



Office of Technology Management

Laulimalide-derived Potent Microtubule Stabilizing Agent

Technology Reference

CV57

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Inventor

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Field

Oncology

Key Words

Synthetic laulimalide

Laulimalide analogs

Microtubule stabilizing agent

License Status

Seeking licensing partners

Patent Status

U.S. and PCT Applications have been filed.

Overview

Amphidinolides, a family of natural compounds that have shown promise as powerful antitumor agents, pose problems for cancer researchers because they are extremely scarce in natural environment. Work by our professor Arun Ghosh may solve this problem.

In this research the inventor has synthesized and evaluated a number of laulimalide-derived compounds as microtubule stabilizing agents. One of the analogs has shown potency similar to laulimalide. Laulimalide belongs to amphidinolides family and is a novel macrocyclic natural product isolated in miniscule quantities from marine sponges. It has been shown to possess significant antitumor properties, sharing the same mechanism of action as the anti-cancer drug Taxol.

Technical Summary

In this research the inventor completed the synthesis of laulimalide, which allowed the preparation and evaluation of various synthetic laulimalide analogs. Additionally, hybrid analogs of laulimalide and epothilone are being synthesized for testing. It has been reported that laulimalide binds at a site on tubulin polymer, which is distinct from the taxoid site. It has been found that laulimalide, while as active as paclitaxel, epothilone A, and eleutherobin in promoting the assembly of cold-stable microtubules, was unable to inhibit the binding of radiolabeled paclitaxel or of 7-O-[N-(2,7-difluoro-4'-fluoresceincarbonyl)-L-alanyl] paclitaxel, a fluorescent paclitaxel derivative, to tubulin. It has also been demonstrated that microtubules formed in the presence of both laulimalide and paclitaxel contained near-molar quantities, relative to tubulin, of both drugs. Laulimalide was active against cell lines resistant to paclitaxel or epothilones A and B on the basis of mutations in the M40 human α -tubulin gene. This synthetic success is showing promising results in laboratory tests against certain cancers previously treated by the drug Taxol, and has shown the ability to kill cells resistant to Taxol. The UIC chemistry professor hopes amphidinolide will prove to be even more effective as an antitumor agent.

Benefits

- Synthesized compound replacing naturally occurring scarce antitumor agent.
- Exhibit microtubule stabilizing properties of Taxol without the disadvantages of Taxol such as multidrug resistance, debilitating side effects and poor aqueous solubility
- Epithilones- similar to Taxol in that they stabilize microtubule assemblies, maintain cytotoxic against P-glycoprotein expressing MDR cells.

Areas of Application

- Laboratory tools
- Drug Discovery
- Cancer treatment
- Research
- Breast carcinomas
- Refractory ovarian carcinomas
- Small cell lung carcinomas
- Metastasis carcinomas
- May be used in TX of breast, ovarian, small-cell lung, myeloid leukemia, Met CA, CA of skin, neck and head

Stage of Development

- Synthesized and evaluated compounds