TRANSDERMAL DRUG DELIVERY TROUGH PHOTOINDUCED PRESSURE WAVES

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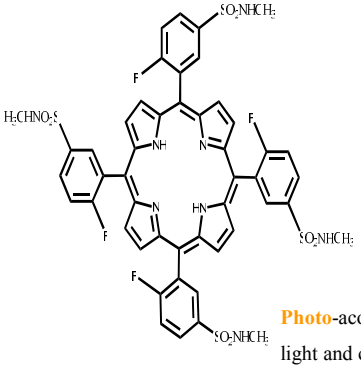
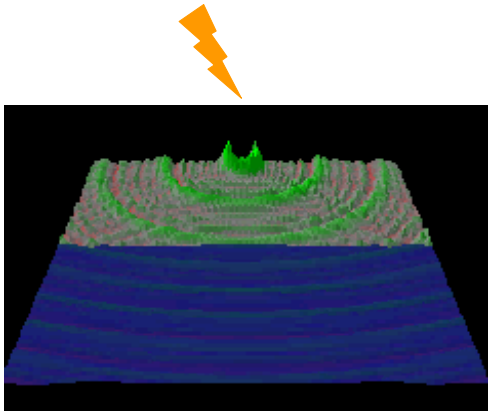
INTRODUCTION

The delivery of drugs with molecular weights in excess of 500 daltons through the *stratum corneum* remains a major obstacle to the widespread use of the transdermal pathway in Medicine. The limited success of chemical enhancers led to the development of many alternative physical processes. Recently, the photomechanical transdermal delivery of insulin was shown to be effective [1]. In this work we explore the use of photoinduced pressure waves [2] to deliver high molecular weight molecules (>1000 dalton) through the stratum corneum. We were able to permeate *ex-vivo* minipigs skin and *in vivo* minipig skin with the 27 kDa green fluorescence protein (GFP). The success of the active method developed in our labs – *LaserLeap* – is evaluated by fluorescence microscopy and confocal microscopy, which provides the tools to follow the delivered molecules. The parameters that control the size and efficiency of the photoinduced pressure waves are evaluated and maximized. It is shown that the pressure waves significantly increase transdermal delivery, when compared with conventional chemical enhancers.

LaserLeap method THEORY

Porphyrin





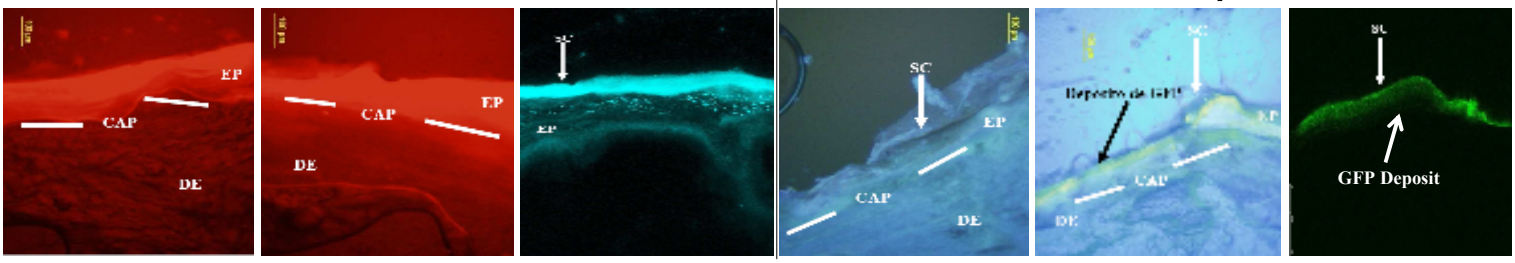
GFP
27 kDa

Photo-acoustic pressure wave formation occurs due to the deposition of heat in the **Target**: the material absorbs laser light and consequent photoexcitation allows a energy decay to the surroundings, where a thermal expansion propagates under the shape of a pressure wave, owing to volume confinement. As it reaches the **Skin**, the pressure wave induces a perturbation of the barrier function facilitating transdermal drug delivery. Our **OBJECTIVE** is to permeate the skin with a porphyrin and a fluorescent protein (GFP).

RESULTS

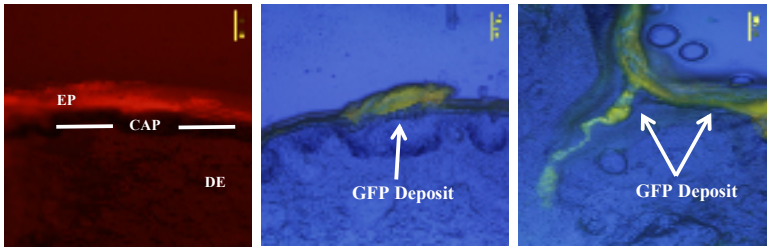
Porphyrin permeation

GFP permeation



***Ex-vivo* minipig Skin: after 15 minutes of contact skin: 6-12 laser pulses, 50-150 mJ.**

***SC* stands for *stratum corneum*, *EP* for epidermis, *CAP* for epidermis:dermis juction and DE for dermis.**



***In vivo* minipig Skin: after 15 minutes of contact skin, 12 laser pulses, 10-50 mJ.**

CONCLUSION: The results shows preferential accumulation of GFP and porphyrin in the minipig epidermis. Porphyrin results show an 10 times increase in the delivering compared with passive methods. High molecular weight GFP is only delivered with the active method proposed. We thus conclude the high potential of the active *LaserLeap* technique for transdermal delivery of biomedical relevant molecules as insulin, botox or vaccination.

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[2] L. G Arnaut, R. A. Caldwell, J. E. Elbert, L. A. Melton, Rev. Sci. Instruments, 63 (**1992**) 5381.

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