

Mathematical Modeling Effect Habbatussauda on Diabetes Mellitus

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Abstract. Habbatussauda is one of the traditional or herbal medicine existed since a long time ago and this is one of the drugs that was recommended by the Prophet Muhammad. Habbatussauda's benefits has been studied extensively in the field of health, habbatussauda also has been widely used to cure various diseases although it takes a long time. One of the benefit is to cure diabetes mellitus. This research will analyze the mathematics models of diabetes using three variables which are glucose, insulin and insulin generalization. Then it will look for the differences before and after consuming habbatussauda by using the mathematics model.

Keywords: Diabetes Mellitus, Habbatussauda, Mathematical Model

INTRODUCTION

The population of Indonesia is 268.015.313 in 2018. Indonesia ranks fourth as the biggest population country, more people living in a country will certainly make many problems arise, one of them is health problem. Some health problems that frequently occur in Indonesia are increased blood sugar, increased blood pressure, obesity, children smoking behavior around 15 years old and older, and many more. While the diseases cause death are stroke, coronary heart disease, diabetes mellitus, respiratory infections, tuberculosis, liver cirrhosis, lung disease, hypertension (high blood pressure).

Diabetes mellitus is a serious chronic disease that occurs because the pancreas does not have insulin (the hormone that regulates blood sugar or glucose), or when the body can't effectively use the produced insulin. According to Consensus Society of Endocrinology Indonesia (PERKENI) 2015 diabetes mellitus diagnosis criteria are the examination of the fasting plasma glucose ≥ 126 mg/dl, the examination of plasma glucose ≥ 200 mg/dl at 2 hours after oral glucose tolerance test (OGTT) with 75 grams of glucose load or plasma glucose tests as ≥ 200 mg/dl with classic complaint or examination HbA1c more than equal to 6.5 per 100 by using a standardized method by the National Glycohaemoglobin Standardization Program (NGSP).

It makes a lot of Indonesian looking for medicine to heal or just make it as a preventer of various disease. One of it with herbal treatments which currently in great demand, one of them is nigella sativa, or commonly known as black seed or habbatussauda.

Habbatussauda is one of the traditional medicine that has begun to be used by physicians to treat various diseases, Prophet Muhammad said that Black Seed can cure all diseases except death. Medicine that uses natural contemporary ways in worldwide have been using the

habbatussauda contains Thymoquinone as a major component. Thymoquinone is a compound found in habbatussauda. Thymoquinone has a function of protection against toxic effects of chemicals toxic to the kidneys (nephrotoxicity) and liver damage caused by chemicals (hepatotoxicity). It also has an antiinamasi activity (relieving inflammation), analgesics (pain relievers), antipyretics (fever), antimicrobial (exterminator microbes).

The development of knowledge about the benefits of habbatussauda in medical science is quite a lot and is still being developed. Habbatussauda's benefits can be analyzed with mathematics, using mathematical modeling. In this model will discuss the modeling of diabetes mellitus which influenced by habbatussauda.

METHOD

Establishment of Model of Diabetes Mellitus

In this study diabetes mellitus model refers to Sandhya and Deepak Kumar journal in 2011, [2], model formulated by using three factors, namely $G(t)$, $X(t)$ and $I(t)$, With $G(t)$ is the plasma glucose concentration at time t (mg/dl), $X(t)$ is equated insulin generalization variable in every part (min^{-1}), and $I(t)$ is the plasma insulin concentration at time t ($\mu\text{U/ml}$). The assumptions used in this model is a suffered disease only diabetes mellitus using only three variables, the amount of plasma glucose, plasma insulin and the amount of insulin generalization of each section.

The amount of three factors above stated $N(t) = G(t) + X(t) + I(t)$. The variables and parameters used in this model are as follows in Table 1.

Table 1. List of Variables and Parameters.

