Pharmacog-enomics

Development of Molecular Targeted Medicines Using Ridaifens (RIDs) from G1 to G5 Synthesized in TUS

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Purpose of Research

Our synthetic team is researching reaction methods that can improve the synthetic yield of pharmaceutical products to the maximum. Ridaifen (RID) can be prepared readily from aromatic aldehydes, allylic nucleophiles, and aromatic nucleophiles in the presence of Lewis acid catalysts by the three-component coupling reaction which was developed at our laboratory as the key process. Development research on drugs for treating leukemia, cancer, osteoporosis, and hyperlipidemia, as well as antimicrobial agents using this agent, is ongoing. Furthermore, a compound that exhibits inhibitory action on cancers that have become resistant to "Velcade," a therapeutic for multiple myeloma, has been discovered. We have a variety of RIDs that have structural features designed from the first generation (G1) to the fifth generation (G5).

Summary of Research

To date, we have provided a compound library of RIDs, which are compounds originally developed at our university using the three-component coupling reaction, and explored several lead compounds for new drugs through investigating structure-pharmacological activity correlations. Ridaifen-B (RID-B) exhibits antitumor activity and outstanding cytostatic effects on certain cancer cell lines.

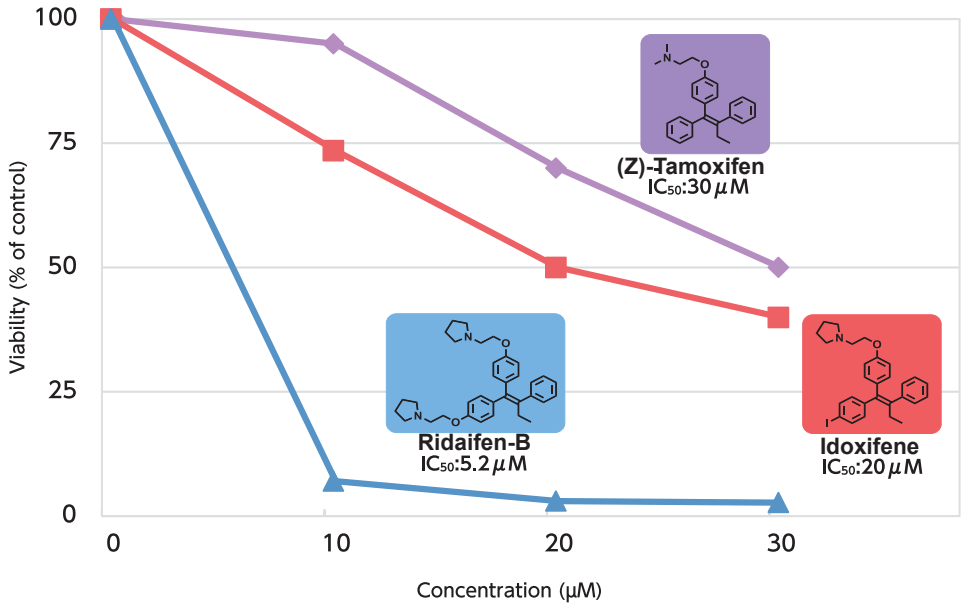

Figure: Potent antitumor activity of ridaifen-B

Points

- **High-efficiency synthesis of Ridaifens using the three-component coupling reaction developed at our university**
- **Low-cost synthesis**
- **Construction of a library of artificial compounds**

Comparison with Conventional or Competitive Technologies

○ Existing (examples)

- Anticancer agent, paclitaxel (Taxol®): Synthesized in 51 steps
- Anticancer agent, M-COPA, under development at our laboratory: Synthesized in 20 steps

○ This research

- "Ridaifens": Synthesized in 4 to 10 steps

Expected Applications

- Therapeutics for leukemia
- Anticancer agents
- Therapeutics for osteoporosis
- Therapeutics for hyperlipidemia

Challenges in Implementation

- Analysis of mechanism
- Development from in vitro to in vivo
- Acquisition of POC in preclinical studies
- Optimization of compound structure
- Establishment of mass-synthesis method

What We Expect from Companies

- Cooperation in exploration of uses
- Cooperation in performance of in vivo studies
- Joint application for large-scale AMED research funds
- Technical cooperation with GLP-level synthesis and GMP synthesis

Future Developments

March 2015 Start of marketing (RID-B: leading compound)
March 2019 The total synthesis yield achieved 50%.
March 2021 Candidate development compound: GLP-level synthesis
March 2022 Preclinical studies of the candidate development compound

- Associated system: AMED Project for Advanced Drug Discovery and Development
- Award: Award for Science and Technology, the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology 2015
- Intellectual Property: Patent No. 05234558 "Anticancer agents containing tamoxifen analogues as active ingredients"
- Sample: Supply is possible after conclusion of contract.

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