IONTOPHORESIS

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Introduction

- ***Iontophoresis*** is a non-invasive method of propelling high concentrations of a charged substance, normally medication or bioactive agents, transdermally by repulsive electromotive force using a small electrical charge approximately (0.5 mA/cm^2) applied to an iontophoretic chamber containing a similarly charged active agent and its vehicle.

- It is a Painless, Sterile, Noninvasive Technique

- Iontophoresis is well classified for use in transdermal drug delivery.

Advantages of Iontophoresis

- Virtually painless when properly applied.
- Provides option for patients unable to receive injections.
- Reduced risk of infection due to non-invasive nature.
- Medications delivered directly to the treatment site.
- Minimizes potential for tissue trauma from an injection.
- Treatments are completed in minutes.

Disadvantages of iontophoresis

- An excessive current density usually results in pain.
- Burns are caused by electrolyte changes within the tissues.
- The high current density and time of application would generate extreme pH, resulting in a chemical burn.
- This change in pH may cause the sweat duct plugging perhaps precipitate protein in the ducts.
- Electric shocks may cause by high current density at the skin surface.
- Ionic form of drug in sufficient concentration is necessary for iontophoretic delivery.

Principles of Iontophoresis

- Electrode placement is dependent on the electric charge of the ion which you are trying to deliver into the tissue.(anode delivers anions)

- A positive ion will be delivered from the positive electrode and a negative ion will be delivered by the negative electrode.

- Electrical energy assists the movement of ions across the stratum corneum according to the basic electrical principle *"like charges repel each other and opposite charges attract each other."*

Movement of Ions In Tissue

- Higher current intensities necessary to create ion movement in areas where skin and fat layers are thick, further increasing chance of burns around negative electrode.

- Sweat ducts are primary paths by which ions move through the skin.

- Once the ions pass through skin they recombine with existing ions and free radicals in the blood thus forming the necessary new compounds for favorable therapeutic interactions.

Components needed for effective iontophoresis delivery

- Power source for generating controlled direct current.
- Electrodes that contain and disperse the drug.
- Negatively or positively charged aqueous medication of relatively small molecule size (<8000 Daltons).
- Localized treatment site.

Current Intensity

- Low amperage currents appear to be more effective as a driving force than currents with higher intensities.
- Higher intensity currents tend to reduce effective penetration into the tissues.
- Recommended current amplitudes used for iontophoresis range between 3-5 mA.

Electrodes

- The electrode materials used for iontophoretic delivery are to be harmless to the body and sufficiently flexible to apply closely to the body surface.
- The most common electrodes used for iontophoretic drug delivery are

✓ Aluminum foil

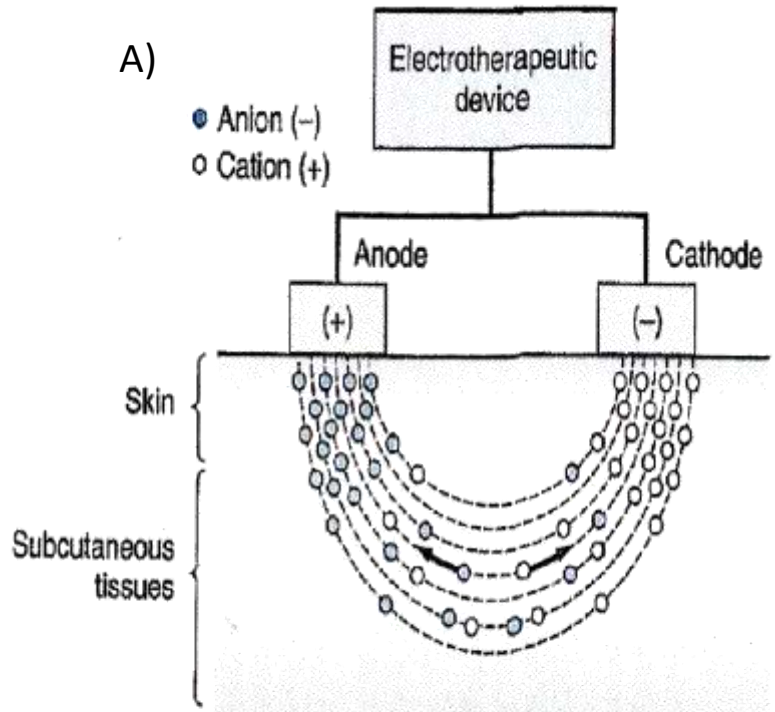
✓ Platinum and

✓ Silver/Silverchloride

❖ A better choice of electrode is silver/silver chloride because it minimizes electrolysis of water during drug delivery.

