SOCIETY FOR SCIENCE AND EDUCATION UNITED KINGDOM

JBEMi JOURNAL OF BIOMEDICAL ENGINEERING AND MEDICAL IMAGING

ISSN: 2055-1266
VOLUME 5 ISSUE 2

The Mathematical Model for Drug Delivery Through Skin

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ABSTRACT

Delivery of the medications is one of the important biomedical applications. It has significant importance for patients. There are a lot of methods for delivery of drugs such as oral, topical, sublingual, inhalation, and nasal and injection routes. Patients are suffering from needles every time they want to take their medications. The oral route is suitable and has the lowest cost, but some drugs can cause gastrointestinal tract irritation and has low bioavailability. Delivery of the medications through skin is the most suitable for patient because it is needleless without any pain for patients. Some medications have large size. Mathematical model for transportation of large molecules of medications and drugs through the skin is described. This model provides a significant reduction of medical complications and improvement in patient compliance. One of the most important parameter is the optimization of the response time of this model. The model shows good stability and response.

Keywords: Biomedical Applications; Medications; Mathematical model; Patients; Skin.

1 Introduction

Medications are very important to patients, they used for diagnosing, treatment, or preventing illness. There are many routes for medications delivery such as oral, topical, sublingual, inhalation, and injection. The most used methodologies for medications delivery are the oral and injection routes, but injection is painful for patients [1-7].

The oral route is the most suitable and has the lowest cost [8, 9]. Some drugs can cause gastrointestinal tract irritation.

The injection route encompasses intravenous (IV), intramuscular (IM), and subcutaneous (SC) administration [10]. Injections act rapidly, with onset of action in 15–30 seconds for IV, 10–20 minutes for IM, and 15–30 minutes for SC [11]. Disadvantages of injections include pain for the patient, and the requirement of trained staff. A hypodermic needle is used for rapid delivery of liquids, or when the injected substance cannot be ingested, such as with insulin because it cannot be absorbed [12, 13].

Jet injection uses the principle of application of high velocities. This principle is such that the drug formulation is propelled from the reservoir at a high speed, bombarding the skin surface and abrading it then creating superficial micro pathways in the skin. The injection of medications using jet affects flow by increasing velocity, decreasing pressure, and increasing momentum. The penetration using the jet damages the skin with its diameter but less than damage of needle [14-16].

DOI: 10.14738/jbemi.52.4252
Publication Date: 25th March 2018
URL: http://dx.doi.org/10.14738/jbemi. 52.4252

The diffusion of medications and drugs through the skin is preferable to injection because it is non-invasive and can be self-administered. This results in a significant reduction of medical complications and improvement in patient compliance. The diffusion is the movement of the solute from high to low concentrations of the solute in the solvent. The microparticles in the fluid are affected by the diffusion force and it will be move based on this force. In general, a small particle diffuses faster than a larger one [17-20].

Transdermal patch is used for systemic delivery. It uses a micro needle which penetrate outer layer of skin then let solution to diffuse to lower layers through the new pores generated by micro needles [20, 21].

In this paper, mathematical model for transportation of medications and drugs through the skin without pain is described. This model provides a significant reduction of medical complications and improvement in patient compliance. This mathematical model uses medical principle for hypoproteinemia according to abnormality of hydrostatic pressure and principles of mass transfer through a porous diaphragm.

Hypoproteinemia is common complication of Nephrotic Syndrome. Nephrotic Syndrome is not a specific illness, but a group of clinical manifestations relate with kidney. Healthy kidneys regulate blood pressure, secrete hormone and purify blood. When kidneys are damaged, they will fail to do these jobs well, because of a series of symptoms appear. Hypoproteinemia refers to a condition where there is an abnormally low level of protein in the blood. In normal condition, when blood flows through kidney, some substances like protein can be kept in the body. However, when kidney structure is damaged, protein will leak into urine and thus form proteinuria. Long-term and severe protein leakage results in hypoproteinemia easily. One of main cause of this disease is hyper blood pressure which increase hydrostatic glomeruli pressure (HGP). This leads to pass of high molecular weight proteins according to increase diameter of pores [14, 22-24].

