



ARTICLE

Solution of Modified Bergman Minimal Blood Glucose-Insulin Model Using Caputo-Fabrizio Fractional Derivative

Ravi Shanker Dubey¹, Dumitru Baleanu^{2,3}, Manvendra Narayan Mishra^{1,*} and Pranay Goswami⁴

¹Department of Mathematics, AMITY School of Applied Science, AMITY University Rajasthan, Jaipur, 302022, India

²Department of Mathematics and Computer Sciences, Cankaya University, Balgat, 06530, Turkey

³Institute of Space Sciences, Magurele-Bucharest, R76900, Romania

⁴School of Liberal Studies, Dr. B.R. Ambedkar University Delhi, Delhi, 110006, India

*Corresponding Author: Manvendra Narayan Mishra. Email: manvendra.mishra22187@gmail.com

Received: 02 December 2020 Accepted: 20 February 2021

ABSTRACT

Diabetes is a burning issue in the whole world. It is the imbalance between body glucose and insulin. The study of this imbalance is very much needed from a research point of view. For this reason, Bergman gave an important model named-Bergman minimal model. In the present work, using Caputo-Fabrizio (CF) fractional derivative, we generalize Bergman's minimal blood glucose-insulin model. Further, we modify the old model by including one more component known as diet $D(t)$, which is also essential for the blood glucose model. We solve the modified model with the help of Sumudu transform and fixed-point iteration procedures. Also, using the fixed point theorem, we examine the existence and uniqueness of the results along with their numerical and graphical representation. Furthermore, the comparison between the values of parameters obtained by calculating different values of t with experimental data is also studied. Finally, we draw the graphs of $G(t)$, $X(t)$, $I(t)$, and $D(t)$ for different values of τ . It is also clear from the obtained results and their graphical representation that the obtained results of modified Bergman's minimal model are better than Bergman's model.

KEYWORDS

Bergman minimal model; blood glucose; Caputo-Fabrizio fractional derivative; uniqueness and existence; fractional calculus

1 Introduction

These days, Mathematical modeling is turning out to be a vital tool in mathematical science. Since it translates real-world problems into mathematical language and after applying the necessary methods, we again translate the results into real-world languages to forecast the objective. In every field, modeling is being used to achieve or predict the future prospective. In recent years, modeling is being used with another important but less interactive field of mathematics—Fractional Calculus (see [1–8]). We have studied several problems and their solutions by ordinary calculus methods, but sometimes fractional calculus gives us better results to describe the model



than the old one. Fractional calculus has several real-world applications. A few of them are Fractional conservation of mass, Groundwater flow problem, Time-space fractional diffusion equation models, Acoustical wave equations, Fractional Schrödinger equation in quantum theory, etc. (see [9–22]).

Nowadays, diabetes is turning out to be a fatal disease. The imbalance between body glucose and insulin causes diabetes. It is categorized into two types. Type-I diabetes is more severe than Type-II. According to a survey, Type-I and Type-II diabetes sufferers are one ratio nine. So, the study of this imbalance was very much needed from a research point of view. For this reason, Bergman gave an important model named-Bergman minimal model (see [23–27]).

Riemann-Liouville and Caputo introduced the initial concept of fractional calculus. But they use a singular kernel in their definition. However, Caputo and Fabrizio recently found specific systems related to material heterogeneities that cannot be well connected with Riemann-Liouville or Caputo derivative. Because of that, Caputo and Fabrizio introduced a new fractional derivative operator involving a non-singular kernel. Due to its memory and non-singularity property, this operator is used to study different models of engineering, science, and bio-mathematical fields. In general, we get more reliable results while using this operator than others for more details of applications of Caputo-Fabrizio derivative (see [28–45]).

Apart from changing the model to fractional-order, we also include the Diet factor in the model that describes the effect of meals on the glucose level. The generalize of Bergman's minimal blood glucose-insulin model gives us a more precise and detailed prediction about the problem.

1.1 The Caputo-Fabrizio Fractional Differential Operator [46–48]

Definition 1: Suppose $h \in H^1(a_1, b_1)$, $b_1 > a_1$, $\beta \in [0, 1]$ hence the Caputo-Fabrizio differential coefficient of fractional order:

$$D_t^\beta (h(t)) = \frac{M(\beta)}{(1-\beta)} \int_a^t h'(x) e^{\left[-\beta \frac{t-x}{1-\beta}\right]} dx, \quad (1)$$

$M(\beta)$ is function of normalization such as $M(0) = M(1) = 1$.

If, $h \notin H^1(a_1, b_1)$, then the derivative is

$$D_t^\beta (h(t)) = \frac{N(\sigma)}{\sigma} \int_a^t h'(x) e^{\left[-\frac{t-x}{\sigma}\right]} dx, \quad N(0) = N(\infty) = 1, \quad (2)$$

also,

$$\lim_{\sigma \rightarrow 0} \frac{1}{\sigma} e^{\left[-\frac{t-x}{\sigma}\right]} = \delta(x-t). \quad (3)$$

One thing is to be noted here that the Caputo-Fabrizio operator has an exponent differential coefficient. We know that the exponential function has no singularity which, means the derivative exists at every point of the territory. So CF operator gives better results in its domain, see [49–56].

Definition 2: The fractional integral of the function $h(t)$ of order β ($0 < \beta < 1$), is

$$I_\beta^t (h(t)) = \frac{2(1-\beta)}{(2-\beta)M(\beta)} h(t) + \frac{2\beta}{(2-\beta)M(\beta)} \int_0^t h(s) ds, \quad t \geq 0. \quad (4)$$

Remark 1: From the above equation, we conclude that the fractional integral of order β ($0 < \beta < 1$), is the mean of h and its anti-derivative. So Nieto et al. gave this condition,

$$\frac{2(1-\beta)}{(2-\beta)M(\beta)} + \frac{2\beta}{(2-\beta)M(\beta)} = 1. \tag{5}$$

$$M(\beta) = \frac{2}{(2-\beta)}, \quad 0 < \beta < 1.$$

Based on the above relation, Nieto and Losada defined the following operator;

$${}_0^{CF}D_t^\beta (h(t)) = \frac{1}{(1-\beta)} \int_{a_1}^t h'(x) e^{\left[-\beta \frac{t-x}{1-\beta}\right]} dx. \tag{6}$$

1.2 Sumudu Transform of Caputo-Fabrizio Operator [57,58]

Suppose $f(t)$ be a function whose Caputo-Fabrizio derivative occurs, hence the Sumudu Transform of Caputo-Fabrizio fractional differential coefficient of $f(t)$ is defined below:

$$ST\left({}_0^{CF}D_t^\beta\right)(f(t)) = M(\beta) \left[\frac{ST(f(t)) - f(0)}{1 - \beta + \beta u} \right] \tag{7}$$

The whole paper is divided into six sections. Section first introduces fractional calculus and mathematical modeling with its brief history. The second section describes the Bergman model’s fractional exponent and an overview of the fractional modified minimal model. The third section discusses the existence and uniqueness of the modified mathematical model with the help of the Caputo-Fabrizio operator. Section 4 is devoted to the solution of the model by using the Sumudu Transform operator. Section 5 deals with numerical solutions along with graphical representations of the modified Bergman model. In section 6, we have concluded our findings.

