α-Amylase Inhibitors: A Review of Raw Material and Isolated Compounds from Plant Source

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ABSTRACT - Inhibition of α-amylase, enzyme that plays a role in digestion of starch and glycogen, is considered a strategy for the treatment of disorders in carbohydrate uptake, such as diabetes and obesity, as well as, dental caries and periodontal diseases. Plants are an important source of chemical constituents with potential for inhibition of α-amylase and can be used as therapeutic or functional food sources. A review about crude extracts and isolated compounds from plant source that have been tested for α-amylase inhibitory activity has been done. The analysis of the results shows a variety of crude extracts that present α-amylase inhibitory activity and some of them had relevant activity when compared with controls used in the studies. Amongst the phyto-constituents that have been investigated, flavonoids are one of them that demonstrated the highest inhibitory activities with the potential of inhibition related to number of hydroxyl groups in the molecule of the compound. Several phyto-constituents and plant species as α-amylase inhibitors are being reported in this article. Majority of studies have focused on the anti-amylase phenolic compounds.

INTRODUCTION

Disorders of carbohydrate uptake may cause severe health problems such as diabetes (1), obesity (2), and oral diseases (3), all of which threaten an increasing worldwide population. Diabetes mellitus (DM) is a metabolic disorder resulting from deficiency in insulin secretion, insulin action, or both, promoting disturbance of carbohydrate, fat and protein metabolism. Long-term complications of diabetes mellitus include retinopathy, nephropathy, neuropathy, micro-angiopathy and increased risk of cardiovascular disease (1, 4, 5).

The therapeutic strategies for the treatment of type 2 diabetes include the reduction of the demand for insulin, stimulation of endogenous insulin secretion, enhancement of the action of insulin at the target tissues and the inhibition of degradation of oligo and disaccharides (6). The drugs commonly used in clinic to handle or control diabetes are insulin, sulfonylureas, biguanide, glucosidase inhibitors, aldose reductase inhibitor, thiazolidinediones, carbamoylmethyl benzoic acid, insulin-like growth factor. The effect of these drugs is aimed to lower the level of blood glucose (4, 7, 8). One therapeutic approach for treating type 2 diabetes mellitus is to decrease the post-prandial glucose levels. This could be done by retarding the absorption of glucose through the inhibition of the carbohydrates-hydrolysing enzymes, α-glucosidase and α-amylase, present in the small intestinal brush border that are responsible for the breakdown of oligosaccharides and disaccharides into monosaccharides suitable for absorption (1, 7, 9, 10). Inhibitors of these enzymes, like acarbose, delay carbohydrate digestion and prolong overall carbohydrate digestion time, causing a reduction in the rate of glucose absorption and consequently blunting the post-prandial plasma glucose rise (1, 4).

Dental caries and periodontal diseases are the most prevalent oral infectious diseases that cause significantly impact a person's overall health, having considerable economic impact, if not adequate treated (3, 11).

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Take part in etiopathology of dental caries, the most abundant enzyme in human saliva, α-amylase salivary, possess at least three distinct biological functions in the oral cavity (12). First, its hydrolytic activity is responsible for the initial break down of starch to oligosaccharides. Second, several lines of evidence indicate that salivary α-amylase bound to tooth enamel or hydroxyapatite may play a role in dental plaque formation. Third, α-amylase in solution binds with high affinity to viridans oral streptococci and bacteria-bound α-amylase is capable of hydrolyzing starch to glucose, which can be used as a food source and then further metabolized to lactic acid. Localized acid production by bacteria can lead to the dissolution of tooth enamel, a critical step in dental caries progression (12, 13). Because of its central role in the oral cavity, α-amylase salivary has been exploited as a target for the structure-assisted design of compounds that might prevent unwanted dental plaque formation and the subsequent process of dental caries formation and progression. Ethnopharmacological approach and bioassay-guided isolation have provided a lead in identifying potential α-amylase inhibitors from plant sources. Currently, methods to determine the levels of α-amylase inhibitor are based on the measurement of α-amylase activity resulting by the different iodine staining power in the presence or absence of an inhibitor during the action of the enzyme on soluble starch or by using an alkaline reactive whose brown reduction products are determined photometrically as reported by Bernfeld (14, 15). This review highlights on the plants and their active constituents so far reported to have α-amylase inhibitory activity.

CHARACTERISTICS OF α-AMYLASE

The α–amylase (α -1,4-glucan-4-glucanohydrolases; E.C. 3.2.1.1) is one of the major secretory products of the pancreas (about 5–6%) (16) and salivary glands, playing a role in digestion of starch and glycogen and can be found in microorganisms, plants and higher organisms (17). The α -amylase constitute a family of endo-amylases that catalyse the initial hydrolysis of starch into shorter oligosaccharides through the cleavage of α-D-(1-4) glycosidic bonds (17-20). Neither terminal glucose residues nor *α*-1,6-linkages can be cleaved by α-amylase (16). The end products of α-amylase action are oligosaccharides with varying length with an α-configuration and α-limit dextrins (21), which constitute a mixture of maltose, maltotriose, and branched oligosaccharides of 6–8 glucose units that contain both *α*-1,4 and *α*-1,6 linkages (16). Others amylolytic enzymes participate in the process of starch breakdown, but the contribution of α-amylase is a prerequisite for the initiation of this process (19).

The human α-amylase is classical calcium-containing enzyme composed of 512 amino acids in a single oligosaccharide chain with a molecular weight of 57.6 kDa (16). There are five α-amylase genes clustered in chromosome 1, at location 1q21, in humans. Three of them code for salivary R-amylase, *AMY1A*, *AMY1B*, and *AMY1C*, and the other two genes *AMY2A* and *AMY2B* are expressed in the pancreas (22, 23). Human salivary and pancreatic α-amylases share a high degree of amino acid sequence similarity with 97% identical residues overall and 92% in the catalytic domains (12, 18).

The amylase presents a three-dimensional structure capable of binding to substrate and, by the action of highly specific catalytic groups, promote the breakage of the glycoside links (20). The protein contains 3 domains: A, B, and C. Domain A, which has a $(\beta/\alpha)_8$ barrel fold, constitutes the catalytic core domain. It contains about 280–300 residues. The catalytic triad (Asp, Asp, Glu) is present in domain A (24, 25). The B domain is inserted between A and C domains and is attached to the A domain by disulphide bond. The C domain presents a β sheet structure linked to the A domain by a simple polypeptide chain and seems to be an independent domain with unknown function. The active site (substrate-binding) of the α-amylase is situated in a long cleft located between the carboxyl end of both A and B domains. The calcium (Ca^{2+}) is situated between A and B domains and may act in stabilizing the three-dimensional structure and as an allosteric activator. The substrate-binding site contains 5 subsites (-3 -2 -1 +1 +2) (26).

α-Amylase catalyze the hydrolysis of starch via a double displacement mechanism involving the formation and hydrolysis of a covalent *β*-glycosyl enzyme intermediate by using active site carboxylic acids for it (27). The residues, in particular, Asp^{197}, Glu^{233}, and Asp^{300} were described to function as catalytic residues (26, 27). Probably, Asp^{197} acts as nucleophil that attacks the substrate at the sugar anomeric center, forming a covalently bound reaction intermediate. In this step, the reducing end of the substrate is cleaved off the sugar skeleton. In a second step a water molecule attacks the anomeric center to

break the covalent bond between Asp^{197} and the substrate, attaching a hydroxyl group to the anomeric center. In both steps Glu^{233} and Asp^{300} either individually or collectively act as acid/base catalysts. As a consequence, the active site of human α-amylase consists of several major binding subsites identified through kinetic studies (26). The same studies show that the "-1", "-2", and "-3" pocket is the core of the catalytic reaction (26).

INHIBITORS OF α-AMYLASE FROM PLANTS

The potential role of the medicinal plants as inhibitors of α-amylase has been reviewed by several authors. A variety of plants has been reported to show α-amylase inhibitory activity and so may be relevant to the treatment of type 2 diabetes. About 800 plant species have been reported to possess antidiabetic properties. A wide range of plant-derived principles belonging to compounds, mainly alkaloids, glycosides, galactomannan gum, polysaccharides, hypoglycans, peptidoglycans, guanidine, steroids, glycopeptides and terpenoids, have demonstrated bioactivity against hyperglycaemia (28). A list of plants reported to have significant α-amylase inhibitory activity is shown in Table 1.

Syzygium cumini L. (syn: *Eugenia jambolana* Lam.) and *Psidium guajava* L. are widely used traditional system of medicine to treat diabetes in India (29). The aqueous extracts from *S. cumini* seeds and *P. guajava* leaves both showed a dose-dependent inhibitory effect on α-amylase activity (29). The extract from seeds of *S. cumini* also significantly decreased the levels of blood glucose on diabetic rats (28, 30). Conforti and cols. (2005) (31) demonstrated that methanol, ethyl acetate and hexane extracts from two varieties of *Amaranthus caudatus* L. seeds (Oscar blanco and Victor red. Oil) showed α-amylase inhibitory activity (above 80% inhibition rate) at 0.25-1mg/mL.

The buffered extracts of several plant species namely *Balanites aegyptiaca* L., *Camellia sinensis* L. Del., *Galega officinalis* L., *Holarrhena floribunda* (Don) Durand & Schinz, *Khaya senegalensis* (Desr.) A. Juss., *Melissa officinalis* L., *Mitragyna inermis* (Willd.) O. Ktze., *Rosmarinus officinalis* L., *Securidaca longepedunculata* Fresen., *Tamarindus indica* L., *Taraxacum officinale* Web. ex Wigg., and *Vaccinium myrtillus* L. were screened for α-amylase activity and showed remarkable inhibitory activity (above 45% inhibition rate at 0.2g/mL) (6). Methanol extracts of 41 plants, used in traditional Mongolian medicine have been tested for α-amylase inhibitory properties and significant inhibition of the enzyme was shown by *Rhodiola rosea* L., *Ribes pullchelum* Turcz, and *Vaccinium uliginosum* L; extracts from *Geranium pretense* L, *Leontopodium ochroleucum* Beauv., *Paeonia anomala* L., and *Pentaphylloides fruticosa* L. Schwarz showed α-amylase inhibitory activity greater than 30% (32). Loizzo and cols (2008) screened the methanol, hexane and chloroform extracts from nine Lebanon traditional medicinal plants recommended in Lebanon for diabetes and found that the methanol extracts of *Salvia acetabulosa* L. and *Marrubium radiatum* Devile ex Benth exerted the highest inhibitory activity against α-amylase (33).

Ayurveda, the traditional Indian herbal medicinal system practiced for over thousands of years have reports of antidiabetic plants with no apparent known side effects (34, 35). Chloroform extracts of six plants namely *Azadirachta indica* A. Juss, *S. cumini*, *Ocimum tenuflorum* L., *Murraya koenigii* (L.) Spreng., and *Linum usitatissimum* L., traditionally used in Ayurveda along with *Bougainvillea spectabilis* Willd. used as a hypoglycemic plant in West Indies, and some parts of Asia were screened for inhibitory activity on α-amylase (34). A significant inhibition was observed with extracts of *O. tenuflorum* (34). Other six Indian medicinal plants were tested for their effect on α-amylase activity. Among them, *Mangifera indica* L., *Embelia ribes* Burm., *Phyllanthus maderaspatensis* Linn. and *Punica granatum* L. showed interesting α-amylase inhibitory activity (36).

The proteinaceous inhibitor of α-amylase (αAI), which inhibits animal salivary and pancreatic a-amylase, has been identified and isolated from various plant species (37). Amongst this plants, seeds of *Phaseolus vulgaris* L. contain proteinaceous inhibitors of the α-amylase and the isoform inhibitor αAI-1 have been isolated and characterized (38, 39). The common bean αAI-1 has been reported to have relatively great potential as an extensive anti-obesity and anti-diabetes remedy (37).

PHYTOCONSTITUENTS WITH α-AMYLASE INHIBITORY ACTIVITY

A wide array of plant has derived numerous chemical compounds that have demonstrated

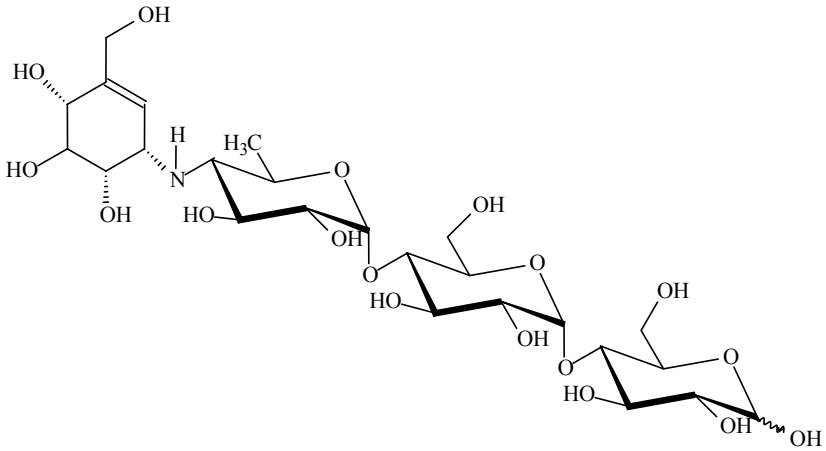
activity consistent with their possible use in the treatment of diabetes. Research on new bioactive compounds from medicinal plants has led to isolation and structure elucidation of a number of exciting new pharmacophores. A list of phyto-constituents having significant α-amylase inhibitory activity is provided in Table 2.

Oligosaccharide inhibitors of the trestatin family that contain the acarviosine moiety (e.g., acarbose ***1***), proteinaceous inhibitors isolated from microbial sources and plant tissues (40) and molecules present in plants comprise the natural inhibitors of α-amylase (41). Acarbose [***1***], a well know drug widely used for clinical treatment of diabetes mellitus, is a pseudotetrasaccharide, produced by *Actinoplanes* sp. fermentation, consisting of a polyhydroxylated aminocyclohexene derivative (valienamine) linked via its nitrogen atom to a 6-deoxyglucose, which is itself α-1,4-linked to a maltose moiety. It is a competitive inhibitor of α-amylase and the mechanism of inhibition seems to be due to the unsaturated cyclohexene ring and the glycosidic nitrogen linkage that mimics the transition state for the cleavage enzymatic of glycosidic linkages (42, 43).

