A Seminar On Iontophoresis Drug Delivery System

Keyur Vasava…
Contents

1. Introduction.......................................................... .................................
2. Theory........................................................................................................
3. Iontophoresis units/devices.................................................................
4. Pathways of iontransport.................................................................
5. Factors affecting iontophoretic transport...........................................
6. Applications of iontophoresis............................................................
   6.1. Hyperhidrosis
   6.2. Diagnosis of cystic fibrosis
   6.3. Anesthesia
   6.4. Facilitation of underlying deep tissue penetration
       of compounds
   6.5. Systemic applications of iontophoresis
   6.6. Miscellaneous
7. Conclusions.......................................................... .................................
8. References.............................................................................................
Introduction:

The concept of drug delivery through the skin hereby referred to as cutaneous drug delivery or systemic indications is now a practical reality and transdermal patches have met with patient acceptability. However, the extension of passive transdermal delivery to a larger number of drugs as been limited by the natural barrier properties of the stratum corneum, the outermost layer of the skin. Conventional transdermal therapy is only applicable to small, potent and lipophilic solutes. There has been a continuous quest for testing strategies to facilitate drug penetration across the stratum corneum barrier. These strategies have included both physical and chemical means and reports have appeared demonstrating the effectiveness of each of these techniques. Most of these strategies have toxicological implications and further work is required before their acceptance in clinical practice.

Iontophoresis is one of such strategies believed to have great potential in facilitating transdermal drug delivery. Iontophoresis may be defined as the facilitated movement of ions of soluble salts across a membrane under an externally applied potential difference. Iontophoresis has been particularly effective in the treatment of palm plantar hyperhidrosis and in the diagnosis of cystic fibrosis. In addition to local indications, the present approach of iontophoresis research for the first time is more focused towards exploiting this technique for systemic delivery of drugs. The technique of iontophoresis has the potential to overcome many of the disadvantages associated with conventional transdermal delivery. The inter and intra subject variability is considerably reduced in iontophoresis since the rate of drug delivery is proportional to the applied current. The dosage regimen can be tailored on an individual basis to deliver drug at preprogramed rates. Iontophoresis is non-invasive drug delivery system with no trauma, risk of infection or damage to the wound and is therefore an important alternative to the injection therapy. Although primarily intended for charged compounds, iontophoresis can also facilitate the delivery of uncharged compounds by the process of electroosmosis. Iontophoresis has shown great promise in the delivery of peptides as well as large molecular weight proteins.

2. Theory

The rate of membrane penetration of drugs may be increased by means of an external energy source. The technique of iontophoresis is novel in providing this external energy source to drug ions in their passage across the skin. It is based on the general principle of electricity i.e. like charges repel each other and opposite charges attract each other. Thus in order to deliver a negatively charged drug across skin, it is placed under the negative electrode where it is repelled and is attracted towards a positive electrode placed elsewhere on the body, the vice versa being true for positively charged ions. Fig I is a
schematic representation of a typical iontophoretic set up. In anodal iontophoresis, the
drug solution containing positive active ion is placed under anode at the desired site of
application while the cathode the receiving electrode, is placed at a different site. The
electrode orientation is reversed in cathodal iontophoresis. The transport of neutral or
uncharged molecules can also be facilitated by iontophoresis.

The Nernst-Planck equation as applied in iontophoresis may be defined as the
combination of flux of an ionic solute, across a membrane by passive diffusion due to
the solute concentration gradient (aC/ax) and as a result of an electrical potential
difference across the membrane:

\[ J_i = -D_i \frac{\partial C_i}{\partial x} - D_i \frac{C_i z_i F}{RT} \frac{\partial E}{\partial x} \]

Fig. 1. Schematic representation of an iontophoresis setup.

