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Inhibition of α -Amylase and α -Glucosidase Activity by Tea and Grape Seed Extracts and their Constituent Catechins

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Abstract

We evaluated the inhibitory effects of plant-based extracts (grape seed, green tea, and white tea) on α -amylase and α -glucosidase activity, glucosidases required for starch digestion. The abundant flavan-3-ol monomers (catechins) in these extracts were also tested for their inhibitory potential and evaluated against the pharmacological glucosidase inhibitor, acarbose. To evaluate relative potency of these extracts and catechins, the concentrations required for 50 and 90% inhibition of enzyme activity were determined. Maximum enzyme inhibition was used to assess an inhibitor's relative efficacy. Results showed that grape seed extract strongly inhibited both α -amylase and α -glucosidase activity, with equal and much higher potency, respectively, than acarbose. While tea extracts and individual catechin 3-gallates were less effective inhibitors of α -amylase, they were potent inhibitors of α -glucosidase. Our data show that plant extracts containing catechin 3-gallates are potent inhibitors of α -glucosidase, and suggest that procyanidins found in grape seed extract strongly inhibit α -amylase activity.

Keywords

α -Amylase; α -glucosidase; enzyme inhibition; tea; grape seed extract; catechins; diabetes

INTRODUCTION

Glycemic control is an effective, long-term therapy for individuals with type II diabetes mellitus, reducing the risk of both cardiovascular and neurological complications in the development of the disease^{1, 2}. Glucosidase inhibitors are commonly prescribed to diabetics to reduce postprandial hyperglycemia induced by the digestion of starch in the small intestine³. These inhibitors are designed to primarily target α -amylase and α -glucosidase, two members of exo-acting glycoside hydrolase enzymes (glucosidases) found in the intestinal tract that are critical for the digestion of carbohydrates. The overall effect of inhibition is to reduce the flow of glucose from complex dietary carbohydrates into the bloodstream, diminishing the postprandial effect of starch consumption on blood glucose levels⁴. However, the leading glucosidase inhibitors, acarbose and miglitol, are often

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reported to produce diarrhea and other intestinal disturbances, with corresponding intestinal pain and flatulence^{4, 5}. Randomized controlled trials with glucosidase inhibitors report these gastrointestinal side-effects as the most common reason for non-compliance and early subject withdrawal⁶.

The consumption of plants or plant-based supplements may be a more acceptable source of glucosidase inhibitors due to low cost and relative safety, including a low incidence of serious gastrointestinal side-effects^{7–9}. Polyphenolic fractions from plants have been shown to inhibit α -amylase and α -glucosidase activity and allow for tighter control of blood glucose^{10–12}. Rich in polyphenolic flavonoid compounds, extracts from grape seed and green tea have been of increasing interest due to their anti-diabetic properties^{13–16}. Green and white teas are particularly abundant in catechins and catechin 3-gallates. The most abundant catechin 3-gallate in green and white tea, epigallocatechin gallate (EGCG), is attributed with providing many of the beneficial, anti-diabetic effects of tea consumption^{13, 17, 18}. In contrast, grape seed extract contains not only catechins and catechin 3-gallates, but also oligomeric flavan-3-ols, called procyanidins^{19, 20}. Procyanidins are a subclass of proanthocyanidins and make up about 20% of total flavonoids in grape seed extract¹⁹. Both monomeric and oligomeric flavan-3-ols interact with glucosidase enzymes^{10, 21–26}, and may act as effective α -glucosidase inhibitors.

Thus, we sought to determine the potential of grape seed, green tea, and white tea extracts to inhibit α -amylase and α -glucosidase activity, and compare their effects to that of the pharmacological inhibitor, acarbose. In addition, catechin constituents of these extracts were also tested for their ability to act as glucosidase inhibitors.

MATERIALS AND METHODS

Chemicals

α -Amylase from human saliva (Type IX-A; 1000 U/mg protein), α -glucosidase from *Saccharomyces cerevisiae* (Type I; 10 U/mg protein), catechin (C), epicatechin (EC), epigallocatechin (EGC), EGCG, galocatechin gallate (GCG), epicatechin gallate (ECG), acarbose, and p-nitrophenyl α -D-glucopyranoside (pNPG) were obtained from Sigma (St. Louis, MO). Tea extracts and Teavigo[®] (DSM Nutritional Products, Heerlen, Netherlands) were supplied by USANA Health Sciences, Inc. (Salt Lake City, UT). EnzChek[®] Ultra Amylase Assay Kit (E33651) was purchased from Life Technologies Corporation (Grand Island, NY).

