Fagron academy

INDUSTRY EDUCATION

Iontophoresis and Phonophoresis

April 22, 2024

Hudson Polonini, BPharm MSc PhD, and Anderson Ferreira BPharm MSc PhD

In the 18th century, Galvani and Volta worked together to combine knowledge about the possibility of electricity moving different metal ions and that these ionic movements might produce electricity. In the same century, the first reference was made to the iontophoresis method, initially described by Pivalti in 1747. However, only in the 20th century did the administration of drugs by iontophoresis begin to gain in prominence after the work of LeDuc, who introduced the term iontotherapy and formulated the laws that govern this process. Ionophoresis is the application of an electrical potential that maintains a constant electrical current through the skin. Using two electrodes on different locations of the skin and a weak current on the order of milliamperes, a circuit is created. As a result, normally uncharged molecules are charged, and the current propels the electrically charged molecule through the skin, without causing pain or irritation.

Iontophoresis is based on the principle that similar charges repel each other and different charges attract each other. An external energy source can be used to increase the penetration rate of drugs through the cell membrane. During iontophoresis, a potential gradient is created across the skin. This energy induces an increase in the migration of ionic substances into the skin through repulsion in an active electrode: the delivery of a positive current directs positively charged molecules on the electrode into the tissues; likewise, a negative current directs negative ions into the tissue. Typical iontophoresis equipment consists of a battery, a microprocessor controller, a medication reservoir, and electrodes. Negative ions are repelled by the negative electrode (cathode) and positive ions are repelled by the positively charged electrode (anode).

There are three possible mechanisms for the resulting effect: The electrophoretic force, according to which charged molecules are repelled from the dosage form by direct interaction of the electrode-generated current; the electro-osmotic force, which is responsible for the transport of non-charged molecules and larger peptides, which are “sucked in” by the flow of proteins in the body; and an increase in skin permeability resulting from the applied voltage, which is not completely understood.

Advantages of iontophoresis include:

- Provides conditions for a controlled-rate release of drugs based on variation in current density, pulsed voltage, drug concentration, and ion concentration
- Eliminates erratic effects on the absorption of certain drugs and first-pass metabolism
- Prevents the gastrointestinal incompatibility of certain drugs
- Reduces the adverse effects of certain drugs and inter-patient variability
- A painless and less traumatic alternative to injectable dosage forms and also lowers the risk of infection, inflammation, and fibrosis due to injection or continuous medication infusion
- Increases patient treatment compliance, providing a convenient and non-invasive therapeutic scheme

The disadvantages include possible skin irritation, burns, or formation of vesicles or blisters on the skin, especially when the electrode is not properly placed or the current intensity and/or application time is exceeded.

Drugs that can be applied by iontophoresis are generally used for the treatment of local or systemic conditions. They must be ionized, positively or negatively charged, and must have a suitable molecule size. In addition, these drugs must be solubilized in an aqueous solution, as drugs in solution undergo iontophoretic transfer—so there is also the occasional need to add other ingredients (such as acids or bases for pH adjustment) to increase the ionized fraction of the drug against the non-ionized fraction present in the solution.

Acoustic method (sonophoresis or phonophoresis)

Combined with topical drug delivery via transdermal patches or other topical dosage forms, an ultrasound device can be used to increase drug flux in a method known as sonophoresis (also known as phonophoresis, ultrasonophoresis, and ultraphonophoresis).

Low frequency ultrasonic waves cause lipid disturbances within the cell membranes of corneocytes. Thus, microcavities are formed that help the drug flow into the deepest strata of the epidermis, because the microvibrations in the epidermis caused by the ultrasonic waves increase the kinetic energy in the molecules of the substances in topical preparations. Sequentially, what occurs is as follows:

1. The ultrasound machine produces high frequency sound waves (not audible by the human ear) from 20–16 MHz.
2. Sound waves cross the skin into the body using a coupling agent (e.g., gel, cream or ointment) applied to the skin as a conductor, which transfers the ultrasonic energy from the ultrasound transducer to the skin.
3. Ultrasound waves support absorption.

A consensus has been reached regarding the mechanism of sonophoresis as it relates to acoustic cavitation, acoustic microflow, and heat generation. Cavitation is the formation of very small air bubbles in the liquid in contact with the ultrasonic waves. Microflow is closely related to cavitation, supporting the dissolution of suspended particles and a higher drug concentration available for absorption close to the skin. Heat generation can occur both on the skin surface and in the deeper layers of the skin. Ultrasound likely acts through several synergistic mechanisms to support skin permeability by disarranging the lipid layer of the cell membrane, increasing substance diffusion and involving heat generation by convection mechanisms (fluid transport is made easier as a result of the conversion of ultrasonic energy into heat).

Drugs typically conveyed by sonophoresis are anti-inflammatory agents (non-steroidal and steroidal). For example, hydrocortisone at concentrations generally ranging from 1%–10%. Therefore, sonophoresis is used therapeutically to treat local inflammatory and/ or painful conditions such as muscle pain, tendinitis, bursitis, and joint pain.

However, ultrasound should be used with caution, with risk/benefit assessment in patients with the following clinical conditions: Infection, cancer, heart problems, use of a pacemaker or with metal, silicone or saline implants, acute or post-acute lesions, epiphyseal areas, thrombophlebitis and areas around the eyes, during pregnancy, and in cases of decreased sensitivity.

The greatest limitation of ultrasound is the fact that it must be used in a medical office, due to the need for an ultrasound source. The performance of the ultrasound equipment depends on correct coupling between the transducer and the patient. Tissues are characterized by acoustic impedance, and applications in direct contact with them require a coupling agent, such as water, gel, and some types of oils such as petrolatum that also remove air bubbles that may form between the transducer and the patient. Although emulsions are used as a coupling medium, they do not perform well. The oil-water interface of emulsions scatters ultrasonic waves, decreasing the intensity of the energy reaching the skin. On the other hand, gels are an ideal vehicle for the delivery of medication by sonophoresis because of their pseudoplastic rheological behavior (their viscosity decreases with friction during application). They provide good ultrasonic energy conduction to the skin.

A preparation containing a vehicle and a drug that is intended for sonophoresis must provide good ultrasonic energy conduction, be homogeneous, smooth and not gritty (the undissolved solid ingredients must be finely dispersed in the vehicle) and have relatively low viscosity for easier application and movement of the ultrasound transducer head.

For further information or questions, please feel free to reach out to us by heading to www.fagronacademy.us!