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A Mathematical Approach on the Study of Glucose-Insulin Model to Quantify the Various Levels of Glucose Uptake in Response to Insulin Behavior

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Abstract: *A mathematical approximation to compute various glucose levels and insulin levels in the case of glucose tolerance test is studied. Variation of food intake is the major consideration of the analysis so as to approximate the effect of circulating hyperglycemia on the rate of pancreatic secretion of insulin. It is observed that glucose stimulates the effective binding of unoxidized glucose along the secretion line which in turn causes the damage of insulin sensitivity in the chemical process. The dynamical model has been formulated using coupled system of differential equations denoting glucose insulin system in the presence of glucose plasma concentration, insulin plasma concentration and time. Numerical computations of G(t) (blood glucose concentration level), I(t) (insulin concentration level), X(t) (Auxiliary function) have been taken for the constant input of amount of insulin dependent glucose under instantaneous administration. This shows the principle of continuity of the requirement of insulin for the food intake. This gives the disappear rate constant of insulin concentration. In the model fitting glucose plasma concentration changes in the blood due to the net glucose uptake chemically reacts with the net available insulin at various time intervals. Solution of system of linear differential equations in the present model describe the blood glucose level balances the insulin secretion for the physiological needs at a rate proportional to concentration of insulin from beta cell of the pancreas so that the end effect of the successive inputs can be seen to maintain the normal blood glucose level. Numerical method (Runge-Kutta Fourth order method) is employed with successive approximations to compute desired degree of accuracy of normal glucose level with a reference to constant amount of insulin and varying amount of insulin.*

Key Words: *insulin, glucose, blood, plasma, cell.*

1. INTRODUCTION:

For every chemical reaction, it is essential to investigate the interaction among the substances. The present model concerns the discussion on the tolerance test of the amount of glucose enters the blood stream in the form of intake of food at various quantities (four different meals). Correspondingly the amount of insulin requirement from β −cell of the pancreas output causes the metabolic process, as a result the release of this process in the form of energy enters hyper thalamus of the brain. The stored energy will be utilized for various purposes as and when human body needs the energy requirement. On the basis of this ideology, we have studied mathematical approach to analyze the average blood glucose level by conducting glucose tolerance test. John B O'Sullivan et. al. [1] discussed the effect of absorption of glucose along with the additional variability of some excluding the use of test using during pregnancy and identified the sources of variation between pregnant and non pregnant stages of women. Byoung G Min et. al. [2] studied a quantitative method to estimate the peripheral tissues insulin resistivity and the hepatic glucose sensitivity from the measured intravenous glucose tolerance test data and the equivalent circuit model. AageValundet. al. [3] discussed a thorough comparative analysis of the results emanated from the two models i.e. Combined model and minimal model in a group of normal subjects with various degrees of insulin sensitivity. Karl Thomasethet. al. [4] investigated a Mathematical model of assess insulin sensitivity of glucose disposal and endogenous glucose production from double-tracer oral glucose tolerance test. Michael Brenner et. al. [5] studied a mathematical model of glucose-insulin homeostasis to estimate the secretion of insulin, glucose uptake by tissues and hepatic handling of glucose. MananPareek et al [6] conducted a prospective population-based cohort study of 4,867men, randomly selected from pre specified birth cohorts between 1921 and 1949,who underwent an oral glucose tolerance test with blood glucose measurements at 0, 1, and 2 h. Wei-Yen Lim et al [7] evaluate the use of HBA1c for diabetes screening, to determine the optimal HbA1c cut-off for screening for diabetes, and to assess if HbA1c could be combined with FPG to detect individuals with diabetes mellitus and impaired glucose tolerance, in a multiracial population living in Asia where the prevalence of diabetes mellitus is high.Marta Balog et al [8] studied the effects of maturation and sex on glucose metabolism during GTT and

ITT. In view of the above researchers contribution we consider the present model needs a study of physiological significance of G(t)(blood glucose concentration level), I(t)(insulin concentration level), X(t)(Auxiliary function) using system of coupled ordinary differential equations. The initial conditions are modeled with the clinical significance for various time intervals with quantity of meals spread over glucose tolerance test period. Numerical scheme is employed to solve the coupled ordinary differential equations with repeated number of approximations to give the average inputs and outputs of food and glucose level respectively.