No.	Symbol	Information	Unit
1.	$G(t)$	The plasma glucose concentration at time t	mg/dl
2.	$X(t)$	The generalized insulin variable for the remote compartment	min^{-1}
3.	$I(t)$	The plasma insulin concentration at time t	$\mu\text{U/ml}$
4.	g_b	This is the basal preinjection value of plasma glucose	mg/dl
5.	i_b	This is the basal preinjection value of plasma insulin	$\mu\text{U/ml}$
6.	m_1	Insulin independent rate constant of glucose rate uptake in muscles, liver and adipose tissue	min^{-1}
7.	m_2	Insulin independent rate constant of glucose rate uptake in muscles, liver and adipose tissue	min^{-1}
8.	m_3	The insulin independent increase in glucose uptake ability in tissue per unit of insulin concentration i_b .	$\text{min}^{-2} \cdot (\mu\text{U/dl})$
9.	m_4	The rate of the pancreatic β -cells' release of insulin after the glucose injection and with glucose concentration above h	$(\mu\text{U/dl}) \cdot \text{min}^{-2}$ $\cdot (\text{mg/dl})^{-1}$
11.	m_5	The threshold value of glucose above which the pancreatic β -cells release insulin.	
12.	m_6	The first order decay rate for insulin in plasma (h^{-1}) pancreatic β -cells release insulin.	min^{-1}

In this model the number of plasma glucose in the body over time t is affected by the declining value of fixed-free insulin to glucose and then multiplied by the number of existing plasma glucose. Total plasma glucose over time t is also affected by increasing levels of glucose reduction, multiplied by the number of existing insulin plasma. In addition the number of plasma glucose at time t is also influenced by the increase of fixed-free insulin value to glucose is multiplied with the glucose initial value before the injection.

Generalization of insulin from any part influenced by the reduction in the rate of reduction of glucose multiplied with generalization of insulin from each section, also influenced by the increased concentration of insulin i_b on every tissue increases insulin free in fasting glucose multiplied by the number of insulin itself, is also affected by a reduction in insulin concentration i_b on every tissue increasing insulin free in fasting glucose but is multiplied with the initial value of insulin before the injected, but it also influenced by the increased in the first decay rate of plasma insulin in pancreas plasma β -cells multiplied with the initial value before insulin injection.

Furthermore, the number of plasma insulin in the body at time t is affected by a reduction of insulin

concentration i_b . In every tissue increasing free insulin on glucose fasting plasma multiplied by the number of insulin in the body. Plasma insulin was also influenced by the increase in the release rate of insulin in pancreatic β -cells after injection of glucose with glucose concentration over h multiplied by the number of plasma glucose in the body. It is also influenced by the increase in the rate of β insulin release in the pancreas after injection of glucose with glucose concentration over h but multiplied by the amount of glucose when cells β in the pancreas releases insulin, the reduced rate of decay of the first insulin on plasma pancreatic β -cells multiplied by the number of plasma insulin that exist in the body, and also by the first decay rate reduced plasma insulin in first decay pancreas plasma β -cells but multiplied by the number of insulin before injection. Therefore is obtained Equation (1), (2), and (3).

$$\frac{dG}{dt} = -m_1 G + m_2 I + m_1 g_b \quad (1)$$

$$\frac{dX}{dt} = -m_2 X + m_3 I - m_3 i_b + m_6 i_b \quad (2)$$

$$\frac{dI}{dt} = -m_3 I + m_4 G + m_4 m_5 - m_6 I + m_6 i_b \quad (3)$$

The Stability of The Equilibrium Point

Obtained equilibrium point value, E_{q0} , of the equations above with notations on this modeling is G_0 , X_0 , and I_0 . Theorem 1 is given as follows.

