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学 位 論 文 要 旨
Dissertation Abstract

氏名： 佐藤 彰彦
Name
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Some of common flavonoids, phytochemicals that may be rich in various vegetables and fruits showed a great suppression of degranulation of RBL 2H3 cells. Isorhamnetin showed the highest suppression of degranulation at 3.1 μmol/L. Flavones and flavonols such as isorhamnetin, luteolin and quercetin bearing double bond between C2 and C3 positions showed high level (IC_{50}: 3.1 μmol/L to 3.7 μmol/L) of the activities in suppression. As antioxidant activities of flavonoids were related with anti-inflammatory activity, chemical structure activity relationship of flavonoids was investigated by TBA tests for antioxidant activity and RBL-2H3 tests for anti-allergic activity. As the results, aromatic ring on C-ring was indispensable for the anti-allergic activity. However, aromatic ring with orth diols on B-ring was essential for antioxidant activity. Therefore the active sites and acting mechanisms of flavonoids for anti-allergic activity and antioxidant activity was found to be a bit different even though polyphenolic character of flavonoids are required in both activities. This kind of information is quite useful for the selection of target plants that may contain valuable flavonoids as nutraceutical ingredients.

The following compounds with higher antiallergic activities were isolated from Eau de Cologne mint leaves: 5,6,4'-trihydroxy-7,8-dimethoxyflavone (**M6**), 5,6,4'-trihydroxy-7,8,3'-trimethoxyflavone (**M7**), 5,6-dihydroxy-7,3',4'-trimethoxyflavone (**M8**), 5,6-dihydroxy-7,8,3',4'-tetramethoxyflavone (**M9**), and 5,6-dihydroxy-7,8,4'-trimethoxyflavone (**M10**). The IC_{50} values of compounds **M6**−**M10** against RBL-2H3

cells were 6.7, 2.4, 5.6, 3.0, and 6.1 μM. Compounds **M7** and **M9** (IC_{50} 2.4 μM and 3.0 μM) had the highest antiallergic activities among the flavonoids previously reported. The amounts of **M7**, **M9**, and **M10** isolated were fairly high, at 177.7 mg/kg, 278.0 mg/kg, and 179.7 mg/kg in the mint, respectively. LD_5 value (index of toxicity) and LD_5/IC_{50} ratio of **M7** and **M9** indicate that the safety is greater than that of luteolin, a typical antiallergic substance. The extract containing powerful antiallergic flavones, **M6**−**M10** with higher hydrophobicity could be selectively separated from the extract containing luteolin and other flavonoids glycosides by partition with dichloromethane and water. Therefore, compounds **M7** and **M9** in mints, and the dichloromethane extract would be the most potent and preventive resources against allergy.

3,4-DHPEA-EA is a kind of secoiridoid first found in three Japanese olive pomaces: Mission, Lucca, and Manzanillo. These varieties showed high activity of 3,4-DHPEA-EA as an antiallergic active substance with IC_{50} at 33.5 ± 0.6 μg/mL. Because 3,4-DHPEA-EA was the most abundant among the active substances in the pomaces and the activity of 3,4-DHPEA-EA was greater than that of hydroxytyrosol and elenolic acid, 3,4-DHPEA-EA, which has the ester linkage of hydroxytyrosol and elenolic acid, should be essential for antiallergic activity. Although a trace amount (1.04 mg/kg) of luteolin in the pomace showed the highest antiallergic activity with IC_{50} at 0.752 ± 0.1 μg/mL, we concluded that the entire antiallergic effect derives from the abundance of 3,4-DHPEA-EA, especially in the green olive pomace of the Mission variety in October, which showed the highest level of 3,4-DHPEA-EA (5033 ± 118 mg/kg). Therefore, the Mission variety had the most effective antiallergy property.

The edible parts of onions used for daily meals have antiallergic activity (IC_{50} = 20.8 to 310.1 μg/mL). The correlation coefficient between the antiallergic activity of eleven onions (eight cultivars, three onions from local markets) and thirty-four peaks in HPLC chromatograms of eleven crude extracts isolated using the QuEChERS method indicated that quercetin 4'-glucoside (**A22**) has a highly-positive correlation (0.91) with antiallergic activity. Quercetin 4'-glucoside (**A22**) isolated from Satsuki cultivar onion showed high antiallergic activity (IC_{50} = 3.0 ± 0.2 μg/mL) and a high amount (69.4 mg/kg). Therefore, we conclude that QuEChERS extraction and correlation coefficient are a systematic method of selection or prediction for main active compounds, without having to isolate all the candidate compounds and biologically test potent fractions. Overall, we also conclude that quercetin 4'-glucoside is a unique flavonol that is water-soluble, has high antiallergic activity, and is abundant in onion.

The entire results raise the value as the antiallergic material of the food used in usual meals (onion and mint), and flavonoid is concerned with the antiallergy mainly. In the olive study, new function as antiallergy was found in secoiridoid, and this result promote more effective use of waste material. This study provides significant and basic information regarding for further development leading compounds of antiallergic drugs or nutraceutical applications.