2. FORMULATION:

Study of Glucose Tolerance Test is considered using Mathematical Modeling with a reference to quantification of Glucose(G(t)), auxiliary function of Glucose(X(t)) and insulin(I(t)) with respect to time (t) numerically for various inputs of meals in relation to Joslin's Principle. For successive computational requirements we have developed analytical formulation for definite comparison of measurements of glucose levels against the intake of meals spread over four different diets per day. It is considered that the major product of glucose is carbohydrate digestion which is important metabolic fuel. This will be utilized by the brain to meet the energy requirement for further process. Insulin produced by the beta cell from the pancreas enhances the glucose metabolism. Governing system of differential equations with change of glucose$\left(\frac{dG(t)}{dt}\right)$, change in insulin $\left(\frac{dI(t)}{dt}\right)$ and the change in Auxiliary Function$\left(\frac{dX(t)}{dt}\right)$ for various time intervals are given by

$$\frac{dG(t)}{dt} = -[p_1 + X(t)]G(t) + p_1 G_b, \quad (1)$$

$$\frac{dX(t)}{dt} = -p_2 X(t) + p_3[I(t) - I_b], \quad (2)$$

$$\frac{dI(t)}{dt} = p_4[G(t) - p_5]t - p_6[I(t) - I_b], \quad (3)$$

Initial conditions

$$G(0) = p_0\,, X(0) = 0, I(0) = p_7 + I_b \quad (4)$$

3. ANALYSIS:

Solution to G, X, I Using RungeKutta Fourth order method and Taylor's Series Method: We discuss two cases of tolerance test for constant and varying uptake of glucose by establishing the mathematically tractable solution of (1), (2) and (3):

- constant glucose uptake and the response of insulin sensitivity
- varying glucose uptake and the response of insulin sensitivity

For Glucose concentration G(t), consider (1)

$$\frac{dG(t)}{dt} = -[p_1 + X(t)]G(t) + p_1 G_b$$

With the initial condition $G(0) = 90$

$$\frac{dG(t)}{dt} = f_1(t, G, X, I)$$

By Runge - Kutta Fourth order method, we compute the blood glucose concentration level at various stages as

$$G = G_0 + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4) \quad (5)$$

For the first stage $G = 90.7031$
For the second stage $G = 91.1589$
For the third stage $G = 91.4546$
For the fourth stage $G = 91.6463$

Model behaves with the use of series solution (Taylor's series) method numerically as analytical expression,

$$\frac{dG(t)}{dt} = -[p_1 + X(t)]G(t) + p_1 G_b, G(0) = 90 \quad (6)$$

i.e.

$$G^1 = -p_1 G + p_1 G_b, G^{11} = -p_1 G^1\ ,\ G^{111} = -p_1 G^{11}\ ,G^{1V} = -p_1 G^{111}\ \ \ldots\ldots$$

We have Taylor's series expansion of G(t) at t = 0 as

$$G(t) = G(0) + tG^1(0) + \frac{t^2}{2!}G^{11}(0) + \frac{t^3}{3!}G^{111}(0) + \frac{t^4}{4!}G^{1V}(0) + \cdots \quad (7)$$

Solution is obtained as

$$G(t) = 90 + t - 0.25t^2 + 0.0417t^3 \quad (8)$$

The variation of G(t) with I(t) gives the proportional increase of G(t) at t: when I(t) is varied as equation (3),

$$\frac{dX(t)}{dt} = -p_2 X(t) + p_3[I(t) - I_b]$$

With the initial condition $X(0) = 0$

$$\frac{dX(t)}{dt} = f_2(t, G, X, I),$$

By Runge - Kutta Fourth order method, we compute the auxiliary function X(t) at various stages as

$$X = X_0 + \frac{1}{6}(g_1 + 2g_2 + 2g_3 + g_4) \quad (9)$$

For the first stage $X = -19.6615$
For the second stage $X = -28.5893$
For the third stage $X = -37.0086$
For the fourth stage $X = -42.1172$
Computation of Auxiliary function by the use of Taylor's Series Method is,

$$\frac{dX(t)}{dt} = -p_2X(t) + p_3[I(t) - I_b], \quad \text{with} \quad X(0) = 0$$

$X^I(t) = -p_2X(t) + p_3[I(t) - I_b], X^{II}(t) = -p_2X^1(t), X^{III}(t) = -p_2X^{11}(t), X^{IV}(t) = -p_2X^{111}(t)$
and so on.
We have Taylor's series expansion of X(t) at t = 0 as

$$X(t) = X(0) + tX^1(0) + \frac{t^2}{2!}X^{11}(0) + \frac{t^3}{3!}X^{111}(0) + \frac{t^4}{4!}X^{1V}(0) + \cdots \quad (10)$$

