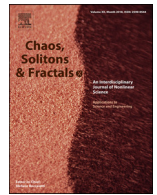




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Computational solutions of the HIV-1 infection of CD4⁺ T-cells fractional mathematical model that causes acquired immunodeficiency syndrome (AIDS) with the effect of antiviral drug therapy

Abdel-Haleem Abdel-Aty^{a,b}, Mostafa M.A. Khater^{c,d}, Hemen Dutta^{e,*}, Jamel Bouslimi^{f,g}, M. Omri^h

^a Department of Physics, College of Sciences, University of Bisha, P.O. Box 344, Bisha, 61922, Saudi Arabia

^b Physics Department, Faculty of Science, Al-Azhar University, Assiut 71524, Egypt

^c Department of Mathematics, Faculty of Science, Jiangsu University, Zhenjiang, 212013, China

^d Department of Mathematics, Obour Institutes, Cairo, 11828, Egypt

^e Department of Mathematics, Faculty of Science, Gauhati University, Guwahati 781014, India

^f Department of Engineering Physics and Instrumentation, National Institute of Applied Sciences and Technology, Carthage University, Tunisia

^g Physics Department, Faculty of Science, Taif University, P.O.Box 888, 21974 Taif, Saudi Arabia

^h Deanship of Scientific Research, King Abdulaziz University, Jeddah, Saudi Arabia

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ABSTRACT

This paper investigates the exact traveling wave solutions of the fractional model of the human immunodeficiency virus (HIV-1) infection for CD4⁺ T-cells. This model also treats with the effect of antiviral drug therapy. These solutions calculate both the boundary and initial conditions that allow employing the septic-B-spline scheme which is one of the most recent schemes in the numerical field. We use the obtained computational solutions via the modified Khater, the extended simplest equation, and sech-tanh methods through Atangana-Baleanu derivative operator. The comparison between the exact and numerical evaluated solutions is illustrated by some distinct sketches. The functioning of our numerical method is tested under three computational obtained solutions.

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1. Introduction

Studying epidemics is one of the most critical and fundamental investigations, especially after discovering many new diseases caused by distinct types of viruses, such as Marburg [1], Ebola [2], Rabies [3], Smallpox [4], Hanta [5], Influenza [6], Dengue [7], Rota [8], SARS [9], SARS-2 [10], MERS [11], Corona [12], ... etc. Nowadays, the world faces a disaster because of a new virus called COVID-19 [13]. SARS-CoV-2 is the main reason for this new virus (COVID-19) [14]. People with chronic diseases, such as diabetes and pneumonia, especially the elderly, are most vulnerable to the complications of this virus. Work in the area of infectious diseases has been of much interest after COVID-19 from different sides, including vaccines production [15], statistics [16], modeling and control

[13], and, social behaviors that affect the spread and infection of the viruses [17].

Long time ago, differential equations were used for simulation and modeling of several phenomena from life and science. The differential equations were a very powerful tool in simulation of the applications in electrical engineering, plasma physics, quantum optics, and nonlinear systems [18–23]. Moreover, mathematical biology is one of the hottest topics that involve several phenomena treated by differential equations [24]. Population dynamics is one of the oldest subjects simulated by the differential equations in the early 15th century [25]. Differential equations have good contributions in the simulation and modeling of the epidemic diseases, with finding new controlling parameters of the transmission and spread of the viruses [16,26,27].

HIV is a virus that attacks the immune system of the human. Untreated HIV breaks and kills CD4 cells, which are a type of immune cell called T cells. Over time, as HIV kills more CD4 cells, the body is more likely to get various types of infections and cancers. In this study, we investigate another virus called HIV-1 [28,29], which is the most serious one. Based on Dr. Amesh Adalja, [30] statistical study, thirty-four million people have died of the HIV-1

* Corresponding author.