Theorem 1. The System (1), (2) and (3) has the equilibrium point, E_{q0} ,

$$G_0 = \frac{m_2 m_4 g_b + m_2 m_4 m_5 + m_2 m_6 i_b}{m_1 m_3 - m_2 m_4 + m_1 m_6} + g_b$$

$$X_0 = \frac{m_1 m_3 (m_4 g_b + m_4 m_5 + m_6 i_b) + (m_6 i_b - m_3 i_b) (m_1 (m_3 + m_6) - m_2 m_4)}{m_2 (m_1 (m_3 + m_6) - m_2 m_4)}$$

$$I_0 = \frac{m_1 m_4 g_b + m_1 m_4 m_5 + m_1 m_6 i_b}{m_1 m_3 - m_2 m_4 + m_1 m_6}$$

Proof. If Equation (1) is substituted to Equation (3), then

$$\text{it is obtained } G_0 = \frac{m_2 m_4 g_b + m_2 m_4 m_5 + m_2 m_6 i_b}{m_1 m_3 - m_2 m_4 + m_1 m_6} + g_b$$

$$\text{and } I_0 = \frac{m_1 m_4 g_b + m_1 m_4 m_5 + m_1 m_6 i_b}{m_1 m_3 - m_2 m_4 + m_1 m_6}. \text{ If } I_0 \text{ is}$$

substituted to Equation (2), then it is obtained

$$X_0 = \frac{m_1 m_3 (m_4 g_b + m_4 m_5 + m_6 i_b) + (m_6 i_b - m_3 i_b) (m_1 (m_3 + m_6) - m_2 m_4)}{m_2 (m_1 (m_3 + m_6) - m_2 m_4)}$$

Theorem 2. The equilibrium point exist if G_0 , X_0 , I_0 is real and non-negative.

Proof. Existence of the equilibrium point above exist if G_0 , X_0 , I_0 is real and non-negative.

1. G_0 is real and non-negative, which $m_1 m_3 + m_1 m_6 - m_2 m_4 > 0$.
2. X_0 is real and non-negative $m_1 m_3 + m_1 m_6 - m_2 m_4 > 0$ and $m_1 m_3 (m_4 g_b + m_4 m_5 + m_6 i_b) + (m_6 i_b - m_3 i_b) (m_1 (m_3 + m_6) - m_2 m_4) \geq 0$.
3. I_0 is real and non-negative, which $m_1 m_3 + m_1 m_6 - m_2 m_4 > 0$. ■

The obtained equilibrium point will be discussed about the stability in the point diabetes mellitus model above.

Theorem 3. The equilibrium point, E_{q0} , System (1) – (3) will be asymptotically stable locally if $(m_1 + m_3 + m_6)^2 = 4[m_1(m_3 + m_6) - m_2 m_4]$.

Proof. The eigenvalues of the Jacobian matrix are as follows.

$$\lambda_1 = -m_2 < 0,$$

$$\lambda_2 = \frac{-(m_1 + m_3 + m_6) + \sqrt{(m_1 + m_3 + m_6)^2 - 4[m_1(m_3 + m_6) - m_2 m_4]}}{2}$$

$$\lambda_3 = \frac{-(m_1 + m_3 + m_6) - \sqrt{(m_1 + m_3 + m_6)^2 - 4[m_1(m_3 + m_6) - m_2 m_4]}}{2}$$

If $(m_1 + m_3 + m_6)^2 = 4[m_1(m_3 + m_6) - m_2 m_4]$, then $\lambda_1 < 0$, $\lambda_2 < 0$, $\lambda_3 < 0$. This means that the equilibrium point is asymptotically stable locally.

RESULT AND DISCUSSION

Simulations

Numerical simulation in this study use Matlab R2016a to provide a value for each parameter used in the model. Numerical simulations are given to illustrate geometrically from diabetes disease model using data of glucose values before and after consuming habbatuassauda with primary data collection. The data obtained directly, conducted on 20 respondents were given habbatuassauda for 14 days which consume 3 capsules per day. The average value of glucose in the blood before taking habbatuassauda is 90.3 mg/dl and the average value of 86.4 mg after consuming habbatuassauda. The value of each parameter is as follows in Table 2.

