

Transdermal drug delivery: approaches and significance

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Transdermal drug delivery systems deliver drugs through the skin as an alternative to oral, intravascular, subcutaneous, and transmucosal routes. Potential advantages of transdermal delivery include, but are not limited to, elimination of first-pass metabolism, steady delivery/blood levels, better patient compliance, reduced systemic drug interactions, possible dose intervention, avoidance of medically assisted drug administration, prolonged drug administration, and overall better therapeutic efficacy.

Patches were the primitive form of transdermal drug delivery systems with conceptually simple engineering. The first representative of the transdermal drug delivery system patch design was Transderm-Scop[®] to treat motion sickness. The success of the scopolamine transdermal system was followed by approval of the nitroglycerin, fentanyl, estradiol, nicotine, and testosterone transdermal systems. Inception of transdermal patch systems paved the way for new medical therapies using existing drugs with the potential for fewer side effects. For example, estradiol patches, with a million users annually, do not cause liver damage, in contrast with oral formulations.¹ As a new medical therapy, transdermal nicotine systems have helped millions of smokers quit smoking and likely increased their lifespan.² Over the last three decades, more than 35 patch products have been approved by the US Food and Drug Administration in a wide range of therapeutic areas.

Need for more delivery systems

Despite this huge initial success, the scientific community soon recognized major obstacles, limiting the transdermal pipeline to just a handful of drugs. Passive permeation depends on the fusion of distinctive physicochemical properties of active pharmaceutical ingredients. Three major constraint characteristics, ie, low molecular weight (<500 Da), high lipophilicity, and low therapeutic dose, often determine the success rate.

Biochemical approaches to increasing skin permeability include synthesis of bioconvertible prodrugs and coadministration of skin metabolism inhibitors. Chemical permeation enhancers also increase skin permeability by increasing partitioning into the stratum corneum and/or solubilizing lipid structures in the stratum corneum. Enhanced solubility of hydrophobic drugs in chemical systems is an attractive advantage of this technique, with examples including oxybutynin, testosterone, and estradiol gel systems.

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Compared with physical techniques, chemical permeation enhancers offer flexibility in formulation design and ease of administration utilizing existing patch designs. A number of known chemical enhancers, eg. surfactants, fatty acids/esters, terpenes, and solvent systems, have been shown to produce significant enhancement towards achieving therapeutic levels.

High-throughput methods to screen transdermal chemical systems have made it possible to establish the enhancement profiles of numerous binary mixtures of known penetration enhancers. High-throughput in transdermal research is an emerging concept enabling throughput of several thousand experiments per day when screening novel formulations for potency.

Physical techniques in active drug delivery systems

A number of physical techniques have been developed into potential systems to facilitate active delivery of drugs across the skin. Most of these active techniques are currently in clinical development and are designed to deliver a wide variety of drugs and biological agents.

Iontophoresis and electroporation involve electric current as the driving force behind actively enhanced drug permeation. Iontophoresis involves movement of charged drug species through the skin under a constant electric current. In contrast with iontophoresis, electroporation establishes reversible aqueous pathways through the lipid bilayers when short pulsed electric current is applied to the skin surface. Large fluxes with a very short lag time have been observed for lidocaine when delivered using this technique.³ Electroporation has major application in minimally invasive intradermal delivery of DNA-based vaccines.

Microneedles are versatile in actively enhancing drug permeation in a number of ways. As a drug delivery system, microneedles disrupt the stratum corneum, forming channels when used as a pretreatment before patch application, leaching drugs into the epidermis when precoated and applied on the skin surface, and infusing large amounts of drug when used in combination with miniature pumps.

When skin is exposed to laser light at low energy levels, the barrier properties of the stratum corneum are altered by rearrangement of lipids and proteins and/or by removal of dead cells. Delivery of vaccines, vitamins, and anti-inflammatory drugs using laser light is currently under investigation.

A paradigm shift

Drug companies manufacturing transdermal are moving towards a rational approach in developing new medical treatments for existing drugs. Such initiatives are concentrating on disease models and justification of existence of such a treatment mode in therapeutic areas like depression, Parkinson's disease, Alzheimer's disease, anxiety, urinary incontinence, allergy, obesity, hypertension, pain, and epilepsy. At least 25 potential drug candidates have been identified so far for future patch development in the aforementioned areas. Increasing global medical needs have tapped the hidden potential of TDDS perfectly. Undoubtedly, the massive growth of research on transdermal and delivery systems is exponential. Transdermal drug delivery research truly has a future all in itself.

Research and Reports in Transdermal Drug Delivery is a unique open access journal dedicated to research on approaches to deliver drugs into and across the skin. The editorial team of the journal invites the researchers to submit their original scientific papers, review articles, and short communications for publication in this esteemed journal.

Disclosure

The author reports no conflicts of interest in this work.

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