沖縄産海洋生物からの抗感染症物質の探索

Form 3

Abstract

Title Search for Anti-Infective Metabolites from Okinawan Marine Organisms

Infectious diseases, without any doubt, have caused a lot of deaths worldwide, especially in developing countries and still remain as domestic and international public health concerns until now. Finding new anti-infective metabolites with stronger activity or newer mechanisms may overcome the problems caused by these diseases.

Okinawa is known for its richness in marine biodiversity. The area is characterized by the northern coral reefs supported by the Kuroshio Current. The high biodiversity provides huge opportunities from the view point of bioresources including new bioactive metabolites as drug candidates. As a thesis project, we worked on the hit extracts against penicillin binding protein (PBP), Nrf2, respiratory syncytial virus (RSV), hepatitis C virus (HCV) NS3 helicase, and cultured cells.

After screening against PBP, five known compounds **1**–**5** have been characterized from three marine sponges. Two known compounds **6**–**7** were identified from extracts of a green alga and a marine sponge, both of which showed activity in Nrf2 assay.

As the extract of the marine dinoflagellate *Vulcanodinium rugosum* was shown to be active against RSV, it was separated to give known portimine (**8**) and a new cyclic imine named kabirimine (**9**). The absolute configuration of **8** was determined by modified Mosher`s method and X-ray diffraction analysis. Partial relative configuration of **9** was deduced by analyzing NOEs/NOESY and JBCA results.

Furthermore, four new aromatic compounds **10**–**13** have been isolated from the crinoid *Alloeocomatella polycladia*. The anticlockwise arrangement at axial chirality of **12** and **13** was elucidated by observing electronic circular dichroism (ECD) spectra. The aromatic sulfates **10**–**13** showed moderate inhibition against NS3 helicase with IC_{50} values of 71, 95, 7, and 5 μM, respectively.

From an extract of an unidentified marine sponge, two new carbonimidic dichlorides **17** and **18** were isolated together with three analogues: axinyssimides C (**19**), reticulidin A (**20**) and **21**. Compounds **17** and **18** showed moderate cytotoxicity against NBT-T2 cell with IC_{50} values of 3.0 and 2.2 μg/mL. In addition, two new cytotoxic molecules **22** and **23** were isolated from a sponge *Leucetta* sp. and an actinomycete *Streptomyces acidiscabies*, respectively.

Name Idam Hermawan