Triterpene glycosides and phenylpropane derivatives from *Staurogyne concinnula* possessing anti-angiogenic effect

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Abstract

In the course of our search for potential anti-cancer agents, four undescribed (**1-3, 5**) and one known oleanane-type triterpene glycosides (**4**), along with five known phenyl propane derivatives (**6-10**) were isolated and characterized from Taiwanese herbal medicine *Staurogyne concinnula* (Hance) Kuntze. Structural elucidation of the undescribed compounds was mainly based on 1D and 2D NMR, as well as LC-MS/MS techniques. Biological evaluation revealed that **4** possessed the significant anti-angiogenic effects (IC_{50} 4.0 ± 0.2 μM). Further mechanism action studies of **4** by inhibition of integrin/FAK/paxillin signaling pathway and its downstream effectors as MMP2 and MMP9 were also presented.

Material and Method

Staurogyne concinnula (Hance) Kuntze

Dried material (5.0 kg)

→ Extracted 3 times with EtOH 95%, at 50 °C; Evaporated under vacuum

Crude extract (550.0 g)

→ Partitioned with *n*-Hexane, EtOAc, *n*-BuOH; Evaporated under vacuum

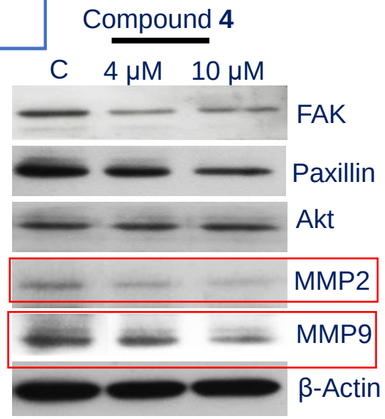
- ***n*-Hexane layer** ǂ (53 g)
- **EtOAc layer** ǂ (150 g)
- ***n*-BuOH layer** ǂ (160 g) → Diaion HP20 column; Mobile phase: MeOH – H_2O

Anti-angiogenic assay

- ✓ Matrigel and cell line EAhy926
- ✓ ǂ samples which were investigated the anti-angiogenic effect

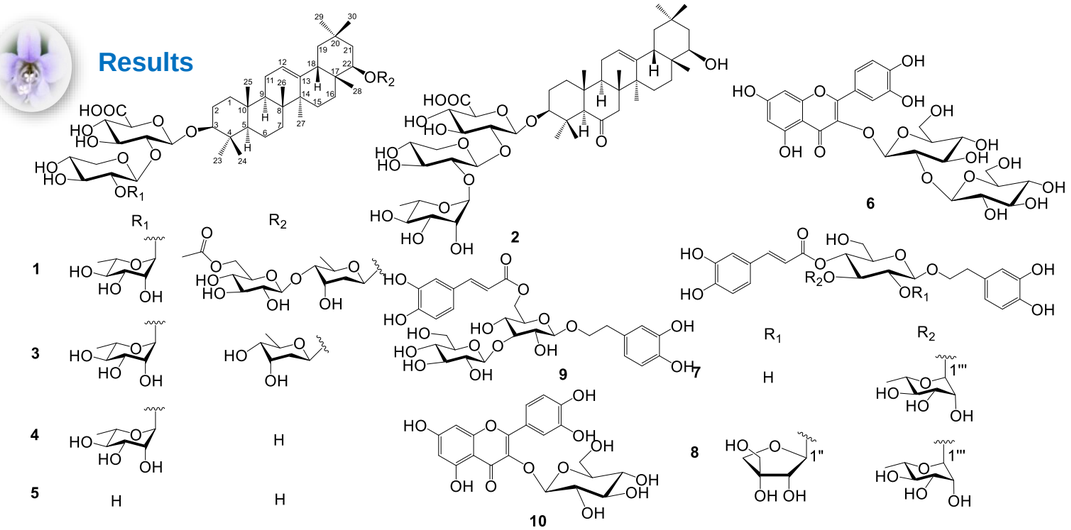
- **Fr. A**ǂ (7.5 g) → Mobile phase: MeOH 35% → Cpds **6-9**
- **Fr. B**ǂ (3.3 g) → Pre-HPLC ODS column; Mobile phase: ACN 50% → Cpds **1-5**ǂ

MS, NMR data, conducting I_2-catalyzed oxidative condensation to confirm sugar moieties by LC-MS/MS → Structural elucidation



The inhibition of integrin/FAK/paxillin signaling pathway of **4**.

Results



Isolated structures from *S. concinnula*

Conclusion

This is the first report that four un-described saponins (**1-3,5**) and known one named baptisiasaponin I (**4**), as well as five phenylpropanoid glycosides (**6-10**), were isolated from *S. concinnula*. Compound **4** proved the significant anti-angiogenic effect via the inhibition of integrin/FAK/paxillin signaling pathway and its downstream effectors as MMP2 and MMP9. Furthermore, the evidence indicated that four isolated saponins possessed the same triterpene with different amounts of sugar moieties implied that the oxidation state of C-6 and the length of sugar chains in sophoradiol saponin would play a crucial role in the anti-angiogenic activity.