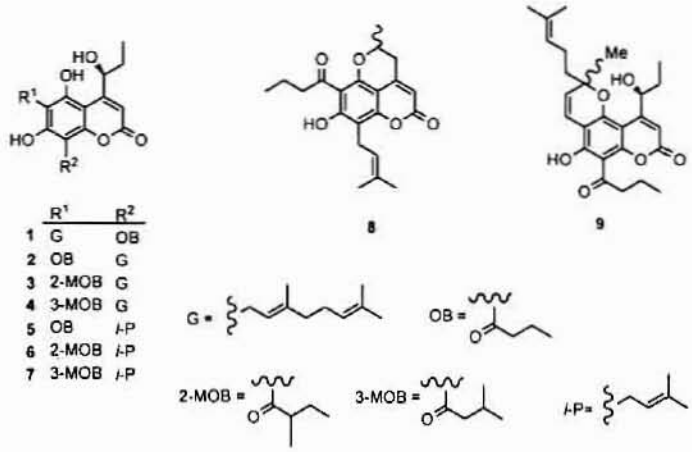
1C-06 Novel anti-cancer agents from the flower of *Kayea assamica* of Myanmar

○ Nwet Nwet Win,[a] Suresh Awale,[a] Hiroyasu Esumi,[b] Yasuhiro Tezuka,[a] Shigetoshi Kadota[a]

[a]*Institute of Natural Medicine, University of Toyama;* [b]*National Cancer Center Research Institute East*

Pancreatic cancer is the fifth leading cause of cancer death with the lowest 5-year survival rate of all cancers. It is largely resistant to conventional forms of chemotherapeutic agents. Therefore there is dire need to search alternative drug candidates to minimize the lost of human life. Among different forms of cancer cells, pancreatic cancer cells have marked tolerance to nutrient starvation that enables them to survive for prolong period of time. Thus the agent that retards the cancer cells tolerance to nutrient starvation (anti-austerity agent) was considered as a novel approach in anti-cancer drug discovery.[1] Under this hypothesis, we have screened the medicinal plants used in Myanmar traditional medicine for their preferential cytotoxicity against human pancreatic cancer PANC-1 cells under nutrient-deprived conditions.[2,3] Recently we discovered that the $CHCl_3$-soluble fraction of 70% EtOH extract of the flower of *Kayea assamica* King & Prain collected in Myanmar exhibited 100% preferential cytotoxicity (PC_{100}) against PANC-1 cancer cells under nutrient-deprived conditions at 1 μg/mL. Thus, detailed bioassay-guided fractionation and isolation was carried out, which afforded nine new coumarins, kayeassamins A–I (**1**–**9**), together with nine known coumarins. All the isolates were evaluated for their *in vitro* preferential cytotoxicity against PANC-1 cells in nutrient-deprived medium. Among them, the novel coumarins, kayeassamins A (**1**), B (**2**), D (**4**), E (**5**), and G (**7**) exhibited the most potent preferential cytotoxicity (PC_{100} 1 μM) in a concentration- and time-dependent manner and induced apoptosis-like morphological change of PANC-1 cells.



References

1. Awale, S.; Lu, J.; Kalauni, S. K.; Kurashima, Y.; Tezuka, Y.; Kadota, S.; Esumi, H. *Cancer Res.* **2006**, *66*, 1751–1757.
2. Win, N. N.; Awale, S.; Esumi, H.; Tezuka, Y.; Kadota, S. *J. Nat. Prod.* **2007**, *70*, 1582–1587.
3. Win, N. N.; Awale, S.; Esumi, H.; Tezuka, Y.; Kadota, S. *Chem. Pharm. Bull.* **2008**, *54*, 491–496.