Extract Analysis

Catechins were identified in the plant extracts using HPLC separation and UV detection at 280nm (Agilent, 1260 series; Santa Clara, CA). Briefly, plant extracts were dissolved in purified water at a concentration of 1 mg/mL, and 1 μ L of the resulting solution was injected on a reverse-phase C18 column (Inertsil, GL Sciences; Torrance, CA). Samples were initially separated with 5% 2-Propanol and 0.03% Formic Acid for 16 minutes, followed by a gradient increased to 15% 2-Propanol. Catechins were quantified based on reference to purified standards, and expressed as total of extract weight (Table 1). Oligomeric content of

grape seed extract was determined after separation on a gel organic column (Phenogel 500A; Phenomenex, Torrance, CA) using a tetrahydrofuran mobile phase and absorbance at 280nm. Oligomeric content (tetramers and large compounds) was expressed as a comparison to grape seed oligomeric proanthocyanidin reference standard (USP Cat# 1298219). Phenolic composition was measured using a modified Folin-Ciocalteu assay and expressed in percentage of gallic acid equivalents (GAE).

α -Amylase Assay

The human salivary α -amylase inhibition assay was adapted from Deutschlander *et al.*²⁷ and Lo Piparo *et al.*²⁶. Extracts were prepared by dissolution in dimethylsulfoxide (DMSO) to a stock concentration of 1 mg/mL immediately before use in experiments. Individual catechins were also dissolved in DMSO to produce an 8 mM stock solution. Various dilutions of test compounds were pre-incubated in 96-well plates for 30 min at room temperature with 250 μ U of α -amylase at a final concentration of 2.5 mU/mL. The incubation buffer consisted of 50 mM NH_2PO_4 , 50 mM NaCl, 0.5 mM CaCl_2 , and 0.1% bovine serum, pH 6.0, and the final volume of the pre-incubation mixture was 75 μ L. To start the reaction, 25 μ L of 20 μ g/mL DQTM starch substrate from the EnzChek® Ultra Amylase Assay Kit (Molecular Probes, Invitrogen), prepared in incubation buffer, was added to achieve a final concentration of 5 μ g/mL starch. The final concentrations of extracts and catechins were between 0.5–500 μ g/mL and 1–1000 μ M, respectively. DMSO concentrations ranged from 0.00625–6.25%. Control incubations showed no effect of these DMSO concentrations on α -amylase activity (data not shown). Acarbose was included in all experiments as a “positive” control.

Amylase enzymatic activity was monitored by digestion of the DQTM starch substrate, resulting in an increase in fluorescence over time. Fluorescence was measured using a SpectraMax GeminiXS Spectrofluorometer (Molecular Devices, Sunnyvale, CA) with excitation and emission wavelengths of 485 nm and 530 nm, respectively. The linear rate of product formation during the initial 15 min of incubation was used to calculate enzyme activity. α -Amylase activity was calculated relative to control incubations without inhibitor added, and expressed as a percentage of that value. Control wells with only test compound, but no enzyme or substrate, were used to determine any background auto-fluorescence. Each incubation was conducted in triplicate, and results are presented as mean $\pm$ standard error from at least three independent experiments, unless indicated otherwise.

α -Glucosidase Assay

The α -glucosidase inhibition assay was adapted from Deutschlander *et al.*²⁷ and Li *et al.*¹¹. Extracts and catechins were prepared as described above. The test compound and 2 mU of α -glucosidase from *S. cerevisiae*, were diluted to 97 μ L in 0.1 M potassium phosphate buffer (pH 6.5) and pre-incubated in 96-well plates at 37 °C for 15 min. The reaction was initiated by adding 3 μ L of 3 mM pNPG as substrate. The plate was incubated for an additional 15 min at 37 °C, followed by addition of 100 μ L 1 M Na_2CO_3 to stop the reaction. All test compounds were prepared in DMSO as described above. The final concentrations of extracts and catechins were between 0.03–10 μ g/mL and 5–1000 μ M, respectively. The final concentration of α -Glucosidase was 20 mU/mL.

Enzyme activity was determined by measuring the release of p-nitrophenol from the pNPG substrate. The reaction was monitored by change of absorbance at 410 nm using a SpectraMax 190 Spectrophotometer (Molecular Devices, Sunnyvale, CA). α -Glucosidase activity was calculated relative to control wells without inhibitor added, and expressed as a percentage of that value. Each incubation was conducted in triplicate, and results are presented as mean $\pm$ standard error from at least three independent experiments, unless indicated otherwise.

