Biophysical transdermal drug delivery system

Heliya Mianmahale
Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
E-Mail: Heliya.mianmahale@yahoo.com

Abstract

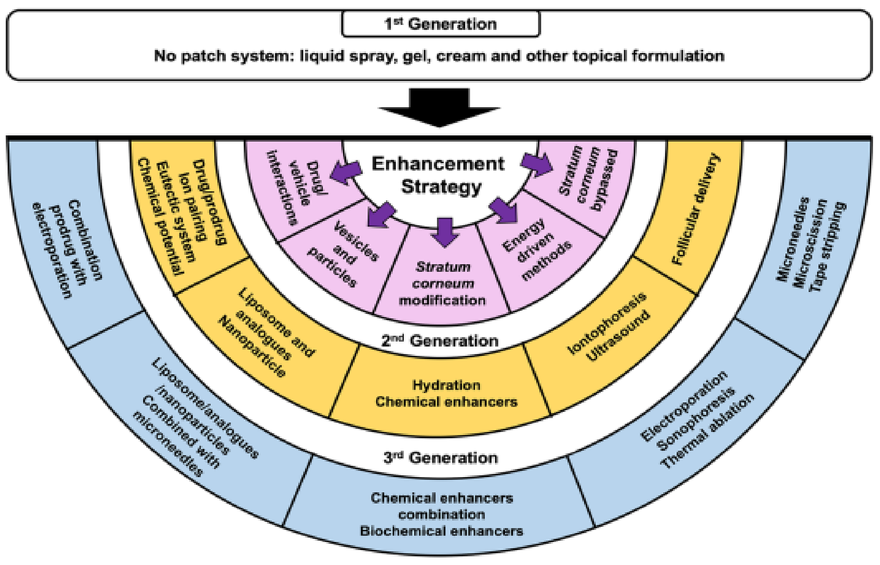
Skin drug delivery is a non-invasive method to transfer therapeutic agents, which has advantages such as slow drug releasing, patient satisfaction due to painlessness and low cost. However, the use of this type of drug delivery is limited due to the function of the internal barriers of the skin; because only small lipophilic molecules (less than 500 Da) can pass through the skin by passive diffusion. The main barrier to deliver the drug to the skin is the stratum corneum, thus it is necessary to use methods to increase the penetration of the skin to transfer the drug. Methods of increasing skin penetration for drug delivery include: Ultrasound, micro-needling, electroporation, thermal ablation (such as laser), iontophoresis and micro/nano carriers. Each of the mentioned methods to increase the permeability of the skin for drugs has its own advantages and disadvantages. Among the studied methods, the electrophoresis method causes cell death due to the high voltage of the electric field; the iontophoresis method is very popular to transfer proteins; the sonophoresis method increases the temperature on the surface and does not have much potential for delivery. Macromolecule microneedles ensure the penetration of the drug in the skin, and thermal methods cause the creation of pores without burns due to the short heating time of the surface, and also micro/nano carriers are structures developed for drug delivery. It is concluded that the use of the mentioned methods is effective for increasing the permeability of the skin to the drug and passing through the stratum corneum. The choice of the method used for drug delivery among the mentioned methods should be based on the structure and characteristics of the drug in order to obtain the best results.
Keywords: Skin, Transdermal drug delivery, Ultrasound, Micro-needles, Electroporation

Introduction

To date, oral delivery systems have been the most preferred method for prescription drugs due to the advantages they offer. Despite these advantages, oral delivery systems have limitations such as poor drug stability in the gastrointestinal tract and exposure to first-pass metabolism. Considering to overcome some of these disadvantages, the transdermal route is another promising way to increase drug delivery. Transdermal drug delivery systems have advantages such as being less invasive (some methods are completely non-invasive), avoiding first-pass metabolism, not requiring specialized personnel, and the potential to reduce the frequency of administration for patients. In addition, this technology has been used to deliver various types of drugs, including hydrophilic and hydrophobic compounds. The purpose of using different transdermal techniques is to modify or break the stratum corneum to increase drug penetration through the skin.

Materials and methods

Over the course of time, three generations of transdermal methods have been developed to increase the permeability of the skin to the drug. The third generation of methods is more important today. The following diagram summarizes the transdermal methods.