Solution for X(t) is,

$$X(t) = -5t + 0.25t^2 - 0.00833t^3 \quad (11)$$

Insulin Concentration I(t),

$$\frac{dI(t)}{dt} = p_4[G(t) - p_5]^+t - p_6[I(t) - I_b], \quad I(0) = p_7 + I_b$$

$$\text{i. e.} \frac{dI(t)}{dt} = f_3(t, G, X, I)$$

By Runge - Kutta Fourth order method, we compute the blood glucose concentration level at various stages as

$$I = I_0 + \frac{1}{6}(m_1 + 2m_2 + 2m_3 + 4_4) \quad (12)$$

For the first stage $I(t) = 5.9648$
For the second stage $I(t) = 7.4425$
For the third stage $I(t) = 8.9275$
For the fourth stage $I(t) = 10.4186$
Model behaves with the use of series solution (Taylor's series) method numerically as analytical expression,

$$\frac{dI(t)}{dt} = p_4[G(t) - p_5]^+t - p_6[I(t) - I_b]$$

$$\text{i. e.} I^1 = p_4[G(t) - p_5]t - p_6[I(t) - I_b]$$

$$I^{11} = p_4[G(t) - p_5] + (p_4t)G^1 - p_6[I^1]$$

and so on
We have Taylor's series expansion of I(t) at t = 0 as

$$I(t) = I(0) + tI^1(0) + \frac{t^2}{2!}I^{11}(0) + \frac{t^3}{3!}I^{111}(0) + \frac{t^4}{4!}I^{1V}(0) + \cdots \quad (13)$$

Considering up to second degree terms,

$$I(t) = 4.5 + (0.25)t + (0.0125)t^2 \quad (14)$$

Blood Glucose concentration with fixed Insulin concentration

In figure (1), we observe that the intake of food in 4 different meals under glucose tolerance test indicates the graph (the increasing trend) which shows there exists no tolerance in the supply of blood glucose concentration

Blood Glucose concentration with varying Insulin concentration

In figure (2), we notice from the graph (the sinusoidal behavior according to pre-prandial and postprandial glucose levels) there exists the tolerance of blood glucose concentration level for the selected 4 different meals. Also the greater variation of insulin will be proportional to the variation of intake of food.

4. RESULTS AND DISCUSSION:

Mathematical analysis has been carried out to quantify the uptake of glucose in response to insulin behavior. The system of simultaneous coupled differential equations have been formulated to assess the glucose level G(t), insulin level I(t) at various time intervals of food intake. Sensitivity parameters imposed in the present model indicate the normal and varying glucose levels of 4 different meals. Two different numerical methods have been used successfully to obtain the results in the form of analytical expression and the set of numerical values respectively by Taylor's series method (sufficient number of derivatives are considered to achieve better approximation) and Runge Kutta 4th order method (iterative scheme). Results indicate good approximation in both the methods with properly chosen sensitivity values.

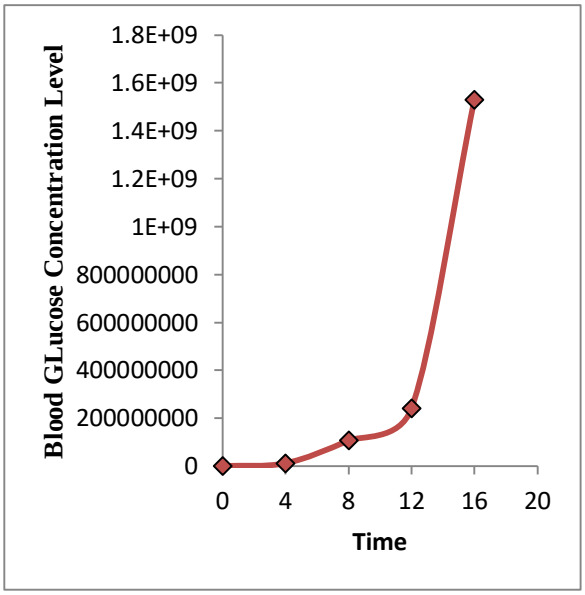

Figure 1: blood glucose concentration level v/s time (with constant Insulin)