E-mail addresses: amabdelaty@ub.edu.sa (A.-H. Abdel-Aty), mostafa.khater2024@yahoo.com (Mostafa M.A. Khater), hemen_dutta08@rediffmail.com (H. Dutta), jamelabouaysem@yahoo.fr (J. Bouslimi), omrimoha2002@yahoo.fr (M. Omri).

since the disease was first discovered in the 1980s. However, the powerful antiviral drugs have made it possible to live with HIV for some years. Despite discovering the powerful antiviral drugs, several countries with low-and middle-income are still suffering from HIV, where 95% of new HIV infections occur. Almost more than two-thirds of the people suffering from HIV worldwide live in Africa, where nearly one in every twenty-five adults in Africa has a positive HIV. All these reasons have forced many researchers in bio-mathematics to form a mathematical model of this virus to study the exact and numerical solutions which present a clear image about dynamical behavior [31,32]. Modeling and simulation of HIV with CD4 Cells by differential equations are reported in many papers [28,29]. Guedj et al. studied the practical parameters that affect the transmission and spread of the HIV, with T-cells, in a model of HIV dynamics based on a system of non-linear Ordinary Differential Equations (ODE) [33]. Global behavior of delay differential equations model of HIV infection with apoptosis was investigated [34,35]. Other papers addressed the control and stability analysis of the spread and transmission of HIV virus [29,36].

In this paper, we investigate the analytical solutions of a bio-mathematical model and use these solutions to evaluate the numerical solutions. This system is given by [37,38]

$$\begin{cases} \mathcal{D}_3^\epsilon \mathcal{G} = \mathfrak{P}_1 - \mathfrak{P}_2 \mathcal{G} - \mathfrak{P}_3 \mathcal{G} \mathcal{Q}, \\ \mathcal{D}_3^\epsilon \mathcal{S} = \mathfrak{P}_3 \mathcal{G} \mathcal{Q} - \mathfrak{P}_4 \mathcal{S}, \\ \mathcal{D}_3^\epsilon \mathcal{Q} = \mathfrak{P}_5 \mathcal{S} - \mathfrak{P}_6 \mathcal{Q}, \end{cases} \quad (1)$$

where $0 < \epsilon < 1$, $\mathcal{G} = \mathcal{G}(3)$, $\mathcal{Q} = \mathcal{Q}(3)$, $\mathcal{S} = \mathcal{S}(3)$ and \mathfrak{P}_i , ($i = 1, \dots, 6$) are arbitrary constants which represent the rate of production of CD4⁺ T-cells, the rate of natural death rate, infected CD4⁺ cells from uninfected CD4⁺ cells, virus producing cell's death, creation of virions viruses by infected cells, and virus particle death. Moreover, system (1) includes some primary biological models such as The HIV-1 two / three / four / general-component models including virions [39,40]. The human immunodeficiency virus causes acquired immunodeficiency syndrome (AIDS) as well as infects, damages, and reduces CD4⁺ T-cells. The body gradually gets more sensitive to infections and loses its safety. AIDS is one of the most serious diseases at the present.

This fractional ODE model of HIV-1 studies the non-local property that depends on both historical and current states of the problem in the contract of the classical calculus. For converting the fractional form of the models to integer form, various fractional operators, such as conformable fractional derivative, fractional Riemann-Liouville derivatives, Caputo, Caputo-Fabrizio definition, and Atangana-Baleanu (AB) fractional operator have been derived [41,42]. Applying the following transformation with AB fractional operator [43]

$$\mathfrak{z} = \frac{\mathfrak{F}(1 - \epsilon) \mathfrak{T}^{-\epsilon m}}{\mathcal{B}(\epsilon) \sum_{m=0}^{\infty} \left(-\frac{\epsilon}{1-\epsilon}\right)^m \Gamma(1 - \epsilon m)}, \quad (2)$$

