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Fractional HCV infection model with adaptive immunity and treatment

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Fractional HCV infection model with adaptive immunity and treatment is suggested and studied in this paper. The adaptive immunity includes the CTL response and antibodies. This model contains five ordinary differential equations. We will start our study by proving the existence, uniqueness, and boundedness of the positive solutions. The model has free-equilibrium points and other endemic equilibria. By using Lyapunov functional and LaSalle's invariance principle, we have shown the global stability of these equilibrium points. Finally, some numerical simulations will be given to validate our theoretical results and show the effect of the fractional derivative order parameter and the other treatment parameters.

Keywords: *fractional order; HCV; cell-to-cell; virus-to-cell; global stability; numerical simulations.*

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1. Introduction

The hepatitis C virus (HCV) is one of the dangerous diseases that can result in severe liver damage [1]. Globally, 51 million are infected by HCV in the world, according to World Health Organization [2]. An infected individual can transmit the virus to someone else through blood-to-blood contact. Nowadays, sharing some specific items or injecting drugs are how most people contract the hepatitis C virus.

Mathematical modeling is an effective tool for understanding the transmission mechanism of most infectious diseases, it permits to give solutions to fight or minimize the side effects of these diseases and also to imagine possible scenarios and health directions [3]. As most biological reactions contain memory, therefore the normal derivative is not sufficient to better describe the transmission dynamics of infectious diseases because this type of derivative does not take into account the memory effect. So, there is another type of derivative called the fractional derivative which takes into consideration this effect [4]. Many works use this derivative to describe the dynamic of transmission of infectious diseases [5–20]. Recently, in [21] suggest a fractional viral epidemic model with antibodies and a cytotoxic T-lymphocyte response as follows:

$$\begin{cases} D^{\alpha}X = \Lambda - \mu_1 x - \dfrac{\alpha_1(1-\varepsilon_{rt})XV}{1+mX+nV}, \\ D^{\alpha}Y = \dfrac{\alpha_2(1-\varepsilon_{rt})XV}{1+mX+nV} - \mu_2 y - \sigma_1 YZ, \\ D^{\alpha}V = \sigma_2(1-\varepsilon_{pi})Y - \mu_3 V - \gamma_1 VW, \\ D^{\alpha}W = \gamma_2 VW - \mu_4 W, \\ D^{\alpha}Z = \sigma_3 YZ - \mu_5 Z, \end{cases}$$

D^{α} means the fractional derivative order where $0 < \alpha \leqslant 1$. The variable X, Y, V, W, and Z design respectively the susceptible cells, the infected cells, the free viruses, the antibodies and cytotoxic T-lymphocyte (CTL) response. Λ means the reproduction rate of susceptible cells, the ratio $\frac{\alpha_1(1-\varepsilon_{rt})XV}{1+mX+nV}$

is the infection function of susceptible cells by a free virus, with m and n two positive constants. The infected particles are killed at $\sigma_1 YZ$, the free viruses are produced at the rate $\sigma_2(1-\varepsilon_{pi})Y$. The Antibodies kill the viruses at the rate $\gamma_1 VW$ and are produced at the rate $\gamma_2 VW$. The CTL grow at rate $\sigma_3 YZ$. The mortality rate of the variables X, Y, V, W, and Z are respectively $\mu_1 X$, $\mu_2 Y$, $\mu_3 V$, $\mu_4 W$, and $\mu_5 Z$. The efficacy of the drugs, reverse transcriptase and protease inhibitors are represented by ε_{pi} and ε_{rt}, where $0 < \varepsilon_{rt}, \varepsilon_{pi} < 1$. The authors have proved the stability of equilibrium points. The disadvantage of this latest model and other models [22–30] they study the dynamic of infections by using only one mode of infection (virus-to-cell) but the hepatits C can transmitted by two within-host modes the first one is called virus-to-cell that is to say that the infection transmits virus to the cell and the second stand is cell-to-cell this means that the infection transmits cell to the cell [31–37]. Recently, Yaagoub and Allali in [38] suggest a HBV model with cell-to-cell and virus-to-cell transmissions and adaptive immunity, they gave the different theorems of existence and well-posedness of all solutions; and also demonstrated the global stability of steady states and they finished their work by giving some numerical simulations.

When the infection by the hepatitis C virus becomes chronic, the treatment is necessary to eliminate the disease or to combat further complications. There is a group of treatment forms recommended by World Health Organization, it depends on the patient's age and also his health situation [2]. Many mathematical models take into consideration the treatment or quarantine to describe the dynamics of some diseases [39–41]. In this work, we suggest the following HCV fractional model with two modes of transmission virus-to-cell and cell-to-cell in which we take into account the treatment of HCV:

$$\begin{cases} D^{\alpha}x = \Lambda - \alpha_1(1-u_1)xv - \alpha_2(1-u_2)xy - \mu_1 x, \\ D^{\alpha}y = \alpha_1(1-u_1)xv + \alpha_2(1-u_2)xy - \sigma_1 yz - \mu_2 y, \\ D^{\alpha}v = \sigma_2 y - \gamma_1 vw - \mu_3 v, \\ D^{\alpha}w = \gamma_2 vw - \mu_4 w, \\ D^{\alpha}z = \sigma_3 yz - \mu_5 z. \end{cases} \tag{1}$$

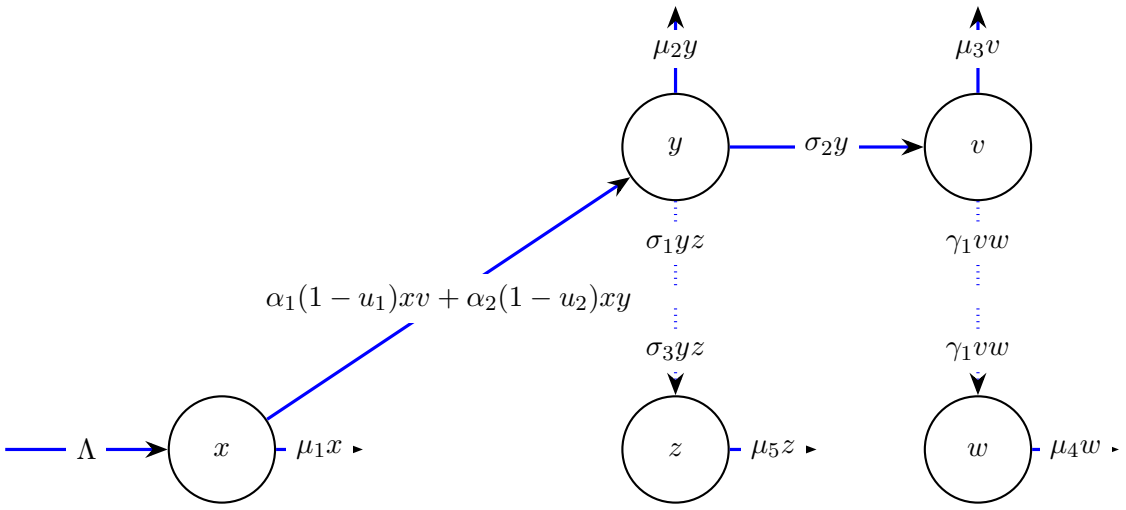

Fig. 1. The diagram of fractional HCV infection model.

