

Iontophoresis

Iontophoresis is a technique which uses an electric current to deliver a medicine or other chemical through the skin. In popular (lay) terms it is sometimes called "an injection without the needle". In the past it has sometimes been called Electromotive Drug Administration, though in modern therapy, this is a rarely employed term.

This is not a new technique - there is recorded iontophoresis activity way back to the 1700's, though most authorities agree that it was not until the work of Le Duc in the early 1900's that the technique really gained momentum, though its use since that time has been sporadic.

Formally, the modality can be defined thus : "... a non-invasive method of propelling high concentrations of a charged substance, (normally a medication or bioactive agent), transdermally by repulsive electromotive force using a small electrical charge applied to an iontophoretic chamber containing a similarly charged active agent and its vehicle". The term iontophoresis is simply defined as ion transfer (ionto = ion; phoresis = transfer).

Iontophoresis is used in therapy, but is not exclusive to this arena, and there are applications in medicine, dentistry, lab sciences and physiology. A literature search will quickly identify thousands of references, though only a relatively small proportion of them will be directly relevant to therapy type applications. There have been several reviews over the years (see references at the end of this material) which will assist those with an interest in following up on the key literature.

There are relatively few practitioners using iontophoresis in the UK, but in the USA it is a mainstream application. In Europe there are pockets of activity, and strong support from many practitioners. The use of iontophoresis worldwide is patchy - with areas of high use and areas where it is almost never employed.

IONTOPHORESIS is NOT the same as PHONOPHORESIS which involves driving ions across the skin with therapeutic ultrasound

Basic Principles

In order to 'drive' the ions into the tissues, a **DIRECT (Galvanic) CURRENT** needs to be employed. Some authorities suggest that the current needs to be continuous, though others have argued that so long as the current is monophasic in nature, a pulsed application can be used. Continuous (classic) DC is most commonly used in practice.

Essentially, the substance to be driven into the tissues NEEDS to be IONIC in nature, and MUST be placed under the electrode with the SAME CHARGE (i.e. positively charged ions placed under the positive electrode (ANODE) and the reverse for a negatively charged ion)

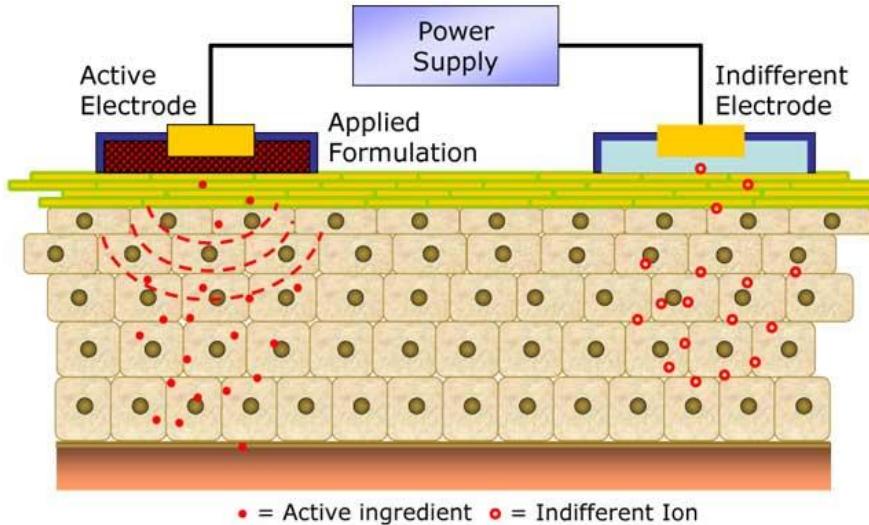
The **positively charged chamber**, called the **anode**, will **repel a positively charged chemical** into the skin.

The **negatively charged chamber**, called the **cathode**, will **repel a negatively charged chemical** into the skin.

Conventionally, the electrode under which the ionic solution is placed is called the ACTIVE electrode (other terms include TREATMENT electrode or DELIVERY electrode). The other electrode, which is used

to complete the circuit is most commonly called the DISPERSIVE, INDIFFERENT, INACTIVE or RETURN electrode. For consistency in this document the terms **ACTIVE** and **INDIFFERENT** electrodes will be used.

Ions with a polarity which is the same as that of the stimulating electrode are repelled into the skin



It is assumed that the effects of the treatment are attributed to the delivered ions and not the direct current - though interestingly, this basic premise has not actually been fully established. Given the wealth of evidence in favour of various DC applications, including a recent resurgence of High Voltage Pulsed Current (HVPC) and the developing use of MICROCURRENT based therapies, it would be surprising if the DC current had no effect in its own right.