to the above system 1, where \mathfrak{F} is an arbitrary constants, yields

$$\mathcal{E}_{\mathfrak{z}}(3) = \frac{1}{\mathfrak{N}^5} \begin{cases} (3 - \mathfrak{z}_{\mathfrak{z}-4})^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}-4}, \mathfrak{z}_{\mathfrak{z}-3}], \\ (3 - \mathfrak{z}_{\mathfrak{z}-4})^7 - 8(3 - \mathfrak{z}_{\mathfrak{z}-3})^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}-3}, \mathfrak{z}_{\mathfrak{z}-2}], \\ (3 - \mathfrak{z}_{\mathfrak{z}-4})^7 - 8(3 - \mathfrak{z}_{\mathfrak{z}-3})^7 + 28(3 - \mathfrak{z}_{\mathfrak{z}-2})^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}-2}, \mathfrak{z}_{\mathfrak{z}-1}], \\ (3 - \mathfrak{z}_{\mathfrak{z}-4})^7 - 8(3 - \mathfrak{z}_{\mathfrak{z}-3})^7 + 28(3 - \mathfrak{z}_{\mathfrak{z}-2})^7 + 56(3 - \mathfrak{z}_{\mathfrak{z}-1})^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}-1}, \mathfrak{z}_{\mathfrak{z}}], \\ (3_{\mathfrak{z}+4} - 3)^7 - 8(3_{\mathfrak{z}+3} - 3)^7 + 28(3_{\mathfrak{z}+2} - 3)^7 + 56(3_{\mathfrak{z}+1} - 3)^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}}, \mathfrak{z}_{\mathfrak{z}+1}], \\ (3_{\mathfrak{z}+4} - 3)^7 - 8(3_{\mathfrak{z}+3} - 3)^7 + 28(3_{\mathfrak{z}+2} - 3)^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}+1}, \mathfrak{z}_{\mathfrak{z}+2}], \\ (3_{\mathfrak{z}+4} - 3)^7 - 8(3_{\mathfrak{z}+3} - 3)^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}+2}, \mathfrak{z}_{\mathfrak{z}+3}], \\ (3_{\mathfrak{z}+4} - 3)^7, & \mathfrak{z} \in [\mathfrak{z}_{\mathfrak{z}+3}, \mathfrak{z}_{\mathfrak{z}+4}], \\ 0, & \text{otherwise.} \end{cases} \quad (8)$$

$$\begin{cases} \mathfrak{F} \mathcal{G}' = \mathfrak{P}_1 - \mathfrak{P}_2 \mathcal{G} - \mathfrak{P}_3 \mathcal{G} \mathcal{Q}, \\ \mathfrak{F} \mathcal{S}' = \mathfrak{P}_3 \mathcal{G} \mathcal{Q} - \mathfrak{P}_4 \mathcal{S}, \\ \mathfrak{F} \mathcal{Q}' = \mathfrak{P}_5 \mathcal{S} - \mathfrak{P}_6 \mathcal{Q}, \end{cases} \quad (3)$$

Substituting third and the second equation of the system 3 into the first equation of the same equation yields,

$$\begin{aligned} & \mathfrak{F}^2 (\mathfrak{F} \mathcal{Q} \mathcal{Q}^{(3)} - \mathfrak{F} \mathcal{Q}' \mathcal{Q}'' + \mathfrak{P}_4 (\mathcal{Q} \mathcal{Q}'' - \mathcal{Q}'^2) + \mathfrak{P}_6 (\mathcal{Q} \mathcal{Q}' - \mathcal{Q}'^2)) \\ & + \mathfrak{P}_3 \mathcal{Q}^2 (\mathfrak{F} \mathcal{Q}' + \mathfrak{P}_6 \mathcal{Q}) + \mathfrak{F} (\mathfrak{F} \mathcal{Q}'' \\ & + \mathfrak{P}_6 \mathcal{Q}') + \mathfrak{P}_2 \mathcal{Q} (\mathfrak{F} \mathcal{Q}' + \mathfrak{P}_6 \mathcal{Q}) + \mathfrak{F} (\mathfrak{F} \mathcal{Q}' + \mathfrak{P}_6 \mathcal{Q}') \\ & - \mathfrak{P}_1 \mathfrak{P}_3 \mathfrak{P}_5 \mathcal{Q}^2 = 0. \end{aligned} \quad (4)$$

By fixing the value of death rate of the virus to equal zero, Eq. 4 transforms to be in the following formula

$$\begin{aligned} & \mathfrak{P}_3 \mathcal{Q}^2 (\mathfrak{F}^2 \mathcal{Q}'' + \mathfrak{F} \mathfrak{P}_4 \mathcal{Q}') + \mathfrak{P}_2 \mathcal{Q} (\mathfrak{F}^2 \mathcal{V}'' + c \mathfrak{P}_4 \mathcal{Q}') \\ & + c^2 (\mathfrak{F} \mathcal{Q} \mathcal{Q}^{(3)} - \mathfrak{F} \mathcal{Q}' \mathcal{V}'' + \mathfrak{P}_4 (\mathcal{V} \mathcal{V}'' - \mathcal{V}'^2)) - \mathfrak{P}_1 \mathfrak{P}_3 \mathfrak{P}_5 \mathcal{Q}^2 = 0. \end{aligned} \quad (5)$$

