Progress in Fractional Differentiation and Applications
An International Journal

http://dx.doi.org/10.18576/pfda/080204

Existence and Uniqueness of Solutions for Mixed Immunotherapy and Chemotherapy Cancer Treatment Fractional Model with Caputo-Fabrizio Derivative

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Received: 6 Mar. 2020, Revised: 12 Jun. 2020, Accepted: 15 Aug. 2020
Published online: 1 Apr. 2022

Abstract: In this article, we aim to analyze the Mixed Immunotherapy and Chemotherapy cancer treatment mathematical model to strengthen cancer research. Firstly, the model is integrated into the Caputo-Fabrizio fractional derivative with a non-singular kernel in order to overcome the limitations of the conventional Riemann-Liouville and Caputo fractional derivatives. After that, the presented mathematical model is examined for the existence of system solutions in detail by applying the fixed-point postulate. We ascertain the conditions under which the uniqueness of this system of solutions can be obtained.

Keywords: Cancer treatment, fractional-order differentialeEquations, fixed-point theorem, Caputo-Fabrizio derivative.

1 Introduction

Mathematical modeling is a powerful tool due to its manifest importance and multifaceted uses against real-world problems in engineering, finance, social sciences and biology. Models have been formulated using classical derivatives. Cancer is foremost among the world's most fatal diseases and there are many contemporary integer order models, with varying treatment approaches presented in [1–4]. However, due to the complexities of real-world problems, the modeling concept was extended to the novel approach, applying fractional derivatives [5–7]. The basics of the fractional derivative, Caputo-Fabrizio, are given in [8, 9]. Thus, some of the studies focused on the multiple applications of fractional operator, Caputo-Fabrizio derivatives, without a singular kernel. A variety of Fractional Models investigation are given in [10–21]. The subsequent research studies refer predominately to cancer treatment models [22–24].

Human anatomy encompasses over 200 standard cell types. These cells develop and regenerate in a controlled manner to balance their decay. However, sometimes when there is a change in the DNA of a cell (for reasons known or unknown), this creates a mutation that increases the cell's growth and division rate in an unprecedented manner. Subsequently, a mass of tissue called a tumor appears. These tumors can grow and adversely affect other body systems like the nervous, digestive, and circulatory systems, That stated, all tumors are not cancerous. Likewise, tumors that are not cancerous are diagnosed benign. Tumors that are cancer are diagnosed malignant. Malignant tumors can proliferate to other parts of the body through the blood or lymphatic system–these are called Metastatic cancers. These malignant tumor cells work as hunters; they can invade any cell and destroy it. We call this an advanced cancer stage. These cancers cannot be completely cured or controlled with treatment. Thus, oncologists determine the possible course of action for treatment by relying on many important factors. Relevant information considered includes patients' past medical history, age of the patient, stage of the tumor, treatment response or type of cancer (such as leukemia, lung cancer, lymphoma and breast cancer). The goal of optimizing cancer treatment is to achieve minimum damage to normal cells and effectuate higher results with lower treatment costs. In general, prevalent cancer treatment methods include surgery, chemotherapy, immunotherapy and radiotherapy.
Immunotherapy treatment provides strength to our immune systems, to combat cancer cells and other forms of disease

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verified by clinical trials and laboratory experiments. The accepted growth model for tumors indicates their increase in size is logistic to the cell population growth law of immune response (supported by data). NK and CD8+T cells are efficient in destroying tumor cells and they react to tumor cells by cytolytic action. Our body's innate immune response system consists of NK cells, which are always present even when there are no traces of tumor cells inside the body. Whereas CD8+T active tumor-specific cells coexist in sizable numbers only in the presence of tumor cells. NK and CD8+T cells move into the indolent state after a few encounters with tumor cells.
Chemotherapy treatment uses cytotoxic antineoplastic drugs (for example doxorubicin), which destroys cells that divide speedily as it is the nature of cancer cells to divide rapidly. As we know our normal body cells (i.e. hair, stomach lining and bone marrow) are harmed by chemotherapy. However, it is of particular importance to note that immune cells originate within bone marrow. Therefore high doses are not permitted in order to save other rapidly proliferating tissues from damage. Ideally, chemotherapeutic drugs are more effective on tumor cells when compared with immune cells [1,4].
Inspired by the aforementioned study, in this article we address the Mixed Chemotherapy and Immunotherapy cancer treatment modality proposed (the FODEs model) for tumor growth under the influence of combined chemotherapeutic drug and immunotherapeutic drug interaction, whose results may be as close as possible to that of the original circumstance. The presented mathematical model consists of four interrelated equations representing the influence of chemotherapeutic drugs and immunotherapeutic drugs on tumor cell biomass and immune cell biomass in the bloodstream.

