SONOPHORESIS: AN ADVANCEMENT IN TRANSDERMAL DRUG DELIVERY SYSTEMS

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ABSTRACT

Sonophoresis is defined as the application of ultrasound to the skin resulting in enhanced transdermal transport of molecules. Low frequency sonophoresis or ultrasound is defined as sonophoresis or ultrasound at a frequency that is less than 2.5 MHz, more typically less than 1 MHz, more preferably in the range of 20 to 100 kHz. The transdermal delivery of biologics—as well as of conventional drugs—is growing in popularity because the technique offers numerous advantages. It reduces pain, bio hazardous waste, and risk of infection. Most importantly, needle-free drug delivery generally increases patient compliance. The present paper highlights the recent advancements in the field of sonophoresis, its mechanism and applications.

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INTRODUCTION

Sonophoresis is a process that exponentially increases the absorption of topical compounds (transdermal delivery) into the epidermis, dermis and skin appendages. Sonophoresis occurs because ultrasound waves stimulate micro-vibrations within the skin epidermis and increase the overall kinetic energy of molecules making up topical agents. It is widely used in hospitals to deliver drugs through the skin. Pharmacists compound the drugs by mixing them with a coupling agent (gel, cream, ointment) that transfers ultrasonic energy from the ultrasound transducer to the skin. The ultrasound probably enhances drug transport by cavitation, microstreaming, and heating. Sonophoresis is also used in Physical Therapy. In addition to its effects in delivering compounds into the skin, sonophoresis is being investigated as a way of drawing compounds such as glucose out of the skin.. During the AAPS National Biotechnology Conference in Boston, held June 19–21, a session entitled “Transdermal Delivery of Proteins,” explored some of the more popular technologies being used today. Among them are iontophoresis, sonophoresis (ultrasound), and microneedles. All of these approaches enhance transdermal drug delivery by increasing skin permeability and allowing the transmission of large molecules. Sonophoresis, or ultrasound, creates holes in the skin, and allows fluids to travel into or out of the body. “When sound is emitted at a particular frequency, the sound waves disrupt the lipid bilayers,” said Mitragotri. He pointed out that the ideal ultrasound frequency range for the transdermal delivery of biologics is 50-60 KHz. “The higher the frequency, the more dispersed the transmission,”

MECHANISM

There are numerous methods of administering drugs to the body, both passive and active. Active methods include the use of penetration enhancers and assisted drug delivery. One of them is sonophoresis (phonophoresis). This term is used to describe the effects of ultrasound on the movement of drugs through intact living skin and into the soft tissues. Although the exact mechanism of sonophoresis is not known, drug absorption may

involve a disruption of the stratum corneum lipids allowing the drug to pass through the skin. In the future, drug release systems aided by ultrasound may be able to provide slow release of vaccines. Researchers are currently exploring the applications in various areas like cutaneous vaccination, transdermal heparin delivery, transdermal glucose monitoring, delivery of acetyl cholinesterase inhibitors for the treatment of Alzheimer's disease, treatment of bone diseases and Peyronie's disease and dermal exposure assessment. The possibilities seem endless. Drug administration through skin patches, with the advent and development of ultrasound-mediated transdermal transport, may soon become the name of the game.

Sonophoresis or ultrasound can be used to create holes in the skin for fluids to travel into or out of the skin. By emitting sound at a particular frequency, the sound waves disrupt the lipid-bilayer of the stratus corneum (outermost layer of skin which has the most barrier properties), creating more and larger microchannels in the skin. Drugs can be administered through these channels, but this project will primarily use this to draw up fluids.