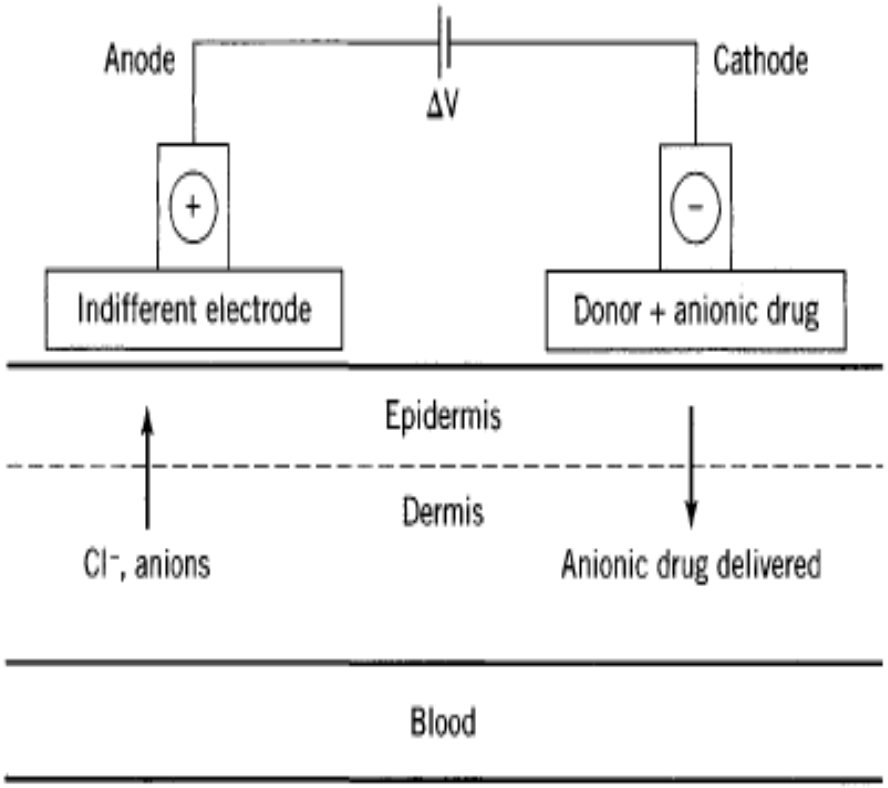
Iontophoresis Diagram

A)



Electrons flowing from the electrotherapeutic device through the lead wires to the electrodes on the patient, inducing ion flow in the biologic tissues beneath the electrodes.

B)



Mechanisms involved in Iontophoresis

(a) ion-electric field interaction provides an additional force that drives ions through the skin.

(b) the flow of electric current increases the permeability of the skin.

(c) electro-osmosis produces bulk motion of solvent that carries ions or neutral species with the solvent stream. Electro-osmotic flow occurs in a variety of membranes and is in the same direction as the flow of counter-ions. It may assist or hinder drug transport.

Treatment Duration

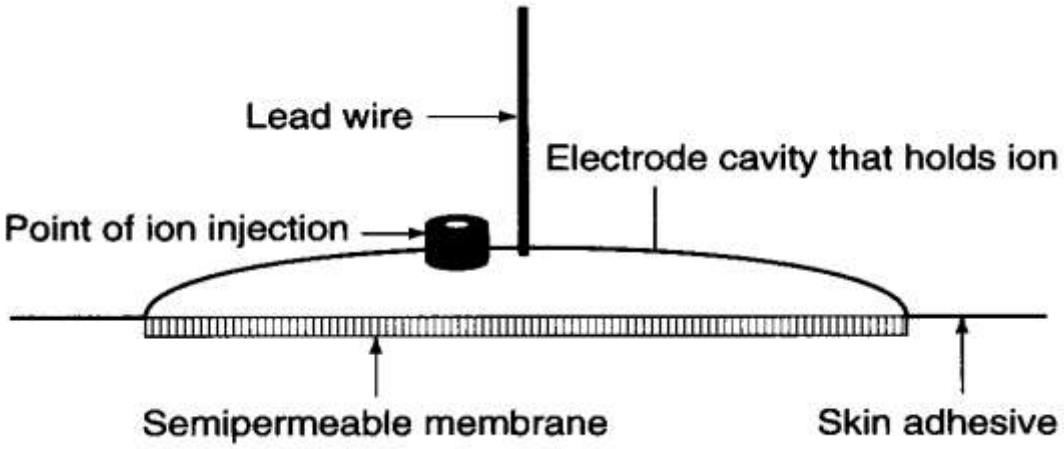
- Treatment duration ranges between 10-20 minutes with 15 minutes being an average.
- Patient should be comfortable with no reported or visible signs of pain or burning.
- Check skin every 3-5 minutes looking for signs of skin irritation.
- Decrease intensity during treatment to accommodate decrease in skin impedance to avoid pain or burning.