The ions are driven into the skin via the pores - hair follicles, sweat gland ducts - rather than through the stratum corneum per se (the stratum has a high resistance, thus limited current passes through it - the ducts are lower resistance, will allow greater passage of current, thus the route of preference).

The ions (ionic solution) used will depend on the therapeutic effects which are intended. The table in this document identifies some of the more commonly employed solutions, their use and the electrode under which they need to be placed in order for the iontophoretic effect to be achieved. These substances range from tap water through to steroid based medicines, and the regulations concerning their use will vary from country to country depending on prescription and therapist autonomy.

IONIC PENETRATION

It is usually considered that the penetration of the ions into the tissues is likely to be less than 1mm. Any deeper penetration is considered to be due to local capillary circulation effects. There is no evidence that the current itself is responsible for penetrations beyond this level (though some authors claim - without explicit evidence - that the ions are driven much further into the tissues. The bulk of the ions that enter the tissues accumulate under the stimulating electrode and it may be possible that recombination of the substance can occur under this (active) electrode, though this remains a controversial issue which has not been fully resolved by the available research evidence.

It is possible that different ions will travel varying distances into the tissues - in other words, there is not a 'set' penetration which is equal for all different substances. This issue has also yet to be fully resolved.

Acid / Alkaline Reactions

Will get **ACID** accumulation under the **POSITIVE** (anode) electrode (weak HYDROCHLORIC ACID) because the negatively charged chloride ions (Cl^- from NaCl) will transit (be attracted) towards the anode.

Will get **ALKALINE** accumulation under the **NEGATIVE** (cathode) electrode (SODIUM HYDROXIDE) because the positively charged sodium ions (Na^+ from NaCl) will move towards the cathode. The Na^+ ions react with water to form sodium hydroxide (NaOH). N.B. it is suggested that the reaction at the negative (cathode) electrode will bring about a softening of the skin, hence its growing use by beauty therapy clinics.

A reactive hyperaemia will be observable under BOTH electrodes due to (chemically mediated) local vasodilation.

The magnitude of the local reaction (independent of the ions utilised) will depend on :

- Current Intensity (more current, greater reaction)
- Time (longer time, stronger reaction)
- Tissue Resistance (greater resistance, stronger reaction)

The evidence is summarised by Belanger (2010) who concludes that based on the available evidence (e.g. Banga et al, 1998 and Anderson et al, 2003) the penetration of the ions is greatest in the region of the pores, the penetration of the substance through the skin is in proportion to the current magnitude, but that the substance is most likely deposited below the stratum corneum, thus acting as a depot. Onward migration of the substance to the deeper tissues is achieved by diffusion rather than being 'driven' deeper by the applied current.

Interestingly, it is also suggested that if there is a strong vasodilation in the blood vessels of the skin, there will be a less effective diffusion to the deeper tissues on the basis that the increased local flow will serve to dilute the subepidermal deposit.

Anodal and Cathodal Reactions in response to Iontophoresis

Cathode	Anode
NEGATIVE electrode	POSITIVE electrode
Attraction of +ve ions	Attraction of -ve ions
Alkaline reaction by the formation of NaOH	Acid reaction by the formation of HCl
Increased density of proteins	Decreased density of proteins
Increased nerve excitability via a depolarisation effect	Decreased nerve excitability via a hyperpolarisation effect (sometimes called anode blockade)

Application Devices

There are many specific (dedicated) machines sold which are solely designed to deliver this type of treatment. Several are for patient home use (especially for the treatment of hyperhidrosis). Most modern multifunction devices will include iontophoresis type currents in their menu options.

Examples of dedicated IONTOPHORESIS devices

Examples of MULTIMODAL devices which include IONTOPHORESIS facilities

Additionally, the so called 'wireless' application devices are gaining popularity, especially for home use. The delivery system is 'self contained' in that the electrodes (self adhesive) and stimulator are in a single housing which the patient applied to the affected area. The electrode patch is preconfigured and delivers a smaller current than is normally employed in the department or clinic (typically 0.1mA). The patch is applied for 12 - 24 hours (depending on the intended dose) after which time, it is removed and discarded (they can not be reused). The illustration of electrode systems (below) includes one such option (top right)

Optimal Current Variables used in Iontophoresis (after Rothstein et al, 1998)

Current Type	DC
Current Amplitude	1.0 - 4.0 mA
Treatment Duration	20 - 40 minutes
Total Current delivered	40-80mA/min

Polarity, Current Intensity and Drug Concentrations

There are some authors who identify very specific substance concentrations, volumes, electrode sizes, current intensity and treatment duration (the critical parameters for an iontophoresis treatment). Others provide general guidance, saying that it is not possible to be specific for a particular patients with a particular clinical presentation.