In this model, all the parameters are defined in the previous paragraph and are displayed in the diagram represented in Figure 1. Finally, we would like to mention that the fractional derivative models have shown their great importance not only in biological systems but also in many other fields [42–44].

This paper consists of the following five sections. In Section 2, some definitions and properties of fractional derivatives were given. In Section 3, the existence, positivity and boundedness of solutions of system (1) were established. In Section 4, we will give the different theorems of the global stability concerning the equilibrium points. Numerical simulation and some discussions are given in Section 5, while the last section concludes the work.

2. Preliminary results

Now we give some results of fractional order derivative which will help us to properly analyze our model (1) later

Definition 1 (Ref. [45]). *The fractional integral of order $\alpha > 0$ of function $G\colon \mathbb{R}_+ \longrightarrow \mathbb{R}$ is defined by*

$$I^{\alpha}G(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} G(s)\, ds,$$

where $\Gamma(z) = \int_0^{\infty} e^{-t} t^{z-t} dt$.

Definition 2 (Ref. [46])). *The Mittag–Leffler function of parameter $\alpha > 0$, noted by E_α is defined as*

$$E_{\alpha}(t) = \sum_{i=0}^{+\infty} \frac{t^i}{\Gamma(\alpha i + 1)}.$$

Let $L\colon \mathbb{R}^n \to \mathbb{R}^n$, where $n \geqslant 1$. We consider the following fractional order system given by

$$D^{\alpha}Y(t) = L(Y), \tag{2}$$

with $Y(0) = Y_0$, $Y_0 \in \mathbb{R}^n$ and $0 < \alpha \leqslant 1$. To prove the uniqueness of solutions of system (2), we give the following proposition.

Proposition 1. If the function L satisfies the two following conditions

1) $L(Y)$ and $\frac{\partial L}{\partial Y}(Y)$ are continuous on $\mathbb{R}^n$;
2) $\|L(Y)\| \leqslant T_1 + T_2\|Y\|$ for all $Y \in \mathbb{R}^n$, with T_1 and T_2 are two positive constants.

Then, the system (2) has a unique solution defined on $\mathbb{R}^n_+$.

Lemma 1 (LaSalle's invariance principle). *Let $\mathbb{C}$ be a compact set of $\mathbb{R}^n_+$. Every solution of the system (2), starting from a point in $\mathbb{C}$ and remains in $\mathbb{C}$ for all t, if there exists a C^1 function $V(x)$ defined over $\mathbb{C}$ satisfies the following condition*

$$D^{\alpha}V \leqslant 0.$$

Let E be the set of all points in $\mathbb{C}$, where $D^{\alpha}V = 0$, and M be the largest invariant set in E. Then, every solution $Y(t)$ starting in $\mathbb{C}$ approaches M as $t \to \infty$.

3. Uniqueness, positivity, and boundedness of solutions

In order to analyze our proposed model (1), we will give the different theorems of existence, uniqueness, and well-posedness of all model solutions.

Theorem 1. *The model (1) has a positive and bounded solution for any initial positive condition.*

Proof. From the different components of the system (1), we have

$$\begin{cases} D^{\alpha}x|_{x=0} = \Lambda > 0, \\ D^{\alpha}y|_{y=0} = \alpha_1(1-u_1)xv \geqslant 0, \\ D^{\alpha}v|_{v=0} = \sigma_1 y \geqslant 0, \\ D^{\alpha}w|_{w=0} = 0 \geqslant 0, \\ D^{\alpha}z|_{z=0} = 0 \geqslant 0. \end{cases}$$

So, the solutions of the system (1) remain positive. For the boundedness of this solution, let the total population

$$\mathcal{N} = x + y + \frac{\mu_2}{2\sigma_2}v + \frac{\mu_2\gamma_1}{2\gamma_2\sigma_2}w + \frac{\sigma_1}{\sigma_3}z.$$

By adding all the equations in system (1), we will have

$$\begin{aligned} D^{\alpha}\mathcal{N} &\leqslant \Lambda - \mu_1 x - \frac{\mu_2}{2} y - \frac{\mu_2\mu_3}{2\sigma_2} v - \frac{\mu_2\gamma_1\mu_4}{2\gamma_2\sigma_2} w - \frac{\sigma_1\mu_5}{\sigma_3} z \\ &\leqslant \Lambda - \theta\mathcal{N}, \end{aligned}$$

with $\theta = \min\left\{\mu_1, \frac{\mu_2}{2}, \mu_3, \mu_4, \mu_5\right\}$. Therefore,

$$\mathcal{N} \leqslant \left(\frac{-\Lambda}{\theta} + \mathcal{N}(0)\right) E_{\alpha}(-\theta t^{\alpha}) + \frac{\Lambda}{\theta},$$

here $E_{\alpha}(\cdot)$ is Mittag–Leffler function.

So, $H := \{x + y + \frac{\mu_2}{2\sigma_2} v + \frac{\mu_2\gamma_1}{2\gamma_2\sigma_2} w + \frac{\sigma_1}{\sigma_3} z \leqslant \frac{\Lambda}{\theta}\}$ is positively invariant for the system (1).

So, all solutions are positive and bounded. ∎

Theorem 2. *For any positive initial condition in H, the system (1) has a unique solution.*

Proof. We can rewrite the system (1) as follow

$$D^{\alpha}Y(t) = L(t, Y(t)),$$

with

$$Y(0) = (x(0), y(0), v(0), w(0), z(0))$$

and

$$L(t, Y(t)) = \begin{pmatrix} \Lambda - \alpha_1(1-u_1)xv - \alpha_2(1-u_2)xy - \mu_1 x \\ \alpha_1(1-u_1)xv + \alpha_2(1-u_2)xy - \sigma_1 yz - \mu_2 y \\ \sigma_2 y - \gamma_1 vw - \mu_3 v \\ \gamma_2 vw - \mu_4 w \\ \sigma_3 yz - \mu_5 z \end{pmatrix}.$$

The function L satisfies the first condition of the Theorem 1. For the condition 2 of this theorem, after some calculation, we have

$$\|L(t, X(t))\| \leqslant \Lambda + \xi\|Y(t)\|, \tag{3}$$

where $\xi = \max\left\{\mu_2, \mu_1, \alpha_1(1-u_1), \alpha_2(1-u_2), \sigma_1, \sigma_2\gamma_1, \mu_4, \gamma_2, \sigma_3, \frac{\sigma_1\Lambda}{\mu_1}, \frac{q\gamma}{\mu_1}, \frac{\gamma_2\Lambda}{\mu_1}, \frac{\sigma_3\Lambda}{\mu}\right\}$.

Therefore, L satisfies two conditions of the Theorem 1. Therefore, the model (1) has a unique solution. ∎

4. Global stability of equilibria

In this section, we will show that the model (1) has one free-equilibrium point and four endemic equilibria. Some results of global stability will be given in this section by using some Lyapunov functional as in [45] and using LaSalle's invariant principle as given in Lemma 1.

