetin derivatives as enzyme inhibitors

Quercetin derivatives	Sources	Target enzyme	Type	Ref
Quercetin-3-O-arabinofuranoside	*Limonium michelsonii*	ACE	Glycosylation	[18]
Quercetin-3-O-galactopyranoside	*Limonium michelsonii*	ACE	Glycosylation	[18]
Quercetin 3-O-rutinoside	Buckwheat	α-Amylase	Glycosylation	[7, 37]
Quercetin 3-O-glucuronide	*Nelumbo nucifera*	α-Glucosidase	Glucuronylation	[23, 56]
3-O-methylquercetin	*Siegesbeckia pubescens*	BNA, β-secretase	Methylation	[46, 58]
4′-O-methylquercetin	*Caragana balchaschensis*	β-Secretase	Methylation	[58]
3,4′-di-O-methylquercetin	*Siegesbeckia pubescens*	BNA, β-secretase	Methylation	[46, 58]
3,7-di-O-methylquercetin	*Siegesbeckia pubescens*	BNA, β-secretase	Methylation	[46, 58]
3,3′-di-O-methylquercetin	*Caragana balchaschensis*	β-Secretase	Methylation	[58]
3,7,3′-tri-O-methylquercetin	*Caragana balchaschensis*	β-Secretase	Methylation	[58]
3,7,4′-tri-O-methylquercetin	*Caragana balchaschensis*	β-Secretase	Methylation	[58]
3,7-di-O-methylquercetin-4′-O-glucoside	*Caragana balchaschensis*	β-Secretase	Methylation, glycosylation	[58]
3,7-di-O-methylquercetin-3′-O-glucoside	*Caragana balchaschensis*	β-Secretase	Methylation, glycosylation	[58]
7-O-prenyl quercetin-4′-O-glucoside	*Melicope glabra*	AChE	Alkylation, glycosylation	[6]
7-O-prenyl quercetin-3′-O-glucoside	*Melicope glabra*	AChE	Alkylation, glycosylation	[6]
8-Prenylquercetin	Turkish mulberry	α-Glucosidase	Alkylation	[16, 47]

Quercetin glucuronide

The representative quercetin glucuronide is quercetin 3-O-glucuronide (Q3G), which is relatively widespread in wine, green beans, and medicinal plants. Q3G has been studied for its inhibitory effects on α-glucosidase, an enzyme involved in carbohydrate digestion and glucose metabolism. This inhibition is particularly relevant for managing type 2 diabetes mellitus (DM) and its complications. Q3G exhibits a reversible and mixed-mode inhibition of α-glucosidase activity. This means that Q3G can bind to both the enzyme and the enzyme-substrate complex, altering the enzyme's activity in multiple ways. The IC_{50} value of Q3G for α-glucosidase inhibition is reported to be 108.11 μM. Molecular docking studies have shown that Q3G enters the hydrophobic pocket of the enzyme and forms multiple hydrogen bonds with amino acid residues. These interactions are crucial for its inhibitory effect on α-glucosidase [56] (Table 1). This makes Q3G a promising candidate for the development of treatments or supplements aimed at managing type 2 diabetes and its related complications.

O-methylated quercetin

O-methylated quercetin derivatives can be found in various plants and herbs such as *Viscum coloratum*, *Sarcocornia fruticose*, *Nasturium officinale*, *Achyrocline satureioides*, *Semecarpus anacardium*, and so on. Among various plant sources, the most studied materials as enzyme inhibitors for these compounds are reported to be *Siegesbeckia* [46], *Melicope* [6], and *Caragana* [58]. Naturally occurring O-methylated quercetins are mainly found in mono, di, and tri-methoxy quercetin. 3-O-Methylquercetin, 3,4′-di-O-methylquercetin, and 3,7-di-O-methylquercetin isolated from the aerial parts of *Siegesbeckia pubescens* have been studied for their potential health benefits, particularly their inhibitory effects on bacterial neuraminidase (BNA). According to previous studies, monomethoxy quercetin (3-O-Methylquercetin, IC_{50}=14.0 μM) is more effective than dimethoxy quercetin (3,4′-di-O- and 3,7-di-O-methylquercetin, IC_{50}=24.3 and 25.8 μM, respectively) against BNA inhibition [46]. Kamila et al. and Aizhamal et al. have been reported those various types of O-methylated quercetins are disclosed to relate to improve cognitive disorder due to their β-secretase inhibition [6, 58]. In present study, various methylated and glycosylated derivatives of quercetin, including mono-, di-, and tri-O-methylated forms, as well as methylated with glycosylated quercetin, were investigated. The O-methylated quercetin demonstrates superior efficacy as a β-secretase inhibitor compared to quercetin and methyl glycosyl quercetins, as evidenced by their respective IC_{50} values. The study reports that O-methylated quercetins exhibits significant effectiveness in β-secretase inhibition, with IC_{50} values ranging from 1.2 to 6.5 μM. Notably, O-methylated quercetins are more effective than the parent com-