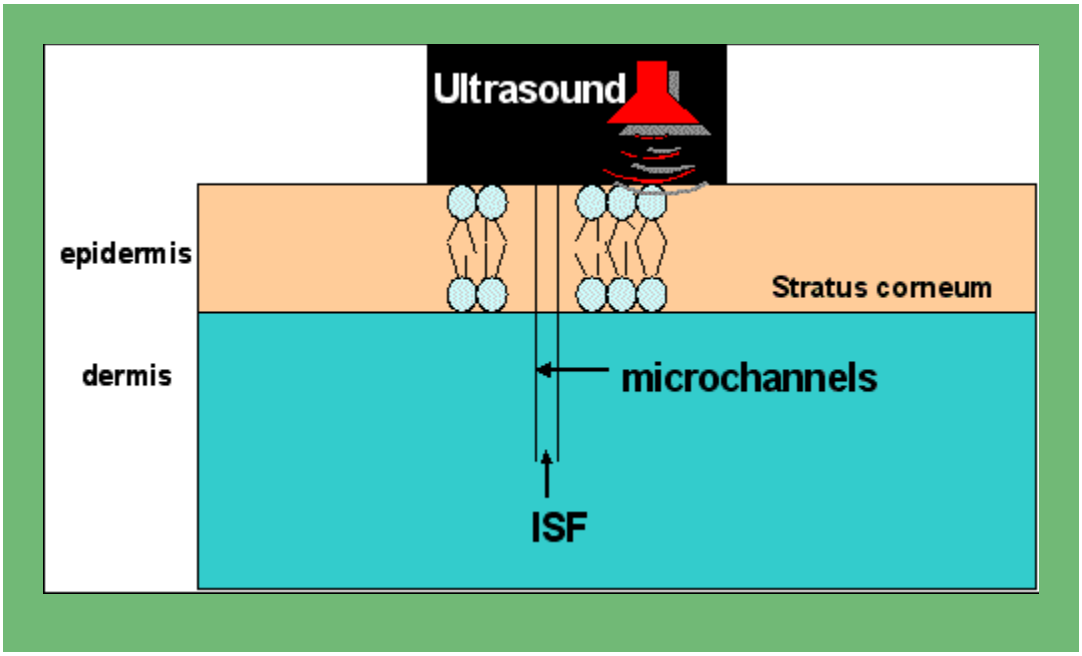

Figure : Picture of how ultrasound disrupts the stratus corneum.

The effects of ultrasound on extracting interstitial fluid (ISF) have been determined by various experiments on rats, cadavers, and human volunteers. Studies showed that low frequency ultrasound (~20 kHz) increased the permeability of the skin by many orders of magnitude better than high frequency ultrasound. Ultrasound treatment at 20 kHz with an intensity of 7 W*cm^-2 for less than 1 minute increased skin permeability for up to 15 hours. There is no pain or damage to the skin associated with this procedure, though it may slightly heat the tisssue. However, further studies assessing the safety of ultrasound after repeated extractions are still required. A low strength vacuum need to be applied for approximately five minutes to extract an adequate amount of interstitial fluid for making glucose measurements. The ultrasound device can be battery powered and be about the size of a deck of cards. Studies showed that low frequency ultrasound can be used to deliver insulin (sonophoresis). Ultrasound enables efficient continuous transdermal monitoring - combined with other techniques, it can decrease the time for extracting ISF to less than 1 minute.

APPLICATIONS

Besides, taking into account the varied possible applications of sonophoretic transdermal drug transport in the fields of biotechnology and genetic engineering, we can envision a whole gamut of newer technologies and products in the foreseeable future. An ultrasonic transducer that operates in flexure mode provides a highly efficient and compact sonophoresis device. Such a device is particularly useful for efficiently enhancing permeation of a substance through a membrane, such as dermal and mucosal membranes for purposes of transdermal/transmucosal drug delivery and/or body fluid monitoring. Many conventional sonophoresis devices have been developed and they are categorized into basic types, namely the disk-type and the horn-type. The literature review has shown that these devices have three major drawbacks: low efficiency, “dead” drug solution, and high electrical power consumption. Transdermal drug delivery offers an attractive alternative to injections and oral medications. However, applications of transdermal drug delivery are limited to only a few drugs as a result of low skin permeability. Application

of low-frequency ultrasound enhances skin permeability, a phenomenon referred to as low-frequency sonophoresis. In this method, a short application of ultrasound is used to permeabilize skin for a prolonged period of time. During this period, ultrasonically permeabilized skin may be utilized for drug delivery. In addition, a sample of interstitial fluid or its components may be extracted through permeabilized skin for diagnostic applications.

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