Where \( D_i \) is the diffusion coefficient of solute across the membrane, \( z_i \) is the solute
charge, \( C_i \) is the concentration of the solute, \( F \) is the Faraday constant, \( R \) is the gas
constant and \( T \) is the absolute temperature. Solvent flow occurs across a membrane
carrying fixed charges when an external electric potential gradient is applied. Given the
skin is negatively charged, this fluid flow will occur in the direction of cation flux. Such
flow will either enhance the transport of cation or retard the transport of anions. Solvent
flux or convective flux or electroosmotic flux is normally added to the Nernst-Planck
equation, Eq. 1, to yield.

\[ J_i = -D_i \frac{\partial C_i}{\partial x} - D_i \frac{C_i z_i F}{RT} \frac{\partial E}{\partial x} \pm C_i J_v \]

where \( J \) is the velocity of convective flow (i.e. volume per unit time per unit area). The
contribution of the convective flux to the overall transport of charged compounds is likely
be small [9,11]. Roberts et al. suggested that on vective flow was likely to contribute only about 5% of the total iontophoretic flux of a solute with a transport number of about 0.2.

3. Iontophoresis units/device

Iontophoresis devices are generally designed to deliver small amounts of therapeutically active materials for a given time. The device is generally operated at a constant voltage so that the current can be varied, depending upon the resistance of the skin being treated. This reduces the chances of electric shocks thus increasing patient compliance and acceptability. The salient considerations for an iontophoretic device include safety, convenience, reliability, cost and portability. Three types of iontophoresis units are commercially available: line-operated units, simple battery operated units, and rechargeable power sources. Line-operated devices are used for the iontophoresis of pilocarpine to diagnose cystic fibrosis. Phoresor is a multifunctional battery-operated device (manufactured by Motion Control Inc., Salt Lake City, current irrespective of the changes in skin resistance and has an automatic control for shut off if the skin/electrode resistance exceeds pre-set limits (Phoresor package insert). Drionic, another battery operated device (General Medical Company, Los Angeles, California) has recently been approved by the Food and Drug Administration and is commercially available for the treatment of hyperhidrosis. It is designed for home self use and has been shown to be clinically safe and effective. Hidrex device (Gesellschaft für Medizin und Technik, Wuppertal, Germany) used for treating palmoplantar hyperhidrosis can be operated by a rechargeable energy source or by batteries. It is also designed for home use and characterized by safety equipment, automatic timing and remote control for amperage adjustment.

4. Pathways of ion transport

Fig. 2 shows a schematic representation of human skin. The major route of iontophoretic transport is believed to be appendageal pores including the sweat ducts and hair follicles. The use of pilocarpine in the diagnosis of cystic fibrosis is in itself a suggestion towards electric current traveling down the sweat ducts. A dot like pattern over the sweat gland
openings following iontophoresis of charged dyes in human skin in vivo has also been observed.

![Diagram of human skin](image)

**Fig. 2. A diagrammatical representation of human skin: (a) appendageal pathway; (b) intercellular pathway.**

Evidence suggesting sweat ducts being an important pathway in iontophoretic transport also comes from the work of Papa and Kligman who observed a direct correlation between methylene blue staining of the skin and the location of sweat ducts. The reduction in blood glucose levels following iontophoretic delivery of insulin in both hairless and regular rats suggests that the drug was being transported mainly through sweat ducts, apocrine and sweat glands. Ion transport through sweat duct units using electrodes was shown by Grimnes, Cullander and Guy used a vibrating probe electrode to identify largest currents in the vicinity of residual hairs. The appendageal pathway for iontophoretic transport has also been shown for mercuric chloride, ferric and ferrous ions by scanning electrochemical microscope and by the observed localization of fluorescein dye at the pores following cathodal iontophoretic transport and by obtaining maximal responses over the pores using microelectrodes.