2 Mathematical Model

2.1 Bergman Model of Fractional Order

Here, we are going to discuss the Bergman model of fractional order. In this model, we consider a glucose chamber and plasma insulin which is inherent to carry out across the isolated chamber to control the final glucose intake. This model, asserts that this is good to satisfy specific validation criteria with minimum parameters. This system is efficient in describing the gesture of interactivity of blood sugar and insulin. In the presented model, we suppose that $G(t)$ is the imbalance of plasma glucose cluster and $I(t)$ is the free plasma insulin cluster, from their initial values. The model was

$$\frac{d^\alpha G(t)}{dt^\alpha} = -(p_1 + X(t)) G(t) + p_1 G_b, \quad 0 < \alpha < 1 \tag{8}$$

$$\frac{d^\beta X(t)}{dt^\beta} = -p_2 X(t) + p_3 (I(t) - I_b), \quad 0 < \beta < 1 \tag{9}$$

$$\frac{d^\gamma I(t)}{dt^\gamma} = p_6 (G(t) - p_5)^+ t - p_4 (I(t) - I_b), \quad 0 < \gamma < 1 \tag{10}$$

with starting conditions $G(0) = G_0$, $X(0) = X_0$, and $I(0) = I_0$.

2.2 Overview of Fractional Modified Minimal Model

Here, we redefined the structure of the previous model. We made some changes in the model and added few parameters. As we have, ‘Diet’ having significant effect on the glucose level. Now the changed structured Bergman modified system has been described in the following equations-

$${}_0^{\text{CF}}D_t^\tau G(t) = -(p_1 + X(t))G(t) + D(t) - X(t)G_b, \quad (11)$$

$${}_0^{\text{CF}}D_t^\tau X(t) = -p_2X(t) + p_3I(t), \quad (12)$$

$${}_0^{\text{CF}}D_t^\tau I(t) = -n[I(t) + I_b] + \frac{u(t)}{V_1}, \quad (13)$$

$${}_0^{\text{CF}}D_t^\tau D(t) = -kD(t). \quad (14)$$

Here one thing is to be noted that $0 < \tau \leq 1$ and initial restrictions are, $G(0) = G_0$, $X(0) = X_0$, $I(0) = I_0$ and $D(0) = D_0$.

This model can be a tool in search of an artificial pancreas. But, unfortunately, it also adopts the problems with the glucose-minimal model. Here, $G(t)$ —blood glucose cluster, $X(t)$ —aftermath of effective insulin, $I(t)$ —blood insulin cluster, $D(t)$ —infusion of exogenous glucose, $u(t)$ —insulin distribution function, G_b —initial blood glucose cluster, I_b —initial blood insulin cluster, V_1 —insulin issuance volume, n —fractional fading rate of insulin, p_1 —insulin free glucose dispensation rate, p_2 —active insulin dispensation rate and p_3 —the increase in absorption capacity caused by insulin.

3 Existence of the Solutions of Described Model

3.1 Theorem 1

Define K_1 , K_2 , K_3 , K_4 and their relations with variables.

Proof: Since the system is

$${}_0^{\text{CF}}D_t^\tau G(t) = -(p_1 + X(t))G(t) + D(t) - X(t)G_b, \quad (15)$$

$${}_0^{\text{CF}}D_t^\tau X(t) = -p_2X(t) + p_3I(t), \quad (16)$$

$${}_0^{\text{CF}}D_t^\tau I(t) = -n[I(t) + I_b] + \frac{u(t)}{V_1}, \quad (17)$$

$${}_0^{\text{CF}}D_t^\tau D(t) = -kD(t). \quad (18)$$

Here one thing is to be noted that $0 < \tau \leq 1$. Then converting the above system into a system of integral equations

$$G(t) - G(0) = {}_0^{\text{CF}}I_t^\tau [-(p_1 + X(t))G(t) + D(t) - X(t)G_b], \quad (19)$$

$$X(t) - X(0) = {}_0^{\text{CF}}I_t^\tau [-p_2X(t) + p_3I(t)], \quad (20)$$

$$I(t) - I(0) = {}_0^{\text{CF}}I_t^\tau \left[-n[I(t) + I_b] + \frac{u(t)}{V_1} \right], \quad (21)$$

$$D(t) - D(0) = {}_0^{\text{CF}}I_t^\tau [-kD(t)]. \quad (22)$$

Then by definition stated by Nieto, we get

$$G(t) = G(0) + \frac{2(1-\tau)}{(2-\tau)M(\tau)}[-(p_1 + X(t))G(t) + D(t) - X(t)G_b] + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t [-(p_1 + X(s))G(s) + D(s) - X(s)G_b] ds, \tag{23}$$

$$X(t) = X(0) + \frac{2(1-\tau)}{(2-\tau)M(\tau)}[-p_2X(t) + p_3I(t)] + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t [-p_2X(s) + p_3I(s)] ds, \tag{24}$$

$$I(t) = I(0) + \frac{2(1-\tau)}{(2-\tau)M(\tau)}[-n[I(t) + I_b] + \frac{u(t)}{V_1}] + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t \left[-n[I(s) + I_b] + \frac{u(s)}{V_1}\right] ds, \tag{25}$$

$$D(t) = D(0) + \frac{2(1-\tau)}{(2-\tau)M(\tau)}[-kD(t)] + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t [-kD(s)] ds. \tag{26}$$

Now let us suppose the kernels are given as

$$K_1(t, G) = -(p_1 + X(t))G(t) + D(t) - X(t)G_b,$$

$$K_2(t, X) = -p_2X(t) + p_3I(t),$$

$$K_3(t, I) = -n[I(t) + I_b] + \frac{u(t)}{V_1},$$

$$K_4(t, D) = -kD(t).$$

3.2 Theorem 2

Show that K_1, K_2, K_3 and K_4 satisfies the Lipchitz condition.

