ISSN: 0975-766X
CODEN: IJPTFI
Available Online through
Research Article
www.ijptonline.com

IONTOPHORETIC TRANSPORT OF IONIC MOLECULE: EFFECT OF CATHODAL AND ANODAL IONTOPHORESIS

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Received on: 28-04-2017 *Accepted on: 05-06-2017*

Abstract

In the transdermal drug delivery, Drug transport using Iontophoresis across biomembrane is increased by applying electric pulse to the membrane. The objective of the present study was to investigate the effects of pulsed current for duty cycles of time and Polarity of the electrodes which gives the electric pulse across biomembrane upon transdermal iontophoretic transport. Enhancementusing iontophoresis drug delivery is by three mechanisms: (a) the ionic and electric field interaction; (b) flow of electric current; (c) electroosmosis. The ionic-electric field interaction provides an additional force which drives ions though the biomembrane. Flow of electric current increases permeability of biomembrane. Electroosmosis produces bulk movement of ionic solvent itself that caries ions. The relative selection of Ionic molecule and importance of cathodal and anodal Electrodes across biomembrane, connected to the iontophoretic Power Supply has been studied. Theoretical Concepts with this respect are reviewed and Experimental observations are explored to clarify the nature of ionic transport and also to define the conditions under which ionic flow is an important effect in transdermal iontophoresis. The Biomembrane used for the study is the Egg membrane. NaCl dissolved in the de-ionized water is used for transport study across biomembrane. For the study Vertical Franz cell with two side arms is used. The mass transported across the biomembrane with Iontophoresis power Supply by changing the cathodal and anodal electrodes which gives the electric pulse to the biomembrane are compared with the mass transport without iontophoresis. Also Effect of both electrodes when altered which gives the electric pulse to the biomembrane.

Keywords: Electroosmosis, cathodal, anodal, biomembrane, Franz cell

Introduction: Iontophoresis is a widely used technique for the transfer of neutral and charged drug molecules into and across the skin by using electric pulse of small current [1].The range of electrical current varies from maximum

of 1 mA. But many researches show the drug is delivered into the skin when the current is below 0.5 mA[2]. In transdermal drug delivery through the skin, the pharmacetical research study requires the flexible iontophoresis power supply with maximum current density of or below 0.5 mA/cm^2 and with different duty cycles of time [3].The mechanisms of iontophoresis contain electro repulsion, which is based on the principle of "like repels like" and electroosmosis where the Ionic molecules are transported from anode to cathode along with the bulk solvent flow[4-5.

The iontophoretic technique is mainly based on the general principle that like charges repel each other[6]. Thus during iontophoresis, if delivery of a positively charged drug (DC) is desired, the charged drug is dissolved in the electrolyte surrounding the electrode of similar polarity, i.e. the anode[7]. On application of an electromotive force the drug is repelled and moves across the stratum corneum towards the cathode, which is placed somewhere else on the body[8]. Communication between the electrodes along the surface of the membrane has been shown to be negligible, i.e. movement of the drug ions between the electrodes occurs through the membrane and not on the surface only.

When the cathode is placed in the donor compartment of a Franz diffusion cell to enhance the flux of an anion, it is termed cathodal iontophoresis and for anodal iontophoresis, the situation would be reversed[9]. On application of electric current Neutral molecules have been observed to move by convective flow as a result of electro-osmotic and osmotic forces.

