Iontophoresis Device: A Review of Technologies and Limitations

Ana Šćekić
Faculty of Electrical Engineering
University of Montenegro
Podgorica, Montenegro
ana.scekic96@gmail.com

Kristina Tomović
Faculty of Electrical Engineering
University of Montenegro
Podgorica, Montenegro
kristinatomx@gmail.com

Abstract— **This paper presents a review of the development of iontophoresis devices and their applications in medicine, including various medical fields such as cancer research and hyperhidrosis. Iontophoresis is a non-invasive drug delivery method that uses an electric current to drive charged ions through the skin and into the body. The technique has been used in a variety of medical fields and is gaining popularity due to its ability to deliver drugs directly to the site of injury or disease, reducing systemic side effects.**

The review covers the historical background of iontophoresis, including early experiments and the evolution of the technology over time. It also discusses the different types of iontophoresis devices available on the market, their mechanisms of action, and the advantages and disadvantages of each. In addition, the review provides an overview of the current clinical applications of iontophoresis, with a focus on the fields of cancer research and hyperhidrosis.

The review concludes with a discussion of the current challenges and future directions of iontophoresis technology. The information presented here will be useful to researchers, clinicians, healthcare professionals, and electrical engineers interested in the latest developments in iontophoresis technology and its applications in medicine.

Keywords: electrotherapy, iontophoresis, home therapy, portable devices, medicine, non-invasive drug delivery

I. INTRODUCTION

In modern times, when talking about the use of drugs for the treatment of a disease or condition, the aim is always to have a targeted effect on the designated area, controlling the dose, the duration of the delivery of the drug, as well as to report as few side effects as possible. Therefore, it is not surprising that iontophoresis as non-invasive method for drug delivery, is being mentioned as promising potential in various fields of medicine.

Iontophoresis (Greek, "ion"-going; "phoros" -bearer, carrier) is a non-invasive medical procedure that involves the use of electrical current to deliver ions of medication or other therapeutic agents through the skin and into underlying tissues. It is a method of enhancing the transdermal delivery of drugs by applying an external electrical potential that promotes the movement of ions across a membrane. Topically applied drugs have an absorption sequence: first, the drug is released by transdermal drug delivery, absorbed by the first skin barrier, the stratum corneum, then the epidermis and dermis to the bloodstream and transported to the site where it is expected to have a therapeutic effect. [2]

Iontophoresis exhibits several advantageous features that make it an attractive option for drug delivery compared to other methods of drug delivery, as illustrated in Figure 1. First, the possibility of using a wide range of drugs - analgesics or anti-inflammatory drugs. Furthermore, since iontophoresis acts directly on the target surface, a smaller dose of the drug is required than would be the case with other types of drug intake - orally or by injection. The smaller the dose of the drug introduced into the body, the lower the possibility that the body will respond with a side effect to that same drug. On the other hand, the targeted action of the drug is an advantage in cases of tumor treatment, for the treatment of pancreatic tumors, breast tumors, and other solid tumors. Then it acts directly on the tumor without disrupting the functioning of untreated surfaces, which allows the body to fight the vicious disease more easily.

targeted delivery	medication is delivered directly to the affected area- less side effects, the medication does not enter the digestive system
reduced dosage	the medication is delivered directly to the affected area, so lower doses of medication are needed
non-invasive	it does not require injections or incisions, suitable for patients who have a fear of needles or who cannot withstand more invasive treatments
convenience	clinical setting, or at home usage, depending on the device and condition
cost-effective	in the long run - reducing the need of visits to the doctor, or more invasive treatments

Figure 1: Advantages of iontophoresis compared to other methods of drug delivery.

II. IONTOPHORESIS IN MEDICINE

A. Historical Background

The therapeutic potential of electricity was first discovered thousands of years ago, as evidenced by its use in ancient Egyptian, Greek, and Roman civilizations. These cultures recognized that electric shocks produced by certain fish species could alleviate pain, including headaches and arthritis. In the 16th to 18th centuries, various electrostatic devices were employed for pain relief. Even though the first proposal for the current medicated drug delivery has been mentioned in the mid-18th century, the 19th century is noted as the period of memorable progress in this field.

