沖縄産海洋生物からの抗感染症物質の探索

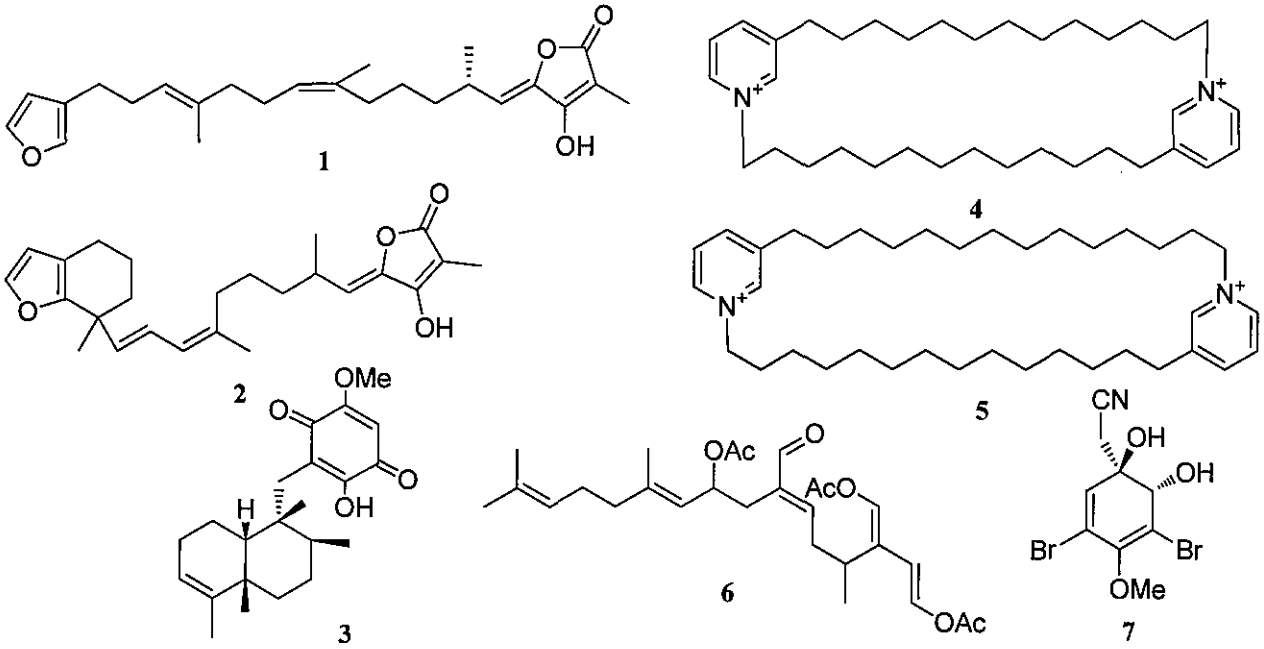
Search for Anti-infective Metabolites from Okinawan Marine Organisms

Idam Hermawan
Advisor: Junichi Tanaka

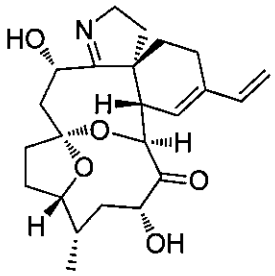
Infectious diseases are still major public health concerns and remain an important cause of mortality, especially in developing countries. Finding new metabolites with stronger anti-infective activity or new mechanisms could help overcome the problems caused by these diseases.

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

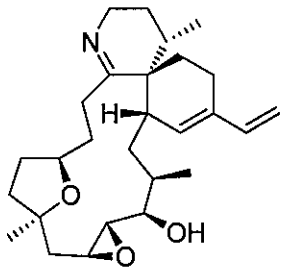
After screening against PBP, five known compounds **1–5** were characterized from three marine sponges. Two known compounds **6–7** were identified from extracts of a green alga and a marine sponge, both of which showed activity in Nrf2 assay.



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 observing NOEs/NOESY and JBCA results.

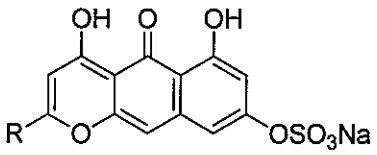


8

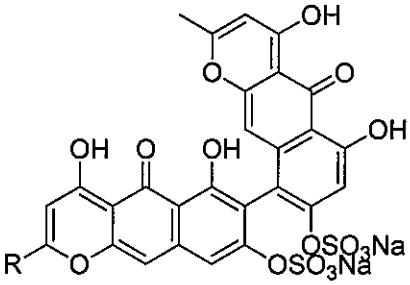


9

In addition, four new aromatic compounds **10–13** were isolated from the crinoid *Alloeocomatella polycladia*. The anticlockwise arrangement at axial chirality of **12** and **13** were determined by observing Electronic Circular Dichroism (ECD) spectrum patterns. The aromatic sulfates **10–13** showed moderate inhibition against NS3 helicase with IC_{50} values of 71, 95, 7, and 5 μM, respectively.

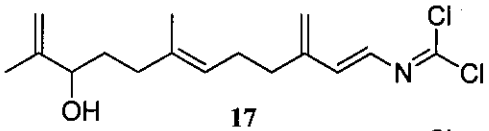


10 R = Me
11 R = Pr

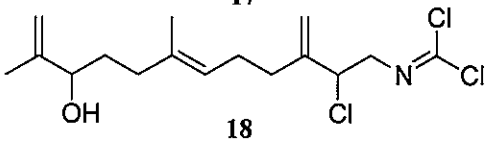


12 R = Me
13 R = Pr

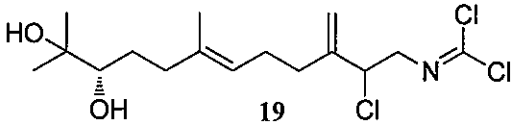
From an extract of an unidentified marine sponge, two new carbonimidic dichlorides **17** and **18** were isolated together with three analogues: axinyssimides C (**19**), reticulidin A (**20**) and **21**. Compounds **17** and **18** showed moderate cytotoxicity against NBT-T2 cells with IC_{50} values 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.



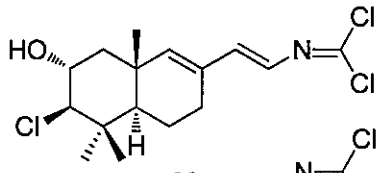
17



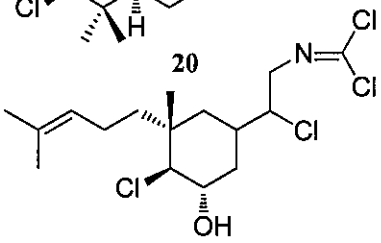
18



19



20



21

The results showed that marine organisms remain interesting sources for finding new anti-infective metabolites.