In the structural study of the human pancreatic α-amylase /acarbose complex, acarbose inhibitor was described to bind subsites "-3" through "+2" (26). In acarbose the valienamine moiety is found in binding subsite -1 and its strong inhibition is believed to result from enhanced binding of this moiety with the side chain of Asp^{197}, Glu^{233}, and Asp^{300}. Kinetic studies also highlighted the importance in catalysis of the presence of hydroxyl groups in the ligand together with the Asp^{197}, Glu^{233}, and Asp^{300} residues in the binding site (substitution of these residues leading to a considerable drop in catalytic activity) (26).

Acarbose [***1***] is metabolised by small and large intestinal carbohydrases to give acarviosine-glucose and glucose (43). The main adverse effects observed with acarbose are gastrointestinal, including abdominal discomfort, flatulence, meteorism and diarrhea (8, 43, 44). These adverse effects might be caused by the increase of degradation products in the intestine resulting in the abnormal bacterial fermentation of undigested carbohydrates (43, 44). Indeed, these main side effects are common to α-amylase inhibitors. Specifically, bloating, abdominal discomfort, diarrhea and flatulence occur in about 20% of patients (45). Frequently such effects lead to therapy discontinuation (7). α-Glucosidase inhibitors are contraindicated in patients with irritable bowel syndrome or severe kidney or liver dysfunction. Inflammatory bowel disease is a relative contraindication (4). There are also reports of an increased of renal tumors occurrence and serious hepatic injury and acute hepatitis (46).

Studies with healthy and type 2 diabetes subjects showed that natural α-amylases inhibitors isolated from wheat (47) and white bean (48) significantly reduced the peak of postprandial glucose. Inhibitory profiles were investigated in green, oolong and black teas and the results suggested that catechins may be responsible for its activity in human salivary α-amylase (49).



1 acarbose

Therefore, the present article reviews and shows in table 1 a list of compounds with human α-amylase inhibitory capacity.

Phenolic compounds are a large group of structurally diverse naturally occurring compounds that possess at least a phenolic moiety in their structures. Most of these compounds possess various degrees of antioxidant or free radical scavenging properties as well as medicinal properties and have long been used as drugs.

Flavonoids are abundant class of natural phenolic compounds with several biological activities. They share a common structural skeleton consisting of two aromatic rings (A and B) linked through three carbons attached to the A-ring, forming an oxygenated heterocycle (ring C) and are divided in groups (Figure 1).

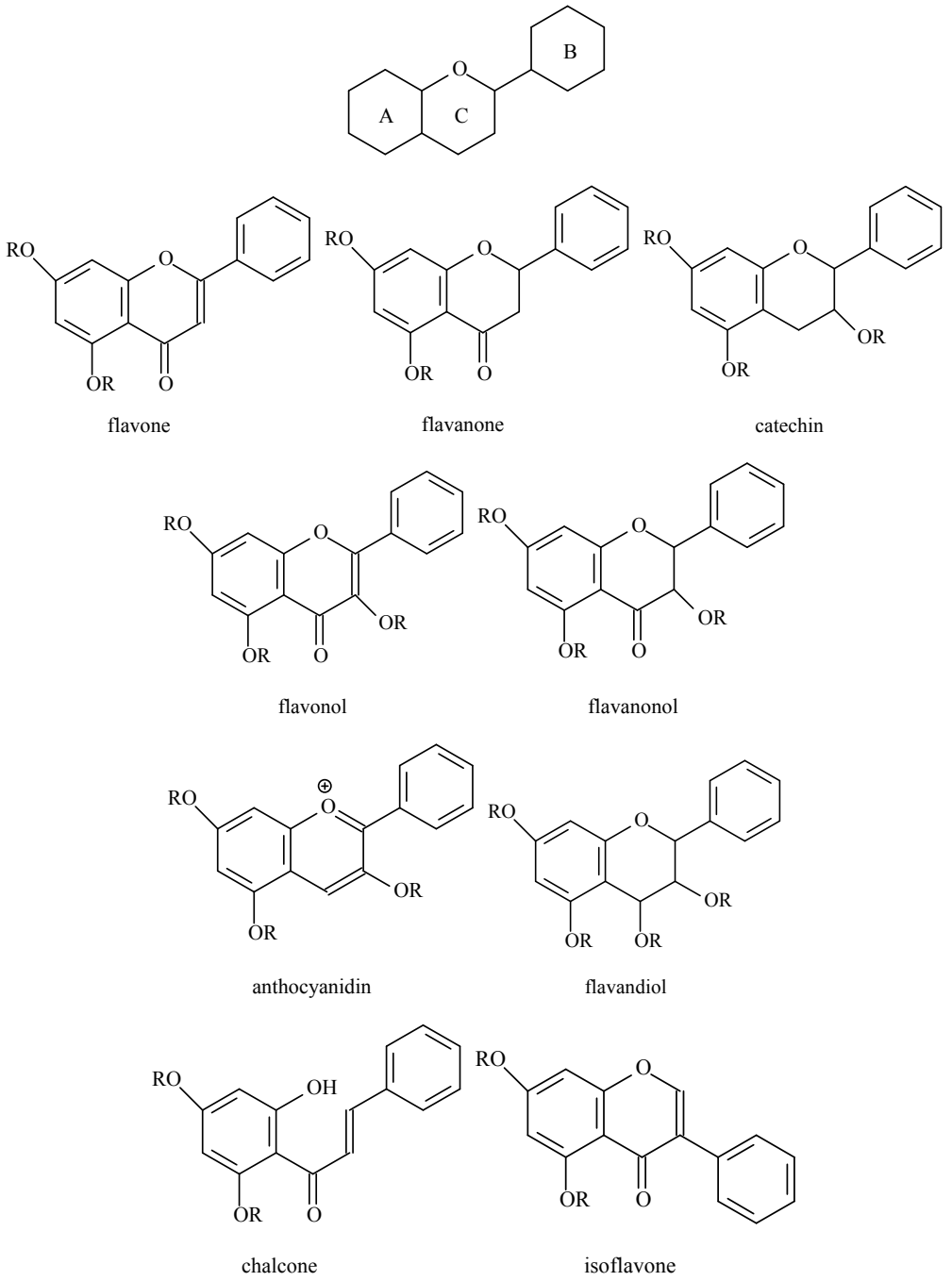
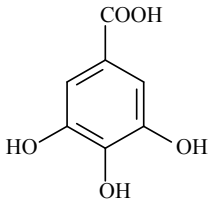


Figure 1. Flavonoids basic skeletons

Lo Piparo *et al*. (2008) investigated the interactions between flavonoids and human α-amylase in order to understand the molecular requirement for enzyme inhibition. They showed that the potency of inhibition is correlated with the number of hydroxyl groups on the B ring of the flavonoid skeleton. The interaction occurs with the formation of hydrogen bonds between the hydroxyl groups in position R6 or R7 of the ring A and position R4' or R5' of the ring B of the polyphenol ligands and the catalytic residues of the binding site and formation of a conjugated π-system that stabilizes the interaction with the active site (41). These results are in general agreement with the mechanism of action proposed for acarbose (50).

Tannins are another heterogenous polyphenol group widely distributed in the plant kingdom that are often present in unripe fruits, but can disappear during ripening. They have a relatively high molecular weight and can be classified into two major classes: hydrolysable tannins and condensed tannins. Hydrolysable tannins are subdivided into gallotannins, derived from gallic acid [***2***] units linked to a sugar moiety), while condensed tannins are complex polymers, where the building blocks are usually catechins and flavonoids (51).



2 gallic acid

Several polyphenolic compounds presenting α-amylase inhibitory activity are shown at Figures 2, 3, and 4. Tannins could cause several effects on the biological system because they are potential metal ion chelators and protein precipitation agents forming insoluble complexes with proteins, as well as biological oxidants (52). Tannic acid and tannin-rich nonalcoholic components of red wine have been shown to reduce serum glucose levels after starch-rich meals in a study of patients with non-insulin dependent diabetes mellitus (53). As the mechanism involved in this anti-hyperglycemic effect is unknown, it is possible that tannins can inhibit α-amylase activity *in situ*. The ability to strongly bind to proteins forming insoluble and indigestible complex is the basis of their extensive use in the leather industry (tanning process), and for the treatment of diarrhea, bleeding, skin injuries (54) and probably it is the action mechanism to cause inhibition of the enzyme α-amylase.

Terpenoids are compounds that comprise various structures commonly found in nature with a several function in plants and animals. They usually arise from head-to-tail joining of isoprene units and a combination of two or more isoprene units divide the terpenoids in monoterpene (C_{10}), sesquiterpene (C_{15}), diterpene (C_{20}), sesterterpene (C_{25}), triterpene (C_{30}) and tetraterpene (C_{40}) (55).

Triterpenoids are a large and structurally diverse group of natural products derived from squalene [***33***] or related acyclic 30-carbon precursors (56) with several potential uses in medicine. Some triterpenoids with well-characterized biological activities include sterols, steroids, and saponins (57).

A range of real and potential usable biological effects are being studied for triterpenoids. Anti-inflammatory, analgesic, antimicrobial, antimycotic, antiviral, antiplasmodial, antiulcerogenic, anticariogenic, immunomodulatory, vascular protective, anti-obese, anticancer and tonic effects are ones the use related uses for this class of compound (58, 59). Hepato and cardioprotective activity were also related for triterpenoids (59-61). Triterpenoids represent a promising and expanding source for biologically active natural compounds whose potential for research and development of new substances with pharmacologic activity. However, despite the fact that triterpenoids are widely distribute in plants, inhibitory α-amylase activity was related only for oleanane, ursane and lupane types and the mechanism by which this activity occur still unknown. Some terpenes presenting inhibitory activity on α-amylase are shown at Figure 5.

CONCLUSION

α-Amylase, a salivary or pancreatic enzyme plays an important role in early breakdown of complex carbohydrates into simple molecules. Modulation of α-amylase activity affects the utilization of carbohydrates as an energy source and stronger is this modulation; more significant is the reduction is the breakdown of complex carbohydrates. Majority of studies have focused on the anti-amylase phenolic compounds.

The action mechanism proposed for inhibitory capacity of flavonoids correlated the

potency of inhibition of these compounds with the number of hydroxyl groups on the B ring of the flavonoid skeleton with the formation of hydrogen bounds between the hydroxyl groups of the polyphenol ligands and the catalytic residues of the binding site of the enzyme. The high inhibitory capacity is observed in flavonols and flavones groups.

The main inhibitory effects of the tannins is related with its the ability to strongly bind to carbohydrates and proteins. However, Kandra *et al*. (2004) suggested that the interaction between tannins, such galloylated quinic acid, and human α-amylase is also correlated with free OH groups in the tannin, that are able to participate in hydrogen bonding (51). However, in this review is possible to note that tannins are not always an effective inhibitor of α-amylase.

The significant differences in inhibitory activity for α-amylase were shown in luteolin-7-*O*-glucoside [***9b***] from different studies. This compound showed 100% of inhibition in one study and 50% of inhibition in another. The same methodology was carried out to evaluate this activity in both studies, however the concentration of tested compound and incubation time of enzyme were different for both (6, 62).

Inhibitory activities ranging from 100% to 50% were also observed for fisetin [***4c***] and luteolin [***9a***]. The analyzed studies showed differences in the concentration of tested compound, incubation time of enzyme and substrate solution used (6, 41, 62), and the impact that changes can be noted in the obtained results.

Differences in percentage of inhibition were also observed for rosmarinic acid [***28***] and daidzein [***15a***]. Inhibitions of 85% and 50% for rosmarinic acid and 23% and 55% for daidzein were shown in the assays using starch and ρ-nitrophenyl-α-D- maltopentaoside (PNPG) as a substrate, respectively (6, 41, 62, 63).

The comparison of inhibitory activity to α-amylase showing in the studies allows to observe significant differences in percentage of inhibition for the same compound. This is due a several number of valuable assay methods for available the amylase activity. Between them, two types of assays are largely used to determine the action of α-amylase. One is based on increase in reducing power of the substrate by the dinitrosalicylic acid (DNS) reagent (64), whereas the other is based on the change of the iodine- staining properties of the substrate (65). Thus, some modifications in this assays reported by researchers could express different results for α-amylase inhibitory activity.

As the intake of phenolic compounds is associated with many beneficial effects, it is also necessary to consider the dose for humans, because it is possible to reduce α-amylase activity by consuming food or medicinal herbs rich in polyphenols with strong α-amylase activity, if it takes in consideration that this source of polyphenols possess different kinds of this compounds in variable concentration. Therefore, more available evidences are necessary about the safety of using natural α-amylase inhibitor.

Also, there is need for novel agents, therapeutic strategies or designing functional foods that could act on the physiological regulation of sugar uptake, blood sugar levels, and prevention of oral diseases.

For the future, a standardized protocol to search potential inhibitors maybe should be designed in order to minimize the differences among obtained results.