Data Analysis

Enzyme activity in the presence of inhibitors was expressed as a percentage of the uninhibited enzyme activity, and plotted versus inhibitor concentration. Non-linear regression was performed using a four-parameter logistic model and GraphPad Prism software (GraphPad Software, La Jolla, CA). As a measure of inhibitory potency, the concentrations required for 50 and 90% inhibition of enzyme activity (IC_{50} and IC_{90} , respectively) were determined. Enzyme inhibition is the reciprocal value of the enzyme activity measured, and expressed as a percentage (where 0% enzyme activity would be reported as 100% inhibition). Maximum enzyme inhibition is determined for each compound when enzyme activity was observed at a minimum for the given range of extracts or catechins provided, and is reported as a measure of the compound's inhibitory efficacy.

Statistics

Differences in calculated IC_{50} and IC_{90} values and percent maximum inhibition values were analyzed by unpaired t-tests and one-way ANOVA employing Tukey-Kramer post-hoc analysis to compare data sets (GraphPad Prism). Differences between means were considered significant if $p < 0.05$, as denoted in applicable tables, figures, and the text.

RESULTS

Isolated α -amylase from human saliva and α -glucosidase from *S. cerevisiae* were incubated with plant extracts (Table 1) or individual catechins, as described in Materials and Methods. Activity data in the presence of varying concentrations of extracts were expressed as percent of uninhibited enzyme activity of either α -amylase (Figure 1a) or α -glucosidase (Figure 1b). As "positive" control, the pharmacological glucosidase inhibitor, acarbose, was used in parallel incubations (Figure 1c). As a measure of potency of the inhibitors tested, IC_{50} and IC_{90} values were calculated from the enzyme activity data. Likewise, as an evaluation of the efficacy of inhibition, the maximum extent of enzyme inhibition achieved by each test compound was also determined from the enzyme activity data.

α -Amylase Inhibition

The inhibitory potencies of grape seed, green tea, and white tea extracts on α -amylase activity are summarized in Table 2. As expected, acarbose showed the lowest IC_{50} , establishing its relative potency as a glucosidase inhibitor. Grape seed extract also was a strong inhibitor of α -amylase, exhibiting an IC_{50} that was slightly but non-significantly higher than that of acarbose. Interestingly, the IC_{90} for grape seed extract was lower than the IC_{90} for acarbose, but again this difference was not statistically significant (Table 2).

Furthermore, percent enzyme inhibition at concentrations of grape seed extract at or exceeding the IC_{90} were not significantly different from the maximum inhibition achieved by acarbose (Figure 2a). These data indicate that grape seed extract is as potent and efficient as the drug, acarbose, in inhibiting α -amylase activity.

Although green tea extract has been suggested to be an effective glucosidase inhibitor¹⁰, we observed only a moderate affinity of this extract for α -amylase, with calculated IC_{50} and IC_{90} values 4–7 times higher than those of acarbose and grape seed extract (Table 2). However, the maximum extent of enzyme inhibition achieved by green tea extract was not significantly different from that of grape seed extract or acarbose (Figure 2a). These data suggest that green tea extract may act as an effective, moderately potent inhibitor of α -amylase.

A commercially available, highly concentrated green tea extract, Teavigo®, exhibited IC_{50} and IC_{90} values similar to those of green tea extract (Table 1); however, maximum enzyme inhibition was considerably lower for Teavigo® compared to green tea extract (Figures 1a and 2a). In contrast, white tea extract only weakly inhibited the enzyme, with an IC_{50} over fifty times higher than that of acarbose (Table 2) and about 50% enzyme inhibition at the highest concentration tested (Figures 1a and 2a).

The vast majority of flavonoids in white and green tea extracts are catechins, whereas grape seed extract also contains a significant amount of procyanidins (Table 1)^{19, 20, 28}. To investigate whether catechins may contribute to the inhibitory effects of the various extracts tested, we determined α -amylase activity in the presence and absence of individual catechins. Consistent with the results obtained with Teavigo® and tea extracts, isolated catechins were considerably less potent than acarbose or grape seed extract in inhibiting α -amylase activity (Table 2). With the exception of GCG, maximum enzyme inhibition was below 50%, even at the highest concentration tested (1 mM), such that reliable IC_{50} and IC_{90} values could not be determined (Fig. 2b and Table 2).