To the best of our knowledge, until now, no one has yet considered the Mixed Immunotherapy and Chemotherapy cancer treatment fractional model with the Caputo-Fabrizio derivative. The other remaining sections appear as follows: sect.2 contains background on definitions related to the Caputo-Fabrizio derivative. Sect.3 deals with modeling the Mixed Immunotherapy and Chemotherapy cancer treatment fractional model with Caputo-Fabrizio derivative whereas sect.4 deals with theorems to prove existence and uniqueness of the solution using the fixed-point postulate. Lastly, sect.5 provides a conclusion.

2 Background for Caputo-Fabrizio fractional derivative

Definition 1 *[8]Let $\Xi \in H^1(b,c)$, $c > b$, $\lambda \in [0,1]$ then, the definition of the arbitary order Caputo-Fabrizio fractional derivative is given by*

$$D_t^{\lambda}(\Xi(t)) = \frac{\mathscr{M}(\lambda)}{1-\lambda}\int_b^t \Xi'(z)\exp\Big[-\lambda\frac{t-z}{1-\lambda}\Big]dz. \tag{1}$$

In the equation (1), $\mathscr{M}(\lambda)$ represents normalization function with conditions $\mathscr{M}(1) = \mathscr{M}(0) = 1$ if Ξ does not belongs to $H^1(b,c)$ then, we obtain

$$D_t^{\lambda}(\Xi i(t)) = \frac{\lambda\mathscr{M}(\lambda)}{1-\lambda}\int_a^t (\Xi(t)-\Xi(z))\exp\Big[-\lambda\frac{t-z}{1-\lambda}\Big]dz. \tag{2}$$

If $\nu = \frac{1-\lambda}{\lambda} \in [0,\infty)$, $\lambda = \frac{1}{1+\nu} \in [0,1]$, under these conditions equation (2) become

$$D_t^{\lambda}(\Xi(t)) = \frac{\mathscr{N}(\nu)}{\nu}\int_a^t \Xi'(z)\exp\Big[-\frac{t-z}{\nu}\Big]dz,\ \ \mathscr{N}(\infty) = \mathscr{N}(0) = 1. \tag{3}$$

further,

$$\lim_{\nu\longrightarrow 0}\frac{1}{\nu}\exp\Big[-\frac{t-z}{\nu}\Big] = \Theta(z-t). \tag{4}$$

Definition 2 *[9] Assume $0 < \lambda < 1$, hence fractional order integral of order λ for function $\Xi(z)$ is denoted as*

$$P_t^{\lambda}(\Xi(t)) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}g(t) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t \Xi(s)ds, t \geq 0. \tag{5}$$

$$\frac{2}{2\mathscr{M}(\lambda)-\lambda\mathscr{M}(\lambda)} = 1, \tag{6}$$

We get $\mathscr{M}(\lambda) = \frac{2}{2-\lambda}$, and with order $0 < \lambda < 1$. The authors in [9] represent the new Caputo derivative in another form as

$$D_t^{\lambda}(\Xi(t)) = \frac{1}{1-\lambda}\int_0^t \Xi'(z)\exp\Big[-\lambda\frac{t-z}{1-\lambda}\Big]dz. \tag{7}$$