A non appendageal pore pathway has also seen suggested recently which probably plies the current flow through “artificial hunts” as a result of temporary disruption of the recoganized structure of stratum corneum. A potential-dependent pore formation in the stratum corneum has also been reported and attributed to the flip-flop movements in polypeptide helices n the stratum corneum. The repulsion between neighboring dipoles form pore openings through which water and charged ions flow and neutralize he dipole moments. The occurrence of par cellular transport for charged and polar solutes has also been demonstrated by confocal microscopy of iontophoretically driven fluorescent ions in the skin intercellular or transepidermal transport may also occur concurrently with
folicular transport but the contribution of this flux to the overall is likely to be small. The skin is believed to be a cation selective membrane facilitating the transport of positively charged ions. The negative charge on the skin is as a result of greater number of protein amino acid residues carrying negative charges e.g. carboxylic groups) as opposed to positive selectivity of the skin induces a net volume flow during iontophoresis, and it has been demonstrated independently by Rein, and Pikal and Shah that this induced volume flow during iontophoresis is in the direction of positive ion transport supporting the belief of cation selectivity of skin.

5. FACTORS INFLUENCING IONTOPHORETIC PROCESS:-

The factors influencing iontophoretic delivery of a drug can be broadly classified into operational and biological factors.

**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

Current profile

Duration of treatment

Electrode material
Polarity of electrodes

Biological Factors
I. Intra and inter subject variability
II. Regional blood flow
III. Skin pH
IV. Condition of skin

Operational Factors

➢ Composition of Formulation

Concentration: Concentration of drug is one of the most important factors affecting iontophoretic process. The effect of the concentration has been studied on a number of drugs. An increase in concentration was shown to increase the apparent steady state flux of a number of drugs e.g., AVP, metoprolol, butyrate, Diclofenac sodium, dopamine agonist 5-OH DPAT, rotigotine, atenolol HCl and ketorolac. All these drugs showed a proportional increase in flux with an increase in concentration. With drugs like benzoate and LHRH, a modest increase was observed. But this is not the general observation since, an increase in concentration increases flux up to a point, after which the flux becomes independent of the donor concentration. This is probably due to the charge saturation of the aqueous conducting pathways of skin also called as boundary layer saturation. Methyl phenidate showed a little change in flux when concentration was increased beyond 0.1M pH: Since iontophoresis is widely used for peptide delivery, pH plays a vital role and it determines the ionization of peptides, which depends upon isoelectric point and respective pKa of charged amino acid. Moreover, skin permeability is also dependent upon pH e.g., AVP (pI-10.8) showed maximum flux when donor having a wide range of pH (4-8) were used [38, 39] but calcitonin (pI-6.5) showed optimum flux at pH 4.0 and not at higher pH. 5-OH DPAT showed enhanced flux when pH was increased from 3 to 5 but not at higher pH. In case of leuprolide (LHRH agonist) a two fold increase in flux at pH 7.2 was observed than at pH 4.5. There was a three fold increase in flux of buprenorphine at pH 4.0 than at pH 5.0. Glibenclamide, when given by pulsed iontophoresis, showed higher flux at pH 8.5 than at pH 7.4 or 8.0. Since pH influences the charge on protein, polarity of electrodes is an important factor to be taken into consideration during drug delivery e.g. anodal delivery of insulin is preferred but below its Isoelectric point whereas in case of pilocarpine a moderate pH of 5.98 is required to achieve maximum permeation. Thus, the optimum pH for iontophoretic delivery of a compound is one where it exists predominantly in an ionized form. The effect of pH of aqueous vehicle on rate and extent of iontophoretic delivery of lidocaine was investigated. The rate was found to be maximum when the drug was in an ionized form. Thus, pH is an important factor governing the
iontophoretic delivery of drugs. Moreover, it also influences the chemical stability of the drug involved.

- **Ionic strength & presence of other ions:**

  In iontophoresis the main aim is that the drug ion should carry maximum charge across the membrane. It follows that an increase in ionic strength will decrease drug delivery, as extraneous ions compete with the drug ions. The buffering agents used to maintain pH of the donor medium is a source of co-ions.