Electro migration of ions during iontophoresis causes convective solvent motion and this solvent motion in turn 'drags' neutral or even charged molecules along with it. This process is termed as electro-osmosis. At pH values above 4, the skin is negatively charged[10], implying that positively charged molecules like Na+ will be more easily transported as they attempt to neutralize the charge in the skin to maintain electro neutrality. Thus the movement of ions under physiological conditions is from anode to cathode[11]. For loss of each cation (e.g.sodium ion) from the electrode in this process, a counter ion, i.e. an anion, Cl^-moves in the opposite direction from the cathode to the anode. It is the transportation number of each ion, which describes the fraction of the total current transferred by the ion and depends on the physicochemical properties of the respective ions. t+ Na is greater than t- Cl and also the skin facilitates movement of Na^+ more than Cl^-, hence there is a net increase in the NaCl in the cathodal compartment and net decrease in NaCl on the anodal side. Due to this electrochemical gradient, osmotic flow of water is induced from the anode to the cathode. If any neutral drug molecules are present at the anode at this time they can be transported

through the skin along with the water. Such water movement often results in pore shrinkage at the anode and pore swelling at the cathode[12].

The objective of the current study was to enhance the transdermal delivery of NaCl by iontophoresis and to compare the effects of pulsed current (less than 0.5 mA/cm^2) iontophoresis on the permeation of biomembrane of thickness 0.0055 cm of 1 molarity solution. Passive diffusion of NaCl was used as the control for the study.

Materials and Methods

Materials: Iontophoresis Power supply using microcontroller with data acquisition system, silver wire of 0.5 mm diameter coated by silver chloride. Vertical Franz cell with two arms, Sodium Chloride as a solute, Deionized water was used to prepare all the solutions required in this study, the computer system.

Methods:

Preparation of Electrodes:

An Electrodes used was made up of silver prepared manually Coated with silver chloride until a uniform and sufficient coat of the silver chloride was obtained.

Conductivity cell: Conductivity cell was designed and constructed with a active silver are of 0.5 x 0.5 cm and the two electrodes were sepearted apart by a distance of 0.25 cm, this results in a cell constant of 1 per cm.

Iontophoresis power Supply and Data Acquisition System

Iontophoresis power supply using microcontroller Atmega 32, of pulsed current less than 0.5 mA/cm^2 and capable of different duty cycles of time was designed, constructed and tested. The power supply is flexible in the sense that the ON time of the pulse and the OFF time of the pulse can be selected using the control panel of the power supply using thumb wheel switch of the push button control. In other words the duty cycle of the square wave pulses being applied to the bio-membrane can be altered according to the need and requirement using the contorl panel of the iontophoresis power supply[13].

For reading the data computer, additional circuitry needed for Data Acquisition system is also designed along with iontophoresis power supply[14]. For controlling the instrument and for data acquisition system serial communication was implemented and computer side controlling program developed in VB. This system had a measuring accuracy of one part in 1024 which is fairly good and acceptable for most of the routine laboratory experiments. Further advantage is that for unattended experiments, tedious task of recording observations over a long time is simplified and ready to use data is available. A typical screenshot while the experiment was in progress is shown in Figure 1.

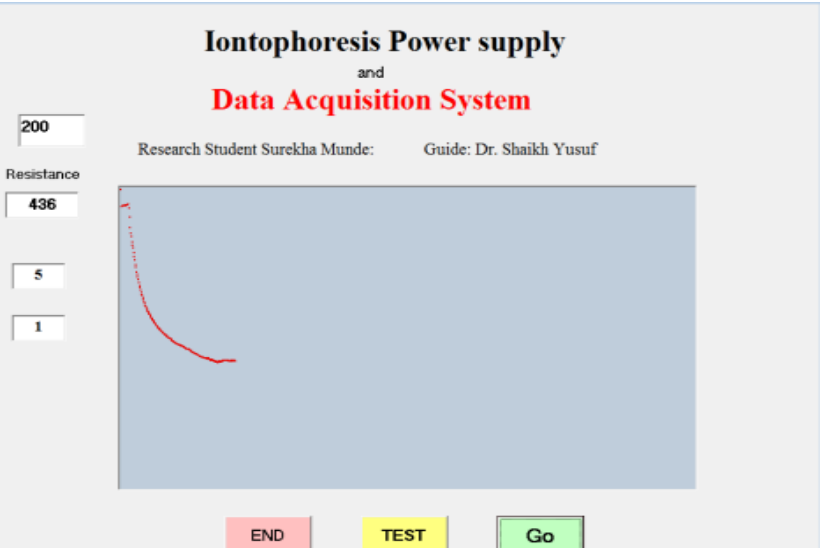

Figure 1: Screen of Data Acquisition Software while recording resistance of the cell.

