TECHNOLOGY

Extending and Maintaining Micropore Viability of Microneedle Treated Skin with Cholesterol Synthesis Inhibitors

OVERVIEW

Transdermal drug delivery is an attractive alternative to oral delivery (which may reduce drug efficacy by first pass metabolism) and hyperdermic injections (which are commonly associated with pain and systemic side effects). A limited spectrum of drugs are able to passively cross the stratum corneum (SC, the outermost layer of the skin), encumbered by the physiochemical properties of the drugs. The addition of microneedles (MN) to transdermal patches provides a minimally invasive solution that enables the delivery of larger, more complex molecules in a relatively pain-free manner. The rate-limiting step of MN-treated skin is the rapid closure of the micropores following insult, which ultimately diminishes the effectiveness of the drug delivery. To address this limitation, this invention is a method in which fluvastatin (FLU), a cholesterol synthesis pathway inhibitor, is used to prolong the duration of pore lifetime for sustained drug delivery. Biochemical inhibitors prevent the synthesis of the essential lipids required for proper healing of the SC, thus extending effective drug delivery time. Local concentrations of specific inhibitors of the three SC-associated lipid synthesis pathways (namely cholesterol, fatty acids, and ceramides) can be used to alter the molar ratio, delaying barrier recovery, thereby extending drug delivery time. These inhibitors can be used as a pretreatment or directly in the formulation during application of the drug.

Preclinical in vivo studies have demonstrated positive safety profiles of FLU and the ability to sustain the lifetime of the micropore and drug delivery for up to 7 days across MN-treated skin. Naltrexone (NTX), a u-opioid receptor agonist used in treatment of opiate and alcohol addiction, was formulated for FLU micropore patch delivery and showed no increase in skin irritation or alterations in skin recovery after occlusion removal. NTX is an ideal candidate drug, given its issues with oral bioavailability, patient compliance, and side effects.

ADVANTAGES

Ø Controlled, continuous drug delivery extends drug delivery window up to 7 days

Ø Good safety profile: does not increase irritation over placebo

Ø Cost-effective: reduced drug volume

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PATENT STATUS

U.S. Patent 10,022,366 issued 07/17/2018

LICENSE STATUS

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AS-2013-103