This study investigates the accuracy of the obtained analytical solutions of the fractional model of the human immunodeficiency virus (HIV-1) infection for CD4⁺ T-cells. This model has been frequently investigated to discover more novel properties of it [44–47]. However, it is the first time to check the accuracy of these studies via taking their obtained analytical solutions, then evaluating the numerical solutions of the model, and calculating the absolute value of error between the analytical and numerical solutions. The future works will be based on the same idea of all previous obtained solutions of the investigated model to show the most accurate solution of this model and to use it in the models of medical applications [47–49].

The other sections of this paper are organized, as follows: Section 2 applies the septic B-spline scheme [32,50] based on the obtained analytical solutions via the modified Khater, extended simplest equation, and sech-tanh expansion methods to the fractional ODE model of the HIV-1 infection of CD4⁺ T-cells to study the numerical solutions via various explicit solutions. Moreover, some sketches of the exact and numerical solutions of the system are presented to illustrate the accuracy of our obtained solutions. Section 4 is devoted to conclusion.

2. Application

This section applies the septic B-spline scheme to Eq. 5 to get the numerical solutions of the fractional model of the human immunodeficiency virus (HIV)-1 infection of CD4⁺ T-cells. This scheme gives the solution of Eq. 5 in the following formula

$$\mathcal{Q}(3) = \sum_{\mathfrak{z}=-1}^{\mathfrak{z}+1} \mathfrak{c}_{\mathfrak{z}} \mathcal{E}_{\mathfrak{z}}, \quad (6)$$

where $\mathfrak{c}_{\mathfrak{z}}$, $\mathcal{E}_{\mathfrak{z}}$ follow the next conditions, respectively:

$$\mathcal{E}_{\mathfrak{z}}(3) = \mathcal{F}(\mathfrak{F}_{\mathfrak{z}}, \mathfrak{B}(\mathfrak{z}_{\mathfrak{z}})) \text{ where } (\mathfrak{z} = 0, 1, \dots, \mathfrak{N}) \quad (7)$$

and

For $\mathfrak{z} \in [-3, \mathfrak{N} + 3]$, we get

$$\begin{aligned} \mathfrak{B}_{\mathfrak{z}}(3) = & \mathfrak{c}_{\mathfrak{z}-3} + 120 \mathfrak{c}_{\mathfrak{z}-2} + 1191 \mathfrak{c}_{\mathfrak{z}-1} + 2416 \mathfrak{c}_{\mathfrak{z}} + 1191 \mathfrak{c}_{\mathfrak{z}+1} \\ & + 120 \mathfrak{c}_{\mathfrak{z}+2} + \mathfrak{c}_{\mathfrak{z}+3}. \end{aligned} \quad (9)$$

Table 1

Exact, numerical, and absolute value of error of Eq. 5 with different values of β according to the obtained solutions via the modified Khater method and septic B-spline scheme.

Value of β	Exact	Numerical	Absolute error
0	-6	-6.00000124	1.2398E-06
0.0001	-5.9997	-5.99970064	6.398E-07
0.0002	-5.9994	-5.99940004	3.98E-08
0.0003	-5.9991	-5.99909944	5.602E-07
0.0004	-5.9988	-5.99879884	1.1602E-06
0.0005	-5.9985	-5.99849824	1.7602E-06
0.0006	-5.9982	-5.99819764	2.3602E-06
0.0007	-5.9979	-5.99789704	2.9602E-06
0.0008	-5.9976	-5.99759644	3.5602E-06
0.0009	-5.9973	-5.99729584	4.1602E-06
0.001	-5.997	-5.99699524	4.7602E-06

Table 2

Exact, numerical, and absolute value of error of Eq. 5 with different values of β according to the obtained solutions via the extended simplest equation method and septic B-spline scheme.