α -Glucosidase Inhibition

Compared to its strong inhibitory effect on α -amylase, acarbose was much less potent in inhibiting α -glucosidase (Figure 1c). The IC_{50} and IC_{90} values of acarbose for α -glucosidase activity were more than 13 times higher than those values for α -amylase (Tables 2 and 3). Even at the highest concentration of acarbose tested (645 μ g/mL, or 1 mM), about 20% of α -glucosidase activity remained (Figures 1c and 3).

Interestingly, all extracts tested were much more potent inhibitors of α -glucosidase than acarbose (Table 3). As with α -amylase, grape seed extract showed strong inhibition of α -glucosidase, but low IC_{50} and IC_{90} values were also observed for all tea extracts. Green tea extract and Teavigo® exhibited significantly lower IC_{50} and IC_{90} values than grape seed and white tea extracts (Table 3). All of the extracts inhibited α -glucosidase activity by more than 90%, which was significantly higher than the maximum inhibition achieved by acarbose (Figures 1b and 3a).

Since Teavigo® and green tea extract were the most potent inhibitors of α -glucosidase, it is likely that the constituent catechins, and specifically EGCG, would also strongly inhibit enzyme activity. As shown in Table 3, some, but not all, of the catechins tested exerted potent inhibitory effects on α -glucosidase activity. The IC_{50} values of catechins with a 3-gallate side group, *i.e.*, EGCG, GCG, and ECG, were much lower than the IC_{50} of acarbose, and—with the exception of ECG—comparable to the IC_{50} values of the extracts. Among the gallated catechins, EGCG was the most potent α -glucosidase inhibitor, with IC_{50} and IC_{90} values basically identical to those of Teavigo®. Furthermore, EGCG and GCG almost completely inhibited α -glucosidase activity, while ECG was somewhat less effective, although the difference was not statistically significant (Figure 3b). In contrast, the non-gallated catechins, C, EC, and EGC, were weak, incomplete α -glucosidase inhibitors (Table 3 and Figure 3b).

DISCUSSION

Our data presented here suggest that extracts of grape seeds and tea as well as 3-gallated catechins show promise as potent glucosidase inhibitors that may limit the digestion of dietary starches. Grape seed and tea extracts are easily available sources of flavonoids, many of which have shown efficacy in controlling the symptoms of diabetes. While all of these plant extracts are rich in flavan-3-ols—flavonoid molecules characterized by their saturated C-ring and 3-OH group—green and white teas are particularly abundant in catechins, *i.e.*, flavan-3-ol monomers, while grape seed extract also contains dimeric, trimeric and oligomeric flavan-3-ols, collectively called procyanidins. It is likely that these differences in extract composition explain the differences in α -amylase and α -glucosidase inhibition observed in the present paper.

Previous studies have determined several key structural features needed for monomeric flavonoids to inhibit α -amylase and α -glucosidase activity^{10, 22, 24, 26}. In agreement with these previous studies^{24, 26}, our data show that extracts abundant in catechins (white tea, green tea, and Teavigo®) along with individual catechins (C, EC, EGC, ECG, GCG, and EGCG) are not particularly strong inhibitors of salivary α -amylase. This is likely due to the lack of an unsaturated C-ring with a 4-keto group in flavan-3-ols, and the lack of specific A- and B-ring hydroxyl groups in the correct stereospecific orientation to effectively interact with the catalytic site of the enzyme²⁶.

For α -glucosidase inhibition, the presence of a gallate group esterified to the 3-position of the C-ring has been suggested to be critical for the interaction of flavan-3-ols with the enzyme^{10, 22}. Our data support this hypothesis, showing that α -glucosidase activity is strongly inhibited by catechin 3-gallates, whereas non-gallated catechins are poor enzyme inhibitors. As green and white tea extracts are abundant in catechin 3-gallates²⁸, primarily EGCG (Table 1), this would explain their relative potency against α -glucosidase activity. Interestingly, grape seed extract does not contain significant amounts of EGCG and other catechin 3-gallates, hence its inhibitory effect on α -glucosidase must be due to some other constituent(s), possibly procyanidin gallates^{19, 20}. Overall, the strongest inhibitors of α -glucosidase identified in our study were EGCG and Teavigo®, which—based on their IC_{50} values—were over 300 times more potent than acarbose. Our results further show that grape