4.1. The basic reproduction number

The basic reproduction number R_0 is defined biologically as the number of newly infected individuals generated by one typical infected individual in a population constituted only by susceptible persons. Mathematically this number is defined as the spectral radius of the next generation matrix FV^{-1} with F designs the matrix of new infections and V is the transfer matrix of infected individuals. Let

$$F = \begin{pmatrix} \alpha_1(1-u_1) & \alpha_2(1-u_2) \\ 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \mu_2 & 0 \\ -\sigma_2 & \mu_3 \end{pmatrix}.$$

So,

$$FV^{-1} = \begin{pmatrix} \frac{\alpha_2(1-u_2)\mu_3+\alpha_1(1-u_1)\sigma_2}{\mu_2\mu_3} & \frac{\alpha_1(1-u_1)}{\mu_3} \\ 0 & 0 \end{pmatrix}.$$

Then,

$$R_0 = \frac{\alpha_2(1-u_2)\mu_3 + \alpha_1(1-u_1)\sigma_2}{\mu_2\mu_3}.$$

4.2. Equilibrium points

The system (1) has a free-equilibrium point other four steady states are given as follows

1. The disease-free equilibrium: $E_1 = \left(\frac{\Lambda}{\mu_1}, 0, 0, 0, 0\right)$.
2. If $R_0 > 1$, then there exists an equilibrium point without immune: $E_1 = (x_1, y_1, v_1, 0, 0)$,
$$x_1 = \frac{-B_1 + \sqrt{B_1^2 + 4A_1C_1}}{2A_1}, \quad y_1 = \frac{\Lambda - \mu_1 x_1}{\mu_2}, \quad v_1 = \frac{\sigma_2}{\mu_3} y_1.$$
Here, $A_1 = \frac{\alpha_1(1-u_1)\mu_1\sigma_2}{\mu_3\mu_2} + \frac{\alpha_2(1-u_2)\mu_1}{\mu_2}$, $B_1 = \frac{-\alpha_1(1-u_1)\Lambda\sigma_2}{\mu_3\mu_2} - \frac{\alpha_2(1-u_2)\Lambda}{\mu_2} - \mu_1$, and $C = \Lambda$.
3. The endemic equilibrium point with CTL response: $E_2 = (x_2, y_2, v_2, 0, z_2)$, where
$$x_2 = \frac{\Lambda\mu_3}{\alpha_1(1-u_1)\sigma_2 + \mu_3(\alpha_2(1-u_2)+\mu_1)}, \quad y_2 = \frac{\mu_5}{\sigma_3}, \quad v_2 = \frac{\sigma_2}{\mu_3} y_2, \quad z_2 = \frac{\Lambda - \mu_1 x_2 - \mu_2 y_2}{\sigma_1 y_2}.$$
4. The endemic equilibrium point with antibodies response: $E_3 = (x_3, y_3, v_3, w_3, 0)$, where
$$x_3 = \frac{-B_3 + \sqrt{B_3^2 + 4A_3C_3}}{2A_3}, \quad y_3 = \frac{\Lambda - \mu_1 x_3}{\mu_2}, \quad v_3 = \frac{\mu_4}{\gamma_2}, \quad w_3 = \frac{\sigma_2 y_3 - \mu_3 v_3}{\gamma_1 v_3}.$$
Here, $A_3 = \frac{\alpha_2(1-u_2)\mu_1}{\mu_2}$, $B_3 = \mu_1 - \frac{\alpha_2(1-u_2)\Lambda}{\mu_2}$, and $C_3 = \Lambda$.
5. The endemic equilibrium point with CTL response and antibodies response: $E_4 = (x_4, y_4, v_4, w_4, z_4)$, where
$$x_4 = \frac{\sigma_3\Lambda\gamma_2}{\alpha_1(1-u_1)\sigma_3\mu_4 + \alpha_2(1-u_2)\gamma_2\mu_2 + \mu_1\gamma_2\sigma_3}, \quad y_4 = \frac{\mu_2}{\sigma_3},$$
$$v_4 = \frac{\mu_4}{\gamma_2}, \quad w_4 = \frac{\sigma_2 y_4 - \mu_3 v_4}{\gamma_1 v_4}, \quad z_4 = \frac{\Lambda - \mu_1 x_4 - \mu_2 y_4}{\sigma_1 y_4}.$$

To show the existence of these equilibria. Let the following numbers:

$$R^{CTLs} = \frac{\sigma_3 y_1}{\mu_5}, \quad R^W = \frac{\gamma_2 v_1}{\mu_4}, \quad R_1^{CTLs,W} = \frac{\gamma_2 v_2}{\mu_4}, \quad R_2^{CTLs,W} = \frac{\sigma_3 y_3}{\mu_5}.$$

With R^{CTLs} means the reproductive number of CTL immune, biologically is the number of CTL cells triggered by contaminated cells when the infection is successful and when the immune response is absent. R^W the reproductive number of humoral immune design the number of CTL cells triggered by the virus the infection is successful and when the immune response is absent. $R_1^{CTLs,W}$ the competitive number of humoral, means the number of antibodies triggered by the virus when the CTL and the immune response exist, and $R_2^{CTLs,W}$ the competitive number of CTL immune, design biologically the number of CTL cells activated by infected cells when CTL immune exist. Now, we show the existence conditions of equilibrium points. For E_0 and E_1 always exist. For E_2 exist when $\Lambda - \mu_1 x_2 - \mu_2 y_2$ positive, which mean $R^{CTLs} > 1$. For E_3 exist when $\sigma_2 y_3 - \mu_3 v_3 > 0$, which means $R^W > 1$. In another way, $w_3 = \frac{\mu_3}{\gamma_1}\left(R^{CTLs} R_1^{CTLs,W} - 1\right)$. Finally, this equilibrium point exists for $R^W > 1$, $R_1^{CTLs,W} > 1$, and $R_2^{CTLs,W} > 1$. For E_4 exist when $w_4 > 0$ and $z_4 > 0$, this means

$$w_4 = \frac{\sigma_2 y_4 - \mu_3 v_4}{\gamma_1 v_4} = \frac{\mu_3}{\gamma_1}\left(R_1^{CTLs,W} - 1\right)$$

and

$$z_4 = \frac{\Lambda - \mu_1 x_4 - \mu_2 y_4}{\sigma_1 y_4} = \frac{\mu_2}{\sigma_1}\left(R_2^{CTLs,W} - 1\right).$$

Then, E_4 exist only for $R_1^{CTLs,W} > 1$ and $R_2^{CTLs,W} > 1$.

4.3. Global stability of steady states

In this subsection, we will give some results of the global stability of the steady states.

