29TM-pm08

Hedgehog/GLI-mediated transcriptional inhibitors from *Acacia pennata* and *Exocoecaria agallocha*

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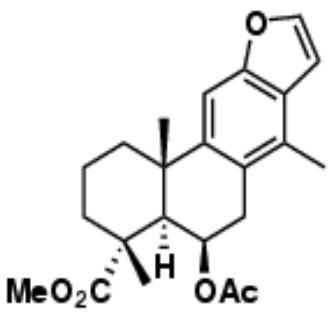
Glioma-associated oncogene (GLI) represents a pathway target gene of Hedgehog (Hh) signaling. In our comprehensive research, we search for active downstream Hh/GLI inhibitors from natural products that could be applicable to GLI-dependent cancers. Terpenoids (**1**, **2**) and flavonoid glycosides (**3**, **4**) from *Acacia pennata* (AP) and *Exocoecaria agallocha* (EA) have been isolated according to activity-guided fractionation. Compound **1**, **2**, **3** and **4** inhibited Hh signaling with IC_{50} of 1.6, 13.5, 10.5 and 43.8 μM respectively. These compounds were also cytotoxic against human pancreatic (PANC1) and prostate (DU145) cancer cell but did not affect normal cell line. Results of western blotting and real time RT-PCR likewise provided similar apparent of inhibition.



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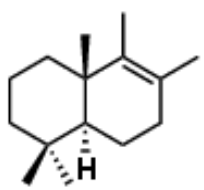

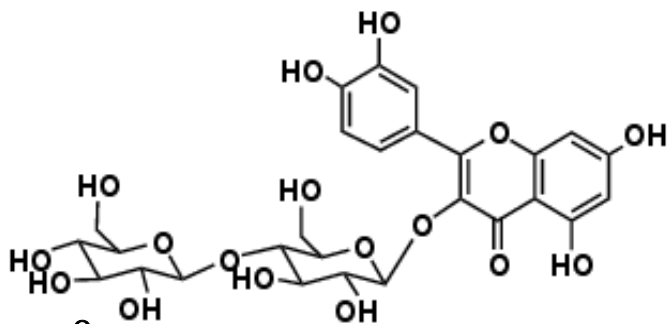

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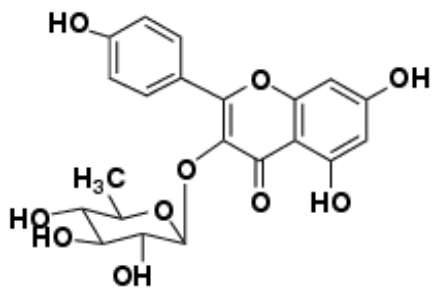

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1) Arai, M. A., Tateno, C., Hosoya, T., Koyano, T., Kowithayakorn, T., Ishibashi, M. *Bioorg. Med.Chem.* **2008**, *16,* 9420-9424.

2) Hosoya, T. , Arai, M. A., Koyano, T., Kowithayakorn, T., Ishibashi, M. *ChemBioChem* **2008**, *9*, 1082-1092.