Experimental design:

For the experiment a specially designed and constructed double layered Vertical Franz cell with two arms was used. For the preparation of 1M sodium chloride solution 5.84 gm NaCl is dissolved in the pure water to have 100 ml of Sodium Chloride solution. In the Acceptor compartment of cell deionized water is used and 1M sodium chloride solution is filled in donor compartment of cell.

Biomembrane used is an egg membrane obtained from egg by dissolving the outer shell in dilute hydrochloric acid and removing the egg white and yoke from the membrane. Egg membrane washed with distilled water is mounted in the cell. A biomembrane is mounted in between donor and acceptor Compartment of Franz cell. Paper clamps are used to hold the two compartments together.To give the electric pulse across biomembrane the electrodes are used. One electrode is inserted from the donor compartment of Franz cell and other electrode is inserted in the lower compartment of Franz cell as shown in figure 2.

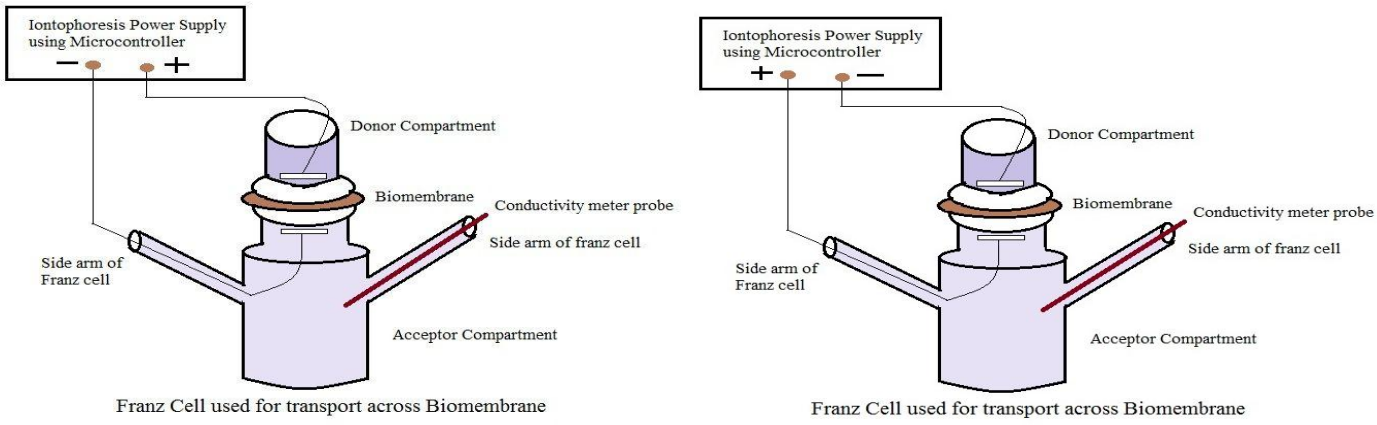

Figure2: Iontophoretic setup that was used for iontophoretic studies of mass transport. The electrodes were connected to a Iontophoresis power supply to perform cathodal and anodal iontophoresis.

These electrodes are connected to the iontophoretic power supply gives the electric pulse adjusted by iontophoretic power supply. A low cost flexible iontophoresis power supply with data acquisition system is used to record the data in terms of resistivity.Iontophoresis power supply is capable of current density below 0.5 mA/cm^{2}and of duty cycles of time adjusted with the help of thumbwheel switch. The ON time and OFF time can be seen on the LCD mounted on front panel of Iontophoresis power supply. The front panel of Iontophoresis power supply is shown in following figure 3. The conductivity cell is inserted from the arm of franz cell connected to the iontophoretic supply records the resistivity in the acceptor compartment of Franz cell.

