GLUCOSE INSULIN SYSTEM SOFTWARE FOR THERAPEUTIC MANAGEMENT OF DIABETES IN HUMANS

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ABSTRACT

In this research work, a computer program was developed using the gut-blood system model as an infinite number of continuous stirred tanks in series and visual basic application tools, where interfaces were developed to read in some measured parameters from a subject. The developed program was used to analyze the information supplied by the subject. The result of this analysis is a prognosis of the subject’s condition that is available to the medical personnel, for decision on treatment.

Keywords: Glucose-Insulin, Diabetes, Mathematical model, Therapy, Software.

1. INTRODUCTION

Diabetes is related to the imbalance of glucose in the human system. A correct glucose metabolism is one of the key factors in keeping a healthy state in mammals. Among other processes, this is accomplished mostly via regulatory action of hormones released by specific cell population inside the pancreas. A very relevant role is played in this process by the hormone, insulin, synthesized by the pancreatic cells. The normal blood glucose concentration level in humans is in a narrow range (70–110 mg/dl) [1]. Exogenous factors that affect the blood glucose concentration level include food in-take, rate of digestion, exercise, reproductive state, etc. The pancreatic endocrine hormones, insulin and glucagons, are responsible for keeping the glucose concentration levels in check.

Diabetes is classified into two main categories: Type 1 diabetes, juvenile onset and insulin-dependent, and Type 2 diabetes, adult onset and insulin-independent. Type 1 diabetes is caused by deficiency of circulating insulin due to the loss of insulin producing β-cells in the Langerhans islets of the pancreas [1], while Type 2 diabetes is caused by the failure of pancreatic beta cells to respond appropriately to the prevailing blood glucose levels [2]. Complications of the disease include retinopathy, nephropathy, peripheral neuropathy and blindness [3]. The ability of insulin to lower blood glucose is referred to as Insulin Sensitivity (IS), while Glucose Effectiveness (GE) is a measure of the fractional ability of glucose to lower its own concentration in plasma independent of increased insulin [4]. To this day, the standard treatment for Type 1 diabetes mellitus is the administration of exogenous insulin to mimic the normal metabolic regulatory system in healthy subjects. Insulin facilitates cellular glucose uptake and stimulates conversion of glucose into glycogen [5].

Several attempts at building a satisfactory model of the glucose-insulin system are available in the literature. The minimal model is the model currently and mostly used in physiological research on the metabolism of glucose [6]. A subsequent model was the Intra-Venous Glucose Tolerance Test (IVGTT) [7]. [8] had identified the two types of diabetes mellitus: the insulin-sensitive and the insulin-insensitive types, by using an insulin-glucose test. Since then, several other methods have been used to quantify insulin action. The tests that have been used to assess insulin sensitivity include: insulinogetic ratio (insulin/glucose) [9], glucose/insulin ratio [10], glucose clamp technique [4], Frequently Sampled Intravenous Glucose Tolerance test (FSIGT) [11] and minimal model technique [6]. Another simple and reliable test, the Short Insulin Tolerance Test (SITT), was developed by [12]. There has been no model study, as far as the authors are aware, on glucose disappearance from blood plasma in Nigerians. However a glucose disappearance study on Nigerians was carried out by [13] using the short insulin tolerance test. No models were developed in that study and glucose disappearance rate constants were determined using the least square method on patient data. [14] developed a model for glucose insulin system by describing the gut-blood system as an infinite number of continuous stirred tanks in series. The model was validated against laboratory data; statistical analysis was carried out that shows there was no difference (p<0.05) between the measured and simulated mean plasma insulin levels and the corresponding plasma glucose levels.

In this study, the gut and blood system is represented as an infinite number of continuous stirred tank reactors in series. The resulting model equations were then utilized for the development of a software with a series of icons that give instructions for diabetic management.
2. MATHEMATICAL FORMULATION
The gut-blood system was modeled as an infinite number of continuous stirred tanks in series. The infinite tanks were used as simulators of the entire blood glucose-insulin system. If a certain amount of Glucose \( N_0 \) is suddenly injected in one shot into the blood stream, and assuming the blood stream can be represented by infinite number of equal volume mixed flow reactors, arrange in series, as shown in Figure 1. The outlet concentration \( C_n \) is then measured. If we first choose an increment of time \( \Delta t \) sufficiently small that the concentration of glucose, \( C(t) \), exiting between time \( t \) and \( t+\Delta t \) is essentially constant. The amount of glucose, \( \Delta N \) leaving the reactor between \( t \) and \( t+\Delta t \) is then:

\[
\Delta N = C(t)F\Delta t
\]

where \( F \) is the effluent volumetric flow rate in other words \( \Delta N \) is the amount of glucose that has spent an amount of time between \( t \) and \( t+\Delta t \) in the reactor.

