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IONTOPHORESIS IN TRANSDERMAL DRUG DELIVERY

RESHMA VALLI KANNAN
Medical Electronics
Electronics And Communication Engineering
St. Xavier's Catholic College Of Engineering
Chunkankadai-629003
Kanyakumari District
Tamil Nadu, India

L.MACEAL TONY
Assistant Professor
Electronics And Communication Engineering
St. Xavier's Catholic College Of Engineering
Chukankadai-629003
Kanyakumari District
Tamil Nadu, India

***Abstract* –This project is designed by keeping in mind the efficiency and ease of drug delivery through transdermal method. Iontophoresis is a process used to deliver drugs through the skin into the body by the flow of electrical current. To deliver the correct dosage, the current flow through the skin must be actively controlled by automated system. Iontophoresis is a non- invasive, non-traumatic and painless modality used to deliver large quantity of medicine into a localized area in a cost effective and portable manner that uses electrical current to administer a transdermal drug over minutes to hours. Since iontophoresis delivers drug transdermally, only small amount of the drug are absorbed into the systemic circulation. Its primary musculoskeletal use is for acute or sub-acute, localized inflammation near the skin's surface.**

Keywords – Iontophoresis, transdermal, electric current, non-invasive.

I. INTRODUCTION

Transdermal drug delivery technologies are divided into passive and active methods. Iontophoresis is an active technique that delivers charged or neutral drugs across the skin by the application of a small electric current which enhances the permeation of drug through the skin non-invasively. The major barrier to transdermal delivery is stratum corneum of skin. It remains a great challenge to enhance transdermal and drug delivery without compromising safety concerns and expand their applications into wide therapeutic areas. Iontophoresis allows controlled drug delivery to the target tissues, thereby reducing the potential adverse effects. Skin is the largest organ of the body with a significant surface area for application of drugs. It consists of several layers: the cellular outermost layer, epidermis, and the inner connective tissue layer, dermis. The outermost layer that is the stratum corneum is the rate limiting factor for drug permeation.Representation of shown in figure 1.The permeation barrier of stratum corneum regulates the regulates transepidermal water loss and maintains homeostasis. Iontophoresis provides the usual advantages of a trandermal route like, "first pass" metabolism, avoidance of inconvenience caused by invasive drug delivery and prevention of variation in the absorption seen with oral administration. It permits the use of a drug with a short biological half life since the drug is delivered to the target area without the need to recirculate in the blood. It provides a rapid termination of the effect by turning off the iontophoretic delivery system.

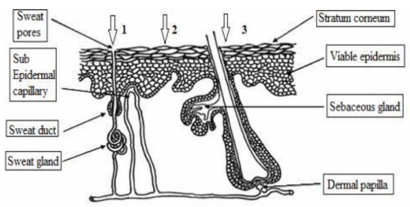

Figure 1: Representation of skin

Limitations of the procedure include the potential for irritation and pain on application of the electric current. Although the technique is considered safe, increase in the intensity of applied current can lead to skin irritation, burning, blisters, necrosis and erythema.

II. SYSTEM

ARCHITECTURE *A. MICROCONTROLLER*

PIC12F683 is an 8-bit PIC microcontroller that has 8-pin interface. It falls under the category of CMOS controllers and comes with nano Watt technology.The figure 2 depicts the pin diagram of PIC12F683 microcontroller.

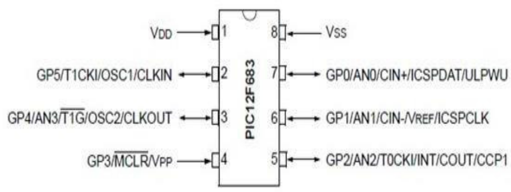

Figure 2. PIC12F683

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B. N-CHANNEL LOGIC LEVEL ENHANCEMENT MODE FIELD EFFECT TRANSISTOR

The MOSFET (Metal Oxide Semiconductor Field Effect Transistor) transistor is a semiconductor device that is used switching and amplifying signals in the iontophoretic device. The MOSFET has four terminals such as source, gate, drain and body terminals. They are represented as S,G, D and B respectively. The figure 3 depicts a typical MOSFET.

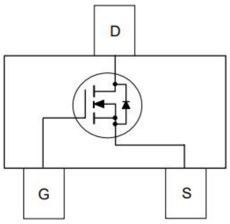

Figure 3. N-channel enhancement mode field effect transistor

C. CAPACITOR NETWORK

The capacitor is an electronic component which has the ability to store energy in the form of an electrical charge producing a Static Voltage across its plates, like a small rechargeable battery. The Figure 4 depicts a typical capacitor model.

Figure 4. A Typical Capacitor

D. INDUCTOR

An inductor is an electronic component that stores energy in the circuit. It is a passive device. An inductor does not allow sudden change of current across it. Therefore it can be used for maintaining constant current in a circuit, thus acting as a choke. The figure 5 depicts a typical inductor.

