AYUSHDHARA
ISSN: 2393-9583 (P)/ 2393-9591 (O)
An International Journal of Research in AYUSH and Allied Systems

Review Article

A REVIEW ON IONTOPHORESIS: A NOBLE DRUG DELIVERY TOOL FOR MANAGEMENT OF PLANTAR FASCIOPATHY USING AYURVEDA DRUGS

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Article info
Article History:
Received: 25-09-2024
Accepted: 27-10-2024
Published: 20-11-2024

KEYWORDS:
Iontophoresis, Plantar fasciopathy, Ayurveda, *Pada-kantaka, Agnikarma.*

ABSTRACT

Iontophoresis is an innovative transdermal drug delivery technique that uses electrical currents to enhance the permeation of drugs through the skin. This method holds significant promise for Ayurveda, a traditional Indian system of medicine that emphasizes holistic healing. This review discusses the mechanisms, applications, advantages, and challenges of using iontophoresis and development of Iontophoresis protocol for Ayurveda drugs. This review article explores the potential of iontophoresis as a transdermal drug delivery method specifically tailored for Ayurvedic medications. Iontophoresis employs electrical currents to facilitate drug absorption through the skin, thus addressing traditional challenges such as low bioavailability and targeted delivery of Ayurvedic formulations. The authors discuss the underlying mechanisms of iontophoresis, including electromigration and electroporation, which enhance drug permeability and absorption. It proposes that this technique aligns well with Ayurvedic principles by allowing for the localized treatment of conditions such as pain and inflammation, thus enhancing therapeutic outcomes. However, the article also addresses significant challenges, such as skin irritation, compatibility of herbal ingredients with iontophoresis, the need for specialized equipment, and regulatory hurdles. It underscores the importance of further research to validate the effectiveness of iontophoresis in Ayurveda and to refine treatment protocols. In conclusion, iontophoresis offers a promising intersection between traditional Ayurvedic practices and modern technology, potentially transforming the delivery of Ayurvedic treatments. Future studies are essential for optimizing formulations and overcoming existing barriers to implementation in clinical settings.

INTRODUCTION

Iontophoresis (IOP) is a technique that uses a mild electric charge to drive a chemical drug through the skin. This non-invasive method employs electrodes with a low electrical charge to propel high concentrations of charged substances across the skin via a repulsive electromotive force. IOP is a well-established approach for transdermal drug delivery, utilizing active transport within an electric field.

Access this article online
Quick Response Code
https://doi.org/10.47070/ayushdhara.v11i5.1737

The main mechanisms involved are electro-migration and electro-osmosis, typically measured in chemical flux (µmol/sq.cm/h). Recently, transdermal drug delivery systems have attracted considerable interest.

Ayurveda emphasizes the use of natural substances for healing, often requiring efficient delivery methods to enhance therapeutic effects. Traditional routes of administration, such as oral and topical applications, may have limitations in bioavailability and targeted delivery. Iontophoresis emerges as a valuable alternative, potentially improving the efficacy of Ayurvedic formulations.

Iontophoresis[1] (Transdermal drug delivery-TDD) offers a convenient alternative to intravenous, intramuscular, and oral administration routes. By

bypassing the first-pass effect in the liver, this method is particularly suitable for drugs with low bioavailability when taken orally or those that may cause adverse effects due to metabolic transformation. Additionally, TDD is painless, noninvasive, easy to apply, and allows for controlled (modified) release, which can extend the therapeutic effect.

For effective TDD, systems must be applied to healthy skin, prompting research into methods that can temporarily interact with the epidermis to enhance permeability for therapeutic substances without degrading the active ingredients or causing skin irritation or damage.

The effectiveness of a transdermal system largely depends on the formulation type. The extent of drug diffusion through the skin varies with the TDD formulation, such as ointments, creams, gels, or transdermal patches. These formulations can include various gel types (like hydrogels, organogels, emulgels, and nano gels), emulsions (including microemulsions, nanoemulsions, and multiple emulsions), and liquid crystals, which are intermediates between solid and liquid states.

AIM AND OBJECTIVES

Aim

To explore the efficacy and potential of iontophoresis as a novel drug delivery system for enhancing the therapeutic effects of Ayurvedic drugs.

Objectives

1. To explain the underlying mechanisms of iontophoresis.
2. To assess the effectiveness of iontophoresis in delivering specific Ayurvedic drugs.

METHODOLOGY

Ayurvedic text books are reviewed for this article. Materials for *Pada-kantaka* and it's management are collected. Modern texts related to iontophoresis in management of Plantar-fasciopathy is also searched from various databases.

RESULT

Conceptual study

Iontophoresis can be categorized under the broader concept of *Agnikarma* in *Ayurveda*, as both techniques utilize the application of energy-heat in the case of *Agnikarma* and electrical energy for iontophoresis-to promote healing and alleviate pain.