Conclusion:

- **Transdermal delivery systems as a solution to overcome problems associated with oral or injectable dosage forms**
- **Skin delivery systems are an efficient method for drug delivery, especially protein and peptide drugs**
- **One of the basic challenges of this method is choosing the most appropriate method among transdermal methods to increase drug permeability and transfer**
- **Advances in these transdermal drug delivery systems could be a driving force for controlling the prevalence of cardiovascular disease:**
  - **Central nervous system**
  - **Diabetes**
  - **Neuromuscular diseases**
  - **Genetic diseases**
  - **Infectious and local infectious diseases**

Results:

Reducing blood sugar by delivering insulin by sonophoresis

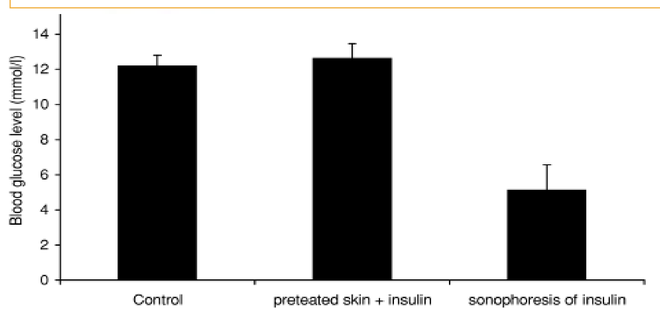


Figure 1: Blood glucose level decreased in mice after insulin delivery by low-frequency sonophoresis

Enhancing delivery of growth hormone-releasing factor (GRF) by iontophoretic method compared to intravenous and subcutaneous injection.

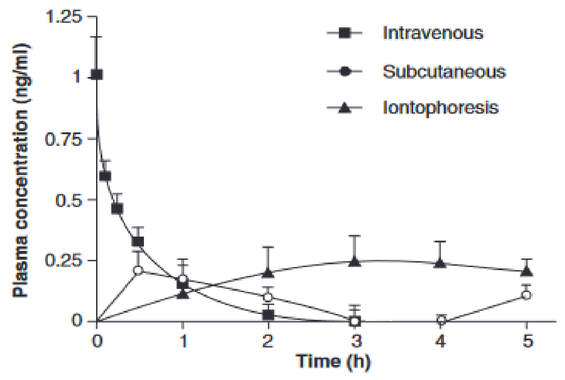


Figure 3: Figure shows growth hormone-releasing factor (GRF) delivery, in which steady-state plasma GRF levels are greater and more stable after iontophoretic delivery than intravenous and subcutaneous injection.

Increasing penetration of peptide drug for the treatment of psoriasis by transdermal method.