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Table 1. Plants with α-amylase inhibitory activity

Plant	Parts used	Type of extract	Activity (% inhibition) (concentration)	Control	References
Acanthaceae					
Andrographis paniculata Nees	Leaf and aerial parts	Ethanol	52.5 (50.9mg/mL) 54.8 (11.3mg/mL)	Acarbose with 50.1% of maxim inhibition at 10mg/mL	(66)
Actinidiaceae					
Actinidia deliciosa (A.Chev.) C.F.Liang & A.R.Ferguson	Leaf	Methanol 90%	50 (0.0429mg/mL)	Voglibose with 50% of inhibition at 0.0466mg/mL	(67)
Amaranthaceae					
Amaranthus caudatus var. Oscar blanco	Seed	Methanol	94.71 (1mg/mL)	Non-treated enzyme	(31)
		Ethyl acetate	93.82 (0.5mg/mL)		
		Hexane	90.64 (0.1mg/mL)		
Amaranthus caudatus var. Victor red	Seed	Methanol	95.12 (1mg/mL)		
		Ethyl acetate	84.03 (0.25mg/mL)		
		Hexane	91.63 (0.1mg/mL)		
Anacardiaceae					
Mangifera indica L.	Bark	Ethanol	84.1 (1mg/mL)	*Phaseolus vulgaris* with 59.4% of inhibition at 0.0125mg/mL	(36)
Apocynaceae					
Holarrhena floribunda (Don) Durand & Schinz	Leaf	Aqueous buffered	20-45 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Asteraceae					
Leontopodium ochroleucum Beauverd	Aerial part	Methanol	35.8 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Taraxacum officinale Web. ex Wigg.	Herb	Aqueous buffered	20-45 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Varthemia iphionoides Boiss	Aerial part	Aqueous Ethanol	67.6 (0.2mg/mL) 70.5 (0.2mg/mL)	Non-treated enzyme	(68)
Balanitaceae					
Balanites aegyptiaca L.	Bark	Aqueous buffered	45-75 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Coniferae					
Ginkgo biloba L.	Leaf	Ethanol	70 (50mg/mL)	Non-treated enzyme	(69)

Crassulaceae					
Rhodiola rosea L.	Rhizome	Methanol	78 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Ericaceae					
Vaccinium myrtillus L.	Leaf	Aqueous buffered	> 75 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Vaccinium uliginosum L.	Leaf and wood	Methanol	80.7 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Euphorbiaceae					
Phyllanthus amarus Schum. et Thonn.	Whole plant	Hexane	24.3 (1mg/mL)	*Triticum aestivum* with 32% of inhibition at 5 unit/mL	(70)
Phyllanthus maderaspatensis L.	Whole plant	Ethanol	47.6 (1mg/mL)	*Phaseolus vulgaris* with 59.4% of inhibition at 0.0125mg/mL	(36)
Geraniaceae					
Geranium pratense L.	Aerial part	Methanol	43.9 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Grossulariaceae					
Ribes pulchellum Turcz.	Aerial part	Methanol	78.9 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Lamiaceae					
Marrubium radiatum Delile ex Benth.	Aerial part	Methanol	50 (0.0611mg/mL)	Acarbose with 50% of inhibition at 0.05mg/mL	(33)
Melissa officinalis L.	Leaf	Ethanol	50 (3.33mg/mL)	Non-treated enzyme	(63)
		Aqueous buffered	50 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Ocimum tenuflorum L.	Leaf	Chloroform	24.57 (10mg/mL)	Acarbose with 50 % of inhibition at 1.22mg/mL	(34)
Origanum vulgare L.	Leaf	Ethanol	42 (3.33mg/mL)	Non-treated enzyme	(63)
Rosmarinus officinalis L.	Leaf	Aqueous buffered	60 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Salvia acetabulosa L.	Aerial part	Methanol	50 (0.0912mg/mL)	Acarbose with 50% of inhibition at 0.05mg/mL	(33)
Fabaceae					
Cajanus cajan L	Seed	Aqueous buffered	100 (2mg protein)	Non-treated enzyme	(71)
Galega officinalis L.	Herb	Aqueous buffered	35 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)

Olneya tesota A.Gray	Seed	Aqueous	65 (0.0044mg/mL)	Non-treated enzyme	(72)
Phaseolus vulgaris L.	Pericarp	Aqueous buffered	45-75 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Tamarindus indica L.	Leaf	Aqueous buffered	90 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Malvaceae					
Hibiscus sabdariffa Linn.	Flower	Methanol 50%	100 (10mL/g fr. wt.)	Non-treated enzyme	(73)
Meliaceae					
Khaya senegalensis (Desr.) A. Juss.	Bark	Aqueous buffered	45-75 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Myrsinaceae					
Embelia ribes Burm. f.	Seed	Ethanol	59.3 (1mg/mL)	*Phaseolus vulgaris* with 59.4% of inhibition at 0.0125mg/mL	(36)
Myrtaceae					
Psidium guajava var. *Pomiferum*	Leaf	Aqueous	98 (200mg/mL)	Non-treated enzyme	(29)
Psidium guajava L.		Ethanol	31.7 (1.5mg/mL)	Acarbose wiith 52.1% of inhibition at 1.5mg/mL	(37)
Syzygium cumini (L.) Skeels	Leaf	Chloroform	22.31 (10mg/mL)	Acarbose with 50 % of inhibition at 1.22mg/mL	(34)
	Seed	Aqueous	98 (200mg/mL)	Non-treated enzyme	(29)
Nyctaginaceae					
Bougainvillea spectabilis Wild.	Leaf	Chloroform	29.43 (25mg/mL)	Acarbose with 50 % of inhibition at 1.22mg/mL	(34)
Paeoniaceae					
Paeonia anomala L.	Root	Methanol	33.1 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Pinaceae					
Cedrus libani A. Rich	Essential oils from cones	Aqueous buffered	31 (1mg/mL)	Acarbose with 50 % of at inhibition 1.22mg/mL	(33)
Polygalaceae					
Securidaca longepedunculata Fresen.	Root	Aqueous buffered	20-45 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Portulacaceae					

Talinum portulacifolium Asch. Ex Schweinf.	Leaf	Methanol	60.66 (1mg/mL)	Acarbose with 50.33% of inhibition at 0.05mg/mL	(74)
Punicaceae					
Punica granatum L.	Fruit rind	Ethanol	68.2 (1mg/mL)	*Phaseolus vulgaris* with 59.4% of inhibition at 0.0125mg/mL	(36)
Rosaceae					
Pentaphylloides fruticosa (L.) O.Schwarz	Leaf and branch	Methanol	31.2 (0.3mg/mL)	Acarbose with 79.6% of inhibition at 0.1mg/mL	(32)
Rubiaceae					
Mitragyna inermis (Willd.) O. Ktze.	Leaf	Aqueous buffered	75 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)
Rutaceae					
Murraya koenigii L.	Leaf	Chloroform	56.64 (25mg/mL)	Acarbose with 50 % of at inhibition 1.22mg/mL	(34)
Saxifragaceae					
Bergenia ciliata, Haw.	Rhizome	Methanol 50% Aqueous Ethyl acetate	93.5 (150mg/mL) 65.3 (150mg/mL) 84.3 (150mg/mL)	Non-treated enzyme	(75)
Theaceae					
Camellia sinensis L. Del.	Leaf	Aqueous buffered	45-75 (200mg/mL)	Acarbose with inhibition higher than 75% at 200mg/mL	(6)

Table 2. Natural compounds with α-amylase inhibition

Compound	Source	Activity	Control	Reference
Flavonol				
quercetin (***3a***)	-	82% of inhibitory activity (50% inhibition at 21,4µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
3,7,3'-trimethoxy quercetin ***(3b***)	*Varthemia iphionoides* Boiss. & Blanche (Asteraceae)	32% of inhibitory activity (100µM)	Non-treated enzyme	(68)
quercetrin (***3c***)	*Kalopanax pictum* (Araliaceae)	± 45% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
rutin (***3d***)	*Sophora japonica* L.(Leguminosae)	± 40% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
kaempferol (***3e***)	-	34% of inhibitory activity (50%	Acarbose with 99% of maxim inhibition	(41)

		inhibition was not determined)	(50% inhibition at 0,996µM)	
5,7,4'- trihydroxy-3-methoxyflavone (***3f***)	*Varthemia iphionoides* Boiss. & Blanche (Asteraceae)	99% of inhibitory activity (100µM)	Non-treated enzyme	(68)
5,4'- dihydroxy-3,7-dimethoxyflavone (***3g***)	*Varthemia iphionoides* Boiss. & Blanche (Asteraceae)	98% of inhibitory activity (100µM)	Non-treated enzyme	(68)
5, 4'- dihydroxy-3, 6, 7-trimethoxyflavone (***3h***)	*Varthemia iphionoides* Boiss. & Blanche (Asteraceae)	77% of inhibitory activity (100µM)	Non-treated enzyme	(68)
astragalin (***3i***)	*Polygala japonica* Houtt. (Polygalaceae)	± 55% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
hyperin (***3j***)	*Kalopanax pictum* (Araliaceae)	± 55% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
isorhamnetin (***4a***)	-	35% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
narcisin (***4b***)	*Sophora japonica* L. (Leguminosae)	± 70% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
fisetin (***4c***)	-	50% inhibition between 0,4-0,6mM	Acarbose with 50% inhibition at < 0,1mM	(6)
	-	85 (50% inhibition at 19,6 µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
myricetin (***4d***)	-	79% of inhibitory activity (50% inhibition at 30,2 µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
quercetin dimer (***5a***)	*Allium cepa* L. (Liliaceae)	87% of inhibitory activity	Acarbose	(76)
(4′-*O*-β-D-glucopyranoside of quercetin dimer) (***5b***)	*Allium cepa* L. (Liliaceae)	56% of inhibitory activity	Acarbose	(76)
Quercetagetin (***6***)	-	97% of inhibitory activity (50% inhibition at 10,2µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
kaempferol–3- O-[6"-O-(3-hydroxy-3-methylglutaroyl) glucoside] ***(7***)	*Polygala japonica* Houtt. (Polygalaceae)	100% of inhibitory activity	Acarbose with 50% inhibition at 5-50µg/mL	(62)
auranetin-5-methylether (***8***)	*Varthemia iphionoides* Boiss. & Blanche (Asteraceae)	18% of inhibitory activity (100µM)	Non-treated enzyme	(68)
Flavone				
Luteolin (***9a***)	*Lonicera japonica* Thunb. (Caprifoliaceae)	100% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)

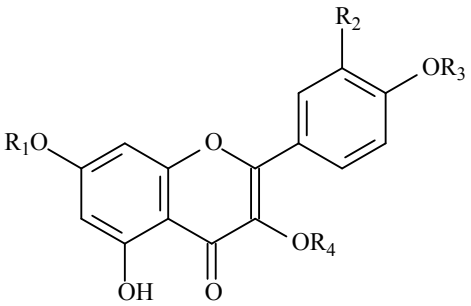
	-	50% inhibition at 0,2mM	Acarbose with 50% inhibition at < 0,1mM	(6)
	-	88% of inhibitory activity (50% inhibition at 18,4 µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
	Allium cepa L. (Liliaceae)	82% of inhibitory activity (50% inhibition was not determined)	Acarbose	(76)
luteolin -7-O-glucoside (***9b***)	*Salix gracilistyla* Miq. (Salicaceae)	100 % of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
	-	50% inhibition between 0,2-0,4mM	Acarbose with 50% inhibition at < 0,1mM	(6)
acacetin (***9c***)	-	14% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
apigetrin (***9d***)	-	50% inhibition at < 0,2mM	Acarbose with 50% inhibition at < 0,1mM	(6)
lonicerin ***(9e***)	*Lonicera japonica* Thunb. (Caprifoliaceae)	± 55 % of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
rhoifolin (***9f***)	*Lonicera japonica* Thunb. (Caprifoliaceae)	± 60 % of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
diosmetin (***10a***)	-	19% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
genkwanin (***10b***)	-	17% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
scutellarein (***11a***)	-	98 % of inhibitory activity (50% inhibition at 9,64 µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
eupafolin (***11b***)	-	99% of inhibitory activity (50% inhibition at 48µM)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
Bilobetin (***12***)	*Ginkgo biloba* L. (Ginkgoaceae)	± 25% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
Flavanone				
naringenin (***13a***)	-	26% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
hesperetin (***13b***)	-	39% of inhibitory activity (50%	Acarbose with 99% of maxim	(41)

		inhibition was not determined)	inhibition (50% inhibition at 0,996µM)	
hesperidin (***13c***)	*Citrus unshiu* (Swingle) Marcow. (Rutaceae)	± 60% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
Flavanonol				
Alliuocide G (***14a***)	*4llium cepa* L. (Liliaceae)	96% of inhibitory activity	Acarbose	(76)
Isoflavone				
daidzein (***15a***)	-	± 55% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
	-	23% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
genistein (***15b***)	-	± 30% of inhibitory activity (5mg/mL)	Acarbose with 50% inhibition at 5-50µg/mL	(62)
	-	25% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
Proanthocyanidin				
catechin (***16a***)	-	13% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
catechin hydrate (***16a***)	-	50% inhibition at > 20 mM	Acarbose with 50% inhibition at 5,7µM	(49)
epicatechin (***16b***)	-	10% of inhibitory activity (50% inhibition was not determined)	Acarbose with 99% of maxim inhibition (50% inhibition at 0,996µM)	(41)
(-)-catechin gallato (***16c***)	*Bergenia ciliate* (Haw) (Saxifragaceae)	50% inhibition at 401 µM	Non-treated enzyme	(75)
(-)-epicatechin gallato (***16d***)	*Bergenia ciliate* (Haw) (Saxifragaceae)	50% inhibition at 739 µM	Non-treated enzyme	(75)
epicatechin gallate (***16d***)	-	50% inhibition at 1,5 mM	Acarbose with 50% inhibition at 5,7µM	(49)
epigallocatechin gallate (***17***)	-	50% inhibition at 1,4 mM	Acarbose with 50% inhibition at 5,7µM	(49)
theaflavin (***18a***)	-	50% inhibition at 67 µM	Acarbose 50% inhibition at 5,7µM	(49)
theaflavin monogallate (***18b***)	-	50% inhibition at 5,5 µM	Acarbose 50% inhibition at 5,7µM	(49)
theaflavin digallate (***18c***)	-	50% inhibition at 2,9 µM	Acarbose 50% inhibition at	(49)