- **Current Drug Deliver:**

  These co-ions are generally more mobile and smaller in size than the drug ions itself and can dominate the penetration into the skin thereby causing a decrease in transdermal flux of the drug. Many peptides widely studied for ionic strength showed a higher flux occurring at low electrolyte concentration. Similarly, drugs like ketorolac showed increased flux with decrease in ionic strength. A 50% reduction in benzoate flux occurred when an approximately equimolar amount of NaCl was added to donor compartment. Salicylic acid flux was found to decrease with the increase in concentration of HEPES buffer and 5-OH DPAT flux decreased with addition of NaCl. But occasionally an increase in ionic strength leads to an increased flux e.g., iontophoresis facilitated an increased skin permeation of AVP as the ionic strength of donor solution increase.

- **Physicochemical Properties:**

  **Molecular size and molecular weight:** The molecular size of the solute is a major factor governing its feasibility for iontophoretic delivery and hence the amount transported. When the iontophoretic delivery of carboxylate ions was studied, flux for acetate was found to be more than that of hexanoate and dodecanoate. This suggests that smaller and more hydrophilic ions are transported at a faster rate than larger ions. Many studies correlating flux as a function of molecular weight have been conducted and it was concluded that for electro repulsive iontophoresis, when all other conditions were kept constant, transport of compounds decreased with increase in molecular weight (chloride> amino acid> nucleotide> tripeptide> insulin). But due to the use of advanced techniques like iontophoresis, electroporation and phonophoresis, delivery of even large molecule like peptides is possible now.

  **Charge:** Charge on a molecule is an important physicochemical property governing iontophoretic transport, since the sign of the charge determines the mechanism by which iontophoresis will proceed e.g., electrorepulsion or electrorepulsion and electroosmosis. Although the transport of cations has been shown to be better than anions for amino acids and peptides, this however is not so simple because an increase in charge will require pH to be decreased, which in turn shall directly decrease the electroosmosis and electro transport process. An increased positive charge on peptide, cause it to bind tightly to the membrane creating a reservoir which in turn can decrease the rate at which the steady state flux will be achieved.
Polarity: Generally, the compounds which are hydrophilic are considered ideal candidates for optimum flux e.g., nalbuphine and its ester showed an increased flux as the lipophilicity of the compound decreased.

➢ Experimental Conditions:

Current strength: Since current can easily be controlled by the use of electronics, it is a convenient mean to control delivery of drugs to the body. However, a large increase beyond the permissible limits causes irritation and can damage the skin. A linear relationship has been observed between the apparent flux of a number of compounds and the applied current. Methylphenidate showed a linear relationship between the applied current and its iontophoretic flux. A linear increase in the flux with current has also been found for TRH, verapamil, GRH, diclofenac and ketorolac. In general, 0.5mA/cm2 is often stated to be the maximum iontophoretic current which should be used on human beings.

Current profile: Mostly, in the studies conducted on animals in vitro, current is kept constant and very low voltage of about 10 V is applied.

Pulsed current: The persistent use of direct current (DC), proportional to time, can reduce the iontophoretic flux because of its polarization effect on the skin. This can be overcome by the use of pulsed DC which is a direct current delivered in a periodic manner [5]. During “off stage” the skin gets depolarized and returns to the initial polarized state. However, Bagniewski and Burnett showed that enhanced skin depolarization can decrease the efficiency of drug transport, if the frequency of pulsed current is very high. A two fold increase in the transdermal flux of vasopressin was observed when pulsed current was used in vivo in rabbits. Enhanced transport of proteins and peptides has been reported using pulsed DC e.g., insulin. But in many cases like sufentanil, fentanyl and ketorolac a decreased flux was observed when pulsed current was used as compared to constant direct current.

Electrode material: Iontophoretic studies have been conducted using both platinum wire and Ag/AgCl wires. However, platinum electrodes or other inert electrodes like nickel or stainless steel have been found to cause pH drift and gas bubbling due to decomposition of water and thus causing production of H+ and OH- ions [26] in the following manner:

Anode: H2O 2H+ + 1/2 O2 + 2e-

Cathode: H2O + e- OH- + 1/2 H2

Thus, Ag/AgCl electrodes with redox potential lower than that of water which help to maintain electroneutrality at both anode and cathode have been used for this purpose. Phipps et al. studied the electrode material selection in optimizing the delivery of lithium across polyvinyl alcohol (PVA) hydrogel membrane. They showed use of platinum anode in donor caused a pH decrease due to production of hydronium ion as shown above, which are more mobile and no efficient
delivery of lithium was observed while the use of Ag/AgCl electrodes in place caused no pH drift and a significant increase in lithium flux almost double of the above case was observed.

