# In Vitro and In Vivo Antipsoriatic Efficacy of Protected and Unprotected Sugar–Zinc Phthalocyanine Conjugates

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Streszczenie

Psoriasis, a chronic immune-mediated skin disorder affecting over 125 million people globally, is characterized by abnormal keratinocyte proliferation and immune cell infiltration. Photodynamic therapy (PDT) remains underutilized in the treatment of psoriasis despite its potential as a promising and effective therapeutic approach. This study aimed to explore the efficacy of zinc phthalocyanine (ZnPc) and its sugar conjugates as potential antipsoriatic agents. We successfully synthesized protected and unprotected sugar-conjugated zinc phthalocyanines and evaluated their potential against cytokine-stimulated HaCaT keratinocytes, as well as an established IMQ psoriasis-like in vivo model. Tetrasubstituted protected glucose–ZnPc (Glu-4-ZnPc-P) demonstrated superior phototoxicity (IC50 = 2.55 µM) compared to unprotected glucose conjugate (IC50 = 22.7 µM), protected galactose–ZnPc (IC50 = 7.13 µM), and free ZnPc in cytokine-stimulated HaCaT cells (IC50 = 5.84 µM). Cellular uptake analysis revealed that IL-17A, a cytokine that plays a central role in the pathogenesis of psoriasis, enhanced unprotected Glu-4-ZnPc uptake by 56.3%, while GLUT1 inhibitor BAY-876 reduced its accumulation by 23.8%. Intracellular ROS generation following Glu-4-ZnPc-P-PDT was significantly increased after stimulation with IL-17A, correlating with in vitro photocytotoxicity. In vivo PDT using Glu-4-ZnPc-P exhibited significant improvement in Psoriasis Area and Severity Index (PASI), inhibiting splenomegaly and restoring normal skin morphology. This study highlights sugar-conjugated zinc phthalocyanines as potential candidates for targeted PDT in psoriasis, providing a basis for further clinical investigations.

Słowa kluczowe

zinc phthalocyanine, sugar conjugates, psoriasis, cytokines, drug uptake

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