seed extract is as potent an α -amylase inhibitor as acarbose. Little is known about the mechanism by which grape seed extract inhibits α -amylase, although the interaction of various grape seed extracts with several digestive enzymes has been reported^{21, 22, 25, 29}. Grape seed extracts can vary in composition based on grape variety, growing season, and other factors. In general, they are similar to the composition listed in Table 1: 5–10% catechin and epicatechin, with an equivalent amount of smaller procyanidins. Since catechin and epicatechin were very weak, incomplete inhibitors of α -amylase, it is likely that the procyanidins in grape seed extract are mainly responsible for the observed inhibitory effect on α -amylase activity. Interestingly, α -amylase normally binds longer polysaccharides than α -glucosidase, and acarbose is a pseudotetrasaccharide containing a non-hydrolyzable nitrogen-linked bond that suppresses α -amylase activity by competitive, reversible inhibition³⁰. Similarly, procyanidins have a non-hydrolyzable oligomeric structure that may occupy the substrate binding pocket of α -amylase, thereby competitively inhibiting the enzyme. Furthermore, gallated procyanidins dimers found in grape seeds have particular “closed” conformations that reportedly enhance interactions with α -amylase²⁵. However, as grape seed extract is a complex mixture of procyanidins, further work is needed to detail these potential interactions of grape seed extract with α -amylase and provide a rationale for the interaction of grape seed extract with α -glucosidase.

To determine the true efficacy of grape seed and tea extracts as glucosidase inhibitors, trials in human subjects are necessary. As such, it is important to consider the interactions of these extracts with the gastrointestinal tract and how this may alter their inhibitory potential. Previous work has shown that both catechins and procyanidins are stable in the acid environment of the stomach^{31, 32}. However, there is some evidence that pancreatic digestion, along with a shift to a slightly alkaline pH, may cause degradation of the polymeric procyanidins to their respective monomeric components^{32, 33}. However, catechins generally remain stable during intestinal transit³³. Despite this degradation of complex procyanidins, studies using simulated digestion models have shown that millimolar concentrations of catechins and procyanidins can be expected in the digestive tract with 300 mg of grape seed extracts³². These concentrations (approximately 0.1–1.0 mg/mL depending on compound in question) would only approach the IC₅₀ values of the most potent inhibitors determined by this study, requiring further dose-response studies to be performed. In addition, non-specific interactions of flavonoids with proteins with the gastric mucosa, intestine, or protein-rich foods may limit the interactions of catechins and procyanidins with glucosidases and require special preparations or the ingestions of large quantities of plant extracts to be effective.

In conclusion, our data suggest the use of plant extracts, especially grape seed and green tea extracts, as viable alternatives to pharmaceutical inhibitors of the glycoside hydrolase enzymes, α -amylase and α -glucosidase. Since these plant extracts are well tolerated, relatively inexpensive, and readily available, they have the potential to be used in many applications for glycemic control. While EGCG appears to be mainly responsible for the inhibitory effects of the plant extracts investigated here on α -glucosidase activity, the contribution of other catechins and catechin 3-gallates should not be discounted. Although further work is required to determine if specific procyanidins are responsible for the inhibitory effects of grape seed extract on α -amylase activity, it is certainly possible that

multiple components of the extract are needed to reach its full inhibitory potential. Clinical trials are currently planned to demonstrate the efficacy of these extracts and EGCG in human volunteers to lower postprandial hyperglycemia.

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ABBREVIATIONS USED

C	Catechin
IC₅₀	concentration required for 50% inhibition of enzyme activity
IC₉₀	concentration required for 90% inhibition of enzyme activity
DMSO	dimethylsulfoxide
EC	epicatechin
EGC	epigallocatechin
EGCG	epigallocatechin gallate
GCG	gallocatechin gallate
ECG	epicatechin gallate
pNPG	p-nitrophenyl α -D-glucopyranoside

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Figure 1a

Figure 1b

Figure 1c

Figure 1. α -Amylase and α -glucosidase inhibition by plant extracts and acarbose
Dose-dependent inhibition of a) α -amylase and b) α -glucosidase activity by grape seed, green tea, and white tea extracts and Teavigo[®]. c) Inhibition of α -amylase and α -glucosidase activity by acarbose, presented on a logarithmic scale to denote differences in inhibitory potency.

Figure 2a

Figure 2b

Figure 2. Efficacy of α -amylase inhibitors

Relative efficacy of α -amylase inhibition was determined as the maximum extent of inhibition (in percent, relative to uninhibited enzyme activity) achieved by either acarbose or

a) plant extracts and b) individual catechins. Significant differences are denoted by unshared letters between columns as determined by ANOVA, as described in Materials and Methods.