3 Mixed immunotherapy and chemotherapy cancer treatment model

In this section, we present the fractional Mixed Immunotherapy and Chemotherapy cancer treatment model with CF derivative, which includes tumor cell biomass denoted by $T(t)$ and immune cell biomass $P(t)$, and chemotherapeutic drug and immunotherapeutic drug at time (t) in blood are denoted by $X(t)$,$Y(t)$ respectively. $r,s,u,w,\alpha_1,\alpha_2,\rho,h,\beta,$ $\mu,\psi,g,\gamma_1,\gamma_2,q_1,q_2$ are the positive real-valued model parameters. FODEs model presented in (8) includes assumptions and descriptions of parameters as per the ordinary differential equation mathematical model presented in the paper [4].The Fractional Mixed Immunotherapy and Chemotherapy cancer treatment model with CF derivative is represented as:

$$
\begin{aligned}
{}_0^{CF}D_t^{\lambda}T &= rT(t)(1-pT(t)) - \alpha_1 T(t)P(t) - q_1X(t)T(t),\\
{}_0^{CF}D_t^{\lambda}P &= \psi + \frac{\rho T^2(t)P(t)}{h+T^2(t)} + \frac{\beta P(t)Y(t)}{g+Y(t)} - \alpha_2 T(t)P(t) - \mu P(t) - q_2P(t)X(t),\\
{}_0^{CF}D_t^{\lambda}X &= u - \gamma_1 X(t),\\
{}_0^{CF}D_t^{\lambda}Y &= w - \gamma_2 Y(t).
\end{aligned} \tag{8}
$$

with initial conditions on (8) as

$$T(0) = n_1 \geq 0, P(0) = n_2 > 0, X(0) = n_3 \geq 0, \text{ and } Y(0) = n_6 \geq 0.$$

4 Existence of solution for cancer treatment FODEs mathematical model

In this section Fixed-point theory is applied to establish that the solution exists for the FODEs model. The fractional integral operator on (8) gives

$$
\begin{aligned}
T(t) - T(0) &= {}_0^{CF}P_t^{\lambda}\{rT(t)(1-\rho T(t)) - \alpha_1 T(t)P(t) - q_1X(t)T(t)\},\\
P(t) - P(0) &= {}_0^{CF}P_t^{\lambda}\left[\psi + \frac{\rho\, T(t)^2P(t)}{h+T(t)^2} + \frac{\beta\, P(t)Y(t)}{g+Y(t)} - \alpha_2 T(t)P(t) - \mu\, P(t) - q_2P(t)X(t)\right],\\
X(t) - X(0) &= {}_0^{CF}P_t^{\lambda}\left[u - \gamma_1 X(t)\right],\\
Y(t) - Y(0) &= {}_0^{CF}P_t^{\lambda}\left[w - \gamma_2 Y(t)\right].
\end{aligned} \tag{9}
$$

Applying Nieto and Losada [9] notations on (9) gives

$$
\begin{aligned}
T(t) - T(0) &= \frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\{rT(t)(1-\rho T(t)) - \alpha_1 T(t)P(t) - q_1X(t)T(t)\}\\
&\quad + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\int_0^t \{rT(t)(1-\rho T(t)) - \alpha_1 T(t)P(t) - q_1X(t)T(t)\}dy,\\
P(t) - P(0) &= \{\psi + \frac{\rho T^2(t)P(t)}{h+T^2(t)} + \frac{\beta P(t)Y(t)}{g+Y(t)} - \alpha_2 T(t)P(t) - \mu P(t) - q_2P(t)X(t)\}\\
&\quad + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\int_0^t \{\psi + \frac{\rho T^2(t)P(t)}{h+T^2(t)} + \frac{\beta P(t)Y(t)}{g+Y(t)}\\
&\quad - \alpha_2 T(t)P(t) - \mu P(t) - q_2P(t)X(t)\}dy,\\
X(t) - X(0) &= \frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\{u - \gamma_1 X(t)\}\\
&\quad + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\int_0^t \{u - \gamma_1 X(t)\}dy,\\
Y(t) - Y(0) &= \frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\{w - \gamma_2 Y(t)\}\\
&\quad + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\int_0^t \{w - \gamma_2 Y(t)\}dy.
\end{aligned} \tag{10}
$$