Treatment Precautions

- Patient has a good understanding of the existing condition which is to be treated
- Uses the most appropriate ions to accomplish the treatment goal
- Uses appropriate treatment parameters and equipment set-up

Commercial Electrodes

- Sold with most iontophoresis systems.
- Electrodes have a small chamber covered by a semipermiable membrane into which ionized solution may be injected.
- The electrode self adheres to the skin.



Commercially developed iontophoretic delivery systems

- ***Lidosite®-*** To deliver lidocaine, an anesthetic agent.
- ***Phoresor® II -*** To deliver botulinum molecule which is used for the treatment of hyperhydrosis.
- ***E-Trans®*** - To deliver fentanyl.
- ***Phoresor®*** - To deliver iontocaine.

Factors Affecting Iontophoretic Delivery of the Drug

❖ **Operational Factors**

I. Composition of formulation:

- Concentration of drug solution
- pH of donor solution
- Ionic strength
- Presence of co-ions

II. Physicochemical properties of the permeant:

- Molecular size
- Charge
- Polarity
- Molecular weight

III. Experimental conditions:

- Current density
- Duration of treatment
- Electrode material
- Polarity of electrodes

❖ **Biological Factors**

- Regional blood flow
- Skin pH
- Condition of skin

EVALUATION OF IONTOPHORETIC DRUG DELIVERY SYSTEM

- In-Vitro Evaluations:Since traditional dose- response studies cannot be performed performed performed, studies of iontophoresis have been limited to demonstrate biological effects.

  these studies, which are numerous, are listed in several of the review srticles.

  this has been especially true for oral dosage forms, where studies in animals have justified studies in man.

- In- Vivo Evaluations: Morimo et al.(1992) described an in-vivo iontophoretic system used in rats for transdermal iontophoretic delivery of vasopressin and analogue in rats.

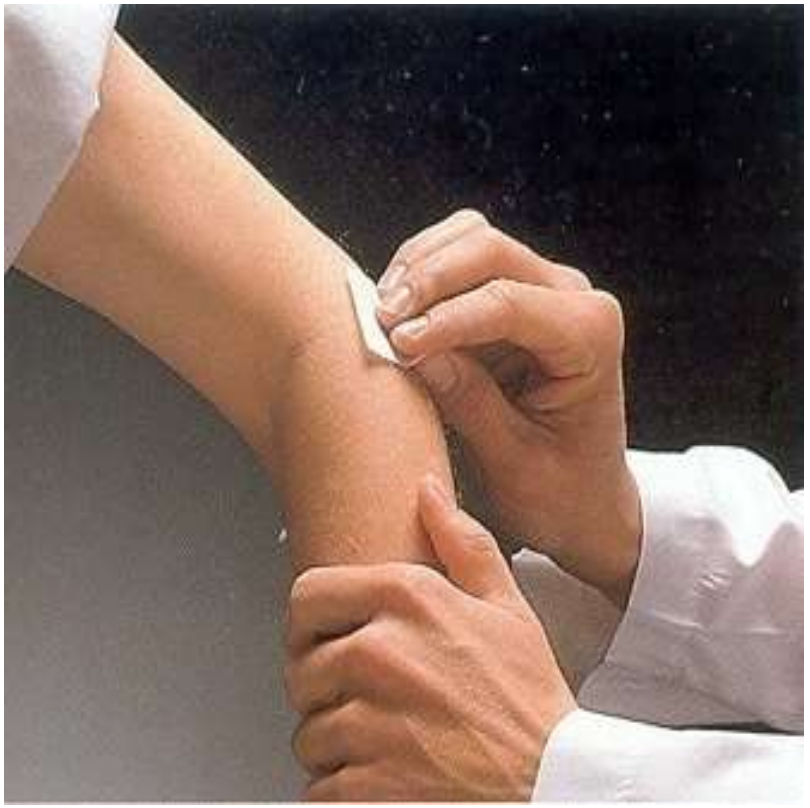
  Two cylindrical polyethylene cells were attached to the abnorminal skin of the rat, a pair of AG/AgCL electrodes was immersed in the solutions, the anode being in the drug solution and the cathode in the 0.9% w/v NaCl solution.

  the electrodes were connected to a constant current power source.

