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|---|---|
| Title | Studies on macrocyclic lactone antibiotics XI. anti-mitotic and anti-tubulin activity of new antitumor antibiotics, rhizoxin and its homologues |
| Sub Title | |
| Author | 高橋, 正明(Takahashi, Masaaki)<br>岩崎, 成夫(Iwasaki, Shigeo)<br>小林, 久芳(Kobayashi, Hisayoshi)<br>奥田, 重信(Okuda, Shigenobu)<br>村井, 知子(Murai, Tomoko)<br>佐藤, 良博(Sato, Yoshihiro)<br>平岡(原口), 徳子(Hiraoka(Haraguchi), Tokuko)<br>長野, 弘(Nagano, Hiroshi) |
| Publisher | 共立薬科大学 |
| Publication year | 1987 |
| Jtitle | 共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.32 (1987. ) ,p.65- 66 |
| JaLC DOI | |
| Abstract | |
| Notes | 抄録 |
| Genre | Technical Report |
| URL | https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000032-0065 |

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# Studies on Macrocyclic Lactone Antibiotics XI. Anti-mitotic and Anti-tubulin Activity of New Antitumor Antibiotics, Rhizoxin and Its Homologues*

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The mode of action of rhizoxin (1a), a new antitumor macrolide, was investigated. Rhizoxin inhibited fusion of the male and the female pronuclei in feritilized sea urchin eggs and inhibited cilia formation in the deciliated sea urchin embryos. *In vitro*, poly-

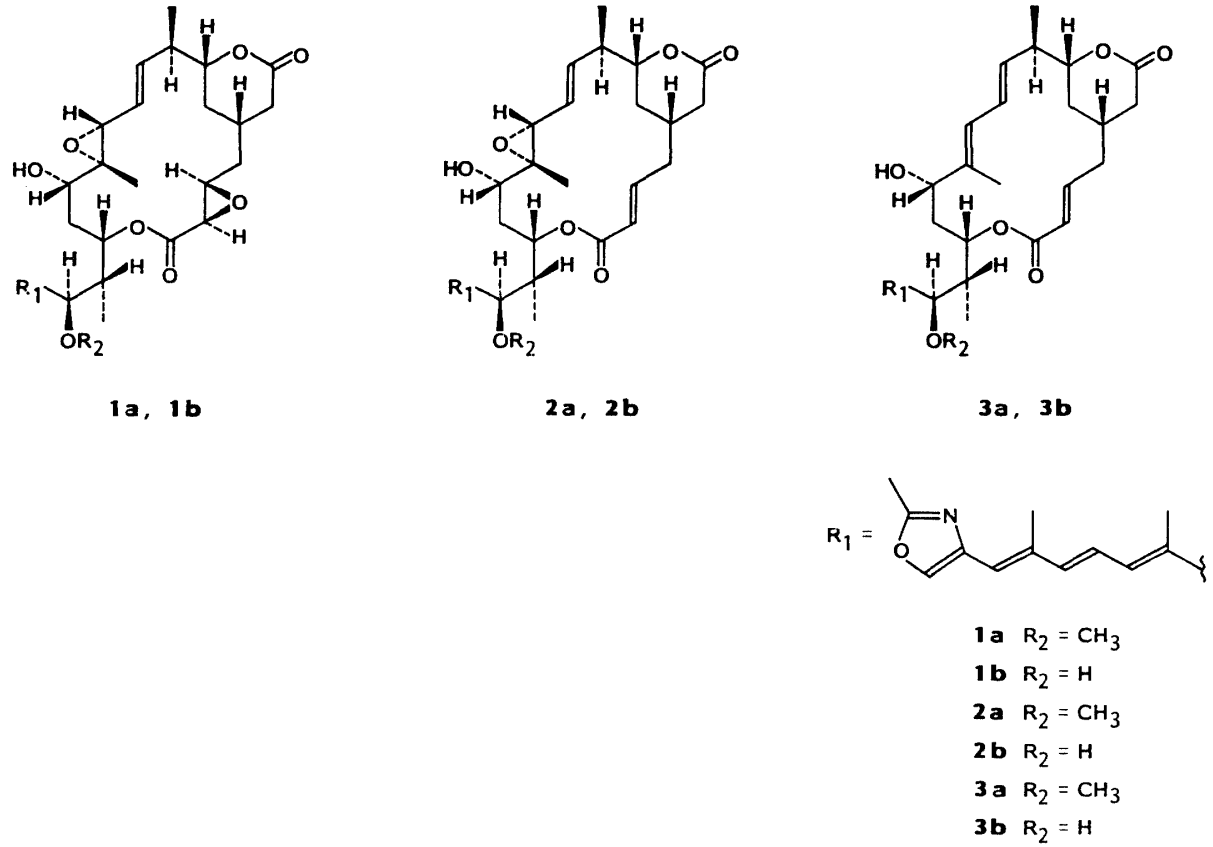


Fig. 1. Structure of naturally occurring rhizoxin homologues.

* 本報告は *J. Antibiotics*, **40**, 66—72 (1987) に発表.

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merization of tubulin isolated from porcine brains was completely inhibited at a $1\times10^{-5}$ M concentration of rhizoxin, and tubulin which had been polymerized by incubation at 37℃ for 30 minutes was depolymerized by addition of $1\times10^{-5}$ M of the drug. Activity of rhizoxin against tubulin polymerization was compared with those of other anti-tubulin drugs such as colchicine, vinblastine and ansamitocin P-3. The homologues of rhizoxin, 1b～3b, also inhibited polymerization of the purified microtubule protein at almost the same extent as rhizoxin.