A Mathematical Model of Glucose - Insulin regulation where glucose and insulin both are influenced by externally ingested glucose

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Abstract: Here we discussed a mathematical model on diabetes mellitus under the influence of ingested glucose where glucose and insulin both are affected by the externally ingested glucose. The new variable E is introduced as the externally ingested glucose which is considered to be taken from external source of food. With the introduction of ingested glucose and its impact on the glucose as well as on insulin, a three variable mathematical model is established. The stability of the model is analyzed under various equilibrium conditions. Numerical simulations are presented to validate and to describe the nature of stability of the model.

Keywords: Modelling; Mathematical Modeling; Diabetes; Glucose-insulin regulatory system; ingested glucose; Stability

1. INTRODUCTION:

Researchers have derived many more mathematical models to understand the different biological and ecological system. The most popular and interesting mathematical models have been derived on different diseases. The most common diseases about which maximum numbers of mathematical models have been derived are Diabetes, Cancer and Asthma. Mathematical modelling in diabetes was firstly introduced by Himsworth and Ker where they approched to measure the insulin sensitivity in VIVO. In 1960, Rosevear and Molnar along with Ackerman and Gatewood [1995] established a model analyzing the blood glucose regulatory system where g is taken to be excess glucose and h as excess insulin at time t.

Depending on the same model many mathematical models on diabetes have been derived till date. We established a model [2016] where a new variable ingested glucose was introduced. The best known $(G-I-E)$ model was an inter relationship between glucose and insulin where the newly introduced variable ingested glucose (E) is affecting the glucose and insulin regulatory system under the following assumptions,

I. Degradation of glucose from body is both insulin independent and insulin dependent with different rate.
II. Insulin secretion will be due to glucose stimulation.
III. The externally ingested glucose follows logistic behaviour. The externally ingested glucose will increase the glucose level
IV. A constant amount of glucose is present in the body.

2. THE MODEL AND ITS ANALYSIS:

We derived a new model as follows,

$$\dot{G}(t) = -aG - bGI + \alpha E + \delta \qquad (2.1)$$

$$\dot{I}(t) = cG - dI - \beta E \qquad (2.2)$$

$$\dot{E}(t) = \beta E(1-\gamma E) \qquad (2.3)$$

Where,

δ : Constant amount of glucose present in the body

a: Rate constant which represents insulin independent glucose disappearance *b*: Rate constant which represents insulin dependent glucose disappearance

c: Rate constant which represents insulin production due to glucose stimulation

d: Rate constant which represents glucose independent insulin degradation

α: Rate constant which represents increase of glucose level due to ingested glucose

β: Intrinsic growth constant of ingested source of glucose

$\frac{1}{\gamma}$: Carrying capacity of ingested source of glucose

The equilibrium points corresponding to the above equations are found equating them to zero are,

$E = 0$ and $E = \frac{1}{\gamma}$

For $E=0$, the equilibrium point is,

$$(G_1, I_1, 0) = \left(\frac{-ad + \sqrt{a^2d^2 + 4bcd\delta}}{2bc}, \frac{-ad + \sqrt{a^2d^2 + 4bcd\delta}}{2bd}, 0 \right)$$

Also for $E = \frac{1}{\gamma}$, the equillibrium point is,

$$(G_2, I_2, \frac{1}{\gamma}) =$$

$$\left(\frac{(b\beta - ad\gamma) + \sqrt{((b\beta - ad\gamma)^2 + 4bcd\alpha\gamma + 4bd\gamma^2\delta}}{2bc\gamma}, \frac{-(b\beta + ad\gamma) + \sqrt{((b\beta - ad\gamma)^2 + 4bcd\alpha\gamma + 4bcd\gamma^2\delta}}{2bd\gamma}, \frac{1}{\gamma} \right)$$

This equillibrium point exists under the condition $a\beta < \alpha + \gamma\delta$

3. STABILITY OF THE MODEL:

3.1 For the equilibrium point $(G_1, I_1, 0)$ we can linearise the model as,

$$\begin{pmatrix} \dot{G} \\ \dot{I} \\ \dot{E} \end{pmatrix} = \begin{pmatrix} -a - bI_1 & -bG_1 & \alpha \\ c & -d & -\beta \\ 0 & 0 & \beta \end{pmatrix} \begin{pmatrix} G - G_1 \\ I - I_1 \\ E \end{pmatrix}$$

From the coefficient matrix the eigen values are,

$$\lambda_1 = \beta \text{ and } \lambda_{2,3} = \frac{-(a + bI_1 + d) \pm \sqrt{(a + bI_1 + d)^2 - 4(ad + bcG_1 + bdI_1)}}{2}$$

Since $\lambda_1 = \beta > 0$, therefore at this equilibrium point the model is unstable.

3.2 For the equilibrium point $(G_2, I_2, \frac{1}{\gamma})$, let us linearise the model as follows,

$$\begin{pmatrix} \dot{G} \\ \dot{I} \\ \dot{E} \end{pmatrix} = \begin{pmatrix} -a - bI_2 & -bG_2 & \alpha \\ c & -d & -\beta \\ 0 & 0 & -\beta \end{pmatrix} \begin{pmatrix} G - G_2 \\ I - I_2 \\ E - \frac{1}{\gamma} \end{pmatrix}$$

From the coefficient matrix the eigen values are,

$\lambda_1 = -\beta$ and $\lambda_{2,3} = \dfrac{-(a+bI_2+d) \pm \sqrt{(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2)}}{2}$

Case 1: Since $\lambda_1 = -\beta < 0$, hence at this equilibrium point the model is stable.