**Regional blood flow:** During iontophoresis, the dermal blood supply determines the systemic and underlying tissue solute absorption. Blood supply however, does not appear to affect the drug penetration fluxes through the epidermis during iontophoretic delivery. Cross and Roberts showed that solute in the upper layer of the skin following iontophoresis was comparable in anaesthetized rats and sacrificed rats. It can thus be presumed that the blood did not affect the penetration through the epidermis since the latter has no blood supply.

**Condition of skin:** In iontophoresis, skin condition also affects the penetrating properties of permeant. Burnt skin, cut, open wounds are not preferred for iontophoresis delivery of drug.

### 6. Applications of Iontophoresis

#### 6.1. Hyperhidrosis

Localized idiopathic hyperhidrosis is a fairly common disorder and socially uncomfortable. The most widespread use of iontophoresis is in the treatment of palmar and plantar hyperhidrosis. The affected region is placed in the tap water and the current passed at a strength just below the threshold for discomfort, for approximately half an hour. The procedure is believed to be safe and effective. The efficacy of tap water iontophoresis for control of palmpplan-tar hyperhidrosis has recently been proven in a large group of patients. A total of seventy one patients with palmpplantar hyperhidrosis were treated. An average current of 15 mA on palms and 20 mA on soles was applied for 30 min. Treatments were carried out preferably once a day and at least three times a week. Hyperhidrosis was completely controlled after lo-12 treatments as revealed by quantitative gravimetric measurements of sweat rates and semiquantitative estimation of starch iodine paper imprints. Maintenance treatments (average 1.3 treatments per week) were carried out.

#### 6.2. Diagnosis of cystic fibrosis

The quantitative pilocarpine iontophoresis test (Q PIT) was introduced by Gibson and Cooke in 1959. Pilocarpine has a stimulatory effect on the endocrine secretion. The chloride content of which is used to assist in the diagnosis of cystic fibrosis. The technique is now universally accepted as the safest and least stressful way to stimulate sweat. The use of pilocarpine iontophoresis to diagnose cystic fibrosis has been approved by FDA and is commonly used by pediatricians. Gibson et al. recommend the application of the current of the order of 0.16 mA/cm² of skin surface for a period of 5 min., and a concentration of 0.5%. The possible use of insulin in cystic fibrosis may also deserve
further attention since a reduction in chloride content of sweat has been reported following insulin treatment.

6.3. Anesthesia

Local anesthesia is often required in conditions like superficial wound excisions, local skin biopsies, eyelid surgery, abscess incision, or in patients who are averse to the use of hypodermic needles. The disadvantages of injecting a local anesthetic include pain. Distortion of tissue, potential systemic absorption. The usefulness of iontophoresis to achieve local anesthesia has been well documented. The advantages of iontophoresis induced anesthesia include no tissue distortion, adequate local and little systemic concentrations of the drug and the procedure is painless. Based on a controlled study employing lidocaine, Gangarosa reported that skin anesthesia was best obtained with solutions containing 1% and 4% lidocaine. Addition of epinephrine prolonged the duration of anesthesia. Russo et al. have reported the penetration of iontophoretically applied lidocaine to the depth of subcutaneous tissue (served by the placement of suture) in humans and observed that lidocaine iontophoresis was an effective means of inducing local anesthesia for about 5 min without using a hypodermic needle and syringe. Riviere et al. have also demonstrated skin penetration of lidocaine after transdermal iontophoresis. Following transdermal iontophoresis in rats, appreciable levels of lidocaine have been observed as deep as underlying muscle. There was minimal systemic uptake of lidocaine which provides evidence for the selective direct penetration of iontophoretically driven lidocaine. Bezzant et al. have demonstrated usefulness of lidocaine iontophoresis for cauterization of spider veins, a procedure poorly served by conventional local anesthesia.