For clarity, we substitute the following

$$E_1(t,T) = rT(t)(1-\rho T(t)) - \alpha_1 T(t)P(t) - q_1 X(t)T(t),$$

$$E_2(t,T) = \psi + \frac{\rho T^2(t)P(t)}{h+T^2(t)} + \frac{\beta P(t)Y(t)}{g+Y(t)} - \alpha_2 T(t)P(t) - \mu P(t) - q_2 P(t)X(t),$$

$$E_3(t,X) = u - \gamma_1 X(t),$$

$$E_4(t,Y) = w - \gamma_2 Y(t). \tag{11}$$

Theorem 1 *The kernels E_1, E_2, E_3 and E_4 will satisfy the Lipchitz condition and contraction if the following inequality holds:*

$$0 \leq (rk + \alpha_1 c + q_1 e) < 1.$$

Proof. We undertake the kernel E_1. Let T and T_1 are two functions. Then, we check the following

$$\begin{aligned} ||E_1(t,T) - E_1(t,T_1)|| &= ||r(T(t)-T(t_1))(1-\rho(T(t)-T(t_1))) \\ &\quad -\alpha_1 P(t)(T(t)-T(t_1)) - q_1 X(t)(T(t)-T(t_1))\}|| \end{aligned} \tag{12}$$

Applying triangular inequality on equation (12) we get

$$\begin{aligned} ||E_1(t,T) - E_1(t,T_1)|| &\leq ||rk\{T(t)-T(t_1)\}|| + ||\alpha_1 P(t)\{T(t)-T(t_1)\}|| \\ &\quad + ||q_1 X(t)\{T(t)-T(t_1)\}||, \\ &\leq \{rk + \alpha_1 ||P(t)|| + q_1 ||X(t)||\}||\{T(t)-T(t_1)\}||, \\ &\leq \{rk + \alpha_1 c + q_1 e\}||\{T(t)-T(t_1)\}||, \\ &\leq \chi_1 ||\{T(t)-T(t_1)\}||. \end{aligned} \tag{13}$$

Taking $\chi_1 = (rk + \alpha_1 c + q_1 e)$, where $||1-\rho(T(t)-T(t_1))|| \leq k$, $||P(t)|| \leq c$ and $||X(t)|| \leq e$, are bounded functions, which prompt the consideration that

$$||E_1(t,T) - E_1(t,T_1)|| \leq \chi_1 ||T(t) - T(t_1)||. \tag{14}$$

Hence, the Lipschiz condition is verified for E_1 and furthermore if $0 \leq (rk + \alpha_1 c + q_1 e) < 1$ then that implies a contraction. Lipschiz condition can be verified for the remaining cases as given below

$$\begin{aligned} &|| E_2(t,P) - E_2(t,P_1) || \leq \chi_2 || P(t) - P(t_1) ||, \\ &||E_3(t,X) - E_2(t,X_1)|| \leq \chi_3 ||X(t) - X(t_1)||, \\ &||E_4(t,Y) - E_2(t,Y_1)|| \leq \chi_4 ||Y(t) - Y(t_1)||. \end{aligned} \tag{15}$$

Considering the previously mentioned kernels, the equation (10) can be written as

$$\begin{aligned} T(t) &= T(0) + \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)} E_1(t,T) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)} \int_0^t (E_1(y,T))dy, \\ P(t) &= P(0) + \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)} E_2(t,P) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)} \int_0^t (E_2(y,P))dy, \\ X(t) &= X(0) + \frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)} E_3(t,X) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)} \int_0^t (E_3(y,X))dy, \\ Y(t) &= Y(0) + \frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)} E_4(t,Y) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)} \int_0^t (E_4(y,Y))dy. \end{aligned} \tag{16}$$

