# Topical Delivery of Methotrexate Via Skin Pretreated With Physical Enhancement Techniques: Low-Fluence Erbium:YAG Laser and Electroporation

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**摘要**

**Abstract**

BACKGROUND AND OBJECTIVE: The high hydrophilicity and molecular weight of methotrexate (MTX) make it difficult to deliver via the skin route for treating psoriasis or rheumatoid arthritis. The objective of this study was to enhance and optimize the skin permeation of MTX using two physical techniques: an erbium:yttrium-aluminum-garnet (Er:YAG) laser and electroporation. METHODS: In vitro skin permeation was performed using horizontal side-by-side diffusion cells. The animal model utilized nude mice. The skin where epidermal hyperproliferation was reproduced by repeated barrier abrogation was also used as a permeation barrier for MTX delivery. RESULTS: Application of the laser and electroporation significantly enhanced the permeation of MTX. The enhancing effect was more pronounced after applying the laser. Er:YAG laser pretreatment on the skin produced a 3- to 80-fold enhancement dependent upon the magnitude of the laser fluence. Using electroporation, treatment with 10 pulses resulted in a twofold increase in MTX flux. A combination of laser pretreatment and subsequent electroporation for 10 minutes resulted in a higher drug permeation than either technique alone. However, this synergistic effect was only observed when the lower laser fluence (1.4 J/cm(2)) was applied. Hyperproliferative skin generally showed a greater variability of MTX flux and lower permeation. CONCLUSION: The results shown in the present study encourage further investigation of laser- and electroporation-assisted topical drug delivery.