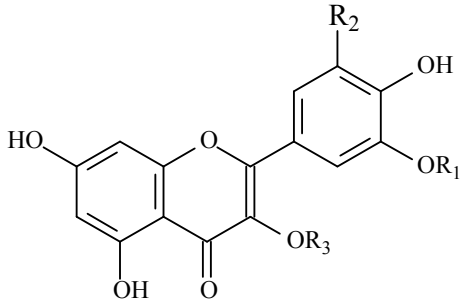
			5,7µM	
Others				
2-(3,4-Dihydroxybenzoyl)-2,4,6-trihydroxy-3 (2*H*)-benzofuranone (***19***)	*Allium cepa* L. (Liliaceae)	88% of inhibitory activity	Acarbose	(76)
Aceronidin (***20***)	*Malpighia emarginata* DC. (Malpighiaceae)	34% of inhibitory activity (50% inhibition at 820µM)	Non-treated enzyme	(77)
Tannin				
"Aleppo tannin" (Gallotanin) (***21***)	"Gall nut"	Dissociation constants of the inhibitor containing complexes EI (K_{EI}) 0,82µg mL^{-1} *vs* dissociation constants of the inhibitor containing complexes ESI (K_{ESI}) 3,32µg mL^{-1}	Acarbose with dissociation constants of the inhibitor containing complexes EI (K_{EI}) 0,45µg mL^{-1} *vs* dissociation constants of the inhibitor containing complexes ESI (K_{ESI}) 0,065µgmL^{-1}	(54)
Pedunculagin (***22a***)	*Rubus suavissimus* S. LEE (Rosaceae)	14% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
1(□)-*O*-galloyl pedunculagin (***22b***)	*Rubus suavissimus* S. LEE (Rosaceae)	56% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
1 (α)- galloyl pedunculagin (***22b***)	*Rubus suavissimus* S. LEE (Rosaceae)	36% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
strictinin (***23a***)	*Rubus suavissimus* S. LEE (Rosaceae)	52% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
sanguiin H5 (***23b***)	*Rubus suavissimus* S. LEE (Rosaceae)	56% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
roshenin B (1-desgalloyl sanguiin H6 (***23c***)	*Rubus suavissimus* S. LEE (Rosaceae)	54% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
sanguiin H2 (***23d***)	*Rubus suavissimus* S. LEE (Rosaceae)	36% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
sanguiin H10 (***23e***)	*Rubus suavissimus* S. LEE (Rosaceae)	23% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)

sanguiin H11 (***23f***)	*Rubus suavissimus* S. LEE (Rosaceae)	1% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
lambertianin A (***23g***)	*Rubus suavissimus* S. LEE (Rosaceae)	36% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
sanguiin H6 (***23h***)	*Rubus suavissimus* S. LEE (Rosaceae)	19% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
rubusuaviin A (***24a***)	*Rubus suavissimus* S. LEE (Rosaceae)	60% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
rubusuaviin B (***24b***)	*Rubus suavissimus* S. LEE (Rosaceae)	60% of inhibitory activity	theaflavin-3,3_-di-*O*-gallate with 83% of inhibition	(78)
rubusuaviin C (***24c***)	*Rubus suavissimus* S. LEE (Rosaceae)	17% of inhibitory activity	theaflavin-3,3-di-*O*-gallate with 83% of inhibition	(78)
rubusuaviin D (***24d***)	*Rubus suavissimus* S. LEE (Rosaceae)	52% of inhibitory activity	theaflavin-3,3-di-*O*-gallate with 83% of inhibition	(78)
rubusuaviin E (***24e)***	*Rubus suavissimus* S. LEE (Rosaceae)	14% of inhibitory activity	theaflavin-3,3-di-*O*-gallate with 83% of inhibition	(78)
rubusuaviin F (***24f***)	*Rubus suavissimus* S. LEE (Rosaceae)	34% of inhibitory activity	theaflavin-3,3-di-*O*-gallate with 83% of inhibition	(78)
	-	50% inhibition at < 0,2mM	Acarbose with 50% inhibition at < 0,1mM	(6)
Tannic acid (***25***)	-	Dissociation constants of the inhibitor containing complexes EI (K_{EI}) between 8-9µg mL^{-1} *vs* dissociation constants of the inhibitor containing complexes ESI (K_{ESI}) between 45-49µgmL^{-1}	-	(51)
Cinnamic acid derivatives				
chlorogenic acid (***26***)	-	50% inhibition between 1,4-1,6mM	Acarbose with 50% inhibition at < 0,1mM	(6)
isochlorogenic acid (***27***)	-	50% inhibition between 0,6-0,8mM	Acarbose with 50% inhibition at < 0,1mM	(6)
rosmarinic acid (***28***)	-	85% of inhibitory activity	Non-treated enzyme	(63)

	-	50% inhibition between 1,4-1,6mM	Acarbose with 50% inhibition at < 0,1mM	(6)
esculin (***29***)	-	50% inhibition between 1,4-1,6mM	Acarbose with 50% inhibition at < 0,1mM	(6)
Terpenes				
Squalene (***33***)	-	30% of inhibitory activity	Non-treated enzyme	(31)
Lupeol (***34***)	-	± 50% of inhibitory activity	α-Amylase inhibitor from wheat seed *Triticum aestivum*	(70)
3-O-[(9Z)-9exadec-9-enoyl]-□-amyrin (***35***)	*Spondias mombin* L. (Anacardiaceae)	57% of inhibitory activity	Acarbose	(79)
oleanolic acid (***36a***)	-	± 55% of inhibitory activity	α-Amylase inhibitor from wheat seed *Triticum aestivum*	(70)
ursolic acid (***36b***)	-	± 87, 5% of inhibitory activity	α-Amylase inhibitor from wheat seed *Triticum aestivum*	(70)
mixture of lambertianin C (***23i***), Sanguiin H10 (***23e***), and Sanguiin H6 (***23h***)	*Rubus idaeus* L. variety Glen Ample (Rosaceae)	± 75% of inhibitory activity	green tea with ± 99% of maxim inhibition	(80)
Mixture of gallic acid ***(2)***, proto-catechuic acid (***30***), caffeic acid (***32a***), ellagic acid ***(31),*** ferulic acid ***(32b)***, quercetin (***3a***) and kaempferol (***3e***)	*Centratherum anthelminticum* (L.) Kuntze (Asteraceae)	90% of inhibitory activity (50% inhibition at 185µg)	Acarbose with 85% of maxim inhibition (50% inhibition at 17µg)	(81)
Isomeric mixture of oleanolic (***36a***) and ursolic acid (***36b***)	*Phyllanthus amarus* Schumach. & Thonn. (Euphorbiaceae)	± 65% of inhibitory activity (50% inhibition at 2,01µg)	α-Amylase inhibitor from wheat seed *Triticum aestivum*	(70)
Mixture of betulinic acid (***37***) and 3, 5, 7, 4'- tetrahydroxy flavanone (***14b***)	*Syzygium cumini* L. (Myrtaceae)	98% of inhibitory activity	Not determined	(29)

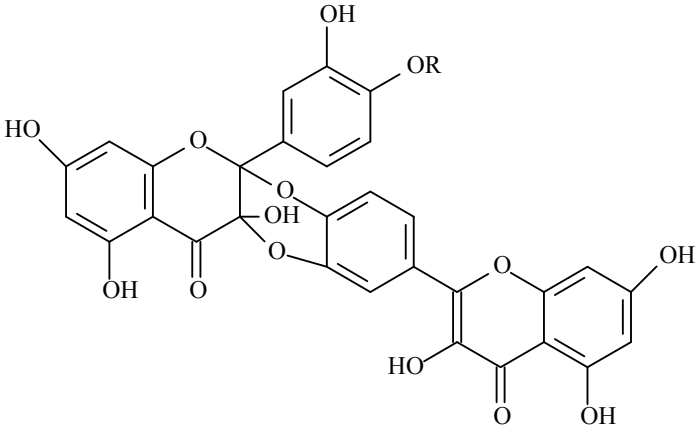


	R_1	R_2	R_3	R_4	
3a	H	OH	H	H	quercetin
3b	CH_3	OH	CH_3	OCH_3	
3c	H	OH	H	rham	quercetrin
3d	H	OH	H	r ham-glu	rutin
3e	H	H	H	H	kaempferol
3f	H	H	H	CH_3	
3g	CH_3	H	H	CH_3	
3h	CH_3	H	CH_3	CH_3	
3i	H	H	H	glu	astragalin
3j	H	OH	H	gal	hyperin

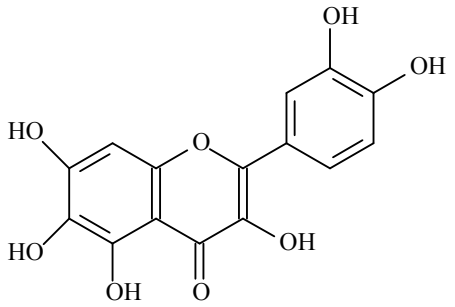


	R_1	R_2	R_3	
4a	CH_3	H	H	isorhamnetin
4b	CH_3	H	rham-glu	narcisin
4c	H	H	H	fisetin
4d	H	OH	H	myricetin

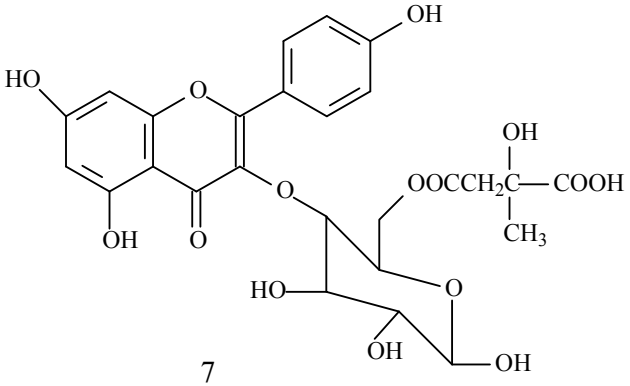
Figure 2. Flavonoids presenting α-amylase inhibition activity



	R
5a	H
5b	glu



6 quercetagetin



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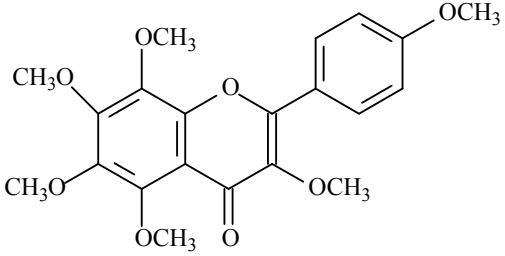
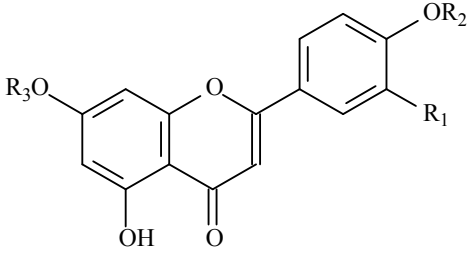
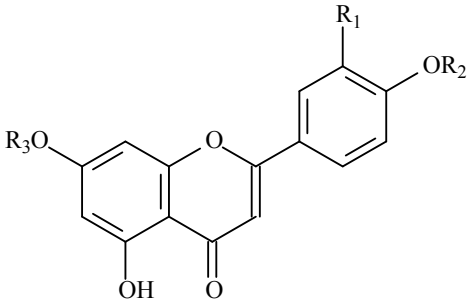


8 auranetin-5-methylether

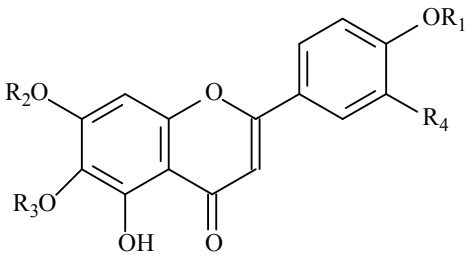


	R_1	R_2	R_3	
9a	OH	H	H	luteolin
9b	OH	H	glu	
9c	OH	CH_3	H	acacetin
9d	H	H	glu	apigetrin
9e	OH	H	glu-rham	lonicerin
9f	H	H	rham-glu	rhoifolin

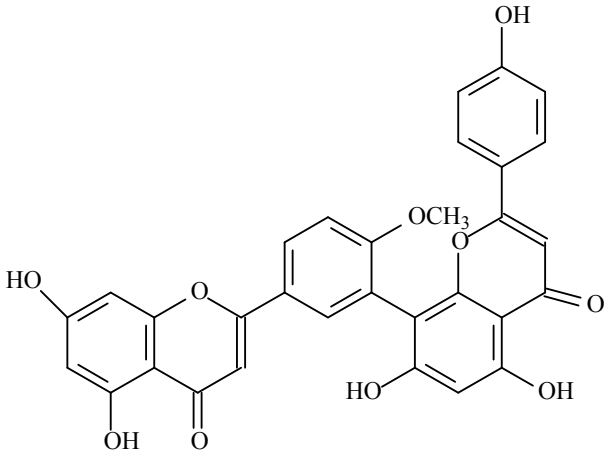
Figure 2. Flavonoids presenting α-amylase inhibition activity (….. Continued)



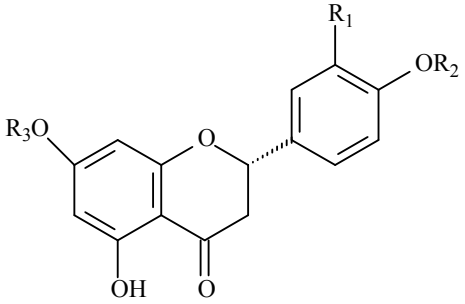
	R_1	R_2	R_3	
10a	OH	CH_3	H	diosmetin
10b	CH_3	CH_3	H	genkwanin



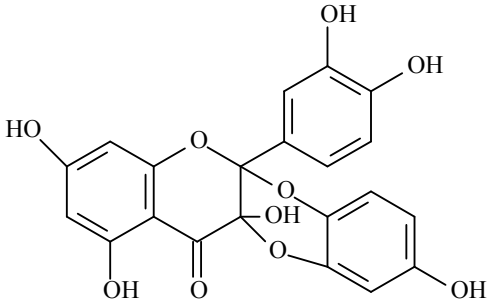
	R_1	R_2	R_3	R_4	
11a	H	H	H	H	scutellarein
11b	H	H	CH_3	OH	eupafolin



12 bilobetin



	R_1	R_2	R_3	
13a	H	H	H	naringenin
13b	OH	CH_3	H	hesperetin
13c	OH	CH_3	rham-glu	hesperidin



14a alliuocide G

Figure 2. Flavonoids presenting α-amylase inhibition activity (….. Continued)