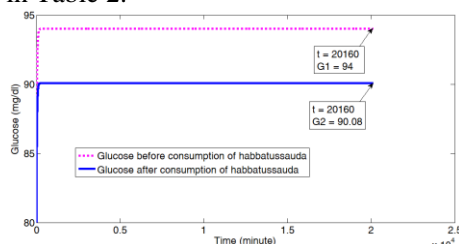


Figure 1. Trajectory glucose before and after consumption of habbatuassauda within 14 days.

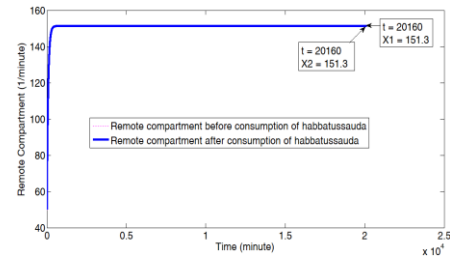


Figure 2. Trajectory remote compartment before and after consumption of habbatuassauda within 14 days.

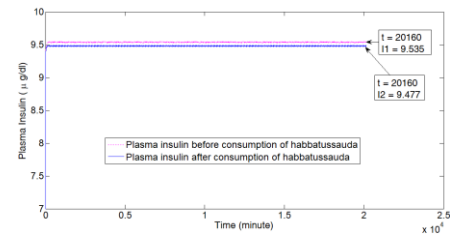


Figure 3. Trajectory plasma insulin before and after consumption of habbatuassauda within 14 days

Table 2. Parameter value of disease diabetes mellitus.

No.	Parameter	Value	Unit
1.	g_b before consumption habbatuassauda	90.3	mg/dl
2.	g_b after consumption habbatuassauda	86.4	mg/dl
3.	i_b	7	$\mu\text{U/ml}$
4.	m_1	0.0317	min^{-1}
5.	m_2	0.0123	min^{-1}
6.	m_3	4.92×10^{-6}	$\text{min}^{-2} \cdot (\mu\text{U/dl})$
7.	m_4	0.0039	$(\mu\text{U/dl}) \cdot \text{min}^{-2} \cdot (\text{mg/dl})^{-1}$
8.	m_5	79.0353	
9.	m_6	0.2659	min^{-1}

The equilibrium point obtained from this model will be shown by numerical simulations in the portrait phase at the equilibrium point using the corresponding parameter values as shown in Table 2. The variables used in this simulation are variables namely glucose and insulin variables, the value before consuming habbatuassauda is 90.3 and the value before consuming habbatuassauda is 86.4. The initial value in this simulation is $(G, X, I) = (80, 50, 7)$.

Figure 1 shows before and after consuming habbatuassauda decreased glucose levels in the body. But the obtained reduction is different, it shows the effect of habbatuassauda consumption decreases glucose levels significantly enough compared to the decreasing rate of glucose levels before taking habbatuassauda. Decreased glucose levels before taking habbatuassauda only reached 90.3 only, while a decrease in glucose levels after consuming habbatuassauda reach 86.4. The rate of this

change would be more significant if habbatussauda consumption in a longer period of time.

Figure 2 shows the remote compartment variable, X , values before and after consumption of Black Seed. To consume habbatussauda or not the remote compartment has not changed. The value of survivors 20160 minutes or 14 days is 151.3 min^{-1} .

Figure 3 shows plasma insulin before and after consuming habbatussauda. After consuming Black Seed there is a decrease though small. Before consuming habbatussauda is $9,535 \mu\text{g/dl}$ and after consuming habbatussauda is $9,477 \mu\text{g/dl}$.

CONCLUSION

Numerical simulation results in the first model showed differences in glucose levels before and after consuming habbatussauda. The results of the second simulation show the same position the content of the remote compartment before and after consuming habbatussauda. Simulation results show the position of a small difference in plasma insulin content before and after consuming habbatussauda.

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