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学 位 論 文 要 旨
Dissertation Abstract

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学位論文題目：
Title of Dissertation

Studies on Isolation and Characterization of Antioxidant and α-Glucosidase Inhibitory Compounds from Woody Plants and Endophytic Fungi
(木本植物およびその内生菌からの抗酸化物質および α-グルコシダ―ゼ阻害物質の単離と特性評価に関する研究)

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Free radicals can cause oxidative damage to the human body, eventually leading to chronic diseases (such as atherosclerosis, cancer, diabetes) and aging. Therefore, antioxidants are considered important because of their many health benefits. However, it has been demonstrated that synthetic antioxidants can accumulate in the human body and possibly cause cancer and other organ damage. Accordingly, using natural antioxidants extracted from plants is highly recommended in food applications for safety, and their potentially nutritional and therapeutic effects. Diabetes mellitus (DM) is the most serious, chronic metabolic disorder and is characterized by high blood glucose levels. One therapeutic approach for diabetes is to postpone absorption of glucose through inhibiting carbohydrate-hydrolyzing enzymes, e.g., α-glucosidase in the digestive organs. Plants are potential sources of drugs and many currently available drugs have been derived from plants. The objective of this research was to search for antioxidant and α-glucosidase inhibitors from several woody plants.

The methanolic extracts of 14 woody plants were evaluated using various in vitro assays: DPPH radical scavenging activity, H_2O_2 radical scavenging activity, β-carotene bleaching assay, and reducing power assay. Total phenol content measurements of several woody plants were determined using Folin-Ciocalteau reagent equivalent to gallic acid and quercetin. The α-glucosidase inhibitory assay was conducted against α-glucosidase from *Saccharomyces cerevisiae*. It was found that *Quercus gilva* Blume and *Quercus phillyraeoides* A. Gray had the highest antioxidant activities (IC_{50}) with 38.53 and 25.00 µg/mL, respectively, whereas *Mallotus japonicus* and *Quercus phillyraeoides* A. Gray had the highest α-glucosidase inhibitory activities (IC_{50}) with 8.46 and 9.88 µg/mL, respectively.

An activity-guided isolation process was used to identify antioxidant compounds in the leaves of *Quercus gilva* Blume. Three compounds were isolated and their structures were identified as catechin (**1**), epicatechin (**2**), and tiliroside (**3**) using instrumental analysis. The antioxidant activity of the isolated compounds was evaluated using various in vitro assays. The α-glucosidase inhibitory assay was conducted against

α-glucosidase from *Saccharomyces cerevisiae*. Compounds **1** and **2** were found to have high antioxidant activity with an inhibitory concentration (IC_{50}) of 40.86 and 22.55 µM, respectively, compared with quercetin as standard with an IC_{50} of 28.08 µM. Compound **3** had the lowest antioxidant activity with an IC_{50} of 160.24 µM. However, compound **3** had the highest α-glucosidase inhibitory activity with an IC_{50} of 28.36 µM, followed by compounds **1** and **2** with 168.6 and 920.6 µM, respectively.

Several α-glucosidase inhibitor compounds were isolated from the methanolic extract of leaves of *Quercus phillyraeoides* A. Gray (*Q. phillyraeoides*) using a bioassay-guided fractionation technique. Further separation and purification of methanolic soluble, the most active fraction, led to isolating constituents with moderate and high activity in inhibiting α-glucosidase: β-sitosterol glucoside (**4**) and condensed tannins (**5**, **6**, **7**, **8, 9**). Constituents **4** to **9** had an inhibitory concentration (IC_{50}) against α-glucosidase from *Saccharomyces cerevisiae* of 118.8, 2.79, 2.78, 3.10, 2.60 and 3.14 µg/mL, respectively, whereas quercetin as standard had an IC_{50} of 4.80 µg/mL. Additionally, significant antioxidant activity using several assays was observed, suggesting a possible application in the treatment of hyperglycaemia-induced oxidative stress.

Xylariaceae sp QGS 01, an endophytic fungus isolated from the stem of *Quercus gilva* Blume, showed the highest α-glucosidase inhibitory activity. Two active constituents, 8-hydroxy-6,7-dimethoxy-3-methylisocoumarine (**10**) and fatty acid fraction (**11**), were isolated from the endophytic fungi *Xylariaceae* sp QGS 01. Compound **10** and fatty acid fraction (**11**) had inhibitory concentration (IC_{50}) values against α-glucosidase from *Saccharomyces cerevisiae* of 41.75 and 5.95 µg/mL, respectively. The results of the present study showed that *Q. gilva*, *Q. phillyraeoides*, and the endophytic fungi *Xylariaceae* sp QGS 01 are potentially a rich source of natural antioxidants and antidiabetic medicine.