Figure 5. Typical Inductor

E. SKIN EQUIVALENT CIRCUIT

Human body consists of tissues that show different electrical properties. Therefore it can be considered as a volume conductor. The conduction that happens in biological tissues is because of the movement of ions. This may represent the conduction that takes place in metallic conductors due to movement of electrons. The skin is composed of different layers and hence it can be considered as a combination of resistance and capacitance. This is depicted in the Figure 6. The equivalent circuit is designed by taking into consideration the characteristic impedance and the capacitance that exist in the layers of human skin. However, the equivalent model of human skin impedance cannot be expressed using a simple passive circuit. This is because the skin has a non-linear property.

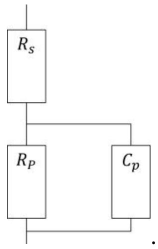

Figure 6.Skin equivalent circuit

III. METHODOLOGY

Iontophoresis is the method that uses electric current for the administration of the drugs through the skin.For this purpose the iontophoresis device must produce sufficient voltage that is necessary to drive the current level so that the required dose of medicine is administered in a specific time period. The main aim of the proposed system is to control the current flow through the skin and ensure that the voltage does not increase excessively. A discontinuous boost regulator topology is used to step up the voltage from a low-voltage battery to sufficient levels to pass the required current through the skin.

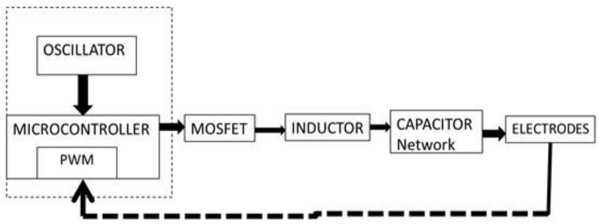

Figure 7. Block diagram of the proposed system

The software used for the implementation of the proposed system monitors the voltage supplied to the skin using the microcontroller's built-in A/D converter, and compares it against a set threshold. When the voltage exceeds the predefined limit, the microcontroller will stop switching the MOSFET, thereby preventing the voltage from being boosted higher. This feature limits the output voltage to a secure level. The predefined limit is set in the software. The applied voltage is maintained between 0 and 3V. The current employed in iontophoresis varies with the medication. The current is controlled by an external resistor and the internal comparator of the PIC12F683. The

comparator threshold is about within the code by shaping the required current level, 0.5 mA-4 mA. The software tests the comparator output to determine the current level. If the present level of current exceeds the

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specified level, then the microcontroller doesn't switch the MOSFET, otherwise the MOSFET is switched to spice up the voltage, driving a lot of current through the skin. The duration of the infusion is controlled using the built -in 16-bit hardware timer plus a 16-bit software timer. When the desired dose is reached, the microcontroller stops switching the MOSFET and goes to Sleep to await a button press

III. RESULT AND DISCUSSION

Initially the microcontroller is programmed with predefined current and voltage limits. The current limits are set in the rage 0.5mA-4mA and the voltage limit ranges from 20V-80V. The internal comparator of the pic microcontroller compares the output voltage with its predefined current and voltage limits and alters the pulse width correspondingly in order to control the boosting of voltage. If the output voltage is greater than the predefined limit or if the output current is greater than the predefined limit, then the controller output which is nothing but the pulse width is increased so as to not boost the MOSFET. Initially the PWM period is set to 5us, during the current delivery there may be variations in the output current and voltage, accordingly the pulse width changes. However the pulse period is monitored such that the PWM period does not fall below 3us. This ensures control of the voltage and current at the output.

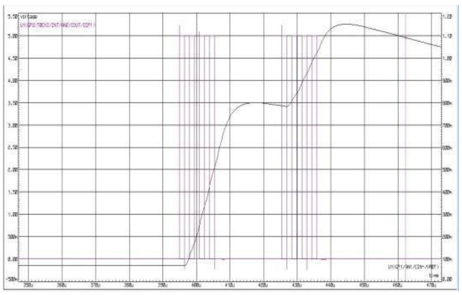

Figure 8. Waveforms obtained from microcontroller input and microcontroller output.

Thus the circuit controls the current flow through the skin effectively as well as ensures that the circuit does not generate high voltages. An inductor is used in the circuit so that it does not allow sudden change of current but allows sudden change of voltage, whereas the capacitors allow sudden change of current and prevents sudden change of voltage. The system works like a choke and monitors both the current and the voltage at the output.

IV. CONCLUSION

The iontophoresis device can be implemented using a small, cost effective microcontroller that controls the boosting of current and voltage in a circuit for the purpose of administering drug through the skin. Without requiring any hardware changes, the software controls can be modified easily for additional features or for altering dose ordrug administering time details. With recent advances in technology, switched mode power supply design, high-performance microcontrollers, the production of low-cost or single-use dispensers for these drugs has become possible.

Thus a low cost, portable and a multipurpose iontophoresis kit was designed and simulated. The proposed system has less transient response which prevents and ensures patient safety from creating burns. It ensures effective drug delivery as well as patient safety.

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