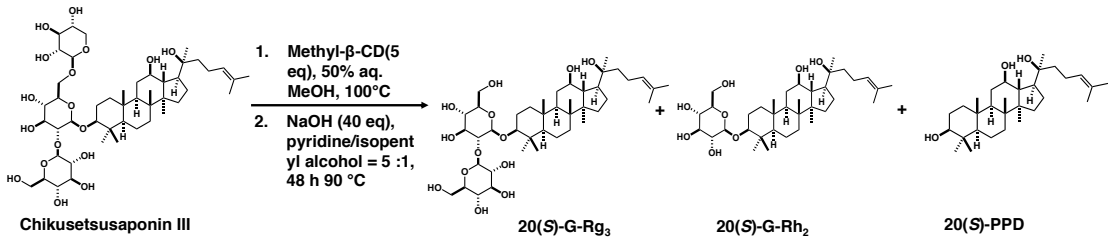
Efficient Isolation and Purification of Monoglucosyl Ginsenoside G-Rh_2 with CNS Protective Activity from an Extract of Chikusetsu Ginseng

([1]*United Graduate School of Drug Discovery and Medical Information Sciences, Gifu University,* [2]*National Center for Geriatrics and Gerontology,* [3]*Faculty of Engineering, Gifu University,* [4]*Gifu University of Medical Science*) ○ Yoshiki Ooshima,[1,2] Hiroko Koyama,[1,3] Aya Ogata,[2,4] Hiroshi Ikenuma,[2] Yasuyuki Kimura,[1,2] Takashi Kato,[1,2] Masaaki Suzuki[2,3]

Keywords: Ginsenoside; Cyclodextrin; Hydrolysis of sugar

Ginsenosides, active components of Korean ginseng as medicinal resources in traditional Chinese medicine, have recently been considered as a potential therapy for central nervous system diseases.[1] We planned to evaluate the brain uptake of highly active metabolites, prosapogenols distinguished as Compound-K, Ginsenoside-Rh_2 (G-Rh_2) and the sapogenin 20(*S*)-protopanaxadiol (PPD) by non-invasive molecular imaging technology positron emission tomography. In this study, we attempted to synthesize and isolate enough amounts of G-Rh_2 and PPD from ginseng extract, which contains various ginsenosides, in order to synthesize the precursors for labeling.

Chikusetsusaponin III contained a three glucose residue in the structure, isolated from Japanese ginseng (Panax japonicus C.A. Meyer), was used to optimize the conditions of glucose hydrolysis. Following the reported conditions, PPD was obtained from Chikusetsusaponin III at 90% yield under NaOH (40 eq)/1-butanol conditions at 90 °C for 24 hours.[2] To selectively obtain the partial hydrolysis intermediate G-Rh_2, we controlled the reaction rate by using co-solvent of non-protonic polar solvent, and protected the resulted structure with cyclodextrin. Actually, the inclusion complex between Chikusetsusaponin III and methyl-β-cyclodextrin was reacted in the presence of NaOH (40 eq) in pyridine/isopentyl alcohol (5:1, *v*/*v*) at 90 °C for 48 hours, resulted in the selective improvement and the 61% isolation yield of objective G-Rh_2.



1) H.-J. Kim, S.-W. Jung, S.-Y. Kim, I.-H. Cho, H.-C. Kim, H. Rhim, M. Kim, S.-Y. Nah, *J. Ginseng Res.,* **2018**, *42*, 401. 2) J.-F. Cui, S. Bystroem, P. Eneroth, I. Bjoerkhem, *J. Org. Chem*., **1994**, 59, 8251.