Now, we demonstrate the following recursive formula:

$$T_n(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)} E_1(t,T_{n-1}) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)} \int_0^t (E_1(y,T_{n-1}))dy,$$

$$P_n(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}E_2(t,P_{n-1}) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_2(y,P_{n-1}))dy,$$
$$X_n(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}E_3(t,X_{n-1}) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_3(y,X_{n-1}))dy,$$
$$Y_n(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}E_4(t,Y_{n-1}) + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_4(y,Y_{n-1}))dy. \tag{17}$$

with following conditions

$$T_0(t) = T(0),\ P_0(t) = P(0),\ X_0(t) = X(0),\ and\ Y_0(t) = Y(0). \tag{18}$$

Now, we obtain the successive terms difference as:

$$\begin{aligned}
\Theta_n(t) &= T_n(t) - T_{n-1}(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}(E_1(t,T_{n-1}) - E_1(t,T_{n-2})) \\
&\quad + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_1(y,T_{n-1}) - E_1(y,T_{n-2}))dy, \\
\zeta_n(t) &= P_n(t) - P_{n-1}(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}(E_2(t,P_{n-1}) - E_2(t,P_{n-2})) \\
&\quad + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_2(y,P_{n-1}) - E_2(y,P_{n-2}))dy, \\
\Phi_n(t) &= X_n(t) - X_{n-1}(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}(E_3(t,X_{n-1}) - E_3(t,X_{n-2})) \\
&\quad + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_3(y,X_{n-1}) - E_3(y,X_{n-2}))dy, \\
\Omega_n(t) &= Y_n(t) - Y_{n-1}(t) = \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}(E_4(t,Y_{n-1}) - E_4(t,Y_{n-2})) \\
&\quad + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t (E_4(y,Y_{n-1}) - E_4(y,Y_{n-2}))dy.
\end{aligned} \tag{19}$$

Which prompts towards the consideration that

$$\begin{cases}
T_n(t) = \sum_{i=1}^{n} \Theta_i(t), \\
P_n(t) = \sum_{i=1}^{n} \zeta_i(t), \\
X_n(t) = \sum_{i=1}^{n} \Phi_i(t), \\
Y_n(t) = \sum_{i=1}^{n} \Omega_i(t).
\end{cases} \tag{20}$$

Using step by step calculation we get

$$\begin{aligned}
||\Theta_n(t)|| = ||T_n(t) - T_{n-1}(t)|| &= ||\frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}(E_1(t,T_{n-1}) - E_1(t,T_{n-2})) \\
&\quad + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\int_0^t (E_1(y,T_{n-1}) - E_1(y,T_{n-2}))dy||.
\end{aligned} \tag{21}$$

Employing triangular inequality on equation (21), we obtain

$$\begin{aligned}
||T_n(t) - T_{n-1}(t)|| &\leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}||(E_1(t,T_{n-1}) - E_1(t,T_{n-2}))|| \\
&\quad + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}||\int_0^t (E_1(y,T_{n-1}) - E_1(y,T_{n-2}))dy||.
\end{aligned} \tag{22}$$

Since kernel satisfies Lipchitz condition, thus we get

$$||T_n(t)-T_{n-1}(t)|| \leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_1||T_{n-1}-T_{n-2}|| + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\chi_1\int_0^t||T_{n-1}-T_{n-2}||dy. \tag{23}$$

Hence, we have

$$||\Theta_n(t)|| \leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_1||\Theta_{n-1}(t)|| + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\chi_1\int_0^t||\Theta_{n-1}(y)||dy. \tag{24}$$

In the same way, we obtain the subsequent results

$$\begin{aligned}
||\zeta_n(t)|| &\leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_2||\zeta_{n-1}(t)|| + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_2\int_0^t||\zeta_{n-1}(y)||dy,\\
||\Phi_n(t)|| &\leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_3||\Phi_{n-1}(t)|| + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_3\int_0^t||\Phi_{n-1}(y)||dy,\\
||\Omega_n(t)|| &\leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_4||\Omega_{n-1}(t)|| + \frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_4\int_0^t||\Omega_{n-1}(y)||dy.
\end{aligned} \tag{25}$$

Considering the above presented results, the following theorem can be established.