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Figure 3a

Figure 3b

Figure 3. Efficacy of α -glucosidase inhibitors

Relative efficacy of α -glucosidase inhibition was determined as the maximum extent of inhibition (in percent, relative to uninhibited enzyme activity) achieved by either acarbose or a) plant extracts and b) individual catechins. Significant differences are denoted by unshared letters between columns as determined by ANOVA, as described in Materials and Methods.

Table 1

Analysis of Plant Extracts Used in Study

	Grape Seed	Green Tea	White Tea	Tea Vigo
GC	-	2.3%	2.1%	-
EGC	-	11.9%	8.6%	-
C	6.6%	0.7%	0.8%	-
EC	4.9%	4.5%	2.5%	-
EGCG	-	34.8%	9.5%	95.2%
GCG	0.4%	1.9%	0.5%	0.1%
ECG	1.3%	8.5%	4.1%	2.1%
CG	-	0.5%	0.2%	-
Procyanidin B1	5.3%	-	-	-
Procyanidin B2	3.1%	-	-	-
Procyanidin C1	1.7%	-	-	-
Procyanidin Oligomers	81.7%	N.D.	N.D.	N.D.
Total Phenolics	86% GAE	74% GAE	34% GAE	94% GAE

Values presented are percent of total weight of extract.

Total phenolics are represented in percent Gallic Acid Equivalents (GAE)

N.D. = Not Determined

Table 2 α -Amylase Inhibition by Tea and Grape Seed Extracts and Individual Catechins

Extracts		IC ₅₀ (µg/mL)	IC ₉₀ (µg/mL)	Catechins	IC ₅₀ (µg/mL)	IC ₉₀ (µg/mL)
Acarbose (<i>positive control</i>)	(n=7)	6.9 ± 0.8 ^a	42.8 ± 4.7 ^e	C	(n=3)	160 ± 67 ^{b,c,d} > 290 [*]
Grape seed extract	(n=3)	8.7 ± 0.8 ^{ab}	28.1 ± 2.0 ^e	EC	(n=3)	N.D. N.D.
Green tea extract	(n=4)	34.9 ± 0.9 ^c	192 ± 15 ^f	EGC	(n=3)	N.D. N.D.
Teavigo®	(n=4)	44.2 ± 6.1 ^c	144 ± 19 ^f	ECG	(n=2)	~27 ~50
White tea extract	(n=4)	378 ± 134 ^d	> 500 [*]	EGCG GCG	(n=2) (n=2)	~24 ~17 ~36 ~144

Different letter superscripts denote significant differences in IC₅₀ or IC₉₀ values as determined by unpaired t-test (p < 0.05)

* Exceeds maximum concentration tested

N.D. = value not determined

Values presented are mean ± standard error or approximate values if weak inhibition was observed

Table 3
 α -Glucosidase Inhibition by Tea and Grape Seed Extracts and Individual Catechins

Extracts		IC ₅₀ (μ g/mL)	IC ₉₀ (μ g/mL)	Catechins	IC ₅₀ (μ g/mL)	IC ₉₀ (μ g/mL)
Acarbose (<i>positive control</i>)	(n=7)	91.0 $\pm$ 10.8 ^a	>645 [*]	C	(n=2)	~31 > 290 [*]
Grape seed extract	(n=3)	1.2 $\pm$ 0.2 ^b	2.1 $\pm$ 0.2 ^f	EC	(n=2)	N.D. > 290 [*]
Green tea extract	(n=3)	0.5 $\pm$ 0.1 ^c	0.8 $\pm$ 0.2 ^g	EGC	(n=2)	N.D.
Teavigo®	(n=3)	0.3 $\pm$ 0.1 ^d	0.4 $\pm$ 0.1 ^g	ECG	(n=3)	3.5 $\pm$ 1.1 ^{b,e} 13.9 $\pm$ 4.1 ^h
White tea extract	(n=3)	2.5 $\pm$ 0.4 ^e	5.7 $\pm$ 1.8 ^{f,h,i}	EGCG GCG	(n=3) (n=3)	0.3 $\pm$ 0.1 ^d 0.4 $\pm$ 0.1 ^g 1.4 $\pm$ 0.1 ^{b,e} 2.9 $\pm$ 0.2 ⁱ

Different letter superscripts denote significant differences in IC₅₀ or IC₉₀ values as determined by unpaired t-test (p < 0.05)

* Exceeds maximum concentration tested

N.D. = value not determined

Values presented are mean $\pm$ standard error or approximate values if weak inhibition was observed