2 Mathematical Methodology

The proposed mathematical model for transportation of medications and drugs through the skin provides a significant reduction of medical complications and improvement in patient compliance. This model uses medical principle for hypoproteinemia according to abnormality of hydrostatic pressure and principles of mass transfer through a porous diaphragm.

For applying this model, there are three mainly steps:

1- Increase the diameter of skin pores by using a specific value of hydrostatic pressure come from blower and controlled by a valve (according to molecular weight of drug), the new pores will be in a very small scale (molecules scale).
2- Transportation of the drug solution through new pores and control the rate of the transportation by hydrostatic pressure (could be critical one or higher with limits to control damage).
3- Skin recovery: The skin recovery is a property of skin which enables pores to get its original diameter. With small scale, the recovery period will be very small.

2.1 Mechanism

As the main mechanism of nephron in kidney, the mechanism should include hydrostatic pressure source, making suitable pores of diaphragm (skin), inner design, and controlling from all sides (power source, on and off, pressure).

1. Hydrostatic pressure source

It will be from a microblower. The blower is considered as the source for the required force.

$$F=P/A \quad (1)$$

Where: F is the required force, P is the hydrostatic pressure, and A is the cross-section area.

The specs of the microblower that be used are: Pressure is up to 1.5 Kpa, Dimension is 20 x 20 x 1.8 mm, Power is from 10 to 20 V.

2. Inner design:

As shown in Figure 1, one-way valve is used as a safety valve and helps in keeping pressure constant, isolator is considered as mass (m) used to prevent blower air from mixing with solution, solution storage is used to keep a specific amount of solution, and skin interface is considered as a non-invasive interface with skin.

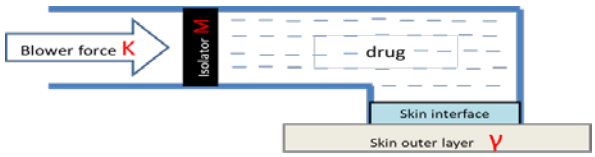

Figure 1. The schematic of the proposed model.

Solution passing through skin is represented as dumper (as in the principle of mass transfer) with gamma factor because they have the same principal. Gamma is considered as overall factors and it represents diffusion constant, skin conditions, and any other effective factors. Gamma can be calculated experimentally and given for user as a numerical value. Therefore, change in the distance (X) can be calculated. It represents the dosage.

3- Microcontroller

Any microcontroller will be used such as Arduino, arm or raspberry pi to control two main things:

Turn on blower for a specific duration till reach a specific pressure then turn off the blower.

Opening the valve to get back the pressure to its normal state after finishing of injection and as a safety for pressure.

In addition, microcontroller will be used for controlling the sensor, showing results, and user interface.

4- Transfer function and the mathematical model

$$Z = ms^2 + \gamma s \quad (2)$$

Where Z is mechanical impedance, M is isolator mass in (Kg), and γ is injection factor in (N.s/m).

The injection factor γ is related to effective condition of skin (as surface area, physical conditions of skin, type of drug, position of injection …… etc.). This factor could be measured experimentally then its range become a given to user in manual of device.

$$T.F = \frac{X(s)}{F(s)} = \frac{1}{ms^2+\gamma s} \tag{3}$$

Where X is output distance in (m), F is input force in (N).

Assume the input force (F) from blower could be represented as unit step function with a gain K.

