Anti-inflammatory Compounds of *Patrinia saniculaefolia*

Ren-Bo An[1,2], KiHwan Bae[3]

[1]Key Laboratory of Natural Resources of Changbai Mountain & Functional Molecules (Yanbian University), Ministry of Education

[2]College of Pharmacy, Yanbian University, Yanji, Jilin, 133000, China

[3]College of Pharmacy, Chungnam National University, Daejeon 305-764, Korea

Patrinia saniculaefolia Hemsley (Valerianaceae) is an endemic species of the genus *Patrinia* in Korea,(1) which has not been clarified as to its constituents. Several plants of the genus *Patrinia* have been used as traditional folk medicine in Korea and China for the treatment of initial stages of appendicitis, perityphlitis, neuralgia, emmenagogue, insomnia in the neurasthenia, psychoses and acute bacterial inflammation.(2) The whole plant was extracted with methanol; the extra was suspended in H_2O and successively partitioned with hexane, CH_2Cl_2 and BuOH. Repeated silica gel column chromatography and reversed phase HPLC from the hexane soluble fraction afforded two new iridoids (**4** and **5**), together with the known compounds *β*-farnesene (**1**), Squalene (**2**), nardostachin (**3**), oleanolic acid (**6**), oleanonic acid (**7**), 3*β*, 23-dihydroxyurs-12-en-28-oic acid (**8**), 3-*O*-α-L-arabinopyranosyl-oleanolic acid (**9**), *β*-sitosteryl-3-*O*-*β*-D-glucopyranoside (**10**), 3-*O*-*β*-D-glucopyranosyl-oleanolic acid (**11**), and 3-*O*-[*β*-D-xylopyranosyl-(1→3)-*β*-D-glucuronopyranoside-6-*O*-butyl ester] (**12**). The molecular formula of compound **4** and **5** were $C_{22}H_{34}O_8$ by high resolution FABMS, and from an analysis of its ^{13}C NMR and DEPT data. On the basis of ^{1}H, ^{13}C NMR, HMQC, HMBC and ^{1}H-^{1}H ROESY spectral data, their structures were established as (1*S*,3*R*,5*R*,7a*R*)-3,5-dimethoxy-7-hydroxymethyl-1-(3-methylbutanoylox-y)-4-(3-methylbutanoyloxymethyl)-1, 3, 5, 7a-tetrahydrocyclopent-4, 6-diene[*e*]pyran and (1*S*,3*S*,5*R*,7a-*R*)-3,5-dimethoxy-7-hydroxymethyl-1-(3-methylbutanoyloxy)-4-(3-methylbutanoyloxymethyl)-1, 3, 5, 7a-tetrahydrocyclopent-4, 6-diene[*e*]pyran, which were named patridoid Ⅰ and patridoid Ⅱ, respectively. Patridoid Ⅱ is unstable in air and it transforms to compound **5-A**, (1*S*,3*S*,5*S*,7a*R*)-3,5-dimethoxy-7-hydroxymethyl-1-(3-methylbutanoyloxy)-4-(3-methylbutanoy-loxymethyl)-1,3,5,7a-tetrahydrocyclopent-4,6-diene[*e*]pyran.

Among these compounds, compound **3** exhibited strong COX-2 inhibitory activity with the IC_{50} value of 3.26 μM.

In the 5-LOX assay, compound **2** showed the most potent activity (IC_{50} = 36.3 μM) among the isolated compounds.

Patridoid Ⅰ and patridoid Ⅱ inhibited both COX-2 and 5-LOX. The IC_{50} values were 8.7 μM (COX-2) and 41.7 μM (5-LOX) for patridoid Ⅰ, and 13.6 μM (COX-2) and 46.9 μM (5-LOX) for patridoid Ⅱ, respectively. Both patridoid Ⅰ and patridoid Ⅱ have a *β*-methoxy group at C-6. This methoxy group may account for the difference in efficacy.

Depending upon their chemical structures, compounds **1-12** exhibited varying degrees of inhibition on the classical pathway of the complement system. In the structure-activity relationships, a carbonyl or hydroxy group at C-3 in the amyrin type triterpene was an essential element for enhancing the anti-complement activity. Compounds **6**, **7** and **8** exhibited inhibitory activity with IC_{50} values of 470.1, 212.2, and 121.0 μM, respectively. However, compounds **1-5**, **5-A**, and **9-12** showed no anti-complement activity.

References:

1. Lee, Y. N. (1996), Flora of Korea, Kyo-Hak Publishing Co., Ltd.

2. Inada *et al*. (1993), Shoyakugaku Zasshi 47, 301-304.