The movement of charged particles in an electric field was first observed as long ago as 1807 by the Russian chemists Pyotr Ivanovich Strakhov (1757–1813) and Ferdinand Frederic Reuss (1778–1852) at the Moscow State University. [3] Before 1908, when Frankhauser used the term "iontophoresis", drug delivery using electrical current was known as "cataphoresis". The first transdermal system that was approved for use in the United States (1979) was a three-day patch that delivers scopolamine to treat motion sickness. [4]

B. Clinical applications of iontophoresis

Iontophoresis is a promising electrotherapy technique for drug delivery that has gained considerable research interest in various medical fields and is being explored for delivering medicines in cases of different conditions. Iontophoresis could be an effective drug delivery approach for the treatment of oral diseases such as tooth decalcification and hypersensitivity and periodontal diseases such as gingivitis and periodontitis. [5]

Ophthalmology is another area where it is necessary to deliver drugs in a controlled and tolerable way. There are in vivo experiments related to this and developed iontophoretic device that could do the work with some limitations, or side effects. [6][7] The clinical uses of iontophoresis via low intensity electric fields have been reported in both animals and humans. Even though the delivery of chemotherapeutic drugs into the tumor is still not well defined, the efforts are being made to enhance its effectiveness.

Iontophoresis has demonstrated notable therapeutic benefits in diverse areas, including musculoskeletal pain, inflammation, dermatological conditions such as psoriasis, and hyperhidrosis. Specifically, the treatment of hyperhidrosis using iontophoresis with tap water or other medicaments has exhibited promising outcomes and there are multiple solutions on the market.

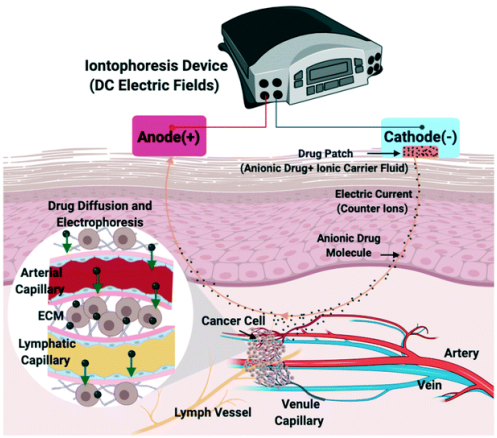

Fig. 2 Iontophoretic transdermal drug delivery into the tumor vasculature in vivo. The schematic shows the in vivo transport of an anionic drug from the artery to the tumor where it eventually drains into the lymph vessel. Iontophoretic transdermal drug delivery includes insertion of the cathode along with the drug patch on the skin from where the anionic drug molecules move to the tumor facilitated by the transport of the counter ions (from carrier solvent) to the anode [9]

III. ANALYSIS OF EXISTING TECHNOLOGIES

There are many variables that can influence iontophoresis. That includes: the cross-sectional skin area and skin as the biggest limiting factor, the time of application of the current and its intensity (Faraday's law), then drug concetration and also physicochemical properties of the drug molecules that are to be delivered. Some of these variables can be adjusted, some should be considered if iontophoresis is a chosen treatment.

The two types of current that are usually utilized in iontophoresis based on the objectives of the treatment and clinicians' preferences are direct current (DC) and pulsed direct current (PDC). [13][14]

A complete circuit forming an iontophoresis device typically consists of electrodes and a DC voltage delivery system, which are connected with wires. Then the adjustments of desired duration of treatment and the current itself. Some solutions offer the choice to choose between DC and PDC. During iontophoresis, the current is conducted from the device through the electrode and the drug solution, leading to the movement of drug ions towards the skin via an ionic flow. The drug molecules are then driven through the trans-appendageal structures and the aqueous pores of the stratum corneum by the repulsive forces. The size of the electrode plays a critical role in determining the required current density for efficient drug transport, and hence, larger electrodes demand higher current supply from the device. Power sources used for these types of devices can be electricity, batteries, or rechargeable power sources.

The machines available in Europe include: Hidroxa [16], SWEAT GUARD®[17], KAWE SwiSto3 [18], MedLight io-

dry [19] etc. These devices can be used as a treatment for hyperhidrosis. Depending on the manufacturer and device, they are used on various parts of the body, for example face, palms, foot. The power source is mostly electricity or rechargeable power source.

In United States, there are also commercial iontophoresis patches, such as Iontopatch[20] most commonly used to treat near surface musculoskeletal conditions. Since they do not need power source, because they have integrated battery, this is their advantage, but they are typically designed for one-time use only and the dose and duration of treatment cannot be manipulated.

So, what the existing solutions have in common is that a greater ability to control the parameters of iontophoresis is needed, as well as the mobility of the device, and the possibility of using the technical solution more than once, because the iontophoresis treatments usually take longer time than one usage of patch, for example.

IV. CONCLUSIONS: CHALLENGES AND PERSPECTIVES

Iontophoresis is a promising drug delivery technique that has garnered significant research interest across various medical fields. It has shown potential in treating oral and ophthalmological conditions, as well as in delivering chemotherapeutic drugs to tumors. Additionally, it has demonstrated therapeutic benefits in treating musculoskeletal pain, inflammation, dermatological conditions, and hyperhidrosis. Specifically, iontophoresis has proven effective in treating hyperhidrosis with tap water or medicated solutions, and multiple solutions are available on the market.