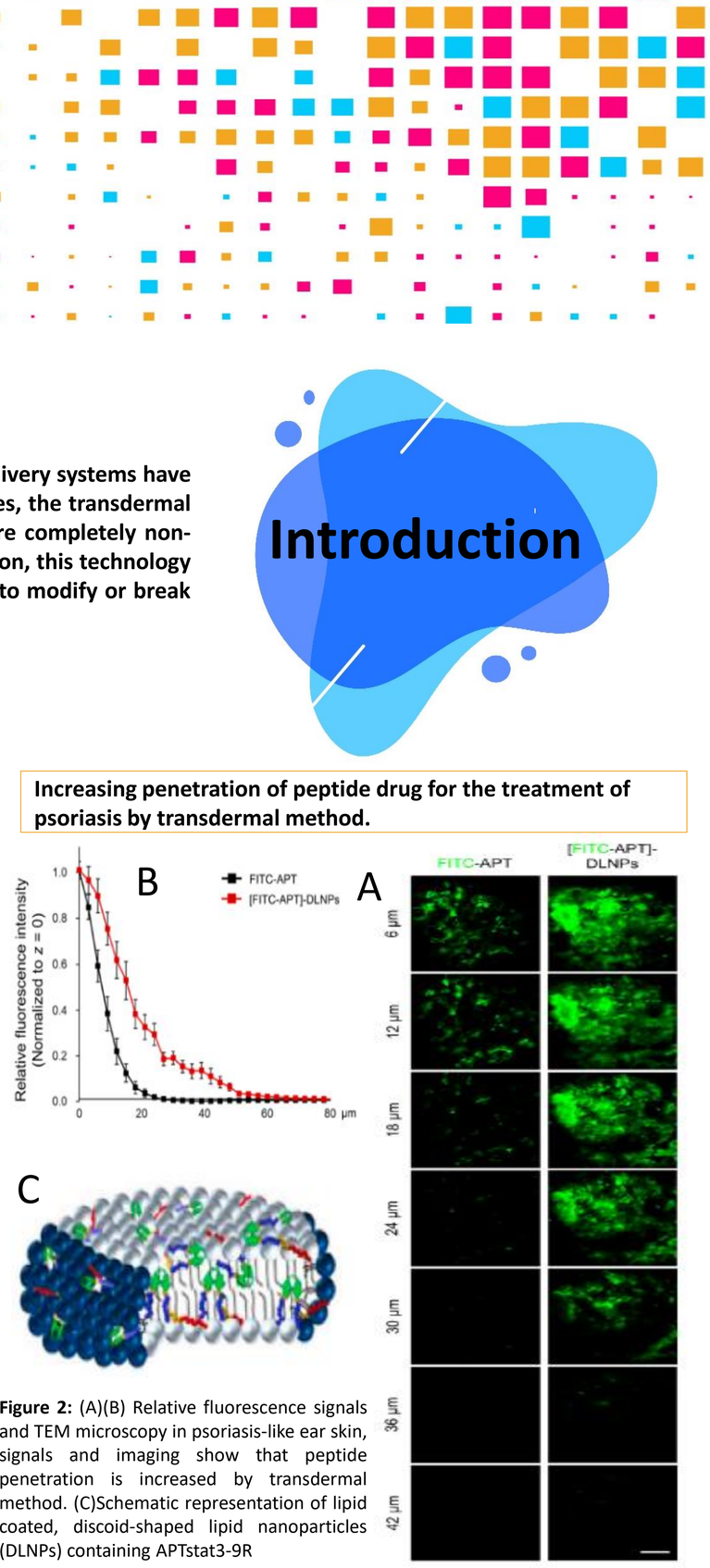


Figure 2: (A)(B) Relative fluorescence signals and TEM microscopy in psoriasis-like ear skin, signals and imaging show that peptide penetration is increased by transdermal method. (C)Schematic representation of lipid coated, discoid-shaped lipid nanoparticles (DLNPs) containing APTstat3-9R

Delivery of LHRH by the combination of electroporation and iontophoresis resulted in a four-fold increase in delivery compared to iontophoresis alone.

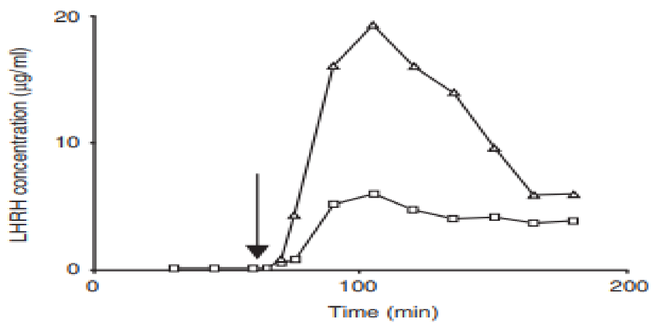


Figure 4: The bottom figure shows the delivery of LHRH in the isolated perfused ear of the pig ear. As seen in the first part of the diagram, LHRH cannot passively permeate across the skin. The combination of electroporation and iontophoresis resulted in an approximately four-fold increase in LHRH delivery compared to iontophoresis alone.

Reference:

1. Chaulagain B, Jain A, Tiwari A, Verma A, Jain SK. Passive delivery of protein drugs through transdermal route. Artificial Cells, Nanomedicine, and Biotechnology. 2018 Oct 31;46(sup1):472-87.
2. Jeong WY, Kwon M, Choi HE, Kim KS. Recent advances in transdermal drug delivery systems: A review. Biomaterials research. 2021 Dec;25(1):1-5
3. Long LY, Zhang J, Yang Z, Guo Y, Hu X, Wang Y. Transdermal delivery of peptide and protein drugs: Strategies, advantages and disadvantages. Journal of Drug Delivery Science and Technology. 2020 Dec 1;60.
4. Peña-Juárez M, Guadarrama -Escobar OR, Escobar-Chávez JJ. Transdermal delivery systems for biomolecules. Journal of Pharmaceutical Innovation. 2021 Jan 6:1-4.
5. Ita KB. Transdermal drug delivery: progress and challenges. Journal of Drug Delivery Science and Technology. 2014 Jan 1;24(3):245-50.