

Glycoconjugated zinc phthalocyanine as a novel photodynamic therapy tool for the treatment of psoriasis

Despite the progress in the development of novel treatment modalities over the past decades, studies reveal that a significant portion of patients with psoriasis remains undertreated relative to the severity of their disease. Psoriatic patients experience treatment failure with, or intolerance to, traditional systemic therapies and/or phototherapy and switch to biologic agents as second-line therapy. However, biologics are costly, inaccessible for general public and require repeated injections. Thus, new, rationally designed agents are needed to replace or complement currently applied therapies.

Recent evidence points that targeting glucose transporter GLUT1 and sugar metabolism offers a novel therapeutic strategy for the treatment of psoriasis and other hyperproliferative skin diseases. In this project, for the first time, we aim to assess the effectiveness of novel photosensitizer - glycoconjugated phthalocyanines (Glu-ZnPc) - in psoriasis therapy. It is expected that coupling multivalent carbohydrates to the porphyrin core allows their interaction with more than one receptor-binding site at the same time and thus increases their affinity, resulting in better cellular recognition and uptake.

The first phase of the project involves synthesis of a glucose-conjugated photosensitizer that is stable, less toxic, and has a more efficient transport system than previously synthesized compounds. The second phase consists of *in vitro* evaluation of the cytotoxic and anti-inflammatory activity and uptake of glycoconjugates, in order to prove their preferential accumulation in highly proliferative psoriatic keratinocytes. The last phase will focus on *in vivo* studies to verify the efficacy and safety of the novel drug in comparison to non-conjugate on psoriatic mice, as well as examine the underlying mechanism of action through evaluation of scoring the severity of skin inflammation and immunohistochemical staining in response to treatment.

It is expected that the glycoconjugated zinc phthalocyanine used in PDT may become a scientific foundation for a novel therapeutic approach in the treatment of psoriasis.