Boron-Containing Dermatologic Drug Design Using Soft-Drug Strategy
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Topical therapeutic application of boron-containing new chemical entities (BNCEs) has been a significant focus of R&D at Anacor Pharmaceuticals. Several BNCEs have been identified as anti-inflammatory agents and are currently undergoing preclinical and clinical development for the topical treatment of psoriasis and atopic dermatitis. For a topically used drug, the possible systemic side effects are expected to be relatively low as compared to the systemic usage. In an ideal case, a topically applied drug exerts its therapeutic action in the target area of the skin and then converts into inactive and non-toxic metabolites if any drug penetrates the skin and reaches systemic circulation. This so-called soft-drug approach may further improve the therapeutic index of BNCEs.

With this strategy, we have designed and synthesized multiple series of BNCEs containing carboxylic ester group(s). These ester BNCEs were found to be excellent anti-inflammatory agents with a range of inhibitory potencies against phosphodiesterase 4 (PDE4). Various ester compounds showed nanomolar-level IC50 for PDE4. These ester compounds were found to be converted in mouse plasma, in vitro or in vivo, to the carboxylic acids, which are inactive against PDE4.

This presentation will describe the design, synthesis and biological data of related BNCEs with soft-drug strategy.

Reference