

## 옻나무(*Rhus verniciflua* Stokes) 주요 단일성분과 그 유도체를 이용한 다중기전 림프부종 치료제 후보물질 개발

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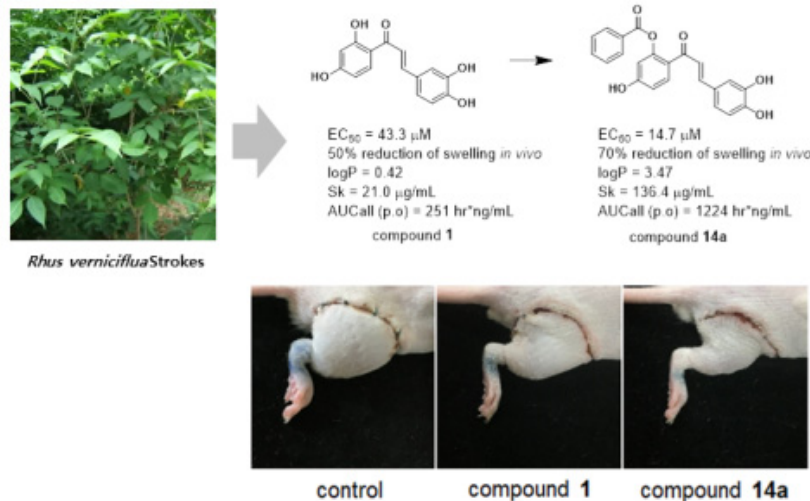
### Development of Drug Candidate for the Treatment of Lymphedema Using Natural Product and its Derivatives from *Rhus verniciflua* Stokes

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Herein, we demonstrate that butein (1) can prevent swelling in a murine lymphedema model by suppressing tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) production. Butein derivatives were synthesized and evaluated to identify compounds with in vitro anti-inflammatory activity. Among them, 20  $\mu$ M of compounds **7j**, **7m**, and **14a** showed 50% suppression of TNF- $\alpha$  production in mouse peritoneal macrophages after lipopolysaccharide stimulation. Compound **14a**, exhibited the strongest potency with an in vitro IC<sub>50</sub> of 14.6  $\mu$ M and suppressed limb volume by 70% in a murine lymphedema model. The prodrug strategy enabled a six-fold increase in kinetic solubility of compound **1** and five-fold higher levels of active metabolite in the blood for compound **14a** via oral administration in the pharmacokinetics study. We suggest that the compound **14a** could be developed as a potential therapeutic agent targeting anti-inflammatory activity to alleviate lymphedema progression.



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