

***Ophioglonol* Suppresses Psoriatic Progression via FOXO1 Nuclear Translocation and Modulation of the PI3K/AKT and NF- κ B Pathways**

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Abstract

Psoriasis is an immune-mediated skin disease characterized by aberrant keratinocyte proliferation and chronic inflammation. This study evaluated the anti-psoriatic activity of *Ophioglossum* extract, identified its key active constituent, and elucidated the underlying molecular mechanism. An imiquimod-induced psoriasis-like mouse model was used to assess the effect of *Ophioglossum* ointment, and the core active constituent was tracked by combining a HaCaT hyperproliferation model with chromatographic separation and drug-likeness evaluation. Keratinocyte inflammation models induced by IL-17A or a TNF- α /IFN- γ cocktail were evaluated using CCK-8 and qPCR. Network pharmacology (PharmMapper, SwissTargetPrediction, and DisGeNET) combined with GO/KEGG enrichment analyses were employed to predict the core pathway. Further validation was performed by using Western blot and nuclear-cytoplasmic fractionation. *Ophioglossum* ointment significantly alleviated erythema, scaling, and epidermal thickening in psoriatic mice, reduced spleen weight, and modulated the proportions of B cells and macrophages in the spleen and lymph nodes, effectively suppressing psoriasis progression. Activity-guided tracking identified two active monomers, ophioglonol and ophioglonin, of which ophioglonol exhibited superior drug-likeness. Ophioglonol (1–5 μ g/mL) markedly inhibited aberrant keratinocyte proliferation, downregulated the pro-inflammatory cytokines IL-1 β , IL-6, and IL-8, and upregulated the anti-inflammatory cytokine IL-10. Target enrichment analysis identified FOXO1 as the core regulatory pathway. Mechanistic validation demonstrated that ophioglonol significantly inhibited IL-17A-induced PI3K/AKT phosphorylation, promoted FOXO1 nuclear translocation, upregulated the downstream cell-cycle inhibitor p21, and suppressed NF- κ B pathway activation, thereby blocking keratinocyte hyperproliferation and the inflammatory cascade. These findings establish ophioglonol as the core active substance underlying the anti-psoriatic effect of *Ophioglossum*, providing a novel candidate compound and theoretical support for the development of natural targeted therapies for psoriasis.

Keywords

Ophioglossum, Ophioglonol, Psoriasis, Foxo1, Pi3k/Akt, Nf-Kb, Keratinocyte