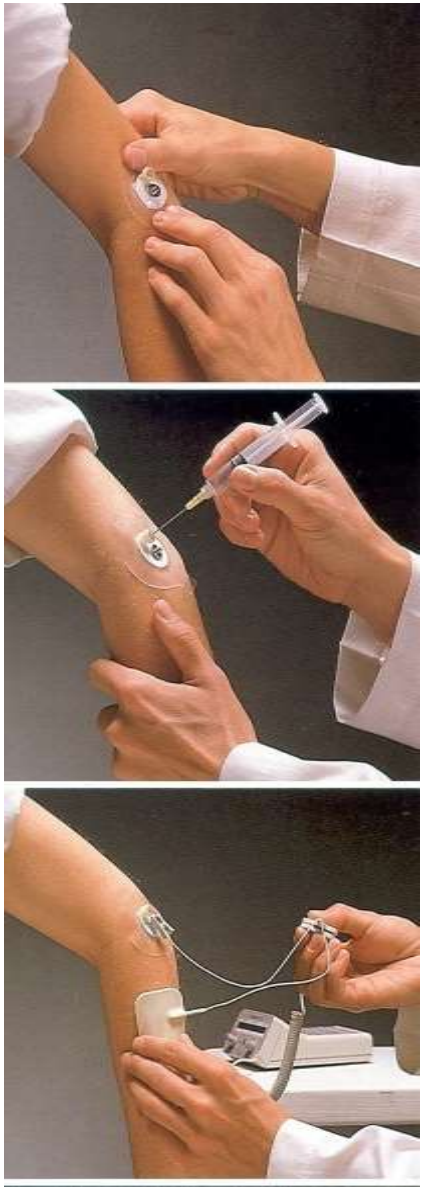
Electrode Preparation

- To ensure maximum contact of electrodes skin should be shaved and cleaned prior to attachment of the electrodes.

- Do not excessively abrade skin during cleaning since damaged skin has lowered resistance to current and a burn might occur more easily.

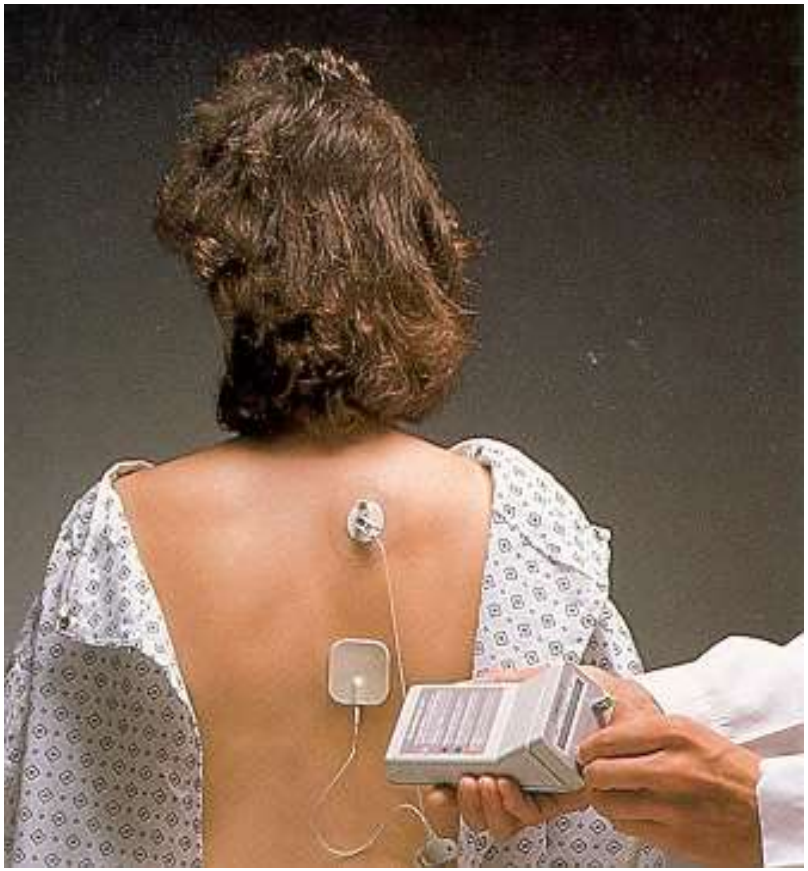


- Attach self-adhering active electrode to skin.
- Inject ionized solution into the chamber.
- Attach self-adhering inactive electrode to the skin and attach lead wires from generator to each.