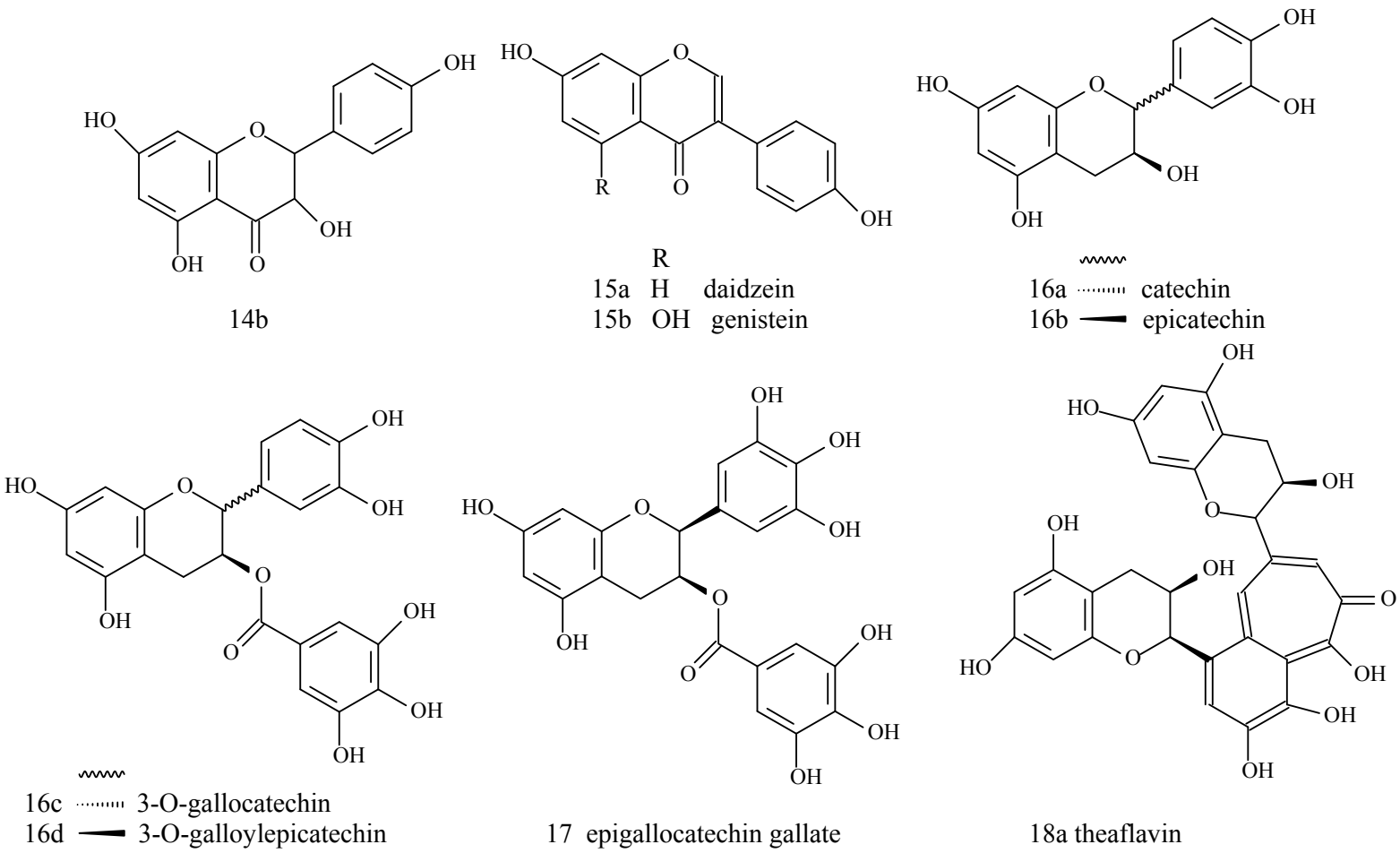
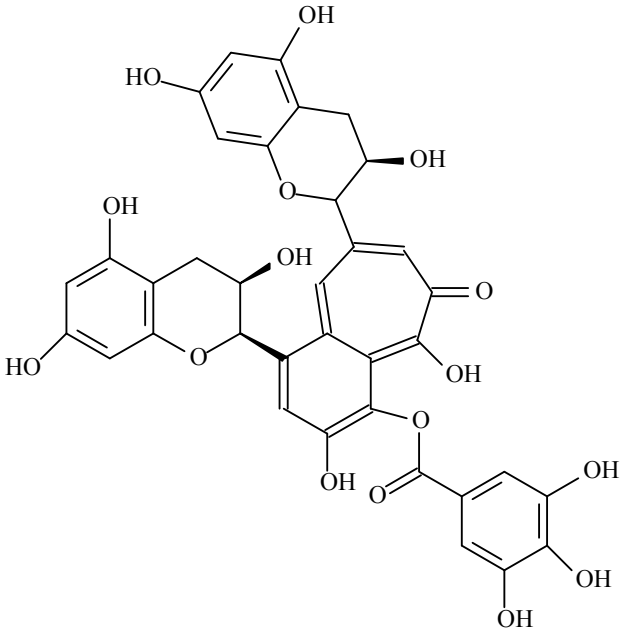
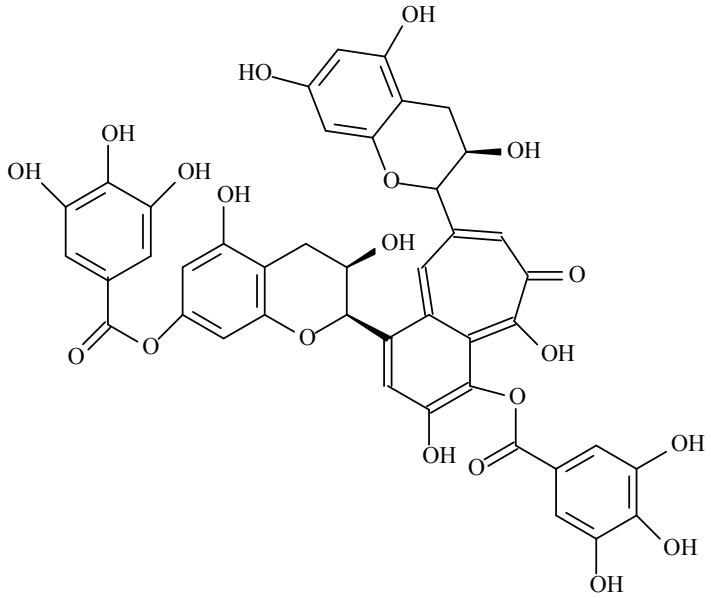


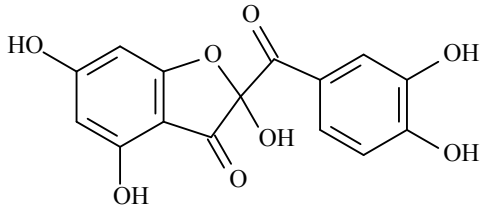
Figure 2. Flavonoids presenting α-amylase inhibition activity (….. Continued)



18b theaflavin monogallate



18c theaflavin digallate



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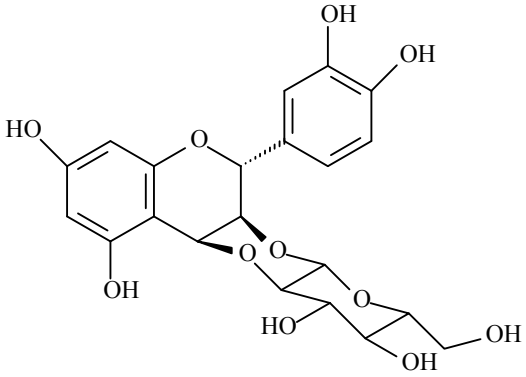
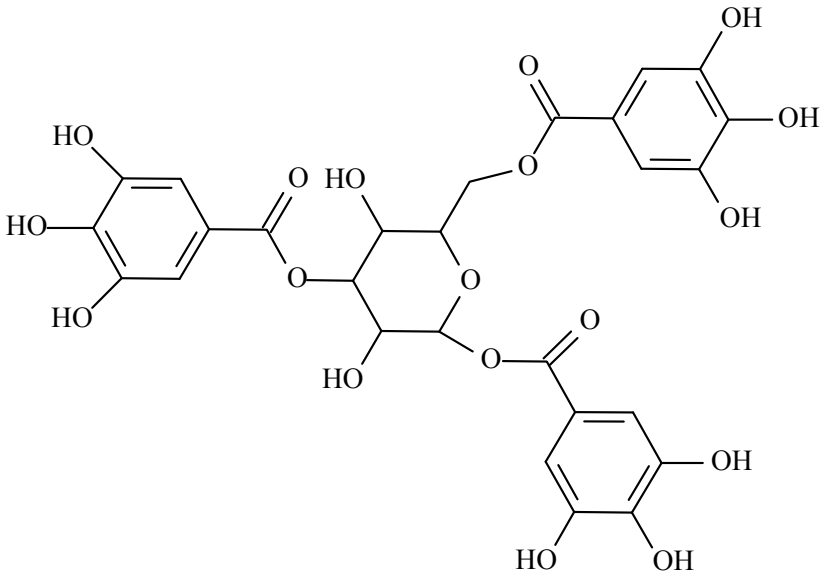
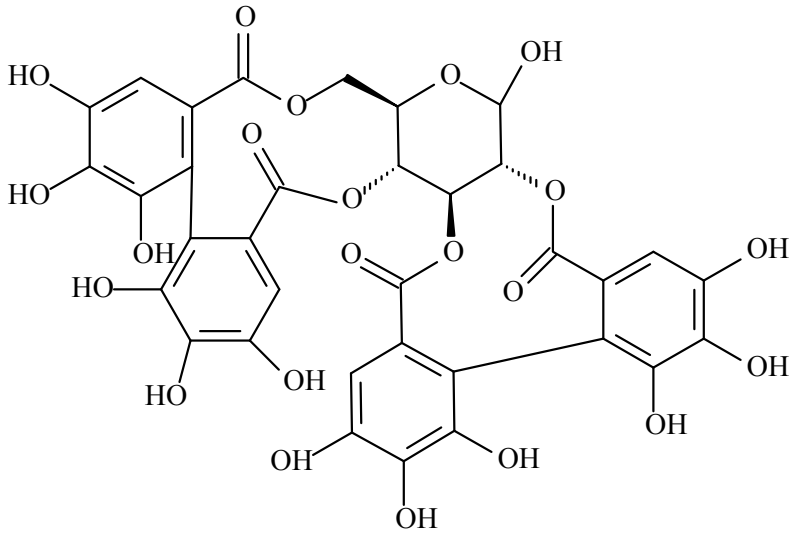


20 aceronidin

Figure 2. Flavonoids presenting α-amylase inhibition activity (Continued)

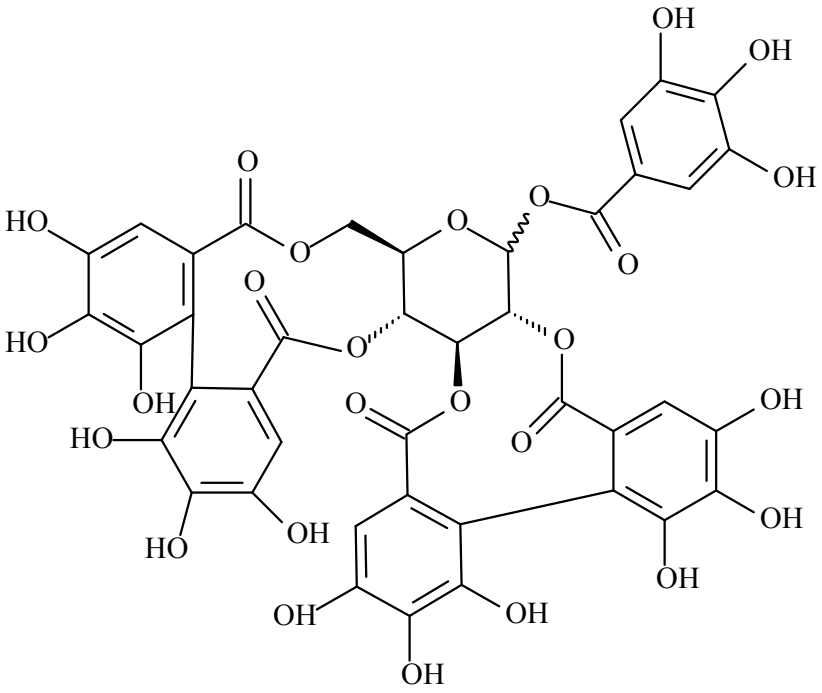


21 gallotannin

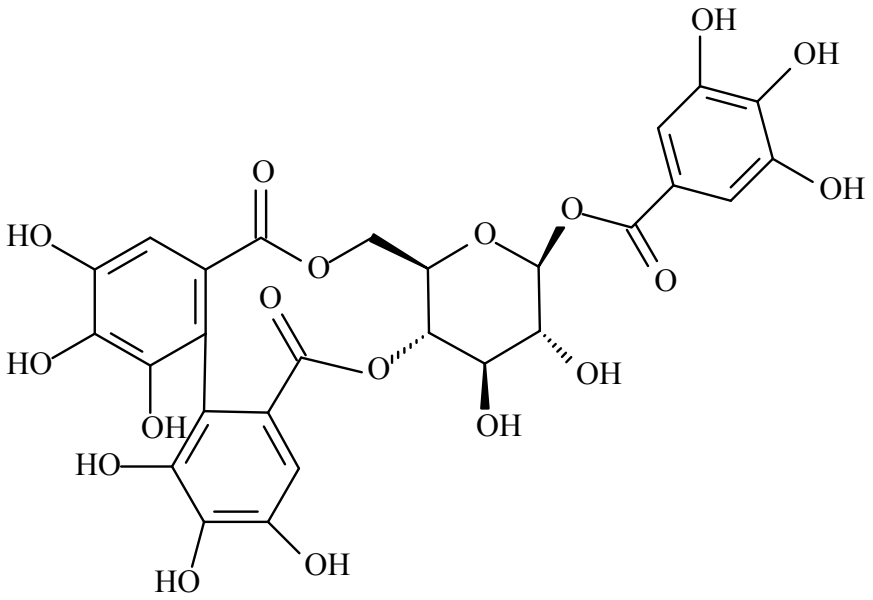


22a pedunculagin

Figure 3. Tannins presenting α-amylase inhibition activity

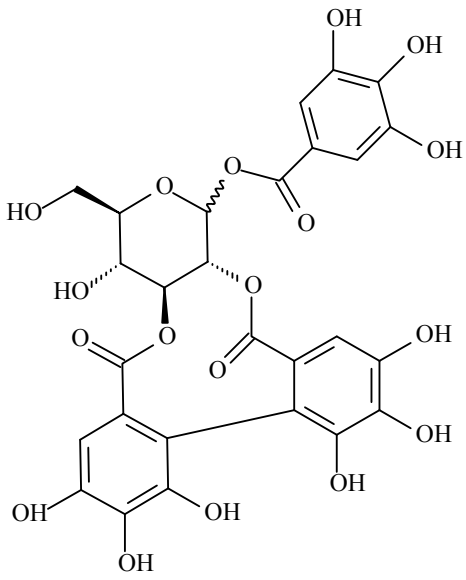


22b 1-O-galloyl pedunculagin

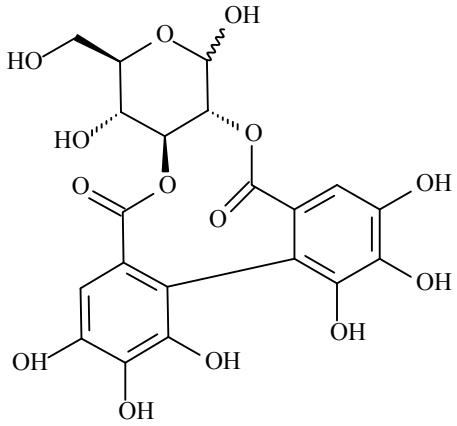


23a strictinin

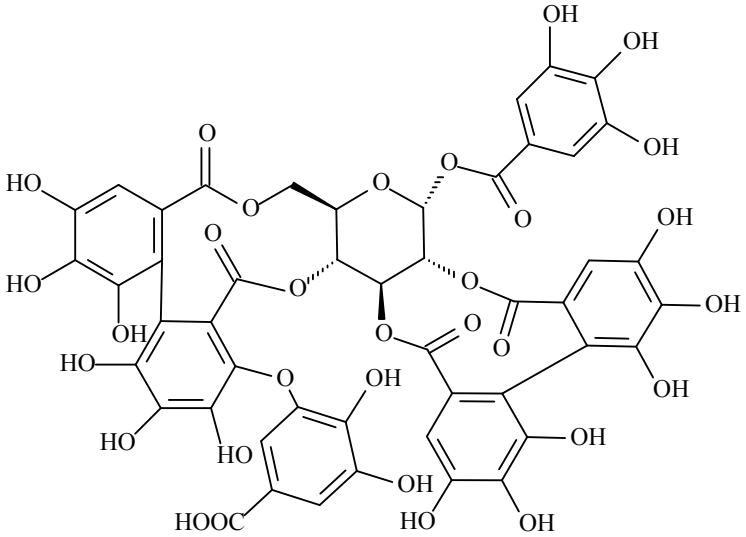
Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