Value of β	Exact	Numerical	Absolute error
0	3	3.000000001	1.2456E-09
0.0001	2.9998	2.999900001	0.000100001
0.0002	2.9996	2.999800001	0.000200001
0.0003	2.9994	2.999700001	0.000300001
0.0004	2.9992	2.999600001	0.000400001
0.0005	2.999	2.999500001	0.000500001
0.0006	2.998800001	2.999400001	0.000600001
0.0007	2.998600001	2.999300001	0.0007
0.0008	2.998400001	2.999200001	0.0008
0.0009	2.998200002	2.999100001	0.0009
0.001	2.998000003	2.999000002	0.000999999

2.1. Modified khater method

The computational obtained solution of Eq. 5 in [51] via the modified Khater method is given by

$$\mathcal{Q}(\beta) = \frac{\sqrt{4\delta\varrho - \chi^2} \sqrt{\mathfrak{P}_3^2(\mathfrak{P}_4 - \mathfrak{P}_6)^2(\chi^2 - 4\delta\varrho)^2 + i\mathfrak{P}_3(\mathfrak{P}_4 - \mathfrak{P}_6)(\chi^2 - 4\delta\varrho)^{3/2} \tanh\left(\frac{1}{2}\beta\sqrt{\chi^2 - 4\delta\varrho}\right)}}{\mathfrak{P}_3^2(4\delta\varrho - \chi^2)^{3/2}}, \quad (10)$$

where $4\delta\varrho - \chi^2 < 0$. Substituting Eq. 9 with the exact solutions 10 into Eq. 5 gives $(\mathfrak{L} + 7)$ of equations. Resolving this system leads to the following values shown in Table 1.

2.2. Extended simplest equation method

The computational obtained solution of Eq. 5 in [51] via the extended simplest equation method is given by

$$\mathcal{Q}(\beta) = a_0 - \frac{a_{-1}\sqrt{-\alpha\mu} \tanh\left(3\sqrt{-\alpha\mu} + \frac{\log(\beta)}{2}\right)}{\alpha}, \quad (11)$$

where $\alpha\mu < 0$. Substituting Eq. 9 with the exact solutions 11 into Eq. 5 gives $(\mathfrak{L} + 7)$ of equations. Resolving this system leads to the following values shown in Table 2.

2.3. Sech-Tanh expansion method

The computational obtained solution of Eq. 5 in [51] via the sech-tanh expansion method is given by

$$\mathcal{Q}(\beta) = a_0 + b_1 \tanh(\beta). \quad (12)$$

Substituting Eq. 9 with the exact solutions 12 into Eq. 5 gives $(\mathfrak{L} + 7)$ of equations. Resolving this system leads to the following values shown in Table 3.

Table 3

Exact, numerical, and absolute value of error of Eq. 5 with different values of β according to the obtained solutions via sech-tanh expansion method and septic B-spline scheme.

Value of β	Exact	Numerical	Absolute error
0	2	2.000215	0.000215
0.0001	2.0004	2.000612846	0.000212847
0.0002	2.0008	2.001010693	0.000210693
0.0003	2.0012	2.001408539	0.00020854
0.0004	2.0016	2.001806386	0.000206386
0.0005	2.002	2.002204232	0.000204233
0.0006	2.0024	2.002602079	0.000202079
0.0007	2.0028	2.002999925	0.000199926
0.0008	2.003199999	2.003397771	0.000197772
0.0009	2.003599999	2.003795618	0.000195619
0.001	2.003999999	2.004193464	0.000193465

3. Results and discussion

This section explains and discusses more about our obtained numerical solutions of the fractional form of the HIV-1 infection of $CD4^+$ T-cells via the septic-B-spline scheme.