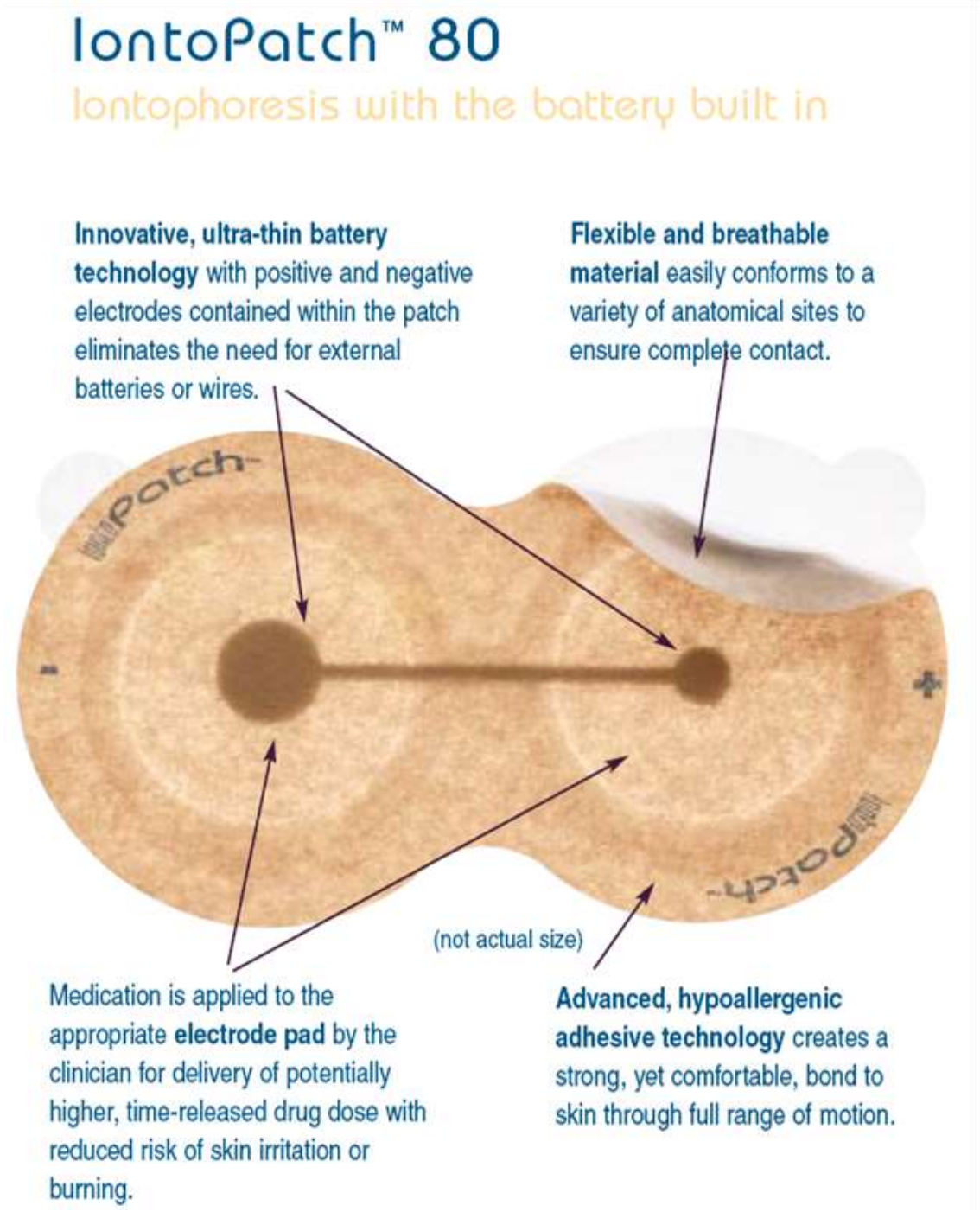


Electrode Placement

- Size and shape of electrodes can cause variation in current density (smaller = higher density)
- Electrodes should be separated by at least the diameter of active electrode
  - Wider separation minimizes superficial current density decreasing chance for burns