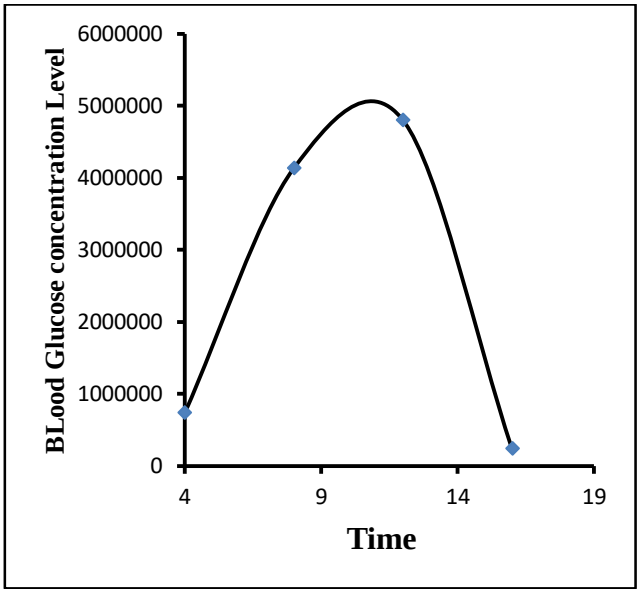

Figure 2: concentration blood glucose level v/s time (with varying Insulin)

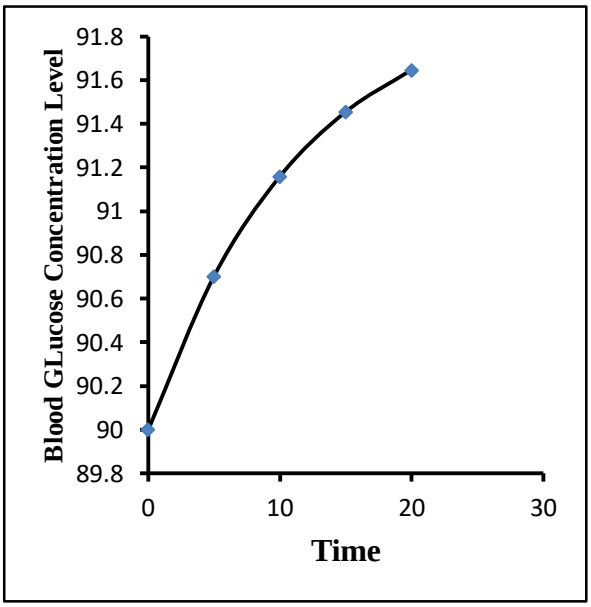

Figure 3: blood glucose concentration level time (R K Fourth Order method)

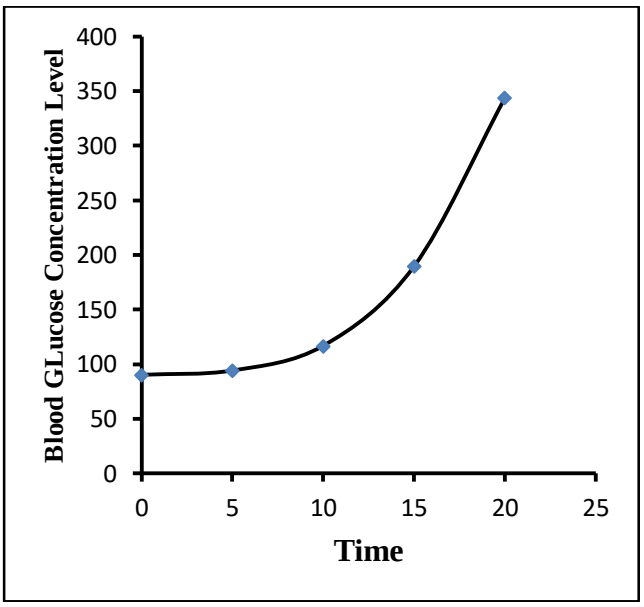

Figure 4: blood glucose concentration level v/s time (Taylor's Series method)

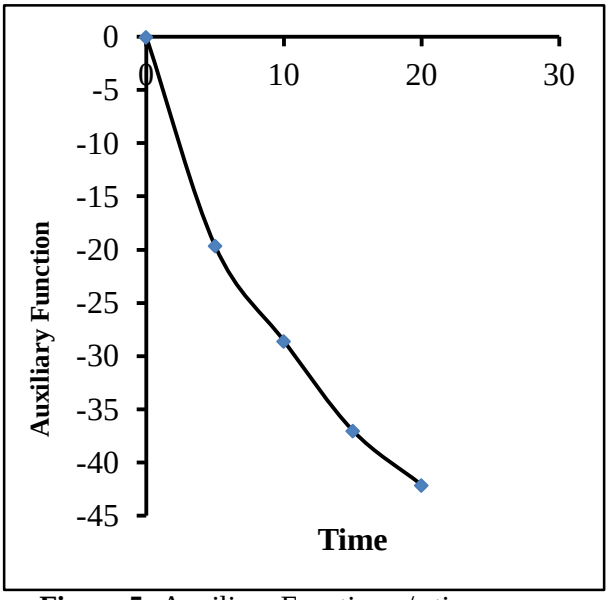

Figure 5: Auxiliary Function v/s time (R K Fourth Order method)

