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Review

Drug Delivery Methods for Compromised Skin

Megha Rajput, B.S[1], Howard Maibach, M.D[2]

[1] College of Osteopathic Medicine, William Carey University, [2] Dermatology, University of California, San Francisco

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Background

Topical and transdermal delivery methods are explored to understand efficient techniques to deliver drugs to damaged skin. The objective of this paper is to review recent studies to interpret drug delivery efficiency when skin has been compromised with disease or treatment.

Methods

Using search engines and inclusive word choices to search and compile recent research on the subject matter of topical drug delivery. After removing articles not benefiting the review, 11 studies were included.

Results

Betamethasone dipropionate spray a topical corticoid cream, improves skin conditions like psoriasis. The Er:YAG laser increased vitamin c levels 86% and microdermabrasion moderately increased vitamin c levels by 20 fold compared to untreated skin. An increased TEWL and a decrease in permeation depth determines effectiveness of GMO-based cubic liquid crystals (Ma et al., 2020). Various microneedles were an effective method to deliver insulin and decrease blood glucose.

Conclusion

Relativity few transdermal drugs are commercialized partially because of the challenge to penetrate stratum corneum; microneedling may offer potential for such purposes. Betamethasone dipropionate spray and GMO-based cubic liquid crystals are novel and may be potentially effective for treating psoriasis and laser damage respectively.

INTRODUCTION

The epidermal water barrier layer is crucial for hydration, but also a passageway for treating disease (Kircik, 2014). Topical and transdermal delivery methods are explored to understand efficient techniques to deliver drugs to damaged/diseased skin. Drug delivery depends on stratum coreum viable epidermis, dermis, or hair follicles.[2] Skin barriers like the stratum corneum and tight junctions in the interfollicular epidermis, hair follicles, and glands challeng drug delivery.[2] Skin damaged by conditions such as psoriasis and eczema results in dry, scaly, painful, and itchy skin and topical corticoids and emollients can help treat such conditions.[3] Tattoos might be removed creating laser damage to the skin; damage is caused by burn and skin degeneration.[1] The size and depth of the burn will determine damage severity that might be repaired with a novel topical GMO-based cubic liquid crystals.[1] The transdermal drug delivery method is only available for a small group of drugs due to inability to penetrate stratum corneum, but microneedling, a relatively new technique, has demonstrated efficiency.[4]

METHODS

Search engines included were Pubmed, Science Direct, and Google Scholar. To narrow the search, one word or short phrases were used to understand the efficiency in the topical medicinal delivery of drugs on compromised skin. The oldest article was published in 2011, the majority are recent. The focus is on microneedle and aqueous creams. The key terms used were transepidermal water loss, atopic dermatitis, eczema, topical delivery of drugs, vitamin c, insulin, methotrexate, and fentanyl, laser injury. Only human studies were reviewed. Eleven relevant articles were identified with a focus on six articles that provide an in-depth update. N=11 scientific studies were reviewed and five are specifically reviewed for an in-depth focus on recent studies.

TOPICAL DELIVERY

A. DFD-01

Betamethasone dipropionate spray (DFD-01) in 0.05% strength, a topical coridcoid, that with the use of its emol-

lient vehicle can improve skin diseases such as psoriasis.[3] Jackson enrolled 18 healthy volunteers that used dry shaving of volar forearms to create a compromised skin barrier. The drug reduced TEWL; increased the capacitance in part one of the experiment, and in the second part, the skin had softened and increased its flexibility.[3] Jackson suggested that reapplication of the cream is required for continued effects.

B. VITAMIN C

Lee et al. examined topical delivery of vitamin c with the prodrug magnesium ascorbyl phosphate via resurfacing techniques such as laser and microdermabrasion. The Er:YAG laser increased vitamin c levels 86% fold compared to only 8.19 increase with CO2 laser. Microdermabrasion moderately increased vitamin c levels by 20 fold compared to untreated skin.

C. CUBIC LIQUID CRYSTAL

Ma et al., discusses the therapeutic effects of Glycerol monooleicate GMO-based cubic liquid crystals on lasers skin damage. TEWL and percutaneous depth of fluorescein isothiocyanate were used to evaluate the treatment of skin with GMO based cubic liquid. The crystals are transparent and viscous. TEWL levels decreased by day 14 and the FITC fluorescence showed a major decrease in permeation depth from day 7 to 14. The first 7 days, the permeation depth did not have significant changes.