Iontophoresis is influenced by many factors, such as skin area, current intensity and duration, drug concentration and properties, and electrode size. Direct current (DC) and pulsed direct current (PDC) are the two main types of current used in iontophoresis, and the complete circuit of an iontophoresis device consists of electrodes, a voltage delivery system, and wires. The size of the electrode affects the current density required for efficient drug transport. Existing devices use power sources such as electricity, batteries, or rechargeable power sources, and vary in terms of their ability to manipulate treatment parameters, mobility, and potential for multiple uses. A greater ability to control iontophoresis parameters, mobility, and multi-use options would improve current solutions.

As research delves deeper into the capabilities of iontophoresis, it is anticipated that advancements in technology and application will continue to broaden its utility in the medical field. The availability and pricing of current solutions present potential areas for further development. Future work in this field may encompass the integration of mobile applications for regulating iontophoresis parameters with simple iontophoresis devices that could include having contact with clinician, with the aim of increasing controllability and accessibility to wider group of people. Moreover, iontophoresis devices hold immense potential for utilization in home therapy for a wide range of treatments. There is also potential for device solutions that combine iontophoresis with other therapeutic modalities since iontophoresis is the most effective when combined with other treatments, or/and a device that enables switching between DC and PDC current, but also being able to have independent power source.

Therefore, this is an area where there is room for further development of the device solutions.

REFERENCES

[1] Kalia YN, Naik A, Garrison J, Guy RH. Iontophoretic drug delivery. Adv Drug Deliv Rev. 2004;

[2] Akhlaq, M.; Hussain, S.; Bakhsh, S. Skin Port: A Novel Route for Drug Delivery. Gomal. J. Med. Sci. 2014;

[3] Strakhov PI, Reuss FF. Über den Electromotorischen Einfluß auf die Bewegung der Flüssigkeiten in Capillar-Röhren [On the electromotive influence on the movement of liquids in capillary tubes]. Ann Phys. 1809;

[4] MR Prausnitz, R Langer „Transdermal drug delivery", Nature Biotechnology, 2008;

[5] Wanasathop A, Li SK. Iontophoretic Drug Delivery in the Oral Cavity. Pharmaceutics. 2018;

[6] Zhang Y, Chen Y, Yu X, Qi Y, Chen Y, Liu Y, Hu Y, Li Z. A flexible device for ocular iontophoretic drug delivery. Biomicrofluidics. 2016;

[7] Wei D, Pu N, Li SY, Wang YG, Tao Y. Application of iontophoresis in ophthalmic practice: an innovative strategy to deliver drugs into the eye. Drug Deliv. 2023;

[8] Lemos CN, de Souza JG, Simão PS, Lopez RFV Iontophoresis Improved Growth Reduction of Invasive Squamous Cell Carcinoma in Topical Photodynamic Therapy. PLOS ONE 11(1), 2016;

[9] Moarefian M, Davalos RV, Tafti DK, Achenie LE, Jones CN (2020) Modeling iontophoretic drug delivery in a microfluidic device. Lab Chip 20(18), 2020;

[10] Bastos CM, Rocha F, Gomes N, Marinho-Reis P. The Challenge in Combining Pelotherapy and Electrotherapy (Iontophoresis) in One Single Therapeutic Modality. Applied Sciences. 2022;

[11] Kim DH, Kim TH, Lee SH, Lee AY. Treatment of Palmar Hyperhidrosis with Tap Water Iontophoresis: A Randomized, Sham-Controlled, Single-Blind, and Parallel-Designed Clinical Trial. Ann Dermatol. 2017;

[12] Blaine D. Griffen | (2018) Proposed mechanism of action of tap water iontophoresis for treatment of hyperhidrosis, Cogent Medicine, 2018;

[13] Reinauer S, Neusser A, Schauf G, Hölzle E. Die gepulste Gleichstrom-Iontophorese als neue Behandlungsmöglichkeit der Hyperhidrosis [Pulsed direct current iontophoresis as a possible new treatment for hyperhidrosis]. Hautarzt. 1995;

[14] Gomez, C.C.S., Servidoni, M.d.F., Marson, F.A.d.L. et al. Pulsed direct and constant direct currents in the pilocarpine iontophoresis sweat chloride test. BMC Pulm Med 14, 198 (2014);

[15] Rai R, Srinivas C R. Iontophoresis in dermatology. Indian J Dermatol Venereol Leprol 2005;

[16] https://www.hidroxa.com/en/

[17] https://sweatguard.co.uk/

[18] https://www.kawemed.com/produkt/swisto3/

[19] https://www.medlight.eu/en/io-dry/

[20] https://www.iontopatch.com/