MICPS2-048-PS

Renieramycins from Thai blue sponge *Xestospongia* sp. and their semisynthetic analogs as potential cytotoxic agants against non-small-cell-lung-cancer cell lines

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Abstract:
Renieramycins constitute a series of marine alkaloids within the bistetrahydroisoquinolinequinone family, which have been sourced from the Thai blue sponge *Xestospongia* sp., discovered at Si-Chang Island in the Gulf of Thailand. The chemical configurations of renieramycin A–Y have been documented. Notably, renieramycin M emerges as the principal chemical constituent. Renieramycin M and its semisynthetic analogs, harboring diverse ester substituents at positions C–5, C–7, and C–8 on ring A as well as C–22 on ring B , were synthesized and assessed for their cytotoxicity against non-small-cell-lung-cancer cell lines. The synthesis involved judicious chemical manipulations, encompassing hydrogenation, light-induced intramolecular photoredox reactions, and Steglich esterification. The findings from the investigation into the structure-cytotoxicity relationship imply that an additional ester motif governs cytotoxic efficacy, predicated on steric hindrance. This augmentation significantly enhances nanomolar cytotoxicity levels against H290 and H460 cell lines, surpassing the potency of renieramycin M by a factor of 5–20 folds.
Keywords: Renieramycin, bistetrahydroisoquinolinequinone, marine alkaloids, *Xestospongia* sp. anticancer, non-small cell lung cancer