Figure 3: Iontophoresis Power supply and Data Acquisition System.

Results and Discussion:

In an experiment we used 1 M sodium chloride solution in the upper compartment of the franz cell fitted with an egg membrane and on the other side of the membrane, the lower comparment, deionised water was used, the nature of experiment did not demand for very high purity double distilled or conductivity water. The two electrodes used for application of the iontophoresis pulse were made from silver and coated with silver chloride, these electrodes were fed with the selected type of electrical pulses from the iontophoresis power supply and the current was set to remain

within the limits discussed earlier (0.5 mA/cm^2). With the help of thumb wheel switch ON time and OFF time was set. The ON time set was 1second and OFF time set was 1 second giving the duty pulse of 50%. When power supply is on the drug is diffused through the membrane in the acceptor compartment of the Franz cell. As drug diffuses in the lower compartment the resistivity decreases. Figure 1 shows the plot of resistance of the cell measured using the microcontroller based data acquisition system of the iontophoresis power supply interfaced with a computer where the readings are saved in a computer file. As discussed above the drug transport is enhanced using iontophoresis power supply when the pulses are given to the bio-membrane. It is seen from the graph that the resistance of the cell falls down rapidly during the initial stages and the change in resistance of the cell becomes slower with time and exhibits a tendency to reach a steady state. The reason for this type of behavior is attributed to the fatigue of the pores of the bio-membrane where the pores become immune to the external stimulus after repeated exposure to the electrical impulses in addition to the behavior showing a sort of saturation effect. This saturation effect comes from the transport of the chemical across the cell wall as a result of osmosis[15].

Initially negative electrode is mounted in the Acceptor compartment of Franz cell on the lower side of biomembrane and positive electrode is mounted in the donor compartment of Franz cell on the upper side of Franz cell. The resistivity in the acceptor compartment was measured using data acquisition system. The resistivity is shown by green line in the following graph. When the electrodes are altered i.e. positive electrode in the acceptor compartment of Franz cell on the lower side of biomembrane and negative electrode in the donor compartment of Franz cell, the resistivity measured in lower compartment is shown by blue line in the following graph. The plot of graph of resistivity against time is shown in the following figure 4

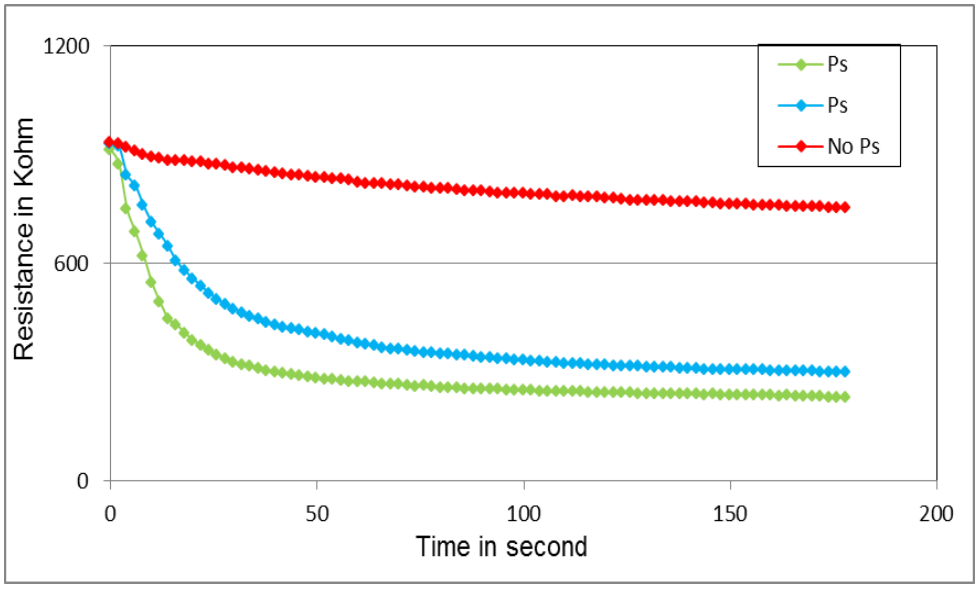

Figure 4: Plot of resistance of the solution in the second compartment versus time.

