Total synthesis of nobiletin and probe molecules

Aiki HIZA

School of Pharmaceutical Sciences, University of Shizuoka

Nobiletin (**1**), which is isolated a polymethylated flavone from Citrus, has received special attention for its remarkable biological activity such as prevention of Alzheimer's Disease (AD). However, it was known that isolation as a pure nobiletin from natural source was required tedious process. Thus, we started approaching total synthesis and introduction of probe units to apply pharmacodynamic studies.

A practical synthesis of nobiletin was accomplished by using our novel flavone synthesis through β-diketone intermediate that was readily obtained by condensation of C-acyl donor and aryl methyl ketone. Additionally, a selective demethylation of synthetic nobiletin and rapid incorporation of ^{11}C atom was accomplished. Subsequently, the synthetic probe was able for a positron emission tomography imaging study.

Additionally, the installation of aminopentyl group to 5-demethyl nobiletin (**2**) was carried out to convert various probe molecules such as a fluorescein probe and a biotin probe. The introduction of probe units was accomplished by using Hüisgen reaction with alkyne and azide. Now, we are applying these probe molecules to pharmacodynamic studies.