Proof: At first, we shall show this for K_1 . Suppose G and G_1 are any functions, so

$$\begin{aligned} \|K_1(t, G) - K_1(t, G_1)\| &= \|-(p_1 + X(t))G(t) + (p_1 + X(t))G_1(t)\| \\ &= \|p_1 + X(t)\| \|G(t) - G_1(t)\| \end{aligned}$$

$$\|K_1(t, G) - K_1(t, G_1)\| \leq H \|G(t) - G_1(t)\|, \quad \text{where } \|p_1 + X(t)\| \leq H < 1.$$

Similarly, we can have

$$\|K_2(t, X) - K_2(t, X_1)\| \leq H_1 \|X(t) - X_1(t)\|, \quad \text{where } \|p_2\| \leq H_1 < 1.$$

$$\|K_3(t, I) - K_3(t, I_1)\| \leq H_2 \|I(t) - I_1(t)\|, \quad \text{where } \|n\| \leq H_2 < 1.$$

and

$$\|K_4(t, D) - K_4(t, D_1)\| \leq H_3 \|D(t) - D_1(t)\| \quad \text{where } \|k\| \leq H_3 < 1.$$

Now consider the recursive formula

$$G_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-1}) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G_{n-1}) ds, \tag{27}$$

$$X_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_2(t, X_{n-1}) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_2(s, X_{n-1}) ds, \tag{28}$$

$$I_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_3(t, I_{n-1}) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_3(s, I_{n-1}) ds, \quad (29)$$

$$D_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_4(t, D_{n-1}) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_4(s, D_{n-1}) ds, \quad (30)$$

Now suppose that the deviation amid two successive terms is

$$\begin{aligned} U_n(t) &= G_n(t) - G_{n-1}(t) \\ &= \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-1}) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G_{n-1}) ds \\ &\quad - \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-2}) - \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G_{n-2}) ds, \end{aligned} \quad (31)$$

$$\begin{aligned} U_n(t) &= \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-1}) - \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-2}) \\ &\quad + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t \{K_1(s, G_{n-1}) - K_1(s, G_{n-2})\} ds. \end{aligned} \quad (32)$$

Now

$$\begin{aligned} \|U_n(t)\| &= \|G_n(t) - G_{n-1}(t)\| \\ &= \left\| \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-1}) - \frac{2(1-\tau)}{(2-\tau)M(\tau)}K_1(t, G_{n-2}) \right. \\ &\quad \left. + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t \{K_1(s, G_{n-1}) - K_1(s, G_{n-2})\} ds \right\|, \\ &\leq \frac{2(1-\tau)}{(2-\tau)M(\tau)} \|K_1(t, G_{n-1}) - K_1(t, G_{n-2})\| \\ &\quad + \frac{2\tau}{(2-\tau)M(\tau)} \left\| \int_0^t \{K_1(s, G_{n-1}) - K_1(s, G_{n-2})\} ds \right\|. \end{aligned} \quad (33)$$

But K_1 satisfies Lipchitz condition so,

$$\|U_n(t)\| \leq \frac{2(1-\tau)}{(2-\tau)M(\tau)}H \|G_{n-1} - G_{n-2}\| + \frac{2\tau}{(2-\tau)M(\tau)}K \int_0^t \|G_{n-1} - G_{n-2}\| ds. \quad (34)$$

Similarly, we have

$$\|V_n(t)\| \leq \frac{2(1-\tau)}{(2-\tau)M(\tau)}H_1 \|X_{n-1} - X_{n-2}\| + \frac{2\tau}{(2-\tau)M(\tau)}J_1 \int_0^t \|X_{n-1} - X_{n-2}\| ds, \quad (35)$$

$$\|W_n(t)\| \leq \frac{2(1-\tau)}{(2-\tau)M(\tau)} H_2 \|I_{n-1} - I_{n-2}\| + \frac{2\tau}{(2-\tau)M(\tau)} J_2 \int_0^t \|I_{n-1} - I_{n-2}\| ds, \tag{36}$$

$$\|T_n(t)\| \leq \frac{2(1-\tau)}{(2-\tau)M(\tau)} H_3 \|D_{n-1} - D_{n-2}\| + \frac{2\tau}{(2-\tau)M(\tau)} J_3 \int_0^t \|D_{n-1} - D_{n-2}\| ds. \tag{37}$$

3.3 Theorem 3

Establish that Bergman Minimal Model with Fractional-order is a minimum system of sugar insulin dynamics.

Proof: Using the recursive technique, we have

$$\|U_n(t)\| \leq \|G(0)\| + \left\{ \frac{2(1-\tau)H}{(2-\tau)M(\tau)} \right\}^n + \left\{ \frac{2\tau Kt}{(2-\tau)M(\tau)} \right\}^n \tag{38}$$

$$\|V_n(t)\| \leq \|X(0)\| + \left\{ \frac{2(1-\tau)H_1}{(2-\tau)M(\tau)} \right\}^n + \left\{ \frac{2\tau J_1 t}{(2-\tau)M(\tau)} \right\}^n \tag{39}$$

$$\|W_n(t)\| \leq \|I(0)\| + \left\{ \frac{2(1-\tau)H_2}{(2-\tau)M(\tau)} \right\}^n + \left\{ \frac{2\tau J_2 t}{(2-\tau)M(\tau)} \right\}^n \tag{40}$$

$$\|T_n(t)\| \leq \|D(0)\| + \left\{ \frac{2(1-\tau)H_3}{(2-\tau)M(\tau)} \right\}^n + \left\{ \frac{2\tau J_3 t}{(2-\tau)M(\tau)} \right\}^n \tag{41}$$

Hence the existence of results is verified, which is continuous too. Now we get

$$G(t) = G_n(t) + P_n(t),$$

$$X(t) = X_n(t) + Q_n(t),$$

$$I(t) = I_n(t) + R_n(t),$$

$$D(t) = D_n(t) + S_n(t),$$

where P_n, Q_n, R_n and S_n are residues of series solution.