Theorem 2 *The Cancer treatment FODEs model (8) coupled solution exists under the condition that, we find* t_0 *which satisfy:*

$$\frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_1 + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\chi_1 t_0 < 1.$$

Proof. Now we know that the Lipchitz condition holds for the kernels and the functions $T(t)$, $P(t)$, $X(t)$, and $Y(t)$ are bounded. Hence, by applying this process recursively [11] on Eqs. (24) and (25), we obtain the inequalities:

$$\begin{aligned}
||\Theta_n(t)|| &\leq ||T_n(0)||\Big[\Big(\frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\chi_1\Big)+\Big(\frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_1 t\Big)\Big]^n,\\
||\zeta_n(t)|| &\leq ||P_n(0)||\Big[\Big(\frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\chi_2\Big)+\Big(\frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_2 t\Big)\Big]^n,\\
||\Phi_n(t)|| &\leq ||X_n(0)||\Big[\Big(\frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\chi_3\Big)+\Big(\frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_3 t\Big)\Big]^n,\\
||\Omega_n(t)|| &\leq ||Y_n(0)||\Big[\Big(\frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}\chi_4\Big)+\Big(\frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\chi_4 t\Big)\Big]^n.
\end{aligned} \tag{26}$$

Thus, the existence and continuity of the above presented solutions are proved. Next to confirm that the functions are the solutions of eq. (8), we fixed

$$\begin{aligned}
T_n(t)-K_n(t) &= T(t)-T(0),\\
P_n(t)-F_n(t) &= P(t)-P(0),\\
X_n(t)-G_n(t) &= X(t)-X(0),\\
Y_n(t)-J_n(t) &= Y(t)-Y(0).
\end{aligned} \tag{27}$$

Thus, we obtain

$$\begin{aligned}
||K_n(t)|| &= \Big|\Big|\frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)}(E_1(t,T)-E_1(t,T_{n-1}))+\frac{2\lambda}{\mathscr{M}(\lambda)(2-\lambda)}\int_0^t(E_1(y,T)-E_1(y,T_{n-1}))dy\Big|\Big|,\\
&\leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}||(E_1(t,T)-E_1(t,T_{n-1}))|| + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\int_0^t||(E_1(y,T)-E_1(y,T_{n-1}))||dy,\\
&\leq \frac{2(\lambda-1)}{(\lambda-2)\mathscr{M}(\lambda)}\chi_1||T-T_{n-1}|| + \frac{2\lambda}{(2-\lambda)\mathscr{M}(\lambda)}\chi_1||T-T_{n-1}||t.
\end{aligned} \tag{28}$$

After the repetition of the same process, we obtain

$$||K_n(t)|| \leq \left(\frac{2(\lambda-1)}{\lambda\mathscr{M}(\lambda)-2\mathscr{M}(\lambda)} - \frac{2\lambda}{\lambda\mathscr{M}(\lambda)-2\mathscr{M}(\lambda)}t\right)^{n+1}\chi_1^{n+1}a. \tag{29}$$

When $t = t_0$

$$||K_n(t)|| \leq \left(\frac{2(\lambda-1)}{\mathscr{M}(\lambda)(\lambda-2)} - \frac{2\lambda}{\mathscr{M}(\lambda)(\lambda-2)}t_0\right)^{n+1}\chi_1^{n+1}a. \tag{30}$$

Employing limits on eq. (30), if $n \to \infty$, we obtain $||K_n(t)|| \to 0$.
In the same manner we obtain $||F_n(t)|| \to 0, ||G_n(t)|| \to 0, ||J_n(t)|| \to 0$.
Hence Hence existence is established.

Moreover, in order to obtain the uniqueness for the solution set of the aforesaid model (8), consider that there exists a separate solution set for (8) as $T_1(t)$, $P_1(t)$, $X_1(T)$, and $Y_1(t)$ thus

$$T(t) - T_1(t) = \frac{2(\lambda-1)}{(\lambda-2).\mathscr{M}(\lambda)}(E_1(t,T) - E_1(t,T_1)) + \frac{2\lambda}{(2-\lambda).\mathscr{M}(\lambda)}\int_0^t (E_1(y,T) - E_1(y,T_1))dy. \tag{31}$$

Employing the norm over the equation (31), we obtain

$$||T(t) - T_1(t)|| \leq \frac{2(\lambda-1)}{(\lambda-2).\mathscr{M}(\lambda)}||E_1(t,T) - E_1(t,T_1)|| + \frac{2\lambda}{(2-\lambda).\mathscr{M}(\lambda)}\int_0^t ||E_1(y,T) - E_1(y,T_1)||dy. \tag{32}$$