Iontopatch by Birch Medical



List of Drugs Investigated Recently for Iontophoretic Delivery

Drug	Animal/ Membrane Model Used	Experimental Conditions	Results
Thiocolchicoside	Rabbit and human skin	*In vitro*: Glass-Franz type cell.	Enhanced flux of the drug over passive control.
Salbutamol	Non rate limiting artificial membrane	*In vitro*: Release of drug from a liquid crystalline vehicle was studied.	Enhanced flux from the vehicle.
Timolol maleate (TM)	Excised rat, rabbit, guinea pig, mouse and human skin	*In vitro*: Valia-Chien side by side diffusion cell. Studied effect of species.	Iontophoretic transport highest in human skin and lowest in rabbits.
Dextran sulphate	Full thickness pig skin or epi-dermis separated from human cadaver skin	*In vitro*: Valia-Chien cell; 500 V; Current- 0.5mA/cm^2; Time – 6 h.	Cumulative amount fluxed from cathode was approximately 300 times more over passive and from anode it was 15 times more.
Diclofenac	Guinea Pig skin	*In vitro*: Current- 0.2 and 0.5 mA/cm^2; Time- 6 h. Studied effect of current on drug delivery.	Full plasma concentration achieved in 1 h. Drug delivery was proportional to current (371± 141 µgm / lt at 0.5 mA/cm^2 and 132 ± 62 µ gm/ lt at 0.2 mA/ cm^2).

Applications

Inflammation With Constant Pain (Red, Hot, and Swollen)

Dexamethasone Sodium Phosphate 0.4% *(negative polarity)* delivered from the cathode for 3 treatments per week for 2-4 weeks.

Diclofenac 5% *(negative polarity)* delivered from the cathode for 3 treatments per week for 2-4 weeks.

Ketoprofen 10% *(negative polarity)* delivered from the cathode for 3-5 treatments per week for 2-6 weeks.

Lidocaine Hydrochloride 4% *(positive polarity)* delivered from the anode for 3-5 treatments per week for 2 weeks.

Conclusion

- Iontophoretic drug delivery has developed a new application system for dermal and transdermal delivery of drugs that is electro-phoretically self-regulated device with electronic indicator.

- The iontophoretic delivery of macromolecules will open the doors to non-invasive transdermal delivery of peptide-based pharmaceuticals.

- Iontophoresis has been explored for many dermatologic and other medical conditions with reports of considerable success.

REFERENCES

- Anderson CR, Morris RL, Boeh SD, et al. “Effects of iontophoresis current magnitude and duration on dexamethasone deposition and localized drug retention.” *Phys Ther.* 2003; 83:161-171.
- Artusi, M.; Nicoli, S.; Colombo, P.; Bettini, R.; Sacchi, A.; Sanli,P. *J. Pharm. Sci*. **2004**, *93* (10), 2431-8.
- Banga, A.K. *Electrically assisted transdermal and topical drug delivery*, Taylor and Francis, London, **1998.**
- Banga, A.K.; Chien, Y.W. *J. Control. Release*, **1988**, *7*(1), 1-24.
- Banga, A.K.; Bose, S.; Ghosh, T.K. *Int. J. Pharm*. **1999**, *179*(1), 1-19.
- Bertolucci, L.E. “Introduction of Anti-inflammatory Drugs by Iontophoresis: Double Blind Study.” *J Orthopedic and Sports Physical Therapy*. 1982;4:103-108 .
- Chou, W.-L.; Cheng, C.-H.; Yen, S.-C.; Jiang, T.-S. *Drug Dev. Ind. Pharm*. **1996**, *22*(9&10), 943-50.
- Clemessy, M.; Couarraze, G.; Bevan, B.; Puisieux, F. *Int. J. Pharm*. **1994**, *101*(3), 219-26.
- Garzione, John E. PT,DPT, D.A.A.P.M. *Alternative Compounds and Advances in Iontophoresis*. 20 June 2006. Sturm. Overuse injury [article]. Available at: http://www.emedicine.com/pmr/topic97.htm. Accessed July 10, 2006.
- Harris PR. “Iontophoresis: Clinical Research in Musculoskeletal Inflammatory Conditions.” *J Ortho Sports PT*. 1982;4:109-112.

Thank you