By compensation at equation (3);

$$X(s) = \frac{K}{s(ms^2+\gamma s)} \tag{4}$$

$$X(s) = \frac{K}{s^2(ms+\gamma)} = \frac{K/\gamma}{s^2\left(1+\frac{m}{\gamma}s\right)} \tag{5}$$

$$X(s) = \frac{K}{\gamma}\left(\frac{1}{s^2\left(1+\frac{m}{\gamma}s\right)}\right) \tag{6}$$

By using partial fraction

$$X(s) = \frac{K}{\gamma}\left(\frac{1}{s^2} - \frac{m/\gamma}{s} + \frac{m/\gamma}{s+\gamma/m}\right) \tag{7}$$

$$X(s) = \frac{K}{\gamma}.\frac{1}{s^2} - \frac{Km}{\gamma^2}.\frac{1}{s} + \frac{Km}{\gamma}.\frac{1}{s+\gamma/m}) \tag{8}$$

By using inverse of Laplacian

$$X(t) = \mathcal{L}^{-1}(X(s)) \tag{9}$$

$$X(t) = \frac{K}{\gamma}t - \frac{Km}{\gamma^2} + \frac{Km}{\gamma^2}.e^{-\frac{\gamma}{m}t} \tag{10}$$

3 Results and Discussions

One of the most important parameter is the optimization of the response time for the proposed model. The response time depends on different parameters according to model equation (10).

After constructing the model and make simulation using MATLAB program, the model shows good stability and response.

It was leading the series of the simulations of the process with changing the values of the injection factor (γ). It can be observed that at M = 0.005 Kg, K = 1.13 N, and at different values of γ = 500, 1000, and 200 N.s/m, by increasing value of gamma it takes more time to reach final value, as shown in Figure 2. Model equation (10) showed that the response time is inversely proportional to the injection factor (γ).

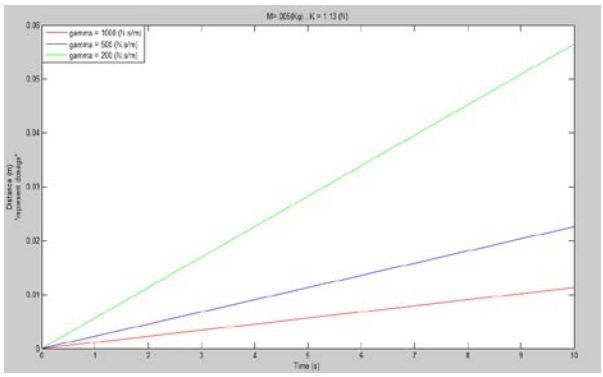

Figure 2. Response time as a function of injection factor (γ).

It was leading the series of the simulations of the process with changing the values of force gain factor (K). It can be observed that at M = 0.005 Kg, γ = 300 N.s/m, and at different values of K = 0.8, 1.13 and 2 N, by increasing value of K it takes less time to reach final value, as shown in Figure 3. Also, it can be observed that the model equation (10) showed that the response time is proportional to the force gain factor (K).

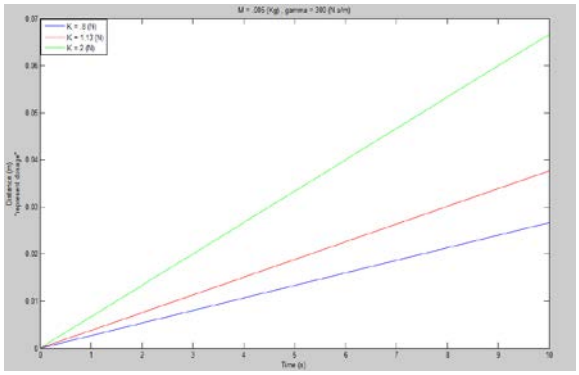

Figure 3. Response time as a function of force gain factor (K).

4 Conclusions

Mathematical model for transportation of medications and drugs through the skin is derivative and described. This model provides a significant reduction of medical complications and improvement in patient compliance. The model shows good stability and response. The response time depends on different parameters according to model equation (10) such as the injection factor (γ) and force gain factor (K). This model is cheap and reliable. The proposed study is simulated by MATLAB program.

The results are demonstrated the proposed study based on a clear procedure. This study is positively led to decrease the patient's pain. In our future works, our study will be used practical experiments.

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