Theorem 3. *If $R_0 \leqslant 1$, the disease-free E_0 equilibrium is globally asymptotically stable.*

Proof. Let the following Lyapunov function L_0

$$L_0 = y + \frac{\alpha_1(1-u_1)}{\mu_3}v + \frac{\sigma_1}{\sigma_3}z.$$

The α derivative of L_0 is given by

$$\begin{aligned} D^\alpha L_0 &\leqslant \alpha_1(1-u_1)xv + \alpha_2(1-u_2)xy - \sigma_1 yz - \mu_2 y + \frac{\alpha_1(1-u_1)\sigma_2}{\mu_3}y - \frac{\alpha_1(1-u_1)\gamma_1}{\mu_3}vw \\ &\quad - \alpha_1(1-u_1)v + \sigma_1 yz - \frac{\sigma_1\mu_5}{\sigma_3}z \\ &\leqslant \alpha_1(1-u_1)v(x-1) + \mu_2 y\left(\frac{\alpha_1(1-u_1)}{\mu_2\mu_3} + \frac{\alpha_2(1-u_2)x}{\mu_2} - 1\right) \\ &\leqslant \alpha_1(1-u_1)v(x-1) + \mu_2 y\left(R_0 - 1\right). \end{aligned}$$

Then, when $\alpha_1(1-u_1)v(x-1) \leqslant 1$, and if $R_0 < 1$, we will have $D^\alpha L_0 \leqslant 1$. Let $P_0 = \{(x,y,v,w,z)|D^\alpha L_0 = 0\}$, then the largest positivity invariant set of P_0 is the singleton E_0. Therefore, from the Lemma 1 we can deduce that the equilibrium point E_0 is globally asymptotically stable. ■

For the global stability of the equilibrium point E_1, we assume the following conditions

$$\left(\frac{v}{v_1} - \frac{x_1}{x}\right)\left(1 - \frac{v_1}{v}\right) \leqslant 0, \quad \forall x,\, v \geqslant 0 \tag{H_1}$$

and

$$\left(\frac{y}{y_1} - \frac{x_1}{x}\right)\left(1 - \frac{y_1}{y}\right) \leqslant 0, \quad \forall x,\, y \geqslant 0. \tag{H_2}$$

Theorem 4. *If $R_0 > 1$, $R^{CTLs} < 1$, and $R^W < 1$, then the equilibrium point E_1 is globally asymptotically stable.*

Proof. Let the following Lyapunov function L_1

$$L_1 = x_1\left(\frac{x}{x_1} - \ln\frac{x}{x_1} - 1\right) + y_1\left(\frac{y}{y_1} - \ln\frac{y}{y_1} - 1\right) + \frac{\mu_2}{\sigma_2}v_1x_1\left(\frac{v}{v_1} - \ln\frac{v}{v_1} - 1\right) + \frac{\sigma_1}{\sigma_3}z + \frac{\mu_2\gamma_1}{\gamma_2\sigma_2}w.$$

The α derivative of L_1 is given by

$$\begin{aligned} D^\alpha L_1 &\leqslant \left(1 - \frac{x_1}{x}\right)D^\alpha x + \left(1 - \frac{y_1}{y}\right)D^\alpha y + \frac{\mu_2}{\sigma_2}\left(1 - \frac{v_1}{v}\right)D^\alpha v + \frac{\sigma_1}{\sigma_3}D^\alpha z + \frac{\mu_2\gamma_1}{\gamma_2\sigma_2}D^\alpha w \\ &\leqslant \Lambda - \mu_1 x - \frac{x_1}{x}\Lambda + \mu_1 x_1 + \alpha_1(1-u_1)x_1v + \alpha_2(1-u_2)x_1y - \alpha_1(1-u_1)xv\frac{y_1}{y} \\ &\quad - \alpha_2(1-u_2)xy\frac{y_1}{y} + \mu_2 y_1 + \sigma_1 y_1 z - \frac{\mu_2\mu_3}{\sigma_2}v - \mu_2 y\frac{v_1}{v}\frac{\mu_2\mu_3}{\sigma_2}v_1 - \frac{\sigma_1\mu_5}{\sigma_3}z + \frac{\mu_2\gamma_1v_1}{\sigma_2}w - \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w. \end{aligned}$$

As

$$\begin{cases} \Lambda = \mu_1 x_1 + \alpha_1(1-u_1)x_1v_1 + \alpha_2(1-u_2)x_1y_1 = \mu_1 x_1 + \mu_2 y_1, \\ \dfrac{y_1}{v_1} = \dfrac{\mu_3}{\sigma_2}. \end{cases}$$

Therefore,

$$\begin{aligned}D^{\alpha}L_1 \leqslant{}& \mu_1 x_1\left(2-\frac{x_1}{x}-\frac{x}{x_1}-1\right)+\alpha_1(1-u_1)x_1v_1\left(4-\frac{xvy_1}{x_1v_1y}-\frac{yv_1}{y_1v}-\frac{v}{v_1}-\frac{x_1v_1}{xv}\right)\\&+\alpha_2(1-u_2)x_1y_1\left(4-\frac{x}{x_1}-\frac{yv_1}{y_1v}-\frac{v}{v_1}-\frac{x_1y_1}{xy}\right)+\alpha_1(1-u_1)x_1v_1\left(\frac{v}{v_1}-\frac{x_1}{x}\right)\left(1-\frac{v_1}{v}\right)\\&+\alpha_2(1-u_2)x_1y_1\left(\frac{y}{y_1}-\frac{x_1}{x}\right)\left(1-\frac{y_1}{y}\right)+\frac{\sigma_1\sigma_3}{\mu_5}\left(R^{CTLs}-1\right)+\frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}\left(R^{W}-1\right).\end{aligned}$$

As E_1 satisfies the both conditions (H_1) and (H_2), we have

$$\left(\frac{v}{v_1}-\frac{x_1}{x}\right)\left(1-\frac{v_1}{v}\right)\leqslant 0$$

and

$$\left(\frac{y}{y_1}-\frac{x_1}{x}\right)\left(1-\frac{y_1}{y}\right)\leqslant 0.$$

As the arithmetic mean is greater than or equal to the geometric mean, we will have

$$2-\frac{x_1}{x}-\frac{x}{x_1}\leqslant 0,$$

$$4-\frac{xvy_1}{x_1v_1y}-\frac{yv_1}{y_1v}-\frac{v}{v_1}-\frac{x_1v_1}{xv}\leqslant 0,$$

and

$$4-\frac{x}{x_1}-\frac{yv_1}{y_1v}-\frac{v}{v_1}-\frac{x_1y_1}{xy}\leqslant 0.$$

Then, if $R^{CTLs}\leqslant 1$ and $R^{W}\leqslant 1$, we will have $D^{\alpha}L_1\leqslant 0$. Let $P_1=\{(x,y,v,w,z)\,|\,D^{\alpha}L_1=0\}$, then the largest positivity invariant set of P_1 is the singleton E_1. Therefore, from the Lemma 1 we can deduce that the equilibrium point E_1 is globally asymptotically stable. ■

For the global stability of the equilibrium point E_2, we assume the following conditions

$$\left(\frac{v}{v_2}-\frac{x_2}{x}\right)\left(1-\frac{v_2}{v}\right)\leqslant 0,\quad \forall x,\, v\geqslant 0, \tag{H_3}$$

$$\left(\frac{y}{y_2}-\frac{x_2}{x}\right)\left(1-\frac{y_2}{y}\right)\leqslant 0,\quad \forall x,\, y\geqslant 0, \tag{H_4}$$

and

$$\left(\frac{v}{v_2}-\frac{y}{y_2}\right)\left(1-\frac{v_2}{v}\right)\leqslant 0,\quad \forall x,\, y\geqslant 0. \tag{H_5}$$

Theorem 5. *If $R^{CTLs}>1$ and $R_1^{CTLs,W}<1$, then the equilibrium point E_2 is globally asymptotically stable.*