So,

$$G(t) - G_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)} K_1(t, G_n) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G_n) ds,$$

$$G(t) - G_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)} K_1(t, G - P_n(t)) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G - P_n(s)) ds.$$

Similarly, we have

$$X(t) - X_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)} K_2(t, X - Q_n(t)) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_2(s, X - Q_n(s)) ds,$$

$$I(t) - I_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)} K_3(t, I - R_n(t)) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_3(s, I - R_n(s)) ds,$$

$$D(t) - D_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)} K_4(t, D - S_n(t)) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_4(s, D - S_n(s)) ds.$$

From the above, it is clear that,

$$G(t) - G_n(t) = \frac{2(1-\tau)}{(2-\tau)M(\tau)} K_1(t, G - P_n(t)) + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G - P_n(s)) ds,$$

$$\begin{aligned} G(t) - G(0) &= \frac{2(1-\tau)K_1(t, G)}{(2-\tau)M(\tau)} - \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G) ds \\ &= P_n(t) + \frac{2(1-\tau)K_1(t, G - P_n(t))}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G - P_n(s)) ds. \end{aligned}$$

Now,

$$\begin{aligned} &\left\| G(t) - \frac{2(1-\tau)K_1(t, G)}{(2-\tau)M(\tau)} - G(0) - \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G) ds \right\| \\ &\leq \|P_n(t)\| + \left\{ \frac{2(1-\tau)H}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} Kt \right\} \|P_n(t)\|, \end{aligned} \quad (42)$$

$$\begin{aligned} &\left\| X(t) - \frac{2(1-\tau)K_2(t, X)}{(2-\tau)M(\tau)} - X(0) - \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_2(s, X) ds \right\| \\ &\leq \|Q_n(t)\| + \left\{ \frac{2(1-\tau)H_1}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} J_1 t \right\} \|Q_n(t)\|, \end{aligned} \quad (43)$$

$$\begin{aligned} &\left\| I(t) - \frac{2(1-\tau)K_3(t, I)}{(2-\tau)M(\tau)} - I(0) - \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_3(s, I) ds \right\| \\ &\leq \|R_n(t)\| + \left\{ \frac{2(1-\tau)H_2}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} J_2 t \right\} \|R_n(t)\|, \end{aligned} \quad (44)$$

$$\begin{aligned} &\left\| D(t) - \frac{2(1-\tau)K_4(t, D)}{(2-\tau)M(\tau)} - D(0) - \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_4(s, D) ds \right\| \\ &\leq \|T_n(t)\| + \left\{ \frac{2(1-\tau)H_3}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} J_3 t \right\} \|T_n(t)\|. \end{aligned} \quad (45)$$

Now taking $n \rightarrow \infty$ we have

$$G(t) = G(0) + \frac{2(1-\tau)K_1(t, G)}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_1(s, G) ds, \quad (46)$$

$$X(t) = X(0) + \frac{2(1-\tau)K_2(t, X)}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_2(s, X) ds, \quad (47)$$

$$I(t) = I(0) + \frac{2(1-\tau)K_3(t, I)}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_3(s, I) ds, \tag{48}$$

$$D(t) = D(0) + \frac{2(1-\tau)K_4(t, D)}{(2-\tau)M(\tau)} + \frac{2\tau}{(2-\tau)M(\tau)} \int_0^t K_4(s, D) ds. \tag{49}$$

On behalf of the above equations, we can state that the solution of the system exists.

3.4 The Uniqueness of Result

To show the uniqueness of results, we suppose that other sets of results exist for the system specified from Eqs. (46) to (49) such that

$$G(t) - G_1(t) = \frac{2(1-\tau)}{M(\tau)(2-\tau)} [K_1(t, G) - K_1(t, G_1)] + \frac{2(\tau)}{M(\tau)(2-\tau)} \int_0^t [K_1(s, G) - K_1(s, G_1)] ds, \tag{50}$$

taking norm both sides, we get

$$\|G - G_1\| = \frac{2(1-\tau)}{M(\tau)(2-\tau)} [\|K_1(t, G) - K_1(t, G_1)\|] + \frac{2(\tau)}{M(\tau)(2-\tau)} \int_0^t [\|K_1(s, G) - K_1(s, G_1)\|] ds, \tag{51}$$

using Lipchitz condition, we obtain

$$\|G - G_1\| < \frac{2(1-\tau)}{M(\tau)(2-\tau)} HD + \left(\frac{2(\tau)}{M(\tau)(2-\tau)} J_1 Dt \right)^n, \tag{52}$$

which is valid for all n , so

$$G = G_1, \tag{53}$$

similarly

$$X = X_1, \quad I = I_1, \quad \text{and} \quad D = D_1. \tag{54}$$

Hence, it claims uniqueness of the system.

4 Result of the Model by Using Sumudu Transform

Considering the system has various equations so it can be challenging to find the exact results. For this, we will adopt the iterative technique together with the Sumudu Transform. Now take Sumudu Transform either sides, side of Eq. (15)

$$ST({}_0^CF D_t^\tau)(G(t)) = ST\{-(p_1 + X(t))G(t) + D(t) - X(t)G_b\},$$

or

$$ST(G(t)) = G(0) + \frac{(1-\tau + \tau u)}{M(\tau)} ST\{-(p_1 + X(t))G(t) + D(t) - X(t)G_b\}.$$

At this moment, take inverse Sumudu Transform on both ends, we have-

$$G(t) = G(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \{-(p_1 + X(t))G(t) + D(t) - X(t)G_b\} \right] \quad (55)$$

Similarly, we have from Eqs. (16)–(18)

$$X(t) = X(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \{-p_2 X(t) + p_3 I(t)\} \right] \quad (56)$$

$$I(t) = I(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \left\{ -n(I(t) + I_b) + \frac{u(t)}{V_1} \right\} \right] \quad (57)$$

$$D(t) = D(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \{-kD(t)\} \right] \quad (58)$$

Then we get the following recurrent form from the above

$$G_{n+1}(t) = G_n(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \{-(p_1 + X_n(t)) G_n(t) + D_n(t) - X_n(t) G_b\} \right] \quad (59)$$

$$X_{n+1}(t) = X_n(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \{-p_2 X_n(t) + p_3 I_n(t)\} \right] \quad (60)$$

$$I_{n+1}(t) = I_n(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \left\{ -n(I_n(t) + I_b) + \frac{u(t)}{V_1} \right\} \right] \quad (61)$$

$$D_{n+1}(t) = D_n(0) + ST^{-1} \left[\frac{(1-\tau+\tau u)}{M(\tau)} ST \{-kD_n(t)\} \right] \quad (62)$$

The result is obtained by

$$G(t) = \lim_{n \rightarrow \infty} G_n(t),$$

$$X(t) = \lim_{n \rightarrow \infty} X_n(t),$$

$$I(t) = \lim_{n \rightarrow \infty} I_n(t),$$

and

$$D(t) = \lim_{n \rightarrow \infty} D_n(t).$$

5 Numerical Solution

For numerical solution, we use the values given below by the experiment defined in [59,60].