23b sanguiin H5

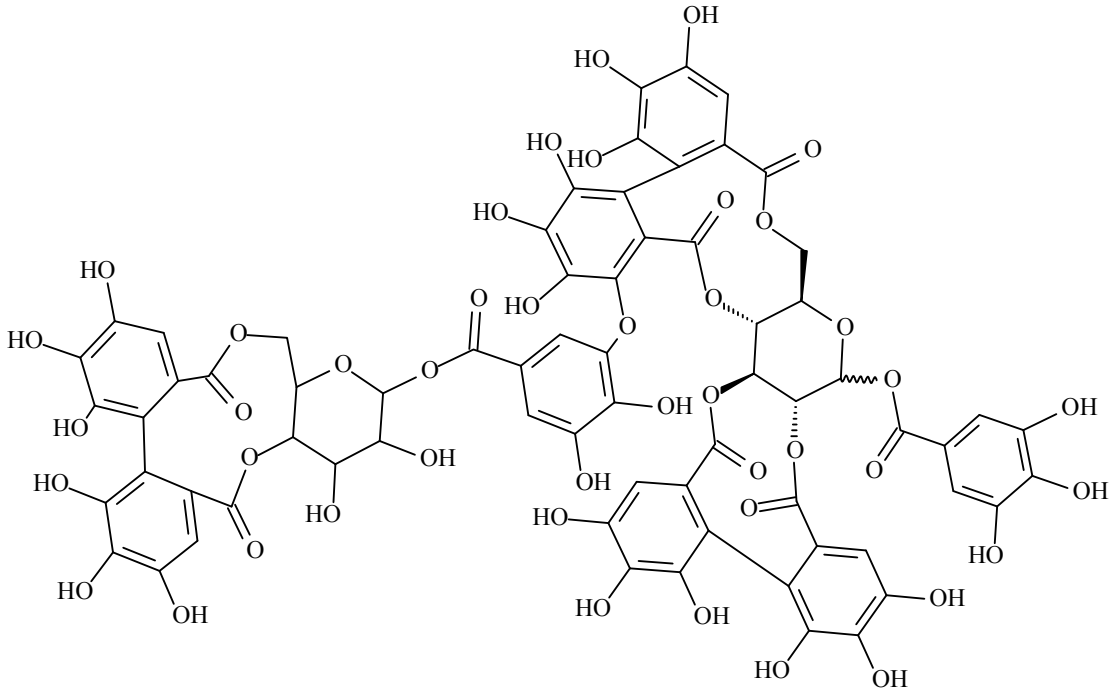


23c roshenin B



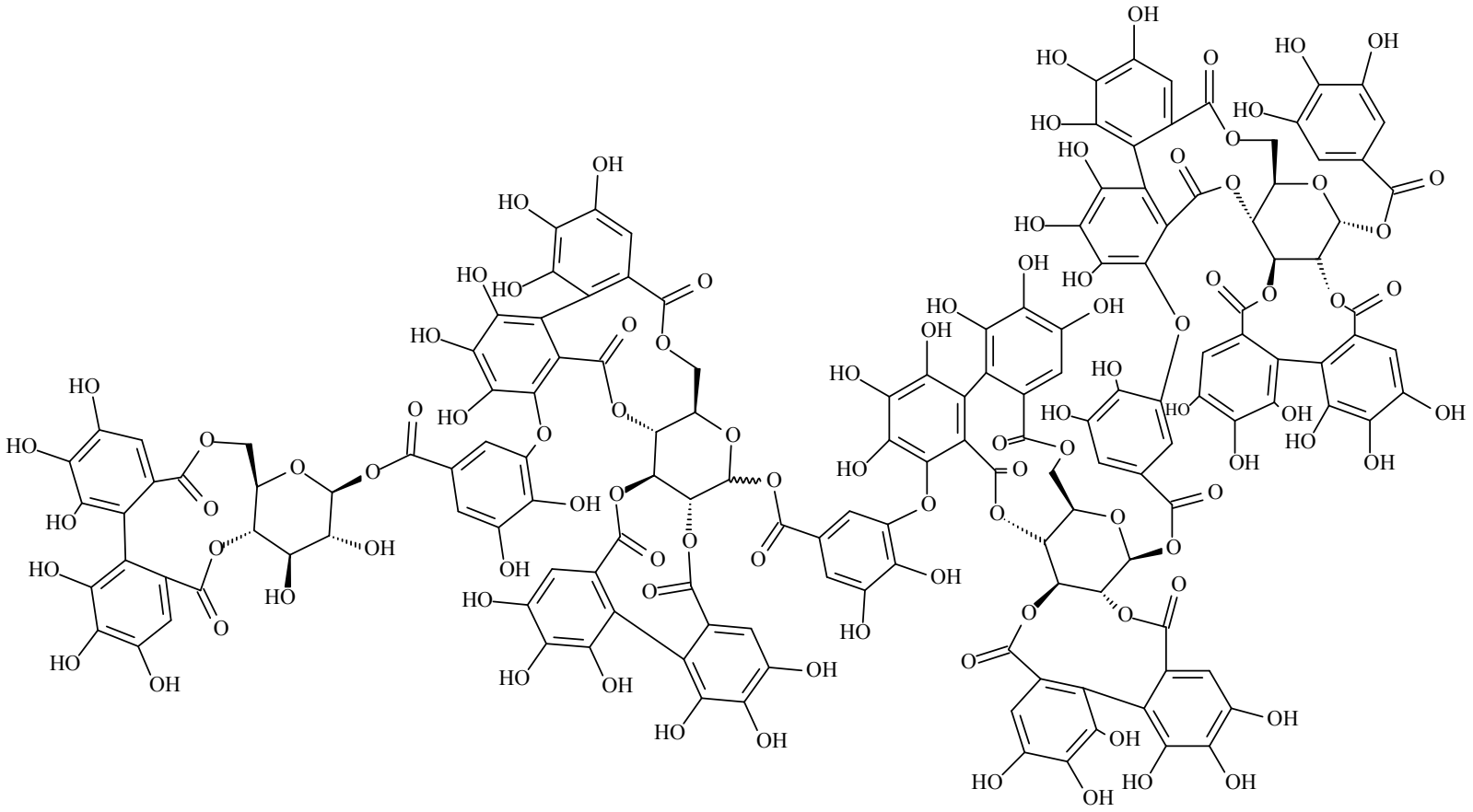
23d sanguiin H2

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



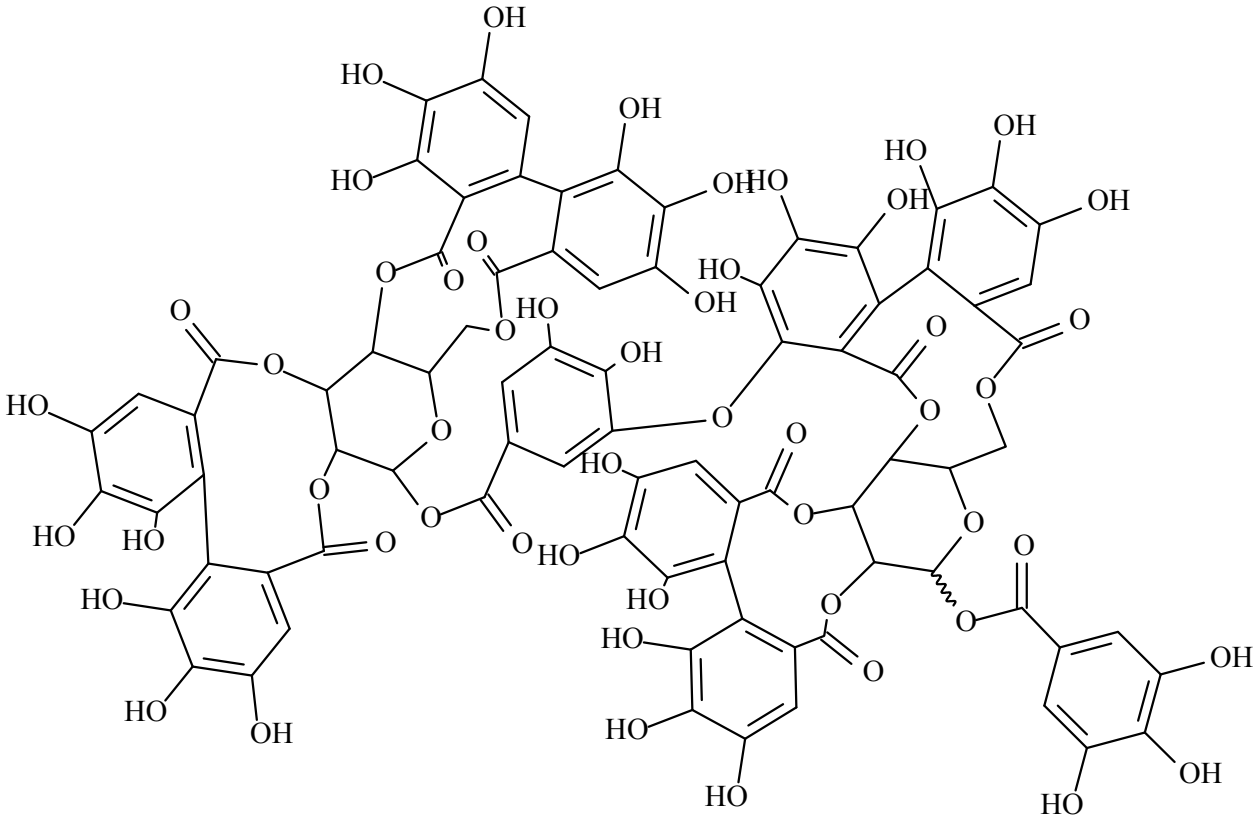
23e sanguiin H10

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



23f sanguiin H11

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



23g ~~~ = β lambertianin A
23h ~~~ = α sanguin H6

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)