In general terms, low current intensities appear to achieve favourable results. The treatment is usually applied with **currents up to 5mA** and with **low ionic concentrations – up to 5%**, though there are certainly reports and treatment suggestions that take the current intensity up to higher levels and employ 'stronger' substance concentrations. Treatment times are typically in the **20 - 40 minute** range.

There is evidence to suggest that using a higher concentration of the substance does not serve to increase the effectiveness of the therapy, and does not increase the amount of the drug delivered to the

tissues - low concentrations of drug (or substance) (typically 2-5%) and a low current intensity (up to 5mA) appears to be the most effective delivery method.

It has been suggested that commonly, the NEGATIVE electrode is made larger (relative to the positive electrode) to avoid skin irritation (whether the ionic driving electrode or not). Figures often cited suggest that the negative (cathode) electrode should be 2 x larger than the positive (anode) electrode.

General Principles of Application

It is preferable to utilise a direct current stimulator, commonly a dedicated iontophoresis device, or the DC/Iontophoresis output on a multi-modal machine.

Constant current is preferable to constant voltage - thus, whatever changes occur in terms of skin resistance, the magnitude of the applied current will not exceed the preset level. Some machines offer you and a choice - and if that is the case, constant current will give you an effective and the most safe application (smaller risk of skin burn).

Constant voltage stimulation can result in a burn more easily (in this case, the voltage is set by the operator. If the skin resistance changes, the current flow through the tissues will vary - and thus give rise to an increased risk of burn)

Safe Current Density

It is important to note that the current density (how strong the current is and also how concentrated it is), measured in mA/cm^2 , is an important factor in these treatments. If the current density reaches too high a level, tissue damage, and especially skin burn, may ensue.

It is suggested (see Belanger, 2010 for the full argument), that **a current density of no more than 0.5mA/cm^2 is applicable at the negative(cathode) electrode and 1.0mA/cm^2 at the positive(anodal) electrode.**

If a current of 2mA is delivered using an electrode of 6cm^2 , the current density will be $2(\text{mA})/6(\text{cm}^2) = 0.33\text{mA/cm}^2$, which is safe at either the positive (anode) or negative (cathode) electrode.

It is possible, using a transposition of the equation, to establish the maximal current that can be applied with a particular electrode whilst ensuring a safe treatment.

Maximum Current (mA) = Maximum Safe Current Density (mA/cm^2) x Electrode area (cm^2)

E.g.

If the (active) electrode to be used is 6cm^2

If the active electrode is to be made NEGATIVE (cathode)

The maximum safe current density is 0.5mA/cm^2

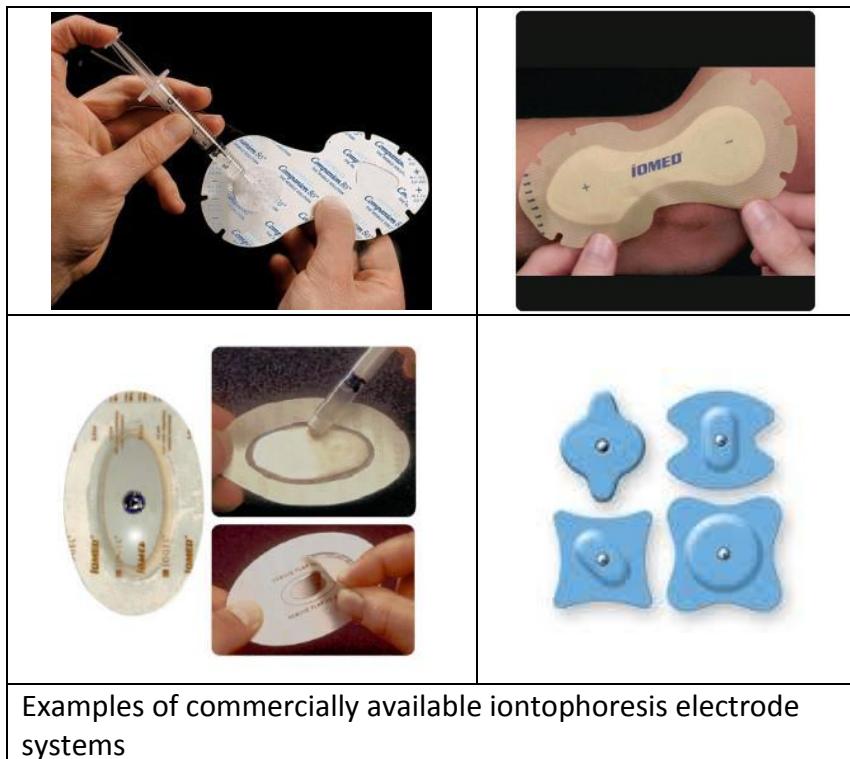
The maximum current that can be safely applied is therefore :

$= 0.5\text{mA/cm}^2 \times 6 (\text{cm}^2) = 3\text{mA}$

Electrodes

The electrodes can be special pre gelled disposable electrodes or standard metal electrodes of various types.