Table 1: Table with initial value and parameters

Parameter	Value
G_0	287 mg/dL

(Continued)

Table 1 (continued)

Parameter	Value
X_0	0
I_0	241 mu/L
D_0	9 mg/dL
G_b	92 mg/dL
I_b	7.3 mu/L
p_1	0.01572
p_2	0.01301
p_3	0.4031×10^{-5}
n	0.3606/min.
k	0.05

Table 2: Comparison between the values of G for different values of t with experimental data

Time	G(tau = 1)	G(tau = 0.95)	G(tau = 0.7)	Exp.	Exp. - G(tau = 1)	Exp. - G(tau = 0.95)	Exp. - G(tau = 0.7)
0	287	287	287	92	195	195	195
4	279.35	279.35	279.36	287	7.65	7.65	7.64
6	275.64	275.71	275.72	251	24.64	24.71	24.72
12	264.71	265.09	265.03	211	53.71	54.09	54.03
18	253.51	253.61	253.41	193	60.51	60.61	60.41
30	224.75	209.89	210.07	149	75.75	60.89	61.07
36	201.98	154.15	156.87	133	68.98	21.15	23.87
38	192.10	124.69	129.23	130	62.1	5.31	0.77

Table 3: Comparison between the values of I for different values of t with experimental data

Time	I(tau = 1)	I(tau = 0.95)	I(tau = 0.7)	Exp.	Exp. - I(tau = 1)	Exp. - I(tau = 0.95)	Exp. - I(tau = 0.7)
0	241	238.74	225.17	11	230	227.74	214.17
4	117.17	117.06	121.96	130	12.83	12.94	8.04
6	81.70	81.97	89.76	85	3.30	3.03	4.76
10	39.72	40.20	48.66	49	9.27	8.80	0.34
14	19.44	19.91	27.11	41	21.56	21.09	13.89
18	11.38	12.36	21.19	32	20.62	19.64	10.81
19	11.40	12.83	23.42	30	18.59	17.17	6.56
20	12.74	14.88	28.19	30	17.26	15.12	1.81

By using the above-defined values, we can easily determine the numerical results for the defined model. In that analysis, we found the numerical result by using the sumudu transform. We found the result for some different τ values and formed a table that shows the comparison of the obtained result with the experimental data (see Tab. 1). In Tab. 2, we discussed G, and in Tab. 3, we discussed I and found from these analyses that the fractional model gives less error than the integer model. We also drew four figures to show the numerical outcomes. In Fig. 1 we showed the values of G at different values of τ , i.e., $\tau = 1$, $\tau = 0.95$, $\tau = 0.9$, $\tau = 0.8$, and $\tau = 0.7$. In Fig. 2, we showed the values of I at different values of τ . In the same way, we drew the Figs. 3

and 4 to show the numerical results of X and D at different values of τ . From the numerical outcome, it is clear that the diet is an essential component of glucose level.

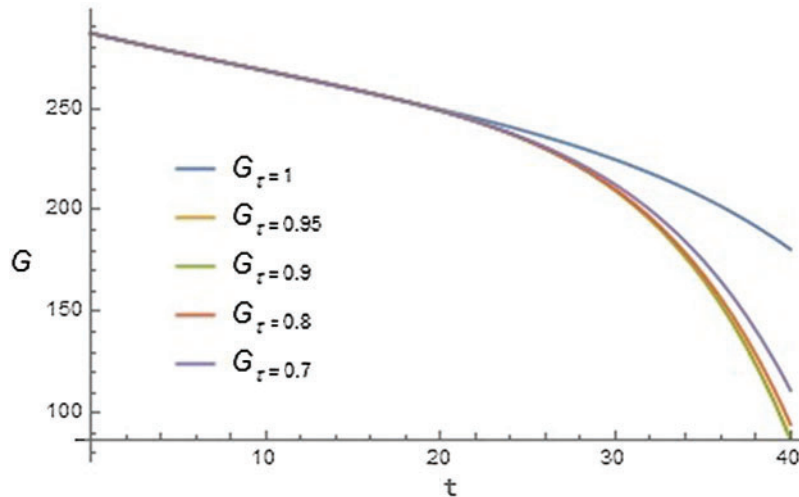


Figure 1: Graph of blood glucose cluster (G) with respect to time t for different values of τ

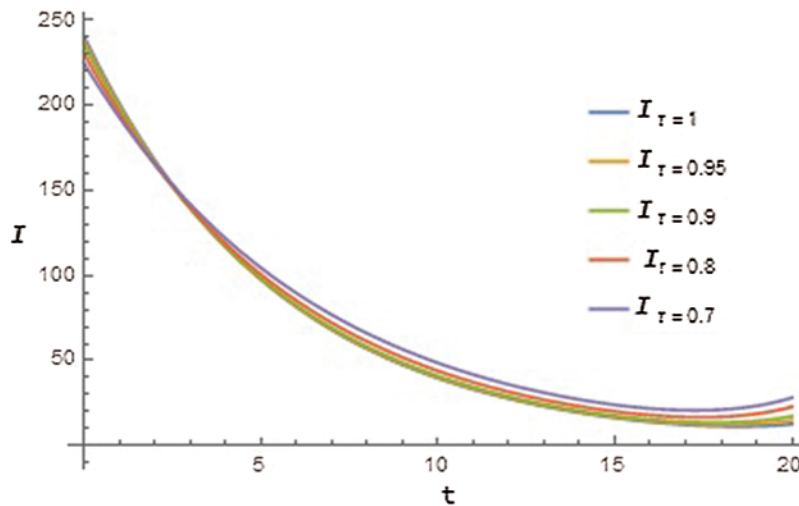


Figure 2: Graph of blood insulin cluster (I) with respect to time t for different values of τ

Furthermore, it has been observed from [Tabs. 2 and 3](#), that the values obtained for G and I with linear order have more error than fractional order. So we can see that the fractional model with Caputo-Fabrizio operator gives better results in contrast to linear model, and our model defined the real-world problem in a better manner.