Proof. Let the following Lyapunov function L_2

$$\begin{aligned}L_2 ={}& x_2\left(\frac{x}{x_2}-\ln\frac{x}{x_2}-1\right)+y_2\left(\frac{y}{y_2}-\ln\frac{y}{y_2}-1\right)+\frac{\mu_2}{\sigma_2}v_2\left(\frac{v}{v_2}-\ln\frac{v}{v_2}-1\right)\\&+\frac{\sigma_1}{\sigma_3}z_2\left(\frac{z}{z_2}-\ln\frac{z}{z_2}-1\right)+\frac{\mu_2\gamma_1}{\gamma_2\sigma_2}w.\end{aligned}$$

The α derivative of L_2 is given by

$$\begin{aligned}D^{\alpha}L_2 \leqslant{}& \left(1-\frac{x_2}{x}\right)D^{\alpha}x+\left(1-\frac{y_2}{y}\right)D^{\alpha}y+\frac{\mu_2}{\sigma_2}\left(1-\frac{v_2}{v}\right)D^{\alpha}v+\frac{\sigma_1}{\sigma_3}D^{\alpha}z+\frac{\mu_2\gamma_1}{\gamma_2\sigma_2}D^{\alpha}w\\\leqslant{}&\Lambda-\mu_1x-\frac{x_2}{x}\Lambda+\mu_1x_2+\alpha_1(1-u_1)x_2v+\alpha_2(1-u_2)x_2y-\alpha_1(1-u_1)xv\frac{y_2}{y}-\alpha_2(1-u_2)xy\frac{y_2}{y}\\&+\mu_2y_2+\sigma_1y_2z-\frac{\mu_2\mu_3}{\sigma_2}v-\mu_2y\frac{v_2}{v}+\frac{\mu_2\mu_3}{\sigma_2}v_2-\frac{\sigma_1\mu_5}{\sigma_3}z+\frac{\mu_2\gamma_1v_2}{\sigma_2}w-\frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w-\sigma_1yz_2+\frac{\sigma_1\mu_5}{\sigma_3}z_2.\end{aligned}$$

As

$$\begin{cases} \Lambda = \mu_1 x_2 + \alpha_1(1-u_1)x_2v_2 + \alpha_2(1-u_2)x_2y_2 = \mu_1 x_2 + \mu_2 y_2 + \sigma_1 y_2 z_2, \\ v_2 = \dfrac{\sigma_2\mu_5}{\mu_3\sigma_3}. \end{cases}$$

Therefore,

$$\begin{aligned} D^\alpha L_2 &\leqslant \mu_1 x_2\left(2 - \frac{x_2}{x} - \frac{x}{x_2}\right) + \alpha_1(1-u_1)x_2v_2\left(4 - \frac{xvy_2}{x_2v_2y} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{x_2v_2}{xv}\right) \\ &+ \alpha_1(1-u_1)x_2v_2\left(-1 - \frac{x_2}{x} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{x_2y_2}{xy}\right) + \alpha_2(1-u_2)x_2y_2\left(4 - \frac{x}{x_2} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{xy_2}{xy}\right) \\ &+ \alpha_2(1-u_2)x_2y_2\left(-1 - \frac{x_2}{x} + \frac{y}{y_2} + \frac{x_2y_2}{xy}\right) + \sigma_1 y_2 z_2\left(-1 - \frac{y}{y_2} + \frac{yv_2}{y_2v} + \frac{v}{v_2}\right) + \frac{\mu_2\gamma_1}{\sigma_2}w\left(v_2 - \frac{\mu_4}{\gamma_2}\right) \\ &\leqslant \mu_1 x_2\left(2 - \frac{x_2}{x} - \frac{x}{x_2}\right) + \alpha_1(1-u_1)x_2v_2\left(4 - \frac{xvy_2}{x_2v_2y} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{x_2v_2}{xv}\right) \\ &+ \alpha_2(1-u_2)x_2y_2\left(4 - \frac{x}{x_2} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{xy_2}{xy}\right) + \alpha_1(1-u_1)x_2v_2\left(\frac{v}{v_2} - \frac{x_2}{x}\right)\left(1 - \frac{v_2}{v}\right) \\ &+ \alpha_2(1-u_2)x_2y_2\left(\frac{y}{y_2} - \frac{x_2}{x}\right)\left(1 - \frac{y_2}{y}\right) + \sigma_1 y_2 z_2\left(\frac{v}{v_2} - \frac{y}{y_2}\right)\left(1 - \frac{v_2}{v}\right) + \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}\left(R_1^{CTLs,W} - 1\right). \end{aligned}$$

As E_2 satisfies the conditions (H_3), (H_4), and (H_5), then

$$\left(\frac{v}{v_2} - \frac{x_2}{x}\right)\left(1 - \frac{v_2}{v}\right) \leqslant 0,$$

$$\left(\frac{y}{y_2} - \frac{x_2}{x}\right)\left(1 - \frac{y_2}{y}\right) \leqslant 0,$$

and

$$\left(\frac{v}{v_2} - \frac{y}{y_2}\right)\left(1 - \frac{v_2}{v}\right) \leqslant 0.$$

As the arithmetic mean is greater than or equal to the geometric mean, we will have

$$2 - \frac{x_2}{x} - \frac{x}{x_2} \leqslant 0,$$

$$4 - \frac{xvy_2}{x_2v_2y} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{x_2v_2}{xv} \leqslant 0,$$

and

$$4 - \frac{x}{x_2} - \frac{yv_2}{y_2v} - \frac{v}{v_2} - \frac{x_2y_2}{xy} \leqslant 0.$$

Then, if $R_1^{CTLs,W} \leqslant 1$, we will have $D^\alpha L_2 \leqslant 0$. Let $P_2 = \{(x, y, v, w, z) \,|\, D^\alpha L_2 = 0\}$, then the largest positivity invariant set of P_2 is the singleton E_2. Therefore, from the Lemma 1 we can deduce that the equilibrium point E_2 is globally asymptotically stable. ∎

For the global stability of the equilibrium point E_3, we assume the following conditions

$$\left(\frac{v}{v_3} - \frac{x_3}{x}\right)\left(1 - \frac{v_3}{v}\right) \leqslant 0, \quad \forall x,\, v \geqslant 0 \tag{H_6}$$

and

$$\left(\frac{y}{y_3} - \frac{x_3}{x}\right)\left(1 - \frac{y_3}{y}\right) \leqslant 0, \quad \forall x,\, y \geqslant 0. \tag{H_7}$$

Theorem 6. *If $R^W > 1$, $R_2^{CTLs,W} < 1$ and $R^W > \frac{1}{R_2^{CTLs,W}}$, then the equilibrium point E_3 is globally asymptotically stable.*

Proof. Let the following Lyapunov function L_3

$$L_3 = x_3\left(\frac{x}{x_3} - \ln\frac{x}{x_3} - 1\right) + y_3\left(\frac{y}{y_3} - \ln\frac{y}{y_3} - 1\right) + \frac{\mu_2}{\sigma_2}v_3\left(\frac{v}{v_3} - \ln\frac{v}{v_3} - 1\right) + \frac{\sigma_1}{\sigma_3}z + \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}\left(\frac{w}{w_3} - \ln\frac{w}{w_3} - 1\right).$$