The same data in figure 4 is then converted to conductivity in the acceptor compartment of Franz cell and the plot of graph is shown in Figure 5 shows the plot of conductivity virsus time for the same data in figure 4.

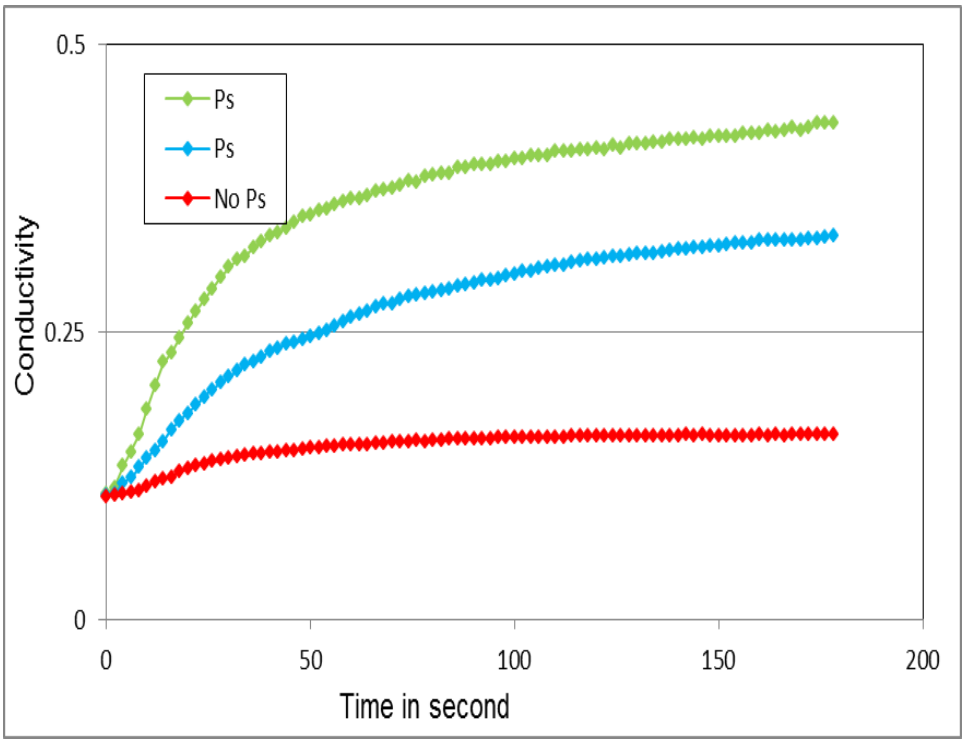

Figure 5: Plot of conductivity of the solution in the second compartment versus.

Conclusion

Results of the iontophoretic studies demonstrated that anodal iontophoresis enhanced the delivery of sodium chloride across the biomembrane. It has been found that the iontophoretic flux of sodium chloride increases linearly with concentration. Also it is concluded that, the single-ion situation allows maximal transport efficiency, which is correlated with aqueous mobility.The presence of sodium as a competing species decreases cation transport numbers in a manner related to the relative aqueous mobilities and molar fractions in the anodal solution.In spite of widely different total cation concentrations at the anode, the sum of cation transport numbers maximizes and it follows that competition from subdermal chloride cannot be eliminated via changes in the iontophoretic delivery i.e. the efficiency of cationic delivery is limited.

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