

PC9

# Exploring the Potential Anti-Psoriatic Properties of A Semi-Synthetic 14-Deoxy-11,12-didehydroandrographolide Derivative

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## ABSTRACT

**Introduction:** Psoriasis is a chronic skin disease characterized by inflammation and hyperproliferation that affects around 2% to 3% of the global population. Currently, no control is available for psoriasis and existing treatments have limitations due to side effects, necessitating the development of safer and more effective anti-psoriatic agents. This study was carried out to determine the anti-psoriatic activity of the 14-deoxy-11,12-didehydroandrographolide (DDAG) derivative via the inhibition of inflammatory pathways, such as nuclear factor kappa light chain enhancer of activated B cells (NF- $\kappa$ B) and mitogen-activated protein kinase (MAPK). **Methods:** Spontaneously immortalized human keratinocyte (HaCaT) and immortalized mouse macrophage (RAW264.7) cells, respectively were treated with andrographolide (AGP), DDAG, SRS49 (semi-synthesized DDAG), and gemcitabine (positive control). The cytotoxicity was evaluated via MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. **Results:** AGP (IC<sub>50</sub>: 3.03  $\mu$ M) and gemcitabine (IC<sub>50</sub>: 0.075  $\mu$ M) exhibited high cytotoxicity against HaCaT cells, while DDAG did not exhibit any toxicity even at high concentration (100  $\mu$ M). AGP and gemcitabine also displayed high cytotoxicity against RAW264.7 cells, with DDAG showing moderate cytotoxicity. SRS49 exhibit higher cytotoxicity against HaCaT cells (IC<sub>50</sub>: 48.67  $\mu$ M) compared to RAW264.7. SRS49 demonstrated anti-proliferative activity against HaCaT cells, indicating potential anti-psoriatic properties. Further studies will be conducted to investigate the effect of SRS49 against proteins involved in NF- $\kappa$ B and MAPK pathways through western blot analysis. **Conclusion:** SRS49 exhibited promising anti-psoriatic properties by selectively inhibiting HaCaT cell proliferation, making it a potential candidate for psoriasis treatment. However, additional studies are needed to determine whether SRS49 has anti-inflammatory activity in HaCaT cells induced with proinflammatory agents, such as tumour necrosis factor-alpha (TNF- $\alpha$ ) and interleukin 17 (IL-17) to further support its efficacy against psoriasis.

**Keywords:** Psoriasis, 14-Deoxy-11,12-didehydroandrographolide, Anti-proliferative, Anti-inflammatory