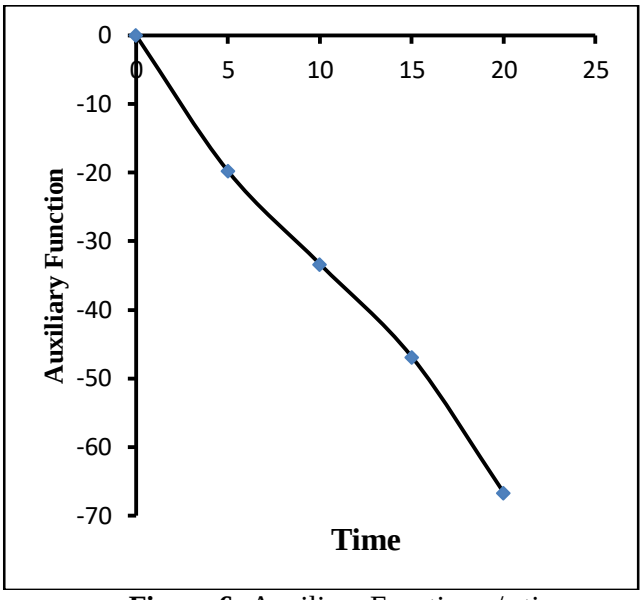

Figure 6: Auxiliary Function v/s time (Taylor's Series method)

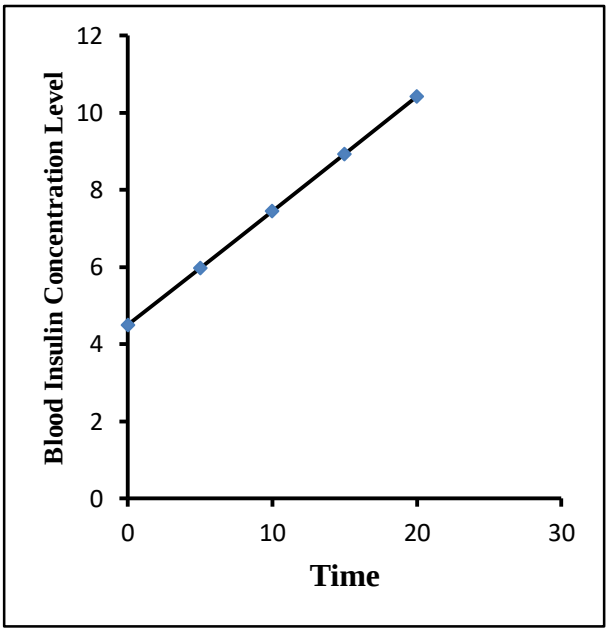

Figure 7: Blood Insulin Concentration Level v/s time (R K Fourth Order method)

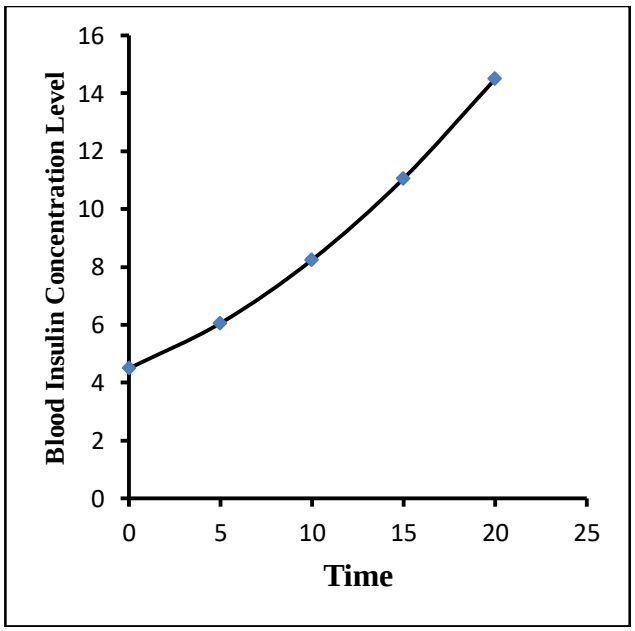

Figure 8: Blood Insulin Concentration Level v/s time (Taylor's Series method)

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