- Solving the biological model (the HIV-1 infection of $CD4^+$ T-cells fractional mathematical model with the effect of antiviral

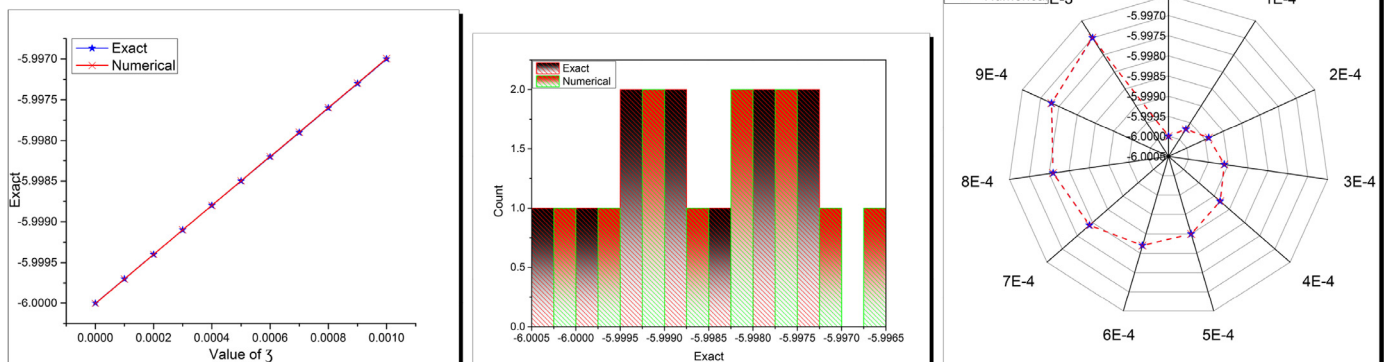


Fig. 1. Exact and numerical solutions of Eq. 5 according to the obtained solution via the modified Khater method and septic-B-spline scheme.

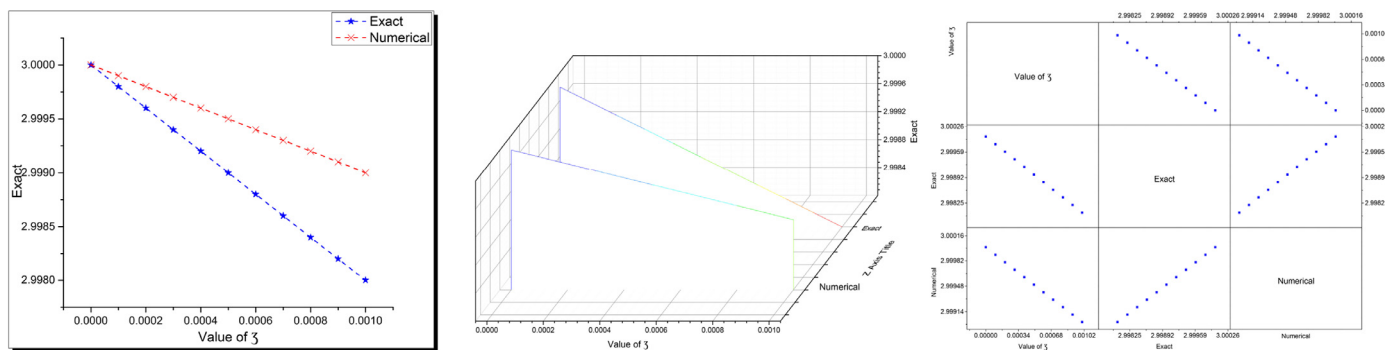


Fig. 2. Exact and numerical solutions of Eq. 5 according to the obtained solution via the extended simplest equation method and septic-B-spline scheme.