The α derivative of L_3 is given by

$$\begin{aligned} D^\alpha L_3 &\leqslant \left(1 - \frac{x_3}{x}\right)D^\alpha x + \left(1 - \frac{y_3}{y}\right)D^\alpha y + \frac{\mu_2}{\sigma_2}\left(1 - \frac{v_3}{v}\right)D^\alpha v + \frac{\sigma_1}{\sigma_3}D^\alpha z + \frac{\mu_2\gamma_1}{\gamma_2\sigma_2}\left(1 - \frac{w_3}{v}\right)D^\alpha w \\ &\leqslant \Lambda - \mu_1 x - \frac{x_3}{x}\Lambda + \mu_1 x_3 + \alpha_1(1-u_1)x_3 v + \alpha_2(1-u_2)x_3 y - \alpha_1(1-u_1)xv\frac{y_3}{y} \\ &\quad - \alpha_2(1-u_2)xy\frac{y_3}{y} + \mu_2 y_3 + \sigma_1 y_3 z - \frac{\mu_2\mu_3}{\sigma_2}v - \mu_2 y\frac{v_3}{v} + \frac{\mu_2\mu_3}{\sigma_2}v_3 + \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w - \frac{\sigma_1\mu_5}{\sigma_3}z \\ &\quad - \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w - \frac{\mu_2\gamma_1 v}{\sigma_2}w_3 + \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w_3. \end{aligned}$$

As

$$\begin{cases} \Lambda = \mu_1 x_3 + \alpha_1(1-u_1)x_3 v_3 + \alpha_2(1-u_2)x_3 y_3 = \mu_1 x_3 + \mu_2 y_3, \\ v_3 = \dfrac{\mu_4}{\gamma_2}, \quad w_3 = \dfrac{\sigma_2 y_3 - \mu_3 v_3}{\gamma_1 v_3}. \end{cases}$$

Therefore,

$$\begin{aligned} D^\alpha L_3 &\leqslant \mu_1 x_3\left(2 - \frac{x_3}{x} - \frac{x}{x_3}\right) + \alpha_1(1-u_1)x_3 v_3\left(4 - \frac{xvy_3}{x_3 v_3 y} - \frac{yv_3}{y_3 v} - \frac{v}{v_3} - \frac{x_3 v_3}{xv}\right) \\ &\quad + \alpha_1(1-u_1)x_3 v_3\left(-1 - \frac{x_3}{x} - \frac{v}{v_3} + \frac{x_3 v_3}{xv}\right) + \alpha_2(1-u_2)x_3 y_3\left(4 - \frac{x}{x_3} - \frac{yv_3}{y_3 v} - \frac{v}{v_3} - \frac{x_3 y_3}{xy}\right) \\ &\quad + \alpha_2(1-u_2)x_2 y_3\left(-1 - \frac{x_3}{x} + \frac{y}{y_3} + \frac{x_3 y_3}{xy}\right) + \sigma_1 z\left(y_3 - \frac{\mu_5}{\sigma_3}\right) \\ &\leqslant \mu_1 x_3\left(2 - \frac{x_3}{x} - \frac{x}{x_3}\right) + \alpha_1(1-u_1)x_3 v_3\left(4 - \frac{xvy_3}{x_3 v_3 y} - \frac{yv_3}{y_3 v} - \frac{v}{v_3} - \frac{x_3 v_3}{xv}\right) \\ &\quad + \alpha_2(1-u_2)x_3 y_3\left(4 - \frac{x}{x_3} - \frac{yv_3}{y_3 v} - \frac{v}{v_3} - \frac{xy_3}{xy}\right) + \alpha_1(1-u_1)x_3 v_3\left(\frac{v}{v_3} - \frac{x_3}{x}\right)\left(1 - \frac{v_3}{v}\right) \\ &\quad + \alpha_2(1-u_2)x_3 y_3\left(\frac{y}{y_3} - \frac{x_3}{x}\right)\left(1 - \frac{y_3}{y}\right) + \sigma_1 y_3 z_3\left(\frac{v}{v_3} - \frac{y}{y_3}\right)\left(1 - \frac{v_3}{v}\right) \\ &\quad + \frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}(R_2^{CTLs,W} - 1). \end{aligned}$$

As E_3 satisfies the both conditions (H_6) and (H_7), then

$$\left(\frac{v}{v_3} - \frac{x_3}{x}\right)\left(1 - \frac{v_3}{v}\right) \leqslant 0,$$
$$\left(\frac{y}{y_3} - \frac{x_3}{x}\right)\left(1 - \frac{y_3}{y}\right) \leqslant 0.$$

As the arithmetic mean is greater than or equal to the geometric mean, we will have

$$2 - \frac{x_3}{x} - \frac{x}{x_3} \leqslant 0,$$
$$4 - \frac{xvy_3}{x_3 v_3 y} - \frac{yv_3}{y_3 v} - \frac{v}{v_3} - \frac{x_3 v_3}{xv} \leqslant 0,$$
$$4 - \frac{x}{x_3} - \frac{yv_3}{y_3 v} - \frac{v}{v_3} - \frac{x_3 y_3}{xy} \leqslant 0.$$

Then, if $R_2^{CTLs,W} \leqslant 1$, we will have $D^\alpha L_3 \leqslant 0$. Let $P_3 = \{(x, y, v, w, z) \,|\, D^\alpha L_3 = 0\}$, then the largest positivity invariant set of P_3 is the singleton E_3. Therefore, from the Lemma 1. We can deduce that the equilibrium point E_3 is globally asymptotically stable. ∎

For the global stability of the equilibrium point E_4, we assume the following conditions

$$\left(\frac{v}{v_4}-\frac{x_4}{x}\right)\left(1-\frac{v_4}{v}\right)\leqslant 0,\quad \forall x,\, v\geqslant 0, \tag{H_8}$$

$$\left(\frac{y}{y_4}-\frac{x_4}{x}\right)\left(1-\frac{y_4}{y}\right)\leqslant 0,\quad \forall x,\, y\geqslant 0, \tag{H_9}$$

and

$$\left(\frac{v}{v_2}-\frac{y}{y_2}\right)\left(1-\frac{v_2}{v}\right)\leqslant 0,\quad \forall v,\, y\geqslant 0. \tag{H_{10}}$$

Theorem 7. *If $R_1^{CTLs,W}>1$ and $R_2^{CTLs,W}>1$, then the equilibrium point E_4 is globally asymptotically stable.*

Proof. Let the following Lyapunov function L_4

$$\begin{aligned}V_4 &= x_4\left(\frac{x}{x_4}-\ln\frac{x}{x_4}-1\right)+y_4\left(\frac{y}{y_4}-\ln\frac{y}{y_4}-1\right)+\frac{\mu_2}{\sigma_2}v_4\left(\frac{v}{v_4}-\ln\frac{v}{v_4}-1\right)\\ &\quad+\frac{\sigma_1}{\sigma_3}z_4\left(\frac{z}{z_4}-\ln\frac{z}{z_4}-1\right)+\frac{\mu_2\gamma_1}{\gamma_2\sigma_2}w_4\left(\frac{w}{w_4}-\ln\frac{w}{w_4}-1\right).\end{aligned}$$