Case 2: For $\lambda_2 = \dfrac{-(a+bI_2+d) - \sqrt{(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2)}}{2}$

i. If $(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2) < 0$, hence λ_2 is imaginary and it has a negative real part which makes the model stable.

ii. If $(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2) > 0$, hence λ_2 is purely real and it is less than zero, which makes the model stable.

Case 3: For $\lambda_3 = \dfrac{-(a+bI_2+d) + \sqrt{(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2)}}{2}$

i. If $(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2) < 0$, hence λ_3 is imaginary and it has a negative real part which makes the model stable.

ii. If $(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2) > 0$, hence the model is stable only when,

$$\frac{-(a+bI_2+d) + \sqrt{(a+bI_2+d)^2 - 4(ad+bcG_2+bdI_2)}}{2} < 0$$

$$\Rightarrow ad + bcG_2 + bdI_2 > 0$$

Which is an obvious condition where the parameter values are considered as follows,

Parameters	a	b	c	d	α	β	γ	δ
values	0.0354	0.0213	0.756	0.0713	0.0132	0.200	0.0124	0.016

4. CONCLUSION :

The stability of the model is discussed numerically with the help of some graphical presentations. The model indicates the instability in the ingested glucose free equillibrium points. At the glucose-insulin-externally ingested glucose existing equillibrium point $\left(G_2, I_2, \frac{1}{\gamma}\right)$ the model is stable. Fig. 1 is to show the stability of the externally ingested glucose (E) and to establish logistic behaviour. Stability of glucose and insulin is shown in Fig. 2. In Fig. 2 the comparative behaviour of glucose and insulin where both are influenced by the externally ingested glucose is seen . Both glucose and insulin became stable after certain period of time under co-existing equillibrium point. The graphs are drawn considering the same parameters values mentioned above.

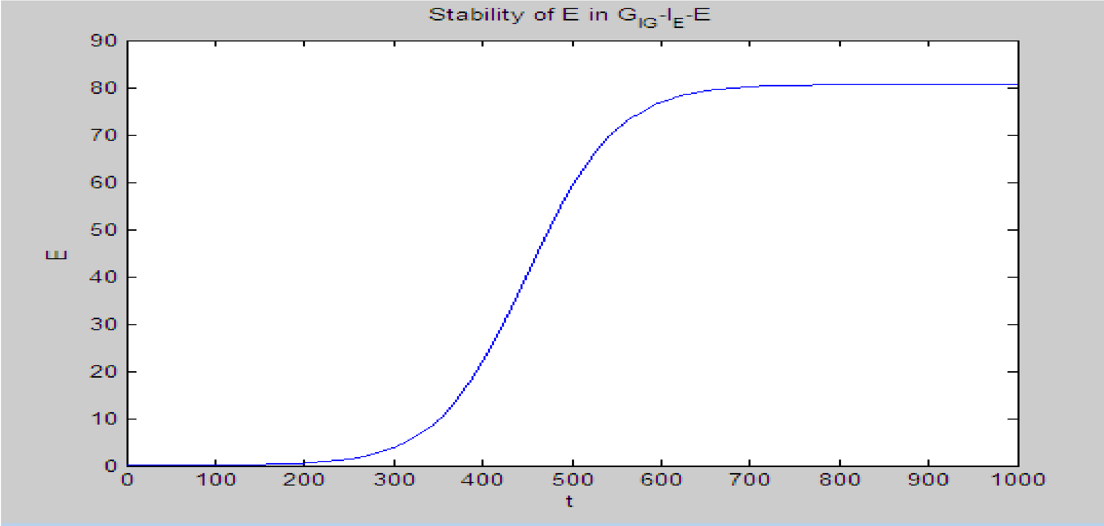

Fig. 1

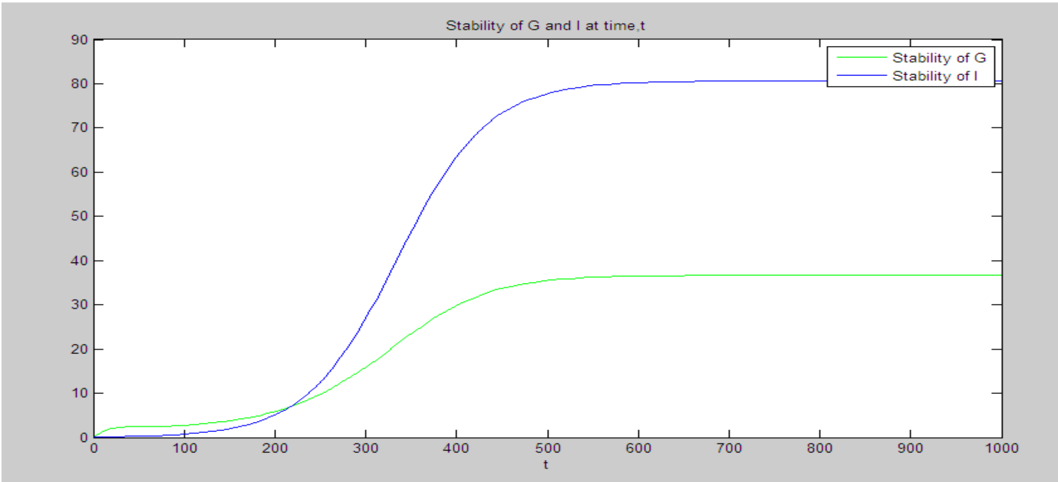

Fig. 2

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