Employing the Lipschitz condition of the kernel, we get

$$||T(t) - T_1(t)|| \leq \frac{2(\lambda-1)}{(\lambda-2).\mathscr{M}(\lambda)}\chi_1||T(t) - T_1(t)|| + \frac{2\lambda}{(2-\lambda).\mathscr{M}(\lambda)}\chi_1 t||T(t) - T_1(t)|. \tag{33}$$

It provides

$$||T(t) - T_1(t)||\left(1 - \frac{2(\lambda-1)}{(\lambda-2).\mathscr{M}(\lambda)}\chi_1 + \frac{2\lambda}{\lambda\mathscr{M}(\lambda)-2\mathscr{M}(\lambda)}\chi_1 t\right) \leq 0. \tag{34}$$

Theorem 3 *A unique solution of the FODEs model presented in (8) exists with the condition*

$$\left(1 - \frac{2(\lambda-1)}{(\lambda-2).\mathscr{M}(\lambda)}\chi_1 + \frac{2\lambda}{\lambda\mathscr{M}(\lambda)-2\mathscr{M}(\lambda)}\chi_1 t\right) > 0.$$

Proof. Assuming the condition provided in (34) exists, then

$$||T(t) - T_1(t)||\left(1 - \frac{2(\lambda-1)}{(\lambda-2).\mathscr{M}(\lambda)}\chi_1 + \frac{2\lambda}{\lambda\mathscr{M}(\lambda)-2\mathscr{M}(\lambda)}\chi_1 t\right) \leq 0. \tag{35}$$

implies that

$$||T(t) - T_1(t)|| = 0. \tag{36}$$

Hence,

$$T_1(t) = T(t). \tag{37}$$

similarly, we get

$$P_1(t) = P(t),$$

$$X_1(t) = X(t),$$

$$Y_1(t) = Y(t). \tag{38}$$

Which completes the proof for the uniqueness of the solution. The FODEs model presented in (8) exists.

5 Conclusion

We extended the Mixed Immunotherapy and Chemotherapy cancer treatment model to fractional calculus by using the CF fractional derivative. To summarize, this derivative has a non-singular kernel and follows exponential distribution, whereas both the fractional derivatives Riemann–Liouville and Caputo, have singular kernels and follow power-law distribution [25]. Existence of the solution for the FODEs cancer treatment model is found by employing the fixed-point theorem. We defined the conditions by which the uniqueness of this system of solutions can be achieved.Similar comparative analysis can be undertaken of other integer order models. Non-integer values of λ the fractional parameter and CF fractional derivative together help to create a significant mathematical model. This is very much in line with in vivo cancer treatment data for accurate prediction and assists in the optimization of immunotherapy and chemotherapy. Ostensibly, this will benefit cancer research by substantially reducing the cost of care.

Conflicts of Interests
The authors declare that they have no conflicts of interests.