![Figure 1: Gut and blood compartment represented as tanks in series (1… 2, n).](image)

A material balance on the glucose in the first and second reactor gives the following equation

\[
\frac{dC_1}{dt} + \frac{C_2}{\tau_i} = \frac{C_0}{\tau_i} e^{-t/\tau_i}
\]

2.1 Model Solution and Simulation of the Glucose and Insulin Kinetics
Three tanks have been determined by [14] to be adequate to model the system. Using Laplace transformation to Equations (2), the analytical solution of the model is as follows:

\[
C_2 = \frac{C_0}{\tau_i} t e^{-t/\tau_i}
\]

The same procedure used for the third reactor gives the expression for the concentration of tracer in the effluent from the third reactor (and therefore from the reactor system):

\[
C_3 = \frac{C_0}{\tau_i^2} t^2 e^{-t/\tau_i}
\]

The volumetric flow rate \( F \) is usually constant, so we can define \( E(t) \) as

\[
E(t) = \frac{C_3(t)}{\int_0^\infty C_3(t)dt}
\]

Substituting Equation (3) in Equation (5) gives:

\[
E(t) = \frac{C_3(t)}{\int_0^\infty C_3(t)dt} = \frac{t^2}{2\tau_i^3} e^{-t/\tau_i}
\]

The effluent concentration from the reactor in generalized form for \( n^{th} \) reactor is:
\[ C^n = \frac{C_0}{(1 + nk)^n} \] (7)

The conversion (depletion of glucose) for these tanks in series would be

\[ X = 1 - \frac{1}{(1 + nk)^n} \] (8)

3. RESULTS AND DISCUSSION

Equations (3)-(8) were used to develop the software. The developed software can be installed from a Compact Disc (CD). Once you insert the CD into your computer, it will take you through the installation and will deposit a shortcut icon on the desktop. Once you click on the icon, Figure 2 will appear. It is the home page which shows the tool bar. Click on diabetes management on the tool bar, a drop down menu bar will appear for you to choose the program of analysis. Clicking on Glusim 1 will take you to the physical data input page as shown in Figure 3. This allows the input of physical and measured data from a patient. Clicking on generate values, the program will take you to Figure 4, showing generated concentration of glucose at different times in the human blood. Clicking on Plot Tab will plot the values of the concentration at different times as shown in Figure 5.

Figure 2. Home page.
Figure 3. Physical Data Input Page.

Figure 4. Analysis showing generated concentration at different times in the human blood.
Clicking Diagnose on Figure 4, will take you to Figure 6, showing you the result of Body Mass Index (BMI) (and waist circumference). The BMI is a measure of your weight relative to your height; waist circumference measures abdominal fat. BMI categories are: underweight ≤ 18.5, normal weight = 18.5-24.9, overweight = 25-29.9 and obesity ≥ 30. For people who are considered obese (BMI greater than or equal to 30) or those who are overweight (BMI of 25 to 29.9) usually have the risk of diabetes. Even a small weight loss just 10 percent of your current weight will help to lower your risk of developing diseases associated with obesity.

If the patient is found to be diabetic, clicking on Treat button on Figure 6, will take you to Treatment Result page in Figure 7, which shows treatment and dietary advice for a diabetic patient. The interface shows the BMI of a patient, total unit of insulin required by the patient to stabilize the glucose concentration, the number of injection to be administered, the insulin units per injection to be administered, the total energy required by the patient, the relative percent of carbohydrate, protein and fat needed by the patient to maintain a normal and good health. The analysis depends on the age, sex, weight, height and the kind of work activity of the patient.
4. CONCLUSION
A computer program was developed using a visual basic applications tools and a model of the gut and blood stream. The gut and blood stream was described mathematically as a compartment/tank with a basal concentration of glucose and insulin. This was modeled as an infinite number of continuous stirred tanks in series, which could be used as simulators of the entire blood glucose-insulin system and the pathway for diabetes development. The model made it possible for the development of a software using visual basic program which can be used for therapeutic management of diabetic patients. The model gives some indicators and parameters that indicate the level of development of the diabetes. Interfaces were developed to read in some measured parameters from a subject and the program analyses the information and gives a feed back on the condition of the subject to medical personnel; they in turn take decision on treatment. The Software can be used to simulate and estimate the Glucose-Insulin parameters.

5. REFERENCES
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