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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 fertilized sea urchin eggs and inhibited cilia formation in the deciliated sea urchin embryos. *In vitro*, poly-

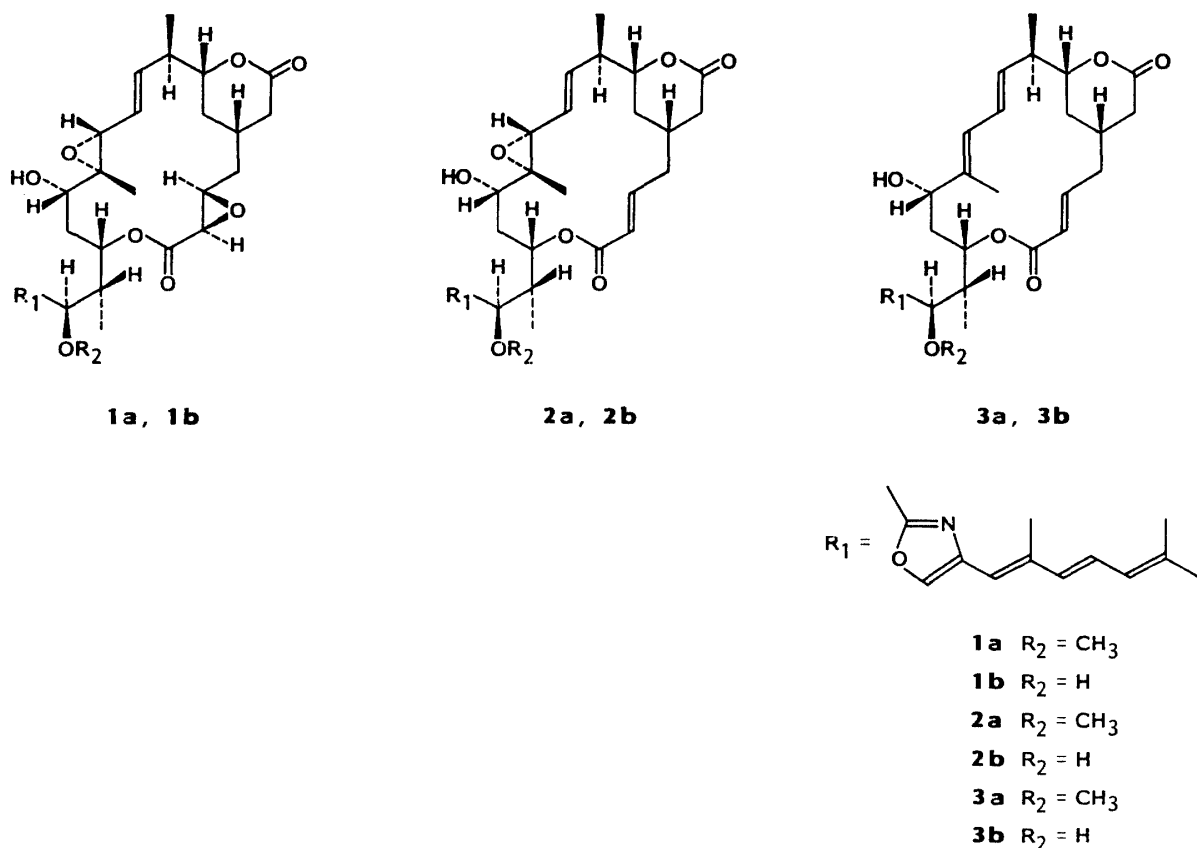


Fig. 1. Structure of naturally occurring rhizoxin homologues.

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merization of tubulin isolated from porcine brains was completely inhibited at a 1×10^{-5} M concentration of rhizoxin, and tubulin which had been polymerized by incubation at 37°C for 30 minutes was depolymerized by addition of 1×10^{-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.