References

[1] L. G. de Pillis, W. Gu and A. E. Radunskaya Mixed immunotherapy and chemotherapy of tumors: modeling, applications and biological interpretations, *J. Theor. Bio.* **238**(4), 841-862 (2006).
[2] L. G. De Pillis and A. Radunskaya A mathematical tumor model with immune resistance and drug therapy: an optimal control approach, *J. Theor. Med.* **3**(2), 79-100 (2001).
[3] F. Castiglione and B. Piccoli, Cancer immunotherapy, mathematical modeling and optimal control, *J. Theor. Biol* **277**(4), 723–732 (2007).
[4] S. Sharma and G. P. Samanta Analysis of the dynamics of a tumor–immune system with chemotherapy and immunotherapy and quadratic optimal control, *Differ. Equ. Dyn. Sys.* **24**(2), 149-171 (2016).
[5] I. Podlubny, *Fractional differential equations*, Academic Press, 1999.
[6] S. Samko, A. Kilbas and O. Marichev, *Fractional integrals and derivatives: theory and applications*, London: Gordon and Breach Science Publishers, 1993.
[7] A. A. Kilbas, H. M. Srivastava and J. J. Trujillo, *Theory and applications of fractional differential equations*, vol. 204.North-Holland, Amsterdam, 2006
[8] M. Caputo and M. Fabrizio, A new definition of fractional derivative with-out singular kernel, *Progr. Fract. Differ. Appl.* **85**, 73–85 (2015).
[9] J. Losada and J. J. Nieto, Properties of the new fractional derivative without singular Kernel, *Progr. Fract. Differ. Appl.* **1**, 87–92 (2015).
[10] S. Ullah, A. Khan and M. Farooq, A new fractional model for the dynamics of the hepatitis B virus using the Caputo-Fabrizio derivative, *Eur. Phys. J. Plus* **133**, 237 (2018).
[11] M. Altaf Khan, S. Ullah, K. O. Okosun and K. Shah A fractional order pine wilt disease model with Caputo–Fabrizio derivative, *Adv. Differ. Equ.* **2018**, 410 (2018).
[12] J. Singh, D. Kumar, M. A. Qurashi and D. Baleanu, A new fractional model for giving up smoking dynamics, *Adv. Diff. Equ.* **2017**, 88–104 (2017).
[13] S. Bushnaq, S. A. Khan, K. Shah and G. Zaman, Mathematical analysis of HIV/AIDS infection model with Caputo-Fabrizio fractional derivative, *Cogent Math. Stat.* **5**(1), 1432521 (2018).
[14] E. J. Moore, S. Sirisubtawee and S. Koonprasert, A Caputo–Fabrizio fractional differential equation model for HIV/AIDS with treatment compartment, *Adv. Differ. Equ.* **200** (2019).
[15] S. A. Khan, K. Shah, G. Zaman and F. Jarad, Existence theory and numerical solutions to smoking model under Caputo-Fabrizio fractional derivative, *Chaos* **29**, 013128 (2019).
[16] J. Singh, D. Kumar, Z. Hammouch and A. Atangana, A fractional epidemiological model for computer viruses pertaining to a new fractional derivative, *App. Math. Comp.* **316**, 504-515 (2018).
[17] D. Baleanu, A. Mousalou and S. Rezapour, A new method for investigating approximate solutions of some fractional integro-differential equations involving the Caputo-Fabrizio derivative, *Adv. Differ. Equ.* **51**, (2017).
[18] A. Atangana and E. F. D. Goufo, The Caputo-Fabrizio fractional derivative applied to a singular perturbation problem, *Int. J. Math. Model. Numer. Opt.* **9**(3), 241 (2019).
[19] D. Kumar, J .Singh, M. A. Qurashi and D. Baleanu, Analysis of logistic equation pertaining to a new fractional derivative with non-singular kernel, *Adv. Mech. Eng.* **9**(2), 1-8 (2017).
[20] X. J. Yang, H. M. Srivastava and J. A. T. Machado, A new fractional derivative without singular kernel: application to the modelling of the steady heat flow, *Therm. Sci.* **20**(2), 753-756 (2016).
[21] B. S. T. Alkahtani and A. Atangana, Controlling the wave movement on the surface of shallow water with the Caputo–Fabrizio derivative with fractional order, *Chaos Soliton Fract.* **89**, 539–546 (2016).

[22] G. H. Erjaee, M. H. Ostadzad, S. Amanpour and K. B. Lankarani, Dynamical analysis of the interaction between effector immune and cancer cells and optimal control of chemotherapy, *Nonlin. Dyn. Psych. Life Sci.* **17**(4), 449-463 (2013).
[23] M. A. Dokuyucu, E. Celik, H. Bulut and H. M. Baskonus Cancer treatment model with the Caputo-Fabrizio fractional derivative, *Eur. Phys. J. Plus* **133**, 92 (2018).
[24] J. E. Solís-Pérez, J. F. Gómez-Aguilar and A. Atangana, A fractional mathematical model of breast cancer competition model, *Chaos Soliton Frac.* **127**, 38-54 (2019).
[25] A. Atangana and J. F. Gomez-Aguilar, Decolonisation of fractional calculus rules: Breaking commutativity and associativity to capture more natural phenomena, *Eur. Phys. J. Plus.* **133**, 166 (2018).