Some commercial iontophoresis electrodes have special wells or receptacle areas for the drug in question.



It is not necessary to use these (commercial) electrodes, and for many years, therapists have used various metal / foil electrodes with the substance needed for the treatment applied to the wet/damp gauze between the metal electrode and the skin surface.

Preparation and Delivery

The skin should be abrasion / cut free and the area carefully washed (soap & water is fine).

Some authorities have advocated the application of heat prior to the iontophoresis, but the experimental evidence does not support this. In fact, it appears to reduce the amount of drug passing through the epidermis and as identified in a previous section, increasing blood flow through the skin and superficial tissues may simply serve to reduce the size of the 'depot' in the skin.

Ensure that all electrode pads are thoroughly soaked in either tap water or other appropriate solution prior to application. Dry electrodes are inappropriate and should not be used.

If pregelled electrodes are being used, ensure that a good even contact is achieved.

Adequate fixation of the electrode and pad to the skin needs to be carefully maintained. Uneven current distribution can easily lead to skin burns and/or irritation

Explain to the patient what is expected and ensure that they know to report immediately if any untoward or painful sensations are felt.

Turn the current up slowly to the required amount

At the end of the treatment time, ensure that the current is turned down slowly.

Table of Commonly Used Medications and Solutions with Iontophoresis (after Rothstein et al (1998) and Belanger (2010)).

Drug / Solution	Main Indication(s)	Rationale	Parameters
Acetic Acid	Calcific tendinitis (myositis ossificans)	Acetate believed to increase solubility of calcium deposits in tendons (and other soft tissues)	2 - 5% aqueous solution NEGATIVE pole
Calcium chloride	Muscle spasm (also hypersensitive peripheral nerves)	Calcium thought to stabilise excitable membranes, appears to decrease excitability threshold in peripheral nerves and skeletal muscle	2% aqueous solution POSITIVE pole
Dexamethasone	Inflammation	(synthetic) anti inflammatory	4mg/mL aqueous solution NEGATIVE pole
Hydrocortisone	Inflammation	Steroid based anti inflammatory	0.5% ointment POSITIVE pole (Rothstein et al)
Hydrocortisone, prednisone	Inflammation	Steroid based anti inflammatory	NEGATIVE pole (Belanger)
Iodine	Adhesive capsulitis Other soft tissue adhesive presentations Infection (microbial)	Iodine acts as a broad spectrum antibiotic. Its actions in relation to adhesive presentations appear not to be fully understood	5 - 10% solution (some use ointment) NEGATIVE pole
Lidocaine	Soft tissue pain Inflammation	Local anaesthetic effects (blocks peripheral nerve activity). May stimulate healing	4 - 5% solution (ointment) POSITIVE pole
Magnesium sulphate (sulfate)	Muscle spasm Myositis	Thought that 'relaxing' effect is achieved by decreased excitability of muscle membrane and reduced activity at neuromuscular junction	2% aqueous solution (ointment) POSITIVE pole
Hyaluronidase	Oedema (local) Subacute and Chronic stages	Increases permeability in connective tissues thus allowing dispersion of accumulated fluid. Hydrolysation of hyaluronic acid	Delivered after reconstitution with 0.9% sodium chloride (Normasol) to give a 150µg/mL solution POSITIVE pole
Salicylates	Muscle and Joint pain Acute and Chronic	Mode of action akin to Asprin - analgesia and anti inflammatory. Inhibits synthesis of prostaglandins	2-3% sodium salicylate solution OR 10% trolamine salicylate ointment NEGATIVE pole

Tolazoline hydrochloride	Ulcers (open wounds)	Stimulates local blood flow Stimulates tissue healing (thought to be via inhibition of local vascular smooth muscle contraction)	2% aqueous solution POSITIVE pole
Zinc Oxide	Open wounds - ulcers Some dermatological conditions	Antiseptic effects related to the zinc. May stimulate healing	20% ointment POSITIVE pole
Tap Water	Hyperhydrosis (illustrations below)	Suppresses sweating in palms, soles of feet, axilla through ?keratin plug formation in ducts	Equal time with POSITIVE and NEGATIVE polarity - use 2 x hand baths. Reverse polarity 1/2 way through treatment (typically 30 minutes : 15+15)



Illustration of tap water iontophoresis for (palmar) hyperhydrosis

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Examples of Iontophoresis Research Publications (there are over 5000 references relating to this subject - this is a SMALL sample!)

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