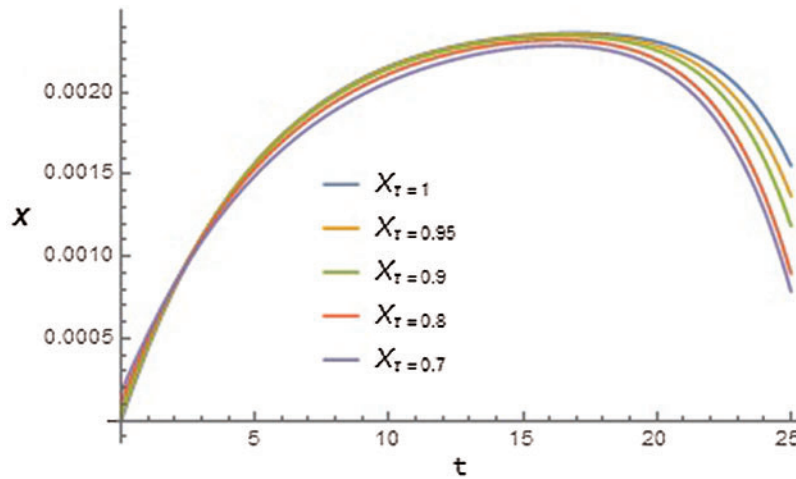


Figure 3: Graph of aftermath of effective insulin (X) with respect to time t for different values of τ

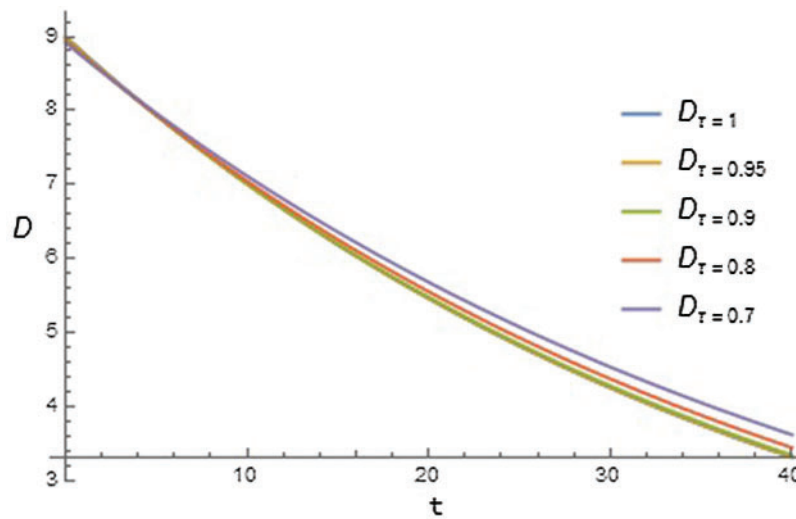


Figure 4: Graph of infusion of exogenous glucose (D) with respect to time t for different values of τ

6 Conclusion

The presented work strives to explain the presence and oneness of the Modified Bergman Minimal Model that is stretched out by Caputo-Fabrizio fractional differential coefficient in the frame of reference of sugar and insulin quantity in blood. From the obtained results, it is clear that the fractional model error reduces compared to integer order. Thus, we get nearby results of a set-up that displays the aftermath of time on the concentrations $G(t)$, $X(t)$, $I(t)$, and $D(t)$. As in future work, we can generalize the model or compare the results using various differential operators.

Acknowledgement: The authors wish to express their appreciation to the reviewers for their helpful suggestions which greatly improved the presentation of this paper.

Funding Statement: The authors received no specific funding for this study.

Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

References

1. Podlubny, I. (1998). *Fractional differential equations: An introduction to fractional derivatives, fractional differential equations, to methods of their solution and some of their applications*. USA: Elsevier, Academic Press.
2. Caputo, M. (1967). Linear models of dissipation whose Q is almost frequency independent-II. *Geophysical Journal International*, 13(5), 529–539. DOI 10.1111/j.1365-246X.1967.tb02303.x.
3. Chaurasia, V. B. L., Dubey, R. S. (2013). Analytical solution for the generalized time-fractional telegraph equation. *Fractional Differential Calculus*, 3(1), 21–29. DOI 10.7153/fdc-03-02.
4. Miller, K. S., Ross, B. (1993). *An introduction to the fractional calculus and fractional differential equations*. New York: John Wiley and Sons.
5. Chaurasia, V. B. L., Dubey, R. S. (2011). Analytical solution for the differential equation containing generalized fractional derivative operators and Mittag–Leffler-type function. *ISRN Applied Mathematics*, 2011(3). DOI 10.5402/2011/682381.
6. Kilbas, A. A., Srivastava, H. M., Trujillo, J. J. (2006). *Theory and applications of fractional differential equations*, pp. 204, Amsterdam, Netherlands: Elsevier.
7. Yang, A. M., Zhang, Y. Z., Cattani, C., Xie, G. N., Rashidi, M. M. et al. (2014). Application of local fractional series expansion method to solve Klein–Gordon equations on cantor sets. *Abstract and Applied Analysis*, 2014(1), 1–6. DOI 10.1155/2014/372741.
8. Baleanu, D., Diethelm, K., Scalas, E., Trujillo, J. J. (2012). *Models and numerical methods, series on complexity*. Singapore, New Jersey, London and Hong Kong: World Scientific Publishing Company. DOI 10.1142/10044.
9. Alkahtani, B. S. T., Atangana, A. (2016). Analysis of non-homogeneous heat model with new trend of derivative with fractional order. *Chaos, Solitons and Fractals*, 89(11), 566–571. DOI 10.1016/j.chaos.2016.03.027.
10. Yang, X. J., Machado, J. T., Cattani, C., Gao, F. (2017). On a fractal LC-electric circuit modeled by local fractional calculus. *Communications in Nonlinear Science and Numerical Simulation*, 47, 200–206. DOI 10.1016/j.cnsns.2016.11.017.
11. Jajarmi, A., Baleanu, D., Sajjadi, S. S., Asad, J. H. (2019). A new feature of the fractional Euler–Lagrange equations for a coupled oscillator using a non-singular operator approach. *Frontiers in Physics*, 7, 196. DOI 10.3389/fphy.2019.00196.
12. Debbouche, A., Torres, D. F. (2014). Approximate controllability of fractional delay dynamic inclusions with nonlocal control conditions. *Applied Mathematics and Computation*, 243(10), 161–175. DOI 10.1016/j.amc.2014.05.087.
13. Alkahtani, B. S., Algahtani, O. J., Dubey, R. S., Goswami, P. (2017). Solution of fractional oxygen diffusion problem having without singular kernel. *Journal of Nonlinear Sciences and Applications*, 10(1), 1–9. DOI 10.22436/jnsa.010.01.28.
14. Dubey, R. S., Alkahtani, B. S. T., Atangana, A. (2015). Analytical solution of space-time fractional Fokker-Planck equation by homotopy perturbation Sumudu transform method. *Mathematical Problems in Engineering*, 2015(2), 1–7. DOI 10.1155/2015/780929.
15. Yang, X. J., Srivastava, H. M., Cattani, C. (2015). Local fractional homotopy perturbation method for solving fractal partial differential equations arising in mathematical physics. *Romanian Reports in Physics*, 67(3), 752–761.