TRANSDERMAL DELIVERY

A. INSULIN THROUGH MICRO-NEEDLING

Zhou et al. performed microneedling with different lengths on diabetic mice to deliver insulin. The greatest delivery method was by using 250- and 500- micrometer needle lengths together.[4] The needles were efficient in delivering insulin and decreasing blood glucose levels compared to no change with the positive control group. Approximately 25% of the initial blood glucose levels were present 1 hour after treatment and that dropped to 18% 3 hours after treatment. Overall, microneedles were effective in the transdermal delivery of insulin in mice.

DISCUSSION

Betamethasone dipropionate provided positive results in psoriasis. The findings suggest importance of the emollient vehicle to reduce itch and increase skin moisture. A future study might focus on a larger number of subjects for a prolonged period to estimate if the results would be lasting.

Micro-needling effectively delivered insulin using microchannels and decreasing blood glucose levels in diabetic mice. This intervention might be promising for diabetics and would benefit from a study with human patients to verify that microneedling is also an effective delivery method of insulin and the 250- and 500- micrometer needles is sufficient as seen in mice.

Laser and microdermabrasion study tested the increase of vitamin c delivery after treatment and showed one form of laser was more effective in increasing vitamin c levels. A newer study observed that there can be damage done by lasers as well which can be treated with cubic liquid crystals. The studies highlight the importance of the increased TEWL levels which indicate a higher absorption of vitamin c. This information is useful for a 2020 study that found an impressive solution to laser damage, GMO- based cubic liquid crystals. Laser damaged skin may be more penetrable; therefore, it increases absorption of nutrients like vitamin C.

CONCLUSION

Few treatments of drug delivery are via transdermal because of the challenge to penetrate the stratum corneum and tight junction, but microneedling is a unique tool that can be used for such purposes. Many topical drugs are present for healing damaged skin Betamethasone dipropionate spray and GMO-based cubic liquid crystals are novel and according to studies discussed potentially effective for treating psoriasis and laser damage respectively. Taken together, recent generations saw numerous transdermals and impaired topicals, but we suggest further innovation.

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Results:

Study	Purpose	Sample size	Outcome measures	Relevant Findings
Jackson et al.[3]	Test if corticoid cream Betamethasone dipropionate spray can heal conditions like psoriasis	18 healthy volunteers for both parts of the study	TEWL measurements using evaporimeter and epidermal hydration measurements in capacitance	-Betamethasone dipropionate spray and its vehicle decreased TEWL, therefore, increasing water retention in study 1 and skin hydration level in capacitance increased. -Study 2 displayed increased moisture and flexibility in skin.
Lee et al.[5]	Test if laser and microdermabrasion increase vitamin C delivery	Pretreated mice	Histological examination, amount of Vitamin C,	-Er:YAG laser showed the largest enhancement of vitamin c inducing a 86.04 fold increase compared to a 8.19 fold increase with CO2 laser at lower fluence. -After microdermabrasion the vitamin c levels were 20 times greater than untreated skin.
Ma et al.[1]	Test if GMO based cubic liquid crystals are in fact therapeutic to laser damaged skin	Guinea pigs	TEWL levels and percutaneous depth of fluorescein isothiocyanate	-Increased TEWL levels by day 14 -decrease in permeation depth shown on the FITC fluorescence from day 7 to day 14 with little to no depth shown. -GMO-based cubic crystals are effective topical treatment for laser damage
Zhou et al.[4]	Evaluate the efficacy of transdermal delivery of insulin with micro-needling treatment	Diabetic mice	Measurements of blood glucose levels, and assessment of various different needle length	-Overall microneedle rollers with different needle lengths can improve drug delivery. -250- and 500-micrometer lengths of needles when used together result in the most promising delivery of insulin. -Needles create micro channels to deliver insulin. -Between the first and third hours of treatment, blood glucose levels decrease to 18% initial amount and the positive control did not change blood glucose levels.

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