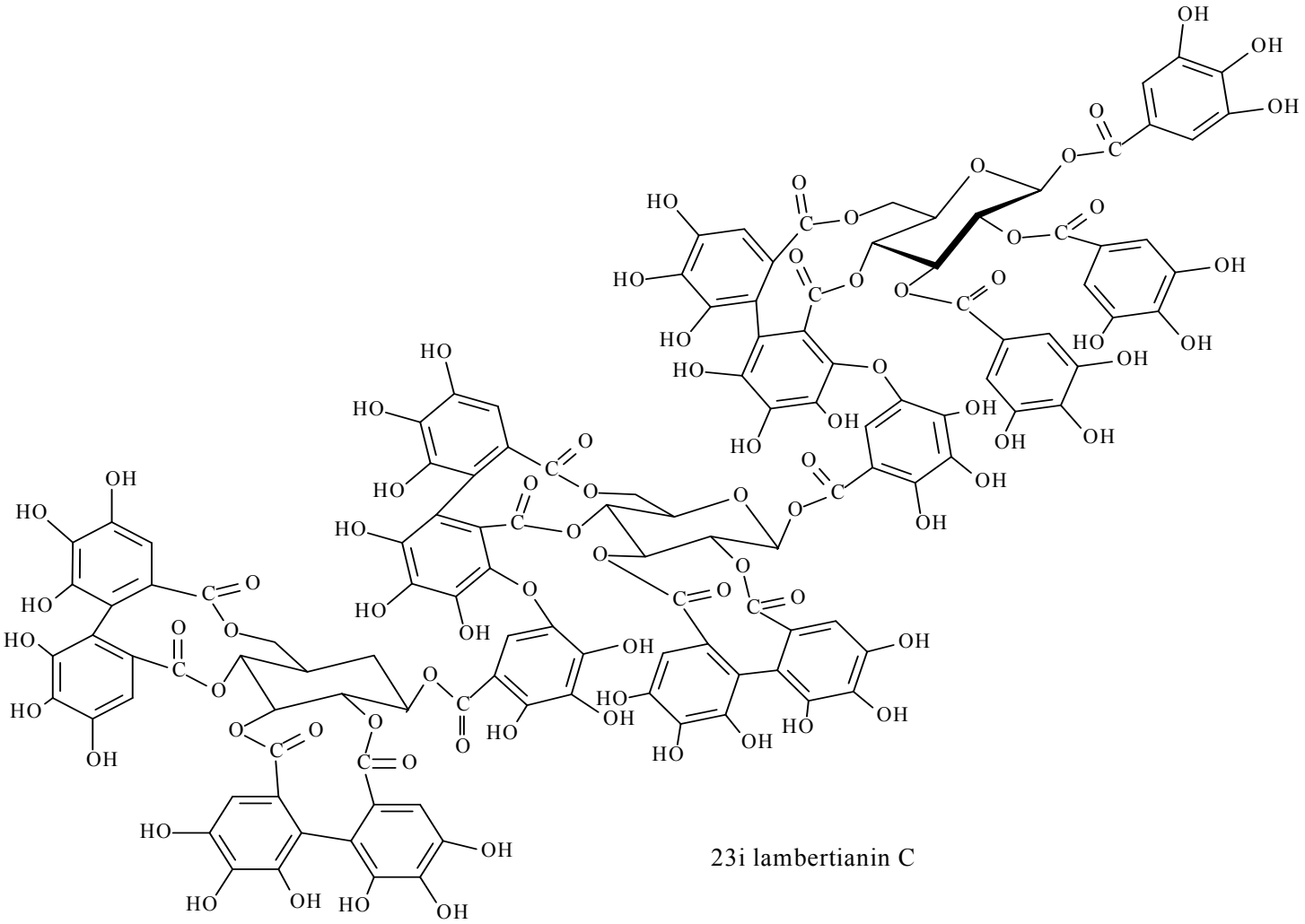
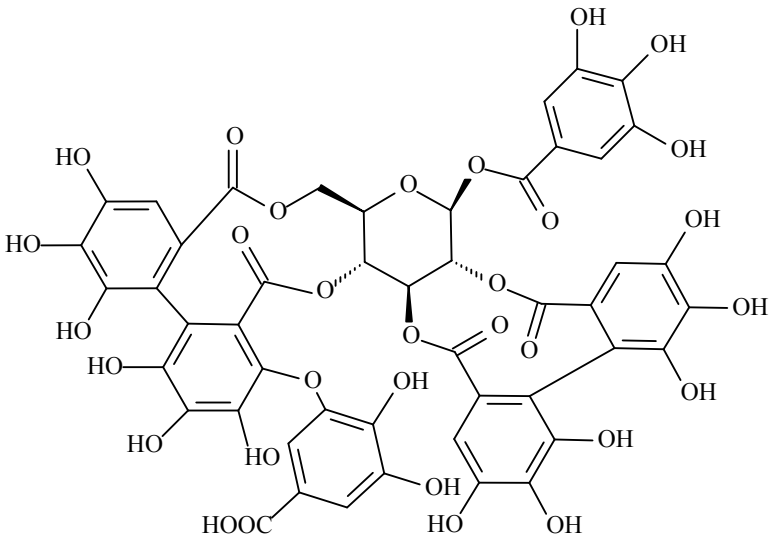
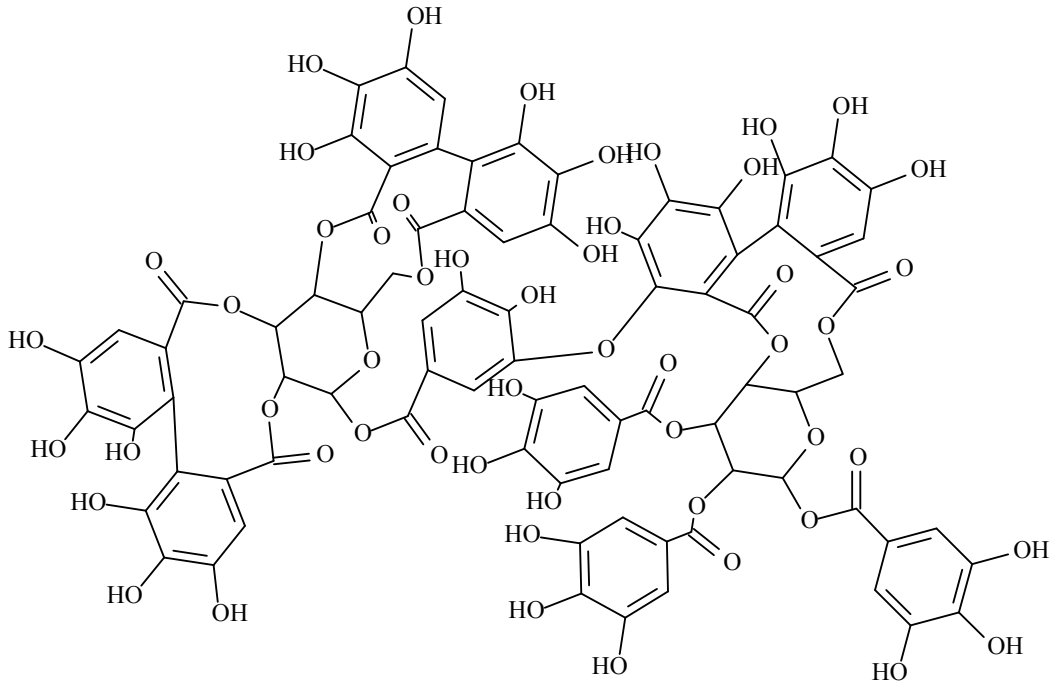


Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



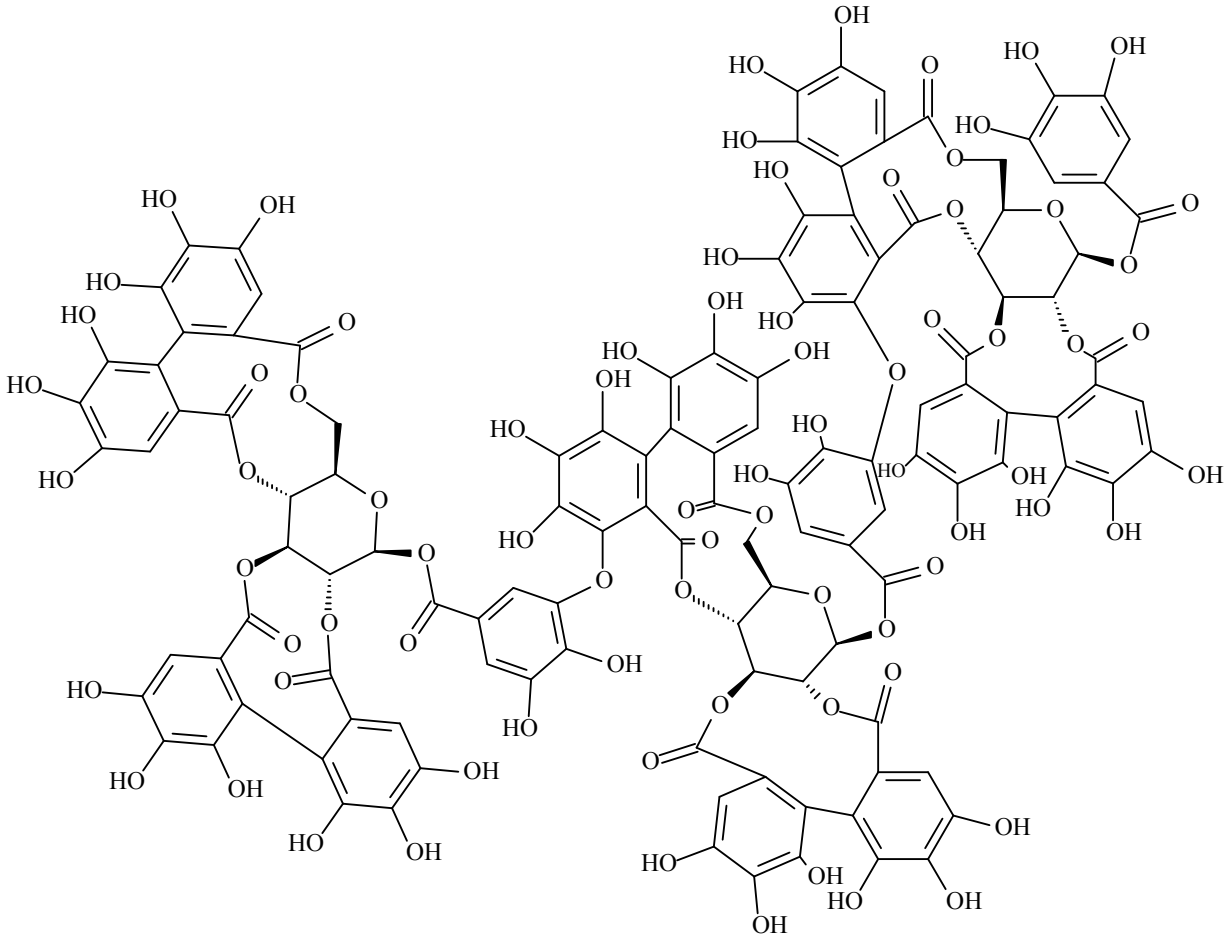
24a rubusuaviin A

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



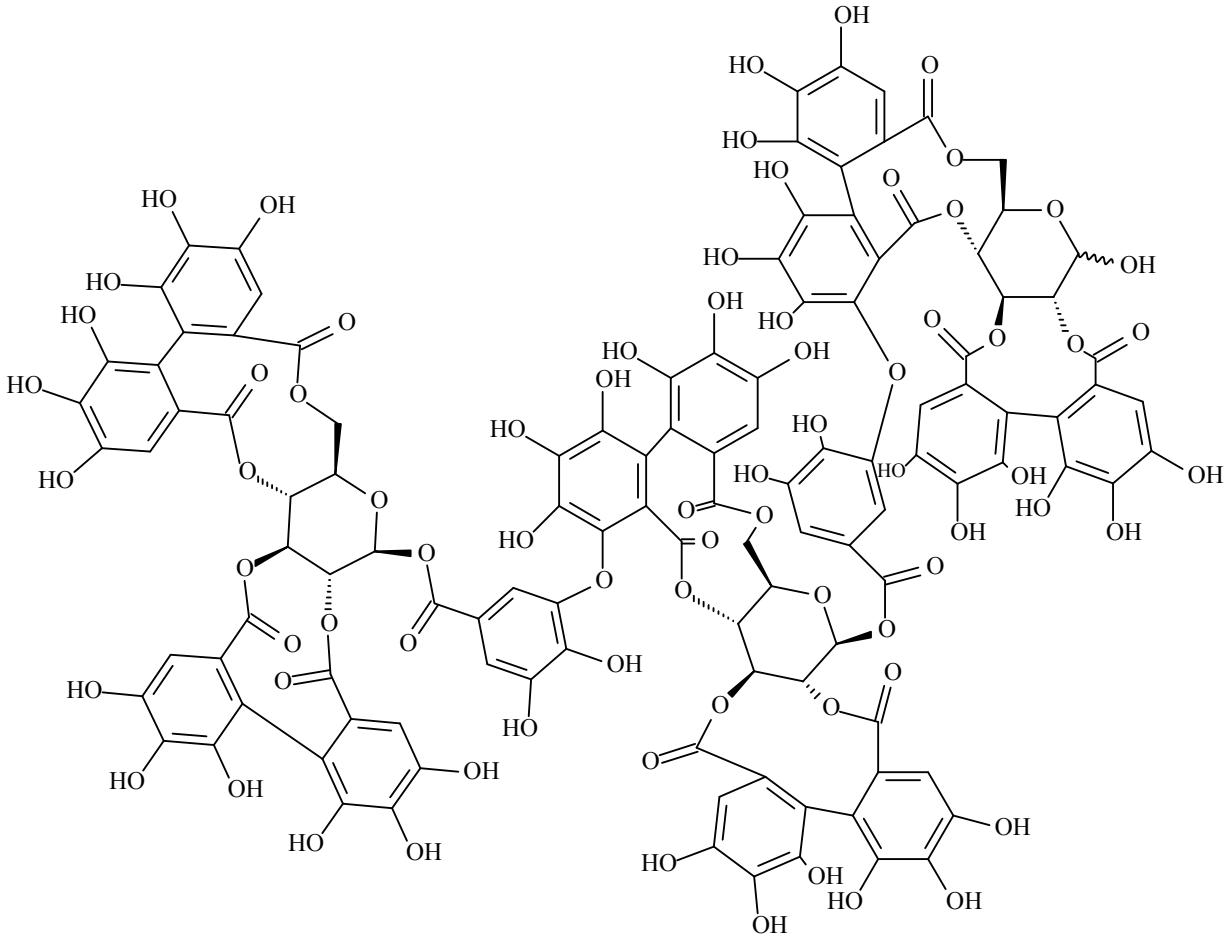
24b rubusuaviin B

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



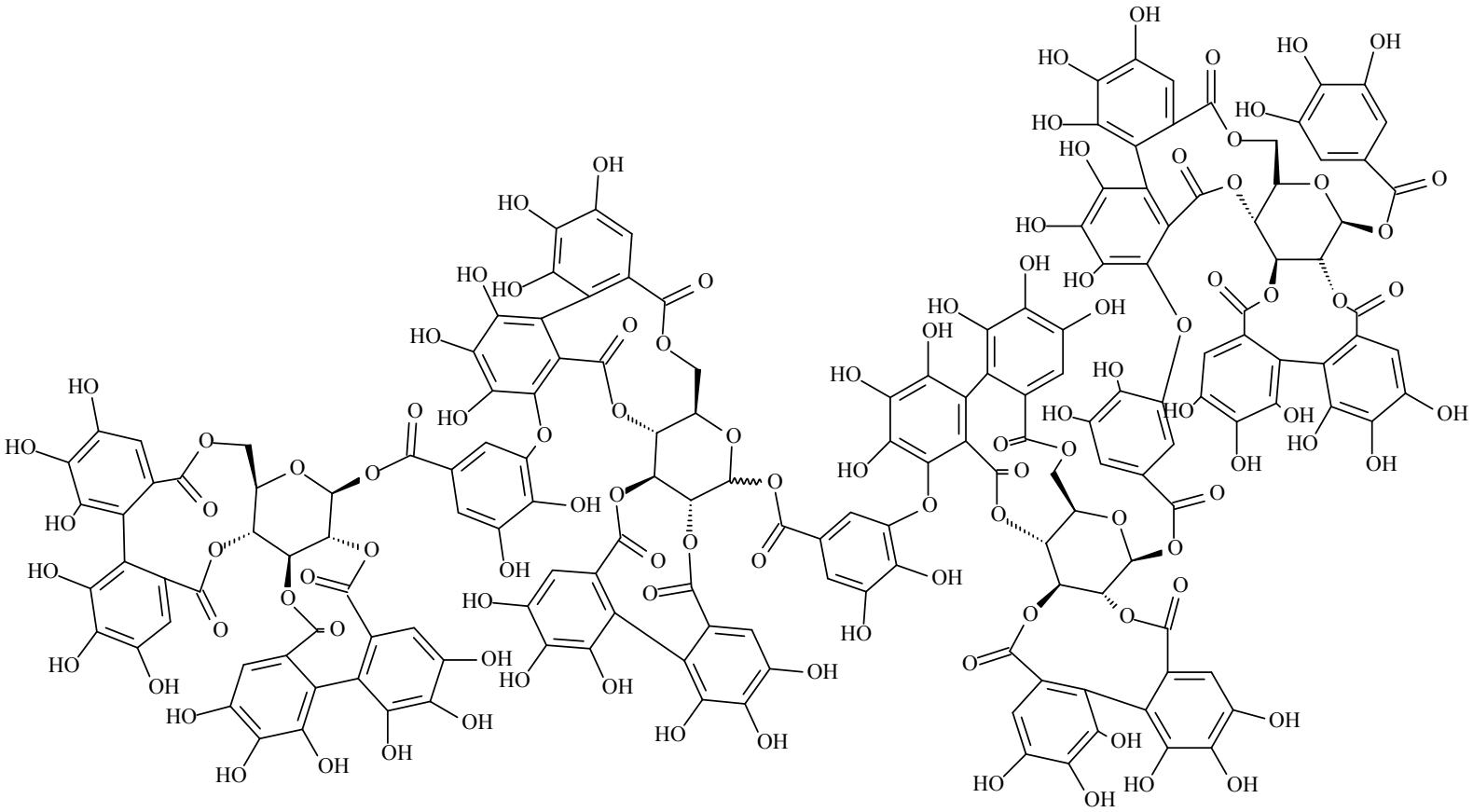
24c rubusuaviin C

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



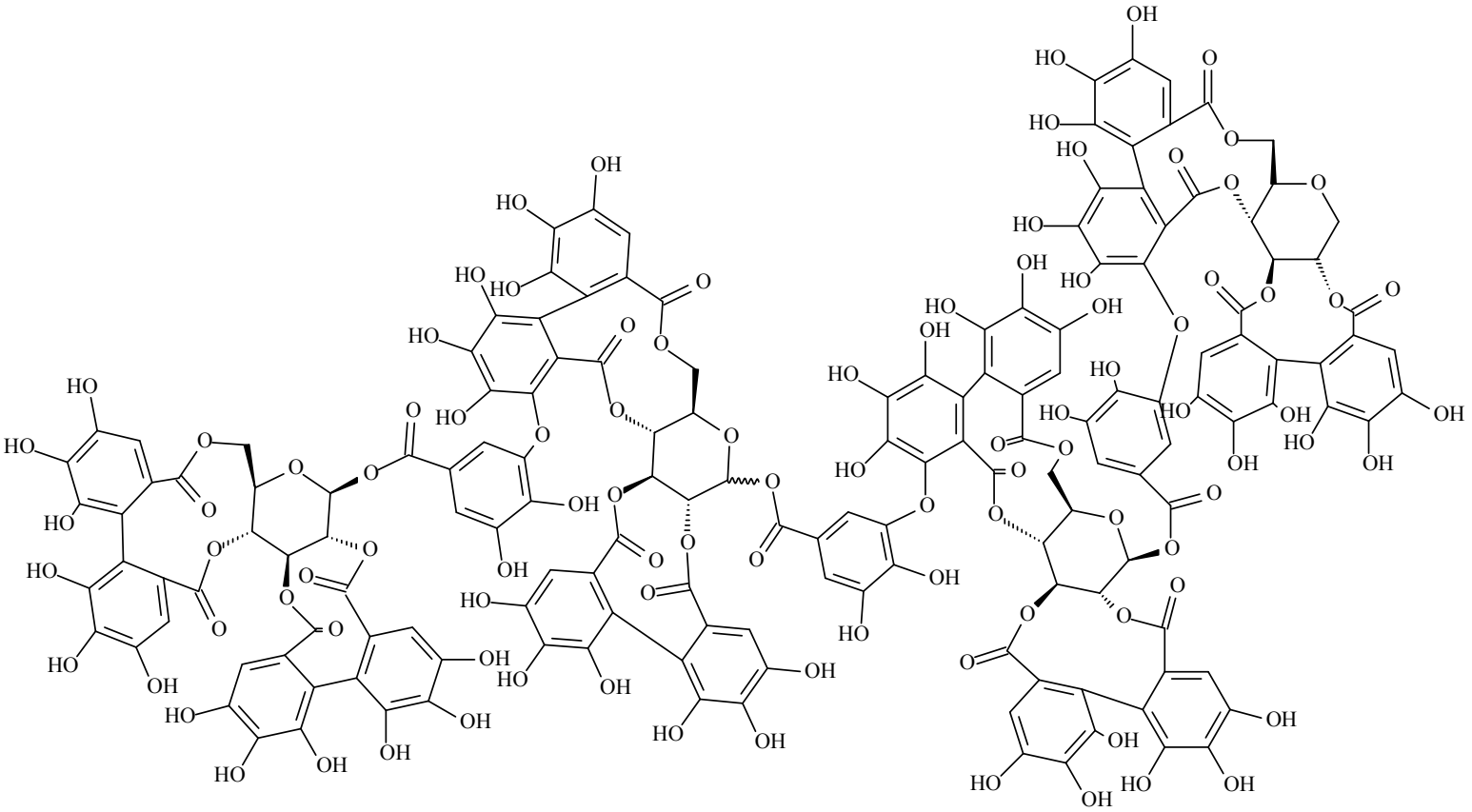
24d rubusuaviin D

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



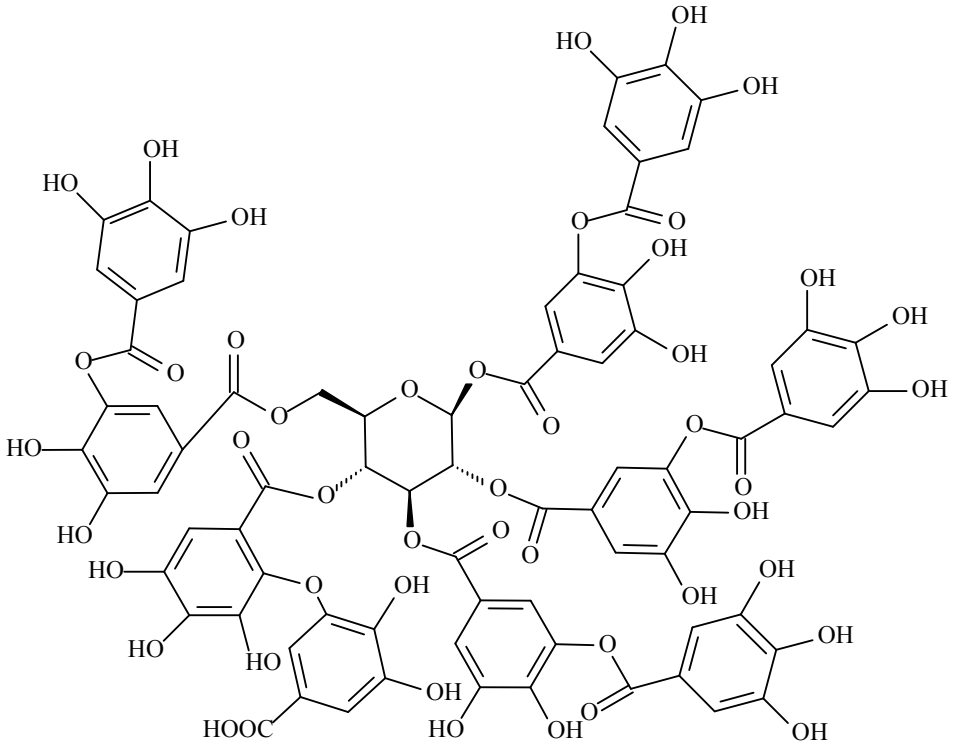
24e rubusuaviin E

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



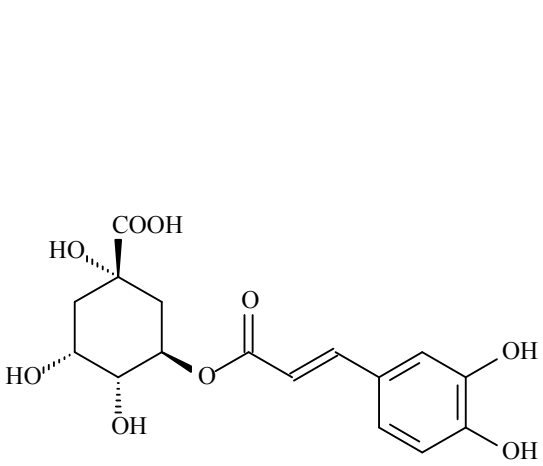
24f rubusuaviin F

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)

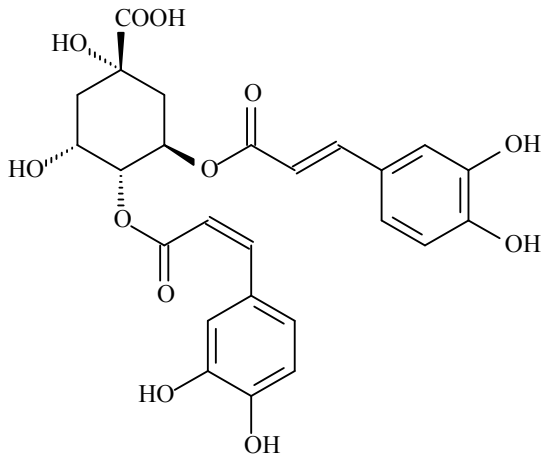


25 tannic acid

Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)

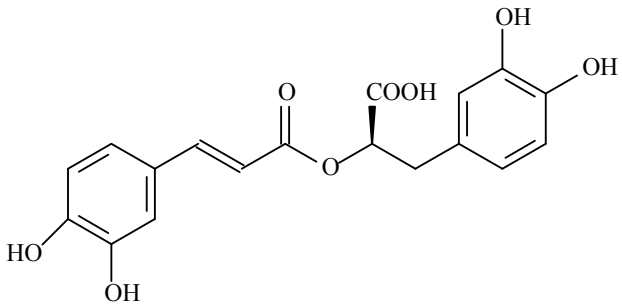


26 chlorogenic acid

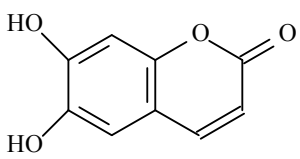


27 isochlorogenic acid

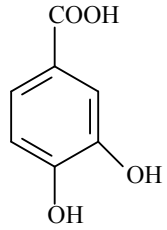
Figure 3. Tannins presenting α-amylase inhibition activity (Continued…..)



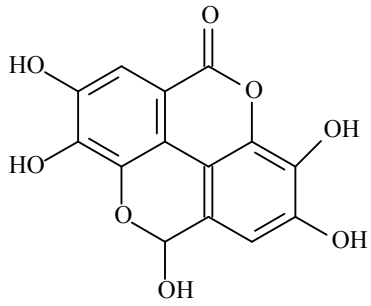
28 rosmarinic acid



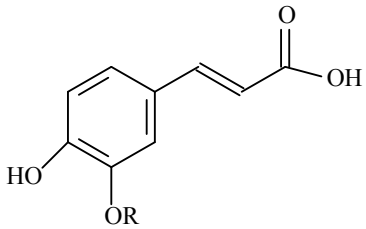
29 esculin



30 protocatechuic acid

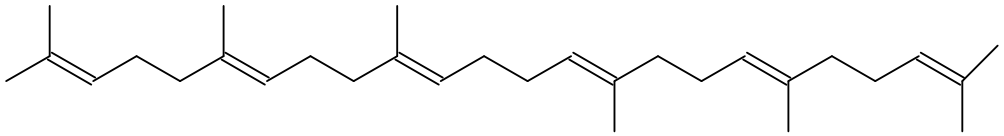


31 ellagic acid

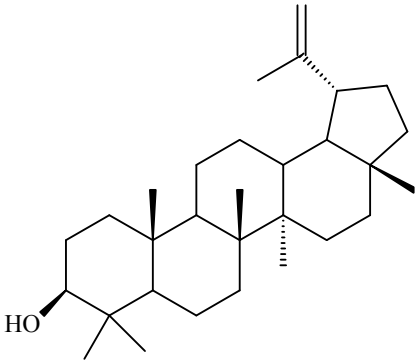


	R	
32a	H	caffeic acid
32b	CH_3	ferulic acid

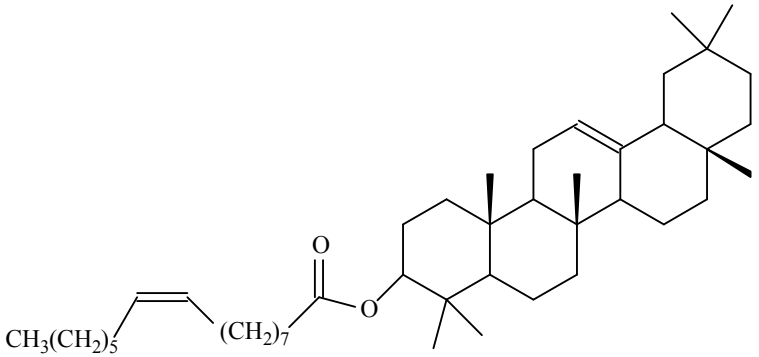
Figure 4. Cinnamic acid derivatives presenting α-amylase inhibition activity



33 squalene

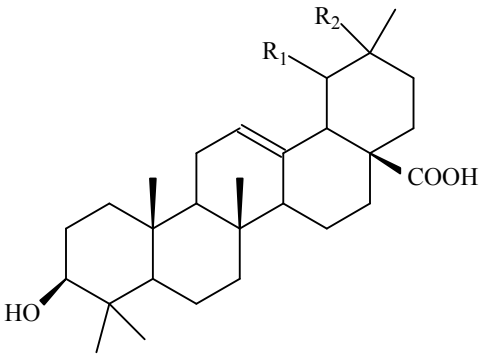


34 lupeol

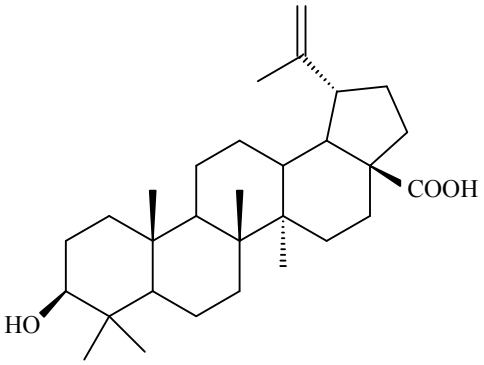


35

Figure 5. Terpenes presenting α-amylase inhibition activity



	R_1	R_2	
36a	H	CH_3	oleanoic acid
36b	CH_3	H	ursolic acid



37 betulinic acid

Figure 5. Terpenes presenting α-amylase inhibition activity (Continued…..)