Both *Agnikarma* and iontophoresis aim to enhance tissue healing and reduce pain through energy application—thermal in *Agnikarma* and electrical in iontophoresis. The common mechanism involves improving blood flow and facilitating drug absorption into targeted tissues. The heat in *Agnikarma* may create a conducive environment for drug efficacy, while iontophoresis directly introduces pharmacological agents.

In treating conditions like plantar fasciopathy (*Pada-Kantaka*), certain Ayurvedic herbs and compounds are utilized in iontophoresis for their anti-inflammatory and analgesic properties. *Nirgundi (Vitex negundo)* Known for its analgesic and anti-inflammatory properties. It contains various bioactive compounds that help in pain relief and swelling reduction.

Guggulu (Commiphora mukul) resin is used for its potent anti-inflammatory effects. It is known to enhance healing and reduce pain, making it suitable for chronic conditions like plantar fasciopathy. *Shallaki (Boswellia serrata)* is well-known for its anti-inflammatory properties. It inhibits leukotriene synthesis, which can help reduce inflammation and improve pain management. *Erandamool (Ricinus communis)* and its components possess anti-inflammatory and analgesic properties. The topical application via iontophoresis may help in reducing pain and inflammation in plantar fasciopathy.

Iontophoresis Procedure

To begin iontophoresis treatment, first assess the patient's condition, medical history, and overall suitability for the procedure. Select appropriate Ayurvedic formulations, choosing from single or multiple drugs based on the patient's specific condition and the drugs' mode of action. Formulations may include extracts such as *Nirgundi Patra* with *Guggulu* resin, *Shallaki* resin, or *Erand mool*. Prepare the selected Ayurvedic drug as a 20% aqueous solution for application.

Before applying the drug, prepare the patient's skin by cleansing the area with an antiseptic to remove any oils or dirt. Apply a conductive gel to the electrodes or immerse them in the prepared solution, placing each electrode on the skin according to the required polarity. Begin with a low current intensity, typically between 1-5 mA, and adjust gradually to a comfortable level. Treatment generally lasts 10-20 minutes, depending on the drug and condition, and is administered in six sessions on alternate days. Continuously monitor the patient throughout the session for any signs of discomfort or adverse reactions.

After the procedure, clean the treated area gently to remove any residue, and assess the patient's response to the treatment, noting any changes in symptoms. Schedule follow-up sessions every 15 days for two months to monitor progress. Throughout the treatment, ensure safety by confirming there are no contraindications, such as pacemakers or skin

infections, and regularly check for signs of skin irritation or allergic reactions to the Ayurvedic drugs.

Fig. no. 1 & 2: Iontophoresis Procedure

Mode of Action of Interventional Drugs

Plantar Iontophoresis with aqueous solutions of *Nirgundi Patra, Guggulu* Resin, *Shallaki* Resin, and *Erand Mool*:

Nirgundi (Vitex negundo) is known for its anti-inflammatory properties, primarily by inhibiting COX-2 receptor activity, targeting COX-2 while sparing COX-1. Research indicates that flavonoids like luteolin and apigenin in *Nirgundi* exhibit anti-inflammatory and anti-arthritic effects and can effectively penetrate human skin (Ginter et al., 2008). The analgesic and anti-inflammatory effects of *Nirgundi* are largely due to its flavonoid content, which inhibits prostaglandin biosynthesis. Additionally, *Vitex negundo* has pain-relieving properties that may stem from its ability to inhibit prostaglandin synthesis, along with antihistamine effects, membrane stabilization, and antioxidant activities.

The active components of *Guggulu* resin can penetrate the intact skin of the sole and reach the plantar fascia, a fibrous tissue with limited blood supply that retains the drug for extended periods. This prolonged retention may enhance the anti-inflammatory and analgesic effects of *Guggulu* resin in treating plantar fasciitis.

Inflammation primarily results from the activation of inflammatory signalling pathways, such as the NF-κB pathway, and the release of inflammatory mediators like pro-inflammatory cytokines (e.g., TNF and IL-1β) and enzymes that generate prostaglandins (e.g., COX-2) and leukotrienes (e.g., lipoxygenase). Cyclooxygenase-2 (COX-2) plays a crucial role in inflammation and pain by converting arachidonic acid into prostaglandins and prostanoids.