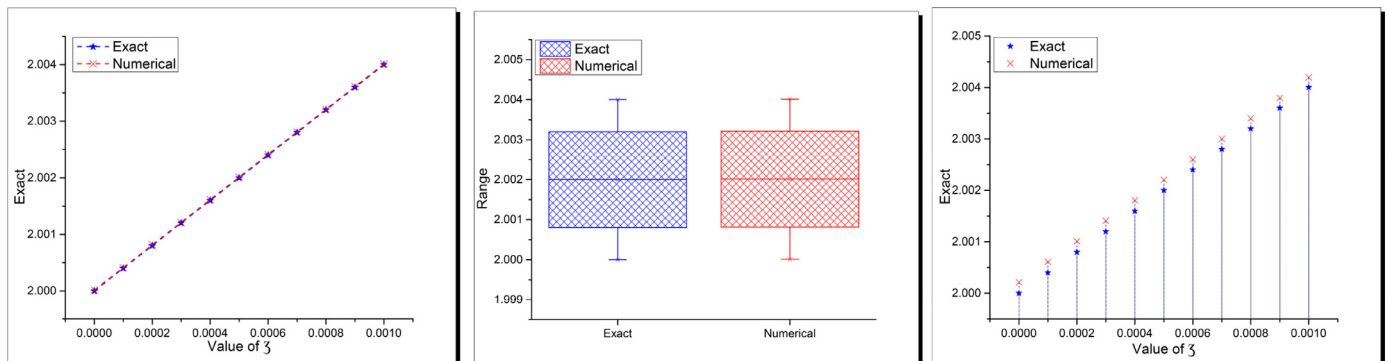


Fig. 3. Exact and numerical solutions of Eq. 5 according to the obtained solution via the sech-tanh expansion method and septic-B-spline scheme.

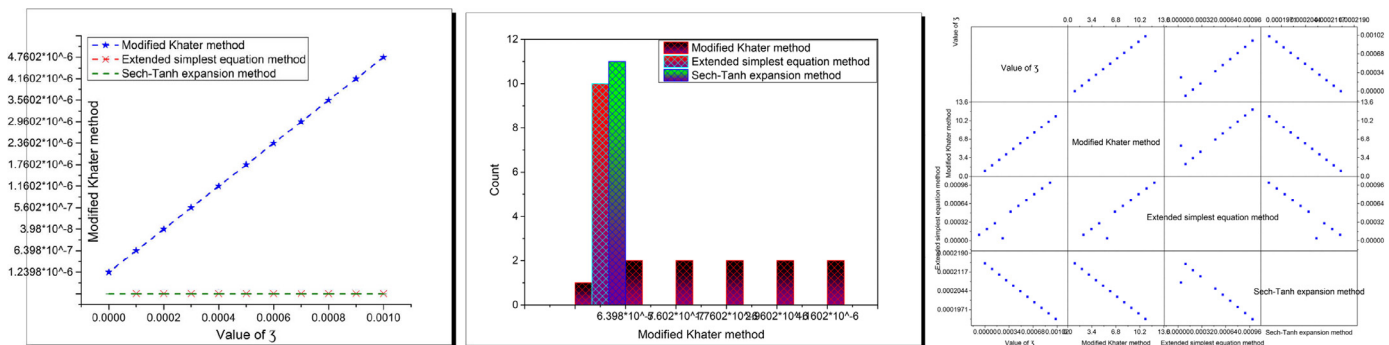


Fig. 4. Absolute error between exact and numerical solutions of Eq. 5 according to the obtained solution via the modified Khater method, the extended simplest equation method, and the sech-tanh expansion method via the septic-B-spline numerical scheme.

drug therapy) gives more explanations of the dynamical behavior of viruses.

- Solving the bio-mathematical model by applying three analytical schemes (the modified Khater method, the extended simplest equation method, the sech-tanh expansion method) gives more distinct types of solutions.
- Using the obtained analytical solutions to calculate the boundary and initial conditions then applying the septic-B-spline to the fractional equation with the evaluated conditions.
- The accuracy of obtained solutions is illustrated by calculating the absolute value of error between exact and numerical solutions.
- Comparison of the effectiveness of the adopted analytical schemes is shown in Fig. 4. It shows that the modified Khater method is more accurate than the extended simplest equation method and the sech-tanh expansion method.
- The septic B-spline is the only member of the B-spline family that can be applied to this kind of equation with the higher order derivative terms.

4. Conclusion

This paper has successfully applied the septic-B-spline scheme to the HIV-1 infection of $CD4^+$ T-cells fractional mathematical model with the effect of antiviral drug therapy. This numerical investigation has been based on three analytical applied schemes (the modified Khater method, the extended simplest equation method, and the sech-tanh expansion method) to evaluate the boundary and initial conditions. Also, the accuracy of the obtained numerical solutions has been illustrated and showed the power of the modified Khater method over the other two analytical used schemes. The obtained solutions show that the used technique can be applied to various forms of nonlinear partial differential equations. Performance of the suggested technique reveals that these methods are appropriate for applying to different formulas of nonlinear partial differential equations.

Credit Statement

Authors 1 & 2 discussed the research problem with Authors 4 & 5 first, and then approached Author 3 for his opinion. All the authors contributed in developing the main results of the paper. In fact, all authors contributed in each section of the paper, and read and approved the paper for submission.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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