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ANTITUMOR ACTIVITY OF *PULSATILLA* SAPONINS AGAINST SOME HUMAN CANCER CELL LINES AND MICE BEARING LL/2

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Seventeen saponins isolated from the root of *Pulsatilla koreana*, 11 known and 6 new saponins, were tested for *in vitro* and *in vivo* antiutmor activity. It was observed that the saponins possessing free carboxylic acid in C-28 showed cytotoxic activity against A549, SK-OV-3, SK-Mel-2 and HCT15 cancer cell lines, whereas their sugar-bonded esters were inactive, implying the importance of the free acid moiety. Among the cytotoxic saponins, 3-*O*-[*O*-α-L-rhamnopyranosyl-(1-2)-*O*-[*O*-β-D-glucopyranosyl-(1-4)-α-L-arabinopyranosyl] oleanolic acid (**SB364**) had the most potent cytotoxicity (an average IC_{50} value of 3.7μg/ml), while hederagenin saponin having the same trisaccharide moiety in C-3 (**SB365**) showed a weaker activity (average IC_{50} value, 9.83μg/ml), meaning that the hydroxyl group in C-23 decreased the cytotoxicity. The cytotoxic activity of lupenoic saponins was much weaker than oleanoic saponins. Among the saccharide moieties in C-3, presence of 3-*O*-[*O*-α-L-rhamnopyranosyl-(1-2) -α-L-arabinopyranosyl] moiety is essential for the activity. Linking one glucopyranosyl group to C-4 of the arabinosyl group improved the activity as recognized in **SB365.** Both of **SB364** and **SB365** acted cell-specifically against SK-Mel-2 cell line showing a strong cell-killing effect (IC_{50}, 3.04 and 1.57μg/ml).

In vivo antitumor activity using BDF1 mice bearing LL/2 was tested for 6 saponins. **SB365** exhibited the highest IR (Inhibition Rate) value of 70% followed by 3-*O*-[*O*-β-D-glucopyranosyl-(1-4)-*O*-β-D-glucopyranosyl-(1-3)-O-α-L-rhamnopyranosyl-(1-2)-α-L-arabinopyranosyl] hederagenin (**SB366**, 50%). **SB364** (32.7%) showing the most potent cytotoxic activity was weaker than **SB365** in the antitumor activity. Possibly, the hydroxyl group in C-23 of **SB365** might enhance the bioavailability in tumor tissue, suggesting that the hederagenin-based saponin is superior to the oleanolic acid-based one in antitumor activity. The structure-activity relationship will be described in more detailed manner for this presentation.