Synopsis of Original Research Paper

Structural Property and Improvement Activity of Skin Barrier Function by Sphingoid Diene in Plant-Derived Glucosylceramide

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We have reported that a glycosylceramide (GlcCer) showed improvement in skin barrier function in mice. Only the GlcCer from pineapple (P-GlcCer) showed the activity among other plant-derived GlcCers. We supposed the specific activity would be originated from the chemical structure of P-GlcCer, especially the moiety of sphingadienine (SD) would have the responsibility for the specificity. Here, we reported the investigation of the structure-activity relationships between the cis/trans geometries of sphingadienines (SD-1~4) and their biological activities. The challenge was initiated to establish the stereoselective synthesis of sphingadienines (SD-1~4). The stereoselective hydrogenolysis of ene–yne was employed to construct the diene moiety. The ene–yne units were prepared by stereoselective addition of acetylide ions of ene–yne units to Garner's aldehyde. Wittig reaction and Johnson–Claisen reaction afforded the required starting ene–ynes. Lindlar catalyst reduced alkyne to afford cis olefin, on the other hand, Red-Al reduction afforded trans olefin. By combination of Wittig/Johonson–Claisen reactions and Lindlar/Red-Al reductions, stereoselective syntheses of SD-1~4 were achieved. Cytotoxicity of SD-1~4 was checked by MTT assay. These compounds showed no cytotoxicity against RBL-2H3 cells at the concentration of 4.71 μg/ml. To confirm the anti-allergic activity of SD-1~4, RBL-2H3 cells were preincubated with each geometric SDs before sensitization of anti-DNP IgE and challenge of DNP-albumin. β-Hexosaminidase released into supernatant was measured as an index of its degradation. It was demonstrated that 4*cis*, 8*cis*-SD possessed the highest activity compared with the other three ones.