The α derivative of L_4 is given by

$$\begin{aligned}D^\alpha L_4 &\leqslant \left(1-\frac{x_4}{x}\right)D^\alpha x+\left(1-\frac{y_4}{y}\right)D^\alpha y+\frac{\mu_2}{\sigma_2}\left(1-\frac{v_4}{v}\right)D^\alpha v\\ &\quad+\frac{\sigma_1}{\sigma_3}\left(1-\frac{z_4}{z}\right)D^\alpha z+\frac{\mu_2\gamma_1}{\gamma_2\sigma_2}\left(1-\frac{w_4}{x}\right)D^\alpha w\\ &\leqslant \Lambda-\mu_1 x-\frac{x_4}{x}\Lambda+\mu_1 x_4+\alpha_1(1-u_1)x_4 v+\alpha_2(1-u_2)x_4 y-\alpha_1(1-u_1)xv\frac{y_4}{y}\\ &\quad-\alpha_2(1-u_2)xy\frac{y_4}{y}+\mu_2 y_4+\sigma_1 y_4 z-\frac{\mu_2\mu_3}{\sigma_2}v+\frac{\mu_2\gamma_1 v_4}{\sigma_2}w-\frac{\sigma_1\mu_5}{\sigma_3}z-\sigma_1 y z_4+\frac{\sigma_1\mu_5}{\sigma_3}z_4\\ &\quad-\frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w-\frac{\mu_2\gamma_1 v}{\sigma_2}w_4+\frac{\mu_2\gamma_1\mu_4}{\gamma_2\sigma_2}w_4-\mu_2 y\frac{v_4}{v}+\frac{\mu_2\mu_3}{\sigma_2}v_4.\end{aligned}$$

As

$$\begin{cases}\Lambda=\mu_1 x_4+\alpha_1(1-u_1)x_4v_4+\alpha_2(1-u_2)x_4y_4=\mu_1 x_4+\mu_2 y_4+\sigma_1 y_4 z_4,\\ y_4=\dfrac{\mu_5}{\sigma_3},\quad v_4=\dfrac{\mu_4}{\gamma_2},\quad w_4=\dfrac{\sigma_2 y_4-\mu_3 v_4}{\gamma_1 v_4}.\end{cases}$$

Therefore,

$$\begin{aligned}D^\alpha V_4 &\leqslant \mu_1 x_4\left(2-\frac{x_4}{x}-\frac{x}{x_4}\right)+\alpha_1(1-u_1)x_4v_4\left(4-\frac{xvy_4}{x_4v_4y}-\frac{yv_4}{y_4v}-\frac{v}{v_4}-\frac{x_4v_4}{xv}\right)\\ &\quad+\alpha_1(1-u_1)x_4v_4\left(-1-\frac{x_4}{x}+\frac{v}{v_4}+\frac{x_4v_4}{xv}\right)+\alpha_2(1-u_2)x_4y_4\left(4-\frac{x}{x_4}-\frac{yv_4}{y_4v}-\frac{v}{v_4}-\frac{x_4y_4}{xy}\right)\\ &\quad+\alpha_2(1-u_2)x_2y_2\left(-1-\frac{x_4}{x}+\frac{y}{y_4}+\frac{x_4y_4}{xy}\right)+\sigma_1 y_4z_4\left(-1-\frac{y}{y_4}+\frac{yv_4}{y_4v}+\frac{v}{v_4}\right)\\ &\leqslant \mu_1 x_4\left(2-\frac{x_4}{x}-\frac{x}{x_4}\right)+\alpha_1(1-u_1)x_4v_4\left(4-\frac{xvy_4}{x_4v_4y}-\frac{yv_4}{y_4v}-\frac{v}{v_4}-\frac{x_4v_4}{xv}\right)\\ &\quad+\alpha_2(1-u_2)x_4y_4\left(4-\frac{x}{x_4}-\frac{yv_4}{y_4v}-\frac{v}{v_4}-\frac{x_4y_4}{xy}\right)+\alpha_1(1-u_1)x_4v_4\left(\frac{v}{v_4}-\frac{x_4}{x}\right)\left(1-\frac{v_4}{v}\right)\\ &\quad+\alpha_2(1-u_2)x_4y_4\left(\frac{y}{y_4}-\frac{x_4}{x}\right)\left(1-\frac{y_4}{y}\right)+\sigma_1 y_4z_4\left(\frac{v}{v_4}-\frac{y}{y_4}\right)\left(1-\frac{v_4}{v}\right).\end{aligned}$$

As E_4 satisfies the conditions (H_8), (H_9), and (H_{10}), then

$$\left(\frac{v}{v_4}-\frac{x_4}{x}\right)\left(1-\frac{v_4}{v}\right)\leqslant 0,$$

$$\left(\frac{y}{y_4}-\frac{x_4}{x}\right)\left(1-\frac{y_4}{y}\right)\leqslant 0,$$
$$\left(\frac{v}{v_4}-\frac{y}{y_4}\right)\left(1-\frac{v_4}{v}\right)\leqslant 0.$$

As the arithmetic mean is greater than or equal to the geometric mean, we will have

$$2-\frac{x_4}{x}-\frac{x}{x_4}\leqslant 0,$$
$$4-\frac{xvy_4}{x_4v_4y}-\frac{yv_4}{y_4v}-\frac{v}{v_4}-\frac{x_4v_4}{xv}\leqslant 0,$$
$$4-\frac{x}{x_4}-\frac{yv_4}{y_4v}-\frac{v}{v_4}-\frac{x_4y_4}{xy}\leqslant 0.$$

Then, if $R_1^{CTLs,W}>1$ and $R_2^{CTLs,W}>1$, we will have $D^\alpha V_4\leqslant 0$. Let $P_4=\{(x,y,v,w,z)\,|\,D^\alpha V_4=0\}$, then the largest positivity invariant set of P_4 is the singleton E_4. Therefore, from the Lemma 1 we can deduce that the equilibrium point E_4 is globally asymptotically stable. ∎

5. Numerical simulations

In this section, we will present some numerical simulations to confirm the results found in the theoretical part concerning the global stability of the equilibrium points, to demonstrate the effect of fractional derivatives and also the effect of the treatment on the infection.

To improve our theoretical results, will present two kinds of numerical simulations, the first one for showing the effect of fractional derivative order on the convergence toward equilibria and the second stand for proving the effectiveness of the parameters of treatment on the HCV infection.