16. Atangana, A., Alabaraoye, E. (2013). Solving a system of fractional partial differential equations arising in the model of HIV infection of $CD4^+$ cells and attractor one-dimensional Keller–Segel equations. *Advances in Difference Equations*, 2013(1), 1–14. DOI 10.1186/1687-1847-2013-94.
17. Odibat, Z., Momani, S. (2008). Modified homotopy perturbation method: Application to quadratic Riccati differential equation of fractional order. *Chaos, Solitons and Fractals*, 36(1), 167–174. DOI 10.1016/j.chaos.2006.06.041.
18. Shaikh, A. S., Shaikh, I. N., Nisar, K. S. (2020). A mathematical model of COVID-19 using fractional derivative: Outbreak in India with dynamics of transmission and control. *Advances in Difference Equations*, 2020(1), 1–19. DOI 10.1186/s13662-020-02834-3.
19. Chaurasia, V. B. L., Dubey, R. S., Belgacem, F. B. M. (2012). Fractional radial diffusion equation analytical solution via Hankel and Sumudu transforms. *International Journal of Mathematics in Engineering Science and Aerospace*, 3(2), 179–188.
20. Baleanu, D., Jajarmi, A., Sajjadi, S. S., Mozyrska, D. (2019). A new fractional model and optimal control of a tumor-immune surveillance with non-singular derivative operator. *Chaos: An Interdisciplinary Journal of Nonlinear Science*, 29(8), 83127. DOI 10.1063/1.5096159.
21. Jajarmi, A., Ghanbari, B., Baleanu, D. (2019). A new and efficient numerical method for the fractional modeling and optimal control of diabetes and tuberculosis co-existence. *Chaos: An Interdisciplinary Journal of Nonlinear Science*, 29(9), 93111. DOI 10.1063/1.5112177.
22. Yildiz, T. A., Jajarmi, A., Yildiz, B., Baleanu, D. (2020). New aspects of time fractional optimal control problems within operators with non-singular kernel. *Discrete and Continuous Dynamical Systems–S*, 13(3), 407. DOI 10.3934/dcdss.2020023.
23. Bergman, R. N., Ider, Y. Z., Bowden, C. R., Cobelli, C. (1979). Quantitative estimation of insulin sensitivity. *American Journal of Physiology–Endocrinology and Metabolism*, 236(6), 667–677. DOI 10.1152/ajpendo.1979.236.6.E667.
24. Bergman, R. N., Cobelli, C. (1980). Minimal modeling, partition analysis, and the estimation of insulin sensitivity. *Federation Proceedings*, 39(1), 110–115.
25. Alkahtani, B. S., Alkahtani, O. J., Dubey, R. S., Goswami, P. (2017). The solution of modified fractional Bergman’s minimal blood glucose-insulin model. *Entropy*, 19(5), 114. DOI 10.3390/e19050114.
26. Dubey, R. S., Belgacem, F. B. M., Goswami, P. (2016). Homotopy perturbation approximate solutions for Bergman’s minimal blood glucose-insulin model. *Fractional Geometry and Nonlinear Analysis in Medicine and Biology*, 2(3), 6. DOI 10.15761/FGNAMB.1000140.
27. Fisher, M. E. (1991). A semiclosed-loop algorithm for the control of blood glucose levels in diabetics. *IEEE Transactions on Biomedical Engineering*, 38(1), 57–61. DOI 10.1109/10.68209.
28. Alshabanat, A., Jleli, M., Kumar, S., Samet, B. (2020). Generalization of Caputo-Fabrizio fractional derivative and applications to electrical circuits. *Frontiers in Physics*, 8(64). DOI 10.3389/fphy.2020.00064.
29. Aydogan, S. M., Baleanu, D., Mohammadi, H., Rezapour, S. (2020). On the mathematical model of rabies by using the fractional Caputo-Fabrizio derivative. *Advances in Difference Equations*, 2020(1), 1–21. DOI 10.1186/s13662-020-02798-4.
30. Baleanu, D., Mohammadi, H., Rezapour, S. (2020). Analysis of the model of HIV-1 infection of $CD4^+$ $CD4^+$ T-cell with a new approach of fractional derivative. *Advances in Difference Equations*, 2020(1), 1–17. DOI 10.1186/s13662-020-02544-w.
31. Moore, E. J., Sirisubtawee, S., Koonprasert, S. (2019). A Caputo-Fabrizio fractional differential equation model for HIV/AIDS with treatment compartment. *Advances in Difference Equations*, 2019(1), 1–20. DOI 10.1186/s13662-019-2138-9.
32. Saleem, M. U., Farman, M., Ahmad, M. O., Rizwan, M. (2017). Control of an artificial human pancreas. *Chinese Journal of Physics*, 55(6), 2273–2282. DOI 10.1016/j.cjph.2017.08.030.
33. Farman, M., Saleem, M. U., Ahmed, M. O., Ahmad, A. (2018). Stability analysis and control of the glucose insulin glucagon system in humans. *Chinese Journal of Physics*, 56(4), 1362–1369. DOI 10.1016/j.cjph.2018.03.037.