pound, quercetin (IC_{50}=25.2 μM). The study also has highlighted the critical role of the O-methyl motif in β-secretase inhibition, with tri-O-methylated quercetin demonstrating the highest potency (3,7,3′- and 3,7,4′-tri-O-methyl, IC_{50}=1.2 and 1.8 μM), followed by di-O-methylated (3,4′-, 3,7-, and 3,3′-di-O-methyl, IC_{50}=3.5, 3.8, and 4.3 μM) and mono-O-methylated (3-O-methyl, IC_{50}=6.5 μM) quercetins [58] (Table 1). The study suggests that the methylated quercetin acts as a noncompetitive inhibitor, while the methylated and glycosylated quercetin functions as a mixed-type inhibitor. This distinction in inhibitory mechanisms highlights the diverse modes of action exhibited by these derivatives in their interaction with the β-secretase enzyme. This comprehensive study not only sheds light on the biochemical properties of O-methylated quercetins but also highlights their broader implications based on the enzyme inhibitors in medicinal chemistry.

O- and C-alkylated quercetin

Alkylated quercetin derivatives offer several distinct advantages as enzyme inhibitors compared to standard quercetin. The process of alkylation modifies the quercetin molecule, which can lead to improved chemical stability and metabolic persistence to enhance its lipophilicity. Lipophilic compounds often exhibit stronger interactions with hydrophobic regions of enzyme active sites. By increasing the lipophilicity of quercetin through alkylation, the binding affinity to target enzymes can be improved. This can lead to more effective inhibition, as the compound can better fit into the enzyme's active site or allosteric sites, disrupting its function more effectively.

One study has been studied for O-alkylated quercetin derivatives isolated from the leaves of *Melicope glabra* such as 7-O-prenylquerctin-4′-O-glucoside and 7-O-prenylquerctin-3′-O-glucoside. The research highlights that O-alkylated quercetins exhibited potent inhibition of human AChE compared to its basic skeleton (quercetin). Specially, 7-O-prenylquerctin-4′-O-glucoside and 7-O-prenylquerctin-3′-O-glucoside reveals a mixed type I mode of inhibition against AChE [6]. The representative C-alkylated quercetin is 8-prenylquercetin from Turkish mulberry [16]. 8-Prenylquercetin has been studied as responsible for its α-glucosidase inhibition. It shows the α-glucosidase inhibitory effects with IC_{50} at 4.38 μM [47] (Table 1). The specific structural modifications (alkylation) significantly improve their ability to inhibit enzymes like AChE and α-glucosidase, compared to the basic quercetin skeleton.

Conclusion

Quercetin, a plant-derived flavonoid that belongs to the polyphenol family. Quercetin has distinct biological properties, making it a valuable natural ingredient in various industries such as pharmaceuticals, cosmetics, and nutraceuticals. Moreover, various quercetin derivatives are found in nature, including glycosylated, methoxylated, and alkylated quercetin based on the quercetin skeleton. These derivatives have unique substituents that display a specific binding pattern with catalytic residue in the enzyme active site. The diverse substituents of quercetin derivatives in the chemical skeleton of quercetin derivatives can affect different targeted bioactive functions in enzyme inhibition. This highlights the potential of quercetin derivatives in the development of new therapeutic strategies. The unique properties of quercetin derivatives, combined with their natural origin, make them an exciting area of research in the pharmaceutical and nutraceutical industries.

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The Conflict of Interest Statement

The authors declare that they have no conflicts of interest with the contents of this article.

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초록 : 천연물질 퀘르세틴 유도체의 다양한 구조 및 효소 저해 활성

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효소 억제제는 인체 내 다양한 대사과정을 조절하는 단백질에 속하는 효소의 작용을 억제하여 특정 질병이나 상태를 치료하는 데 도움을 준다. 퀘르세틴은 폴리페놀 계열에 속하는 플라보노이드의 일종으로 식물에서 발견되는 이차 대사산물이다. 이러한 퀘르세틴은 구조적 이점을 바탕으로 효소의 활성부위에 결합하여 α-glucosidase, acetylcholinesterase, bacterial neuraminidase, xanthine oxidase에 대한 억제 활성을 갖는 것으로 보고된다. 또한, 퀘르세틴은 glycosylation, methoxylation, alkylation 등을 통해 특징적인 치환기를 가질 수 있으며 이러한 천연 퀘르세틴 유도체는 효소 활성 부위의 촉매 잔기와 특이적인 결합 패턴을 나타내어 더욱 우수한 효소저해활성을 가질 수 있다. 따라서, 본 논문에서는 퀘르세틴 및 그 유도체의 특징적인 구조에 대해 알아보고 이들의 효소저해활성을 통해 유도체별 다양한 질병을 목표로 하는 효과적인 효소 저해제 개발에 유망한 후보가 될 수 있음을 시사한다.