Recently, a two-center open-label study was reported using iontophoretic administration of 4% lidocaine with epinephrine (1:50000). Iontophoretic local anesthesia was 80 to 100% effective for pain relief for injections, abrasions, laser surgery, and cautery and relatively less effective for dermal excisions. In a double blind, placebo-controlled evaluation, iontophoresis of lidocaine was observed to be significantly effective in reducing the discomfort of pulsed dye laser ablation of port-wine stains in adults and children over 7 years of age. The rapidity of the technique was confirmed when an average of only 12 min was required for iontophoretic treatment as compared to 60 min required for anesthesia using a eutectic mixture of local anesthetics.

6.4. Facilitation of underlying deep tissue penetration of compounds

The use of iontophoresis to facilitate underlying deep tissue penetration of drugs after topical application will be most beneficial in the treatment of osteoarthritis, soft-tissue rheumatism, tendonitis and other deep rooted local inflammatory conditions associated with sports injuries or other minor accidental injuries. Reports have appeared in literature showing appreciable levels of certain drugs in underlying deeper tissues following their
transdermal iontophoretic application Glass et al. have demonstrated the penetration of dexamethasone in tissues below the applied site in monkeys. The drug was observed at sufficient tissue depths including tendinous structures and cartilaginous tissue. Russo et al. have reported the penetration of iontophoretically applied lidocaine to the depth of subcutaneous tissue (observed by the placement of suture) in humans. Iontophoresis of water soluble glucocorticoids dexamethasone, hydrocortisone and prednisolone up to a depth of 1.25 cm below the applied was also demonstrated by Murray et al.. Recently, Singh and Roberts studied the depth of penetration of lidocaine and salicylic acid after their transdermal iontophoresis in rats. Iontophoresis yielded high concentrations of lidocaine in underlying tissues up to a depth of about 1.2 cm as compared to the passive application to rat epidermis (Fig. 4). In contrast, similar concentrations of salicylic acid were observed in underlying tissues after both transepidermal iontophoretic and passive dermal (epidermis re- moved) application. The direct penetration of iontophoretically driven lidocaine relative to salicylic acid was evident when almost all of the absorbed lidocaine was recovered in underlying tissues following 2 h transdermal iontophoresis whereas only 30% salicylic acid (majority being in the skin) was found in underlying tissues for the similar duration of iontophoresis.

![Graph showing tissue distribution of lidocaine after epidermal iontophoretic and passive epidermal treatments.](image)

**Fig. 4.** Tissue distribution of lidocaine after epidermal iontophoretic (■) and passive epidermal treatments (□). The vertical axis represents fraction of applied concentration.

### 6.5. Systemic applications of iontophoresis

The therapeutic importance of peptides and proteins has gained growing recognition in past few years due to the development of systematic methods to produce therapeutic peptides and the success of recombinant DNA technology, e.g. insulin in the treatment of diabetes mellitus, vasopressin for diabetes insipidus (791, certain growth hormone releasing factors effective in promoting linear growth in short-statured children [SO], reproductive
hormone luteinizing hormone releasing hormone. Peptide and protein molecules are generally inactive when given orally, because of their high susceptibility to degradation by proteolytic enzymes in the gastrointestinal tract, poor absorption because of their polar nature and extensive hepatic first pass metabolism. Parenteral administration is thus required for peptides to be therapeutically effective. Because of their relatively short half lives, frequent injections become necessary to maintain the desired therapeutic levels. This treatment often exposes the patient to constant pain and health hazards. One of the attractive alternatives is the transdermal drug delivery, but then again since peptide and protein macromolecules are mostly hydrophilic in nature and often of large molecular size their passive delivery through skin is limited. The application of transdermal iontophoresis has shown promise in delivering charged and large molecular weight solutes across the skin. A literature has now been established showing the use of iontophoresis to facilitate the delivery of protein and peptide drugs across the skin.

