Therapeutic effects of the marine natural product 11-*epi*-sinulariolide acetate on rats with adjuvant-induced arthritis.

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In recent years, a significant number of metabolites with potent anti-inflammatory properties have been discovered in marine organisms, and several of these compounds are now under clinical trials. We have isolated 11-epi-sinulariolide acetate (Ya-s 11), a cembrane-type compound from the soft coral Sinularia querciformis. Preliminary screening revealed that in lipopolysaccharide (LPS)-stimulated murine macrophages, 11-epi-sinulariolide acetate significantly inhibited the expression of proinflammatory proteins, nitric oxide synthetase, and cyclooxygenase-2. It is known that inflammation plays a critical role in the development of rheumatoid arthritis (RA), which affects about 1% of the world population. In the present study, we examined the therapeutic effect of 11-epi-sinulariolide acetate on adjuvant-induced RA in rats. RA was induced by injecting 10.01 of heat-killed Mycobacterium butyricum in Freund's incomplete adjuvant in the base of the tail of female Lewis rats. After adjuvant injection from day 7 to 28, the rats were subcutaneously injected with 3 or 9 mg/kg 11-epi-sinulariolide acetate once every 2 days. Animal experiments have shown that 11-epi-sinulariolide acetate significantly inhibits adjuvant-induced ankle edema and arthritis. Moreover, using histological analysis, we had found that 11-epi-sinularolide acetate also improved the histopathologic features of RA. We concluded that 11-epi-sinulariolide acetate attenuated the expression of proinflammatory proteins and the disease progression in the RA model. Hence, 11-epi-sinularolide acetate may serve as a useful therapeutic agent for the treatment of RA.