Guggulsterone and other active compounds in the aqueous solution of Guggulu resin help prevent cytokine-induced cellular damage. Guggulsterone reduces inflammation by inhibiting inducible nitric oxide synthase (iNOS) expression in macrophages, which is induced by lipopolysaccharide. Inflammation is mediated by NF-κB activation, and Guggulsterone can suppress the DNA binding of NF-κB activated by TNF. The COX-2 inhibitory action of *Guggulu* enhances its anti-inflammatory effects in plantar fasciitis. Furthermore, boswellic acids inhibit 5-lipoxygenase, an enzyme responsible for producing pro-inflammatory leukotrienes from arachidonic acid, and can also decrease the activity of human leukocyte elastase (HLE) enzymes.

Erand mool contains active compounds, particularly from its root extract, which exhibit various pharmacological activities through different mechanisms:

- Alkaloids: These interact with opioid receptors in the central nervous system, modulating pain perception and producing analgesic effects, as well as influencing neurotransmitter levels for anti-inflammatory actions.
- Flavonoids: Known for inhibiting prostaglandin synthesis, flavonoids can reduce inflammation and alleviate pain by blocking inflammatory pathways.
- Saponins: These compounds may disrupt cell membranes, leading to histamine release and the activation of other inflammatory mediators. They also possess immunomodulatory properties that help reduce inflammation and pain.
- Terpenoids: Recognized for their anti-inflammatory effects, terpenoids can inhibit the release of pro-inflammatory cytokines, contributing to their analgesic properties.
- Tannins: With astringent properties, tannins can help reduce inflammation and pain while modulating nociception-related signaling pathways.
- Carbohydrates and Glycosides: These serve as energy sources for cells and may be involved in various biological processes, with some glycosides linked to anti-inflammatory and analgesic effects.

DISCUSSION

Iontophoresis involves applying a low electrical current to facilitate the movement of charged drug molecules through the skin. This technique can enhance drug absorption by: Electromigration: Charged drugs are propelled toward the opposite electrode. Iontophoresis employs a small electrical current to drive ionized drugs toward the target site.

Positively charged drugs move toward the negative electrode and vice versa. This directional movement increases the concentration of the drug at the skin's surface, leading to higher permeation rates. Electroporation: The electrical current temporarily disrupts the lipid bilayer of skin cells, increasing permeability. The electrical current can create transient pores in the skin's lipid bilayer, significantly increasing permeability. This process allows larger molecules, which typically have low skin permeability, to enter the systemic circulation more effectively. Thermal Effects: Iontophoresis generates heat, which can enhance skin permeability. Elevated temperatures can improve blood flow to the area, further facilitating drug absorption. The application of electrical current can increase the kinetic energy of drug molecules, enhancing their diffusion through the stratum corneum (the outermost layer of skin). This increased mobility can lead to higher absorption rates.

Iontophoresis, with its ability to enhance drug delivery through the skin, presents several promising applications in the field of Ayurveda. By improving the bioavailability and efficacy of Ayurvedic formulations, iontophoresis can support various therapeutic interventions. Here are some key applications: Pain Management-Herbal Analgesics: Iontophoresis can be used to deliver herbal formulations containing analgesic properties, such as *Nirgundi*[2] *Patra*, *Guggulu* resin, *Shallaki* resin[6], and *Erand mool*[3] extracts. This method allows for targeted pain relief in conditions like Plantar Fasciopathy, arthritis, muscle pain, and neuropathic pain. Anti-inflammatory Applications-Localized Delivery: Conditions characterized by inflammation, such as tendinitis and bursitis, can benefit from the localized delivery of anti-inflammatory Ayurvedic substances. Iontophoresis can facilitate the absorption of herbs like *Ashwagandha* and Boswellia[5], known for their anti-inflammatory properties. Musculoskeletal Disorders- Iontophoresis can be utilized for conditions affecting the musculoskeletal system, such as back pain and joint disorders. By delivering muscle relaxants or anti-inflammatory agents directly to the affected area, patients may experience quicker relief.

CONCLUSION

Iontophoresis presents a promising avenue for enhancing the delivery of Ayurvedic drugs. By improving bioavailability and providing targeted therapies, Iontophoresis represents a significant advancement in transdermal drug delivery. By utilizing electrical currents to overcome skin barriers, this technique not only improves the efficacy of treatments but also aligns with the principles of Ayurveda by utilizing natural substances in a more effective manner. It can potentially bridge the gap between traditional practices and modern medical technology. Future research should focus on optimizing formulations and addressing challenges to fully integrate iontophoresis into Ayurvedic treatment protocols.

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Cite this article as:
Vivek Singh Bhadauria, Narinder Singh, P. Hemantha Kumar, Monika Singh, Satya Santosh Sahoo. A Review on Iontophoresis: A Noble Drug Delivery Tool for Management of Plantar Fasciopathy Using Ayurveda Drugs. AYUSHDHARA, 2024;11(5):238-241.
https://doi.org/10.47070/ayushdhara.v11i5.1737
Source of support: Nil. Conflict of interest: None Declared

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