34. Khalid, A., Khan, I., Khan, A., Shafie, S. (2015). Unsteady MHD free convection flow of Casson fluid past over an oscillating vertical plate embedded in a porous medium. *Engineering Science and Technology: An International Journal*, 18(3), 309–317. DOI 10.1016/j.jestch.2014.12.006.
35. Sheikh, N. A., Ali, F., Saqib, M., Khan, I., Jan, S. A. A. et al. (2017). Comparison and analysis of the Atangana–Baleanu and Caputo–Fabrizio fractional derivatives for generalized Casson fluid model with heat generation and chemical reaction. *Results in Physics*, 7(2), 789–800. DOI 10.1016/j.rinp.2017.01.025.
36. Owolabi, K. M., Atangana, A., Akgul, A. (2020). Modelling and analysis of fractal-fractional partial differential equations: Application to reaction-diffusion model. *Alexandria Engineering Journal*, 59(4), 2477–2490. DOI 10.1016/j.aej.2020.03.022.
37. Owolabi, K. M., Shikongo, A. (2020). Mathematical modelling of multi-mutation and drug resistance model with fractional derivative. *Alexandria Engineering Journal*, 59(4), 2291–2304. DOI 10.1016/j.aej.2020.02.014.
38. Shaikh, A., Tassaddiq, A., Nisar, K. S., Baleanu, D. (2019). Analysis of differential equations involving Caputo–Fabrizio fractional operator and its applications to reaction-diffusion equations. *Advances in Difference Equations*, 2019(1), 1–14. DOI 10.1186/s13662-019-2115-3.
39. Tarasov, V. E. (2019). Caputo–Fabrizio operator in terms of integer derivatives: Memory or distributed lag. *Computational and Applied Mathematics*, 38(3), 1–15. DOI 10.1007/s40314-019-0767-y.
40. Qureshi, S., Rangaig, N. A., Baleanu, D. (2019). New numerical aspects of Caputo–Fabrizio fractional derivative operator. *Mathematics*, 7(4), 374. DOI 10.3390/math7040374.
41. Abro, K. A., Memon, A. A., Abro, S. H., Khan, I., Tlili, I. (2019). Enhancement of heat transfer rate of solar energy via rotating Jeffrey nano fluids using Caputo–Fabrizio fractional operator: An application to solar energy. *Energy Reports*, 5(20), 41–49. DOI 10.1016/j.egy.2018.09.009.
42. Ali, F., Sheikh, N. A., Khan, I., Nisar, K. S. (2020). Caputo–Fabrizio fractional derivatives modeling of transient MHD Brinkman nano liquid: Applications in food technology. *Chaos, Solitons and Fractals*, 131(12), 109489. DOI 10.1016/j.chaos.2019.109489.
43. Atangana, A., Khan, M. A. (2020). Modeling and analysis of competition model of bank data with fractal-fractional Caputo–Fabrizio operator. *Alexandria Engineering Journal*, 59(4), 1985–1998. DOI 10.1016/j.aej.2019.12.032.
44. Khan, M. A., Alfinyah, C., Alzahrani, E. (2020). Analysis of dengue model with fractal-fractional Caputo–Fabrizio operator. *Advances in Difference Equations*, 2020(1), 1–23. DOI 10.1186/s13662-020-02881-w.
45. Gomez-Aguilar, J. F. (2018). Fundamental solutions to electrical circuits of non-integer order via fractional derivatives with and without singular kernels. *The European Physical Journal Plus*, 133(5), 197. DOI 10.1140/epjp/i2018-12018-x.
46. Caputo, M., Fabrizio, M. (2015). A new definition of fractional derivative without singular kernel. *Progress in Fractional Differentiation and Applications*, 1(2), 73–85. DOI 10.12785/pfda/010201.
47. Shrahili, M., Dubey, R. S., Shafay, A. (2020). Inclusion of fading memory to Banister model of changes in physical condition. *Discrete and Continuous Dynamical Systems-S*, 13(3), 881–888. DOI 10.3934/dcdss.2020051.
48. Srivastava, H. M., Shanker Dubey, R., Jain, M. (2019). A study of the fractional order mathematical model of diabetes and its resulting complications. *Mathematical Methods in the Applied Sciences*, 42(13), 4570–4583. DOI 10.1002/mma.5681.
49. Singh, J., Kumar, D., Baleanu, D. (2020). A new analysis of fractional fish farm model associated with Mittag–Leffler-type kernel. *International Journal of Biomathematics*, 13(2), 2050010. DOI 10.1142/S1793524520500102.
50. Baleanu, D., Wu, G. C. (2019). Some further results of the laplace transform for variable order fractional difference equations. *Fractional Calculus and Applied Analysis*, 22(6), 1641–1654. DOI 10.1515/fca-2019-0084.
51. Baleanu, D., Etemad, S., Rezapour, S. (2020). A hybrid Caputo fractional modeling for thermostat with hybrid boundary value conditions. *Boundary Value Problems*, 2020(1), 1–16. DOI 10.1186/s13661-020-01361-0.

52. Odibat, Z., Baleanu, D. (2019). A Linearization based approach of homotopy analysis method for non-linear time fractional parabolic PDEs. *Mathematical Methods in the Applied Sciences*, 42(18), 7222–7232. DOI 10.1002/mma.5829.
53. Velasco, M. P., Usero, D., Jiménez, S., Vázquez, L., Vázquez-Poletti, J. L. et al. (2020). About some possible implementations of the fractional calculus. *Mathematics*, 8(6), 893. DOI 10.3390/math8060893.
54. Jajarmi, A., Yusuf, A., Baleanu, D., Inc, M. (2020). A new fractional HRSV model and its optimal control: A non-singular operator approach. *Physica A: Statistical Mechanics and Its Applications*, (547), 123860. DOI 10.1016/j.physa.2019.123860.
55. Shahmorad, S., Ostadzad, M. H., Baleanu, D. (2020). A Tau-like numerical method for solving fractional delay integro-differential equations. *Applied Numerical Mathematics*, 151(1–2), 322–336. DOI 10.1016/j.apnum.2020.01.006.
56. Dizicheh, A. K., Salahshour, S., Ahmadian, A., Baleanu, D. (2020). A novel algorithm based on the Legendre wavelets spectral technique for solving the Lane-Emden equations. *Applied Numerical Mathematics*, (153), 443–456. DOI 10.1016/j.apnum.2020.02.016.
57. Katatbeh, Q. D., Belgacem, F. B. M. (2011). Applications of the Sumudu transform to fractional differential equations. *Nonlinear Studies*, 18(1), 99–112.
58. Dubey, R. S., Goswami, P., Belgacem, F. B. M. (2014). Generalized time-fractional telegraph equation analytical solution by Sumudu and Fourier transforms. *Journal of Fractional Calculus and Applications*, 5(2), 52–58.
59. Khan, M. W., Abid, M., Khan, A. Q. (2019). Fractional order Bergman’s minimal model-A better representation of blood glucose-insulin system. *International Conference on Applied and Engineering Mathematics*, pp. 68–73. Taxila, Pakistan, IEEE. DOI 10.1109/ICAEM.2019.8853741.
60. Pacini, G., Bergman, R. N. (1986). MINMOD: A computer program to calculate insulin sensitivity and pancreatic responsivity from the frequently sampled intravenous glucose tolerance test. *Computer Methods and Programs in Biomedicine*, 23(2), 113–122. DOI 10.1016/0169-2607(86)90106-9.