5.1. Effect of fractional order derivative

In this subsection, we present some numerical simulations that value our theoretical results concerning the global stability of equilibria and show the effectiveness of fractional order derivative on the stability of equilibrium points using the value of the different parameters presented in Table 1 with the value of fractional derivative order between 1 and 0.4. We are using Matlab to perform this numerical simulation and using also the following schema like in [47]:

$$\begin{aligned}Y(t_j)=&\frac{h^\alpha}{\Gamma(\alpha+2)}\left((j-1)^{\alpha+1}-(j-\alpha-1)j^\alpha\right)G(Y(t_0))+Y(t_0)\\&+\frac{h^\alpha}{\Gamma(\alpha+2)}\sum_{i=1}^{j-1}\left((j-i+1)^{\alpha+1}-2(j-i)^{\alpha+1}+(j-i-1)^{\alpha+1}\right)G(Y(t_i))\\&+\frac{h^\alpha}{\Gamma(\alpha+2)}G\left(Y(t_{j-1})+\frac{h^\alpha}{\Gamma(\alpha+1)}G(Y(t_{j-1}))\right),\end{aligned}$$

where $t_j=t(j-1)+h$, for $j=0,1,\ldots,N-1$, with the following initial condition $Y_0=(12,10,8,7,5)^T$.

Figure 2 shows the evolution of the infection of the different compartments. We can observe that all curves represent the compartments x, y, v, w, and z converge to the point $(20,0,0,0,0)$ for the different values of fractional derivative order parameter. The value of the basic reproduction number with the value of different parameters given in column two of Table 1 is given by $R_0=0.775$ (see Table 2). This value verified the conditions of global stability of this free equilibrium point E_0 given in Theorem 3.

In Figure 3, we can notice that all curves representing the different variables of our model converge to the point $(0.715,39.285,78.200,0,0)$ for the different values of the fractional order derivative parameter. The value of basic reproduction number R_0, the CTL immune reproductive number R^{CTLs} and the humoral immune reproductive number R_W are given by $R_0=1.4$, $R^{CTLs}=0.24$, and $R^W=0.22$ (see the second column of Table 2). These values check the Theorem 4 conditions of global stability of E_1.

Table 1. Values of the model (1) parameters.

Parameters	Fig. 2	Fig. 3	Fig. 4	Fig. 5	Fig. 6	Fig. 7
Λ	4	4	4	4	4	4
u_1	0.5	0.8	0.8	0.8	0.8	–
u_2	0.6	0.85	0.85	0.85	0.85	–
α_1	0.3	0.2	0.2	0.2	0.2	0.2
α_2	0.4	0.4	0.4	0.4	0.4	0.4
μ_1	0.1	0.1	0.1	0.1	0.1	0.1
μ_2	0.0.15	0.1	0.1	0.1	0.1	0.1
μ_3	0.2	0.1	0.1	0.1	0.1	0.1
μ_4	0.35	0.7	0.7	0.7	0.3	0.3
μ_5	0.4	0.8	0.3	0.15	0.3	0.3
σ_1	0.1	0.1	0.1	0.1	0.1	0.1
σ_2	0.2	0.2	0.2	0.2	0.2	0.2
σ_3	0.15	0.005	0.09	0.003	0.03	0.03
γ_1	0.15	0.15	0.15	0.1	0.15	0.15
γ_2	0.2	0.002	0.002	0.002	0.2	0.2

Table 2. Values of the model (1) reproductive numbers.

E_0	E_1	E_2	E_3	E_4
$R_0 = 0.775$	$R_0 = 1.4$ $R^{CTLs} = 0.24$ $R^{W} = 0.22$	$R^{CTLs} = 1.5$ $R_1^{CTL,W} = 0.02$	$R^{W} = 2.24$ $R_2^{CTLs,W} = 0.78$	$R_1^{CTLs,W} = 1.33$ $R_2^{CTLs,W} = 2$

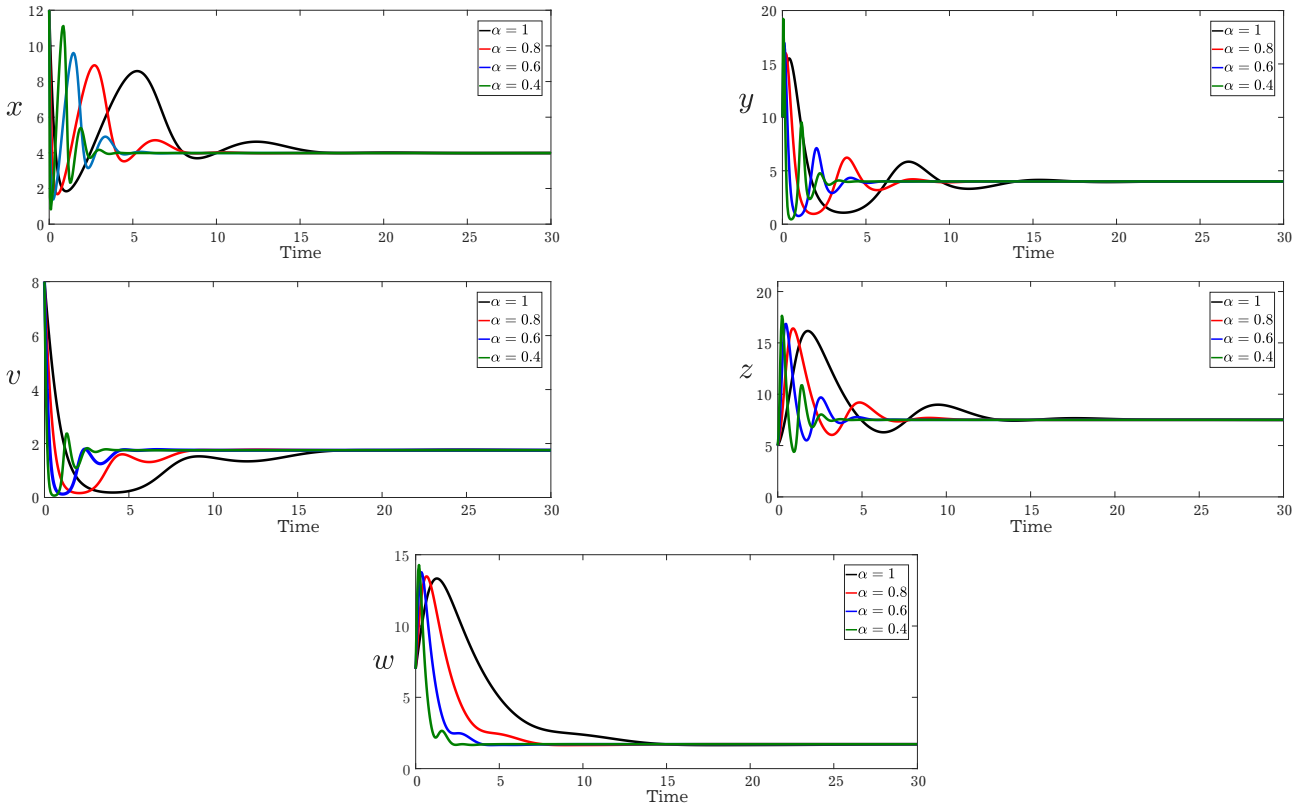

Fig. 2. Global stability of E_0 with the different value of fractional derivative order.

The Figure 4 describes the dynamics of HCV infection, and we can notice that all curves converge toward the point $(3.3648, 6.4706, 9.7059, 0, 0)$. The CTL immune reproductive number R^{CTL} and the humoral immune reproductive number $R_1^{CTL,HUM}$ in this case are given in column three of Table 2 by $R^{CTL} = 1.5$ and $R_1^{CTLs,W} = 0.02$, these values coincide with the conditions of Theorem 6 concerning the global stability of E_2.