6.6. Miscellaneous

Iontophoresis has been used to deliver antiviral chemotherapeutic agents for the treatment of herpes simplex virus infection in mice. Iontophoresis of adenine arabinoside monophosphate has been suggested as a method of choice for the treatment of HSV-1 skin lesions in hairless mice. 80% of hairless mice treated by cathodal iontophoresis of adenine arabinoside monophosphate survived Herpes Simplex Virus Type 2 infections (p < 0.05), when compared with saline iontophoresis and other topically treated groups. Iontophoresis of idoxyuridine and acyclovir has been shown to be an effective remedy in the treatment of oral herpes and recurrent herpes labialis. Recently, iontophoresis of vinblastin in HIV-1 - infected patients untolerable to systemic vinblastin has been shown to be a viable alternative for control of cosmetically unacceptable or painful cutaneous lesions of Kaposi’s sarcoma. By iontophoresing sympathetic agonists and antagonists into the finger skin and evaluating the resulting change in local blood flow by laser Doppler velocimetry, adrenoreceptor function in subjects with Raynaud’s disease has been evaluated. Iodine iontophoresis has also been shown to be effective in reducing scar tissue. Zinc iontophoresis has been shown to accelerate wound healing of ischemic skin ulcers. Iontophoresis (2 mA, 10 min) of salicylate ion in patients with plantar warts was found to be effective in removing the warts in 2-3 treatments . Iontophoresis has also been employed to deliver meladinine for the treatment of vitiligo, copper iontophoresis for male contraception and epidermophytosis, steroids for treating Peyronie’s disease. In veterinary practice, positive iontophoresis of 2% methylene blue was effective against heavy infestations of Demodex folliculorum from canine skin while negative iontophoresis of potassium iodide alleviated Trichophyton verrucosum infection of bovine skin. Histamine iontophoresis has been used to induce local capillary dilatation in order to obtain accurate determination of blood gases and also suggested as an aid in the healing
of chronic sclerotic ulcers. Histamine iontophoresis has also been demonstrated to be a reliable model for the study of inflammatory skin responses.

Some other applications of iontophoresis include acetic acid iontophoresis into joints for calcium deposits, cisplatin iontophoresis in the treatment of superficial skin cancers, and histamine iontophoresis in the treatment of fibrosis. Iontophoresis is also employed to study blood vessel responses to iontophoretic administration of various drugs. In order to study the vasodilator system component of skin blood flow, local iontophoresis of bretylium has been performed to selectively abolish the adrenergic vasoconstrictor system. The use of iontophoresis as a method of investigation for contact dermatitis has also been advocated. The potential of using iontophoresis to extract compounds from within the skin (“reverse iontophoresis”) to diagnose systemic conditions has also been suggested.

7. Conclusions

The use of iontophoresis to treat local conditions is well known. Iontophoresis may also be useful for targeting deeper underlying tissues e.g. muscle in conditions such as osteoarthritis, musculoskeletal spasms and other local inflammations associated with sports injuries or accidents. More recently, iontophoresis is being exploited for the controlled delivery of drugs for systemic indications. It is believed to be practical alter-native to parenteral therapy since comparable plasma levels may be obtained by two methods and the pain and discomfort associated with repeated injection therapy can be overcome by iontophoresis. Iontophoresis may be particularly useful for the effective delivery of peptide and protein drugs since these compounds exist in a charged form at physiological pH. Using iontophoresis, transdermal delivery of insulin, thyrotropin releasing hormone, leuprolide, gonadotropin-releasing hormone, arginine-vasopressin and some tripeptides has been demonstrated. The proper understanding of protein chemistry in the formulation and within the skin under a closed electrical circuit, however, has not been investigated in detail and research in this area will help to further optimize iontophoretic delivery of protein and peptide drugs. The use of direct/pulsed current in terms of iontophoresis efficiency and skin irritation also needs to be evaluated.

References

• Controlled and novel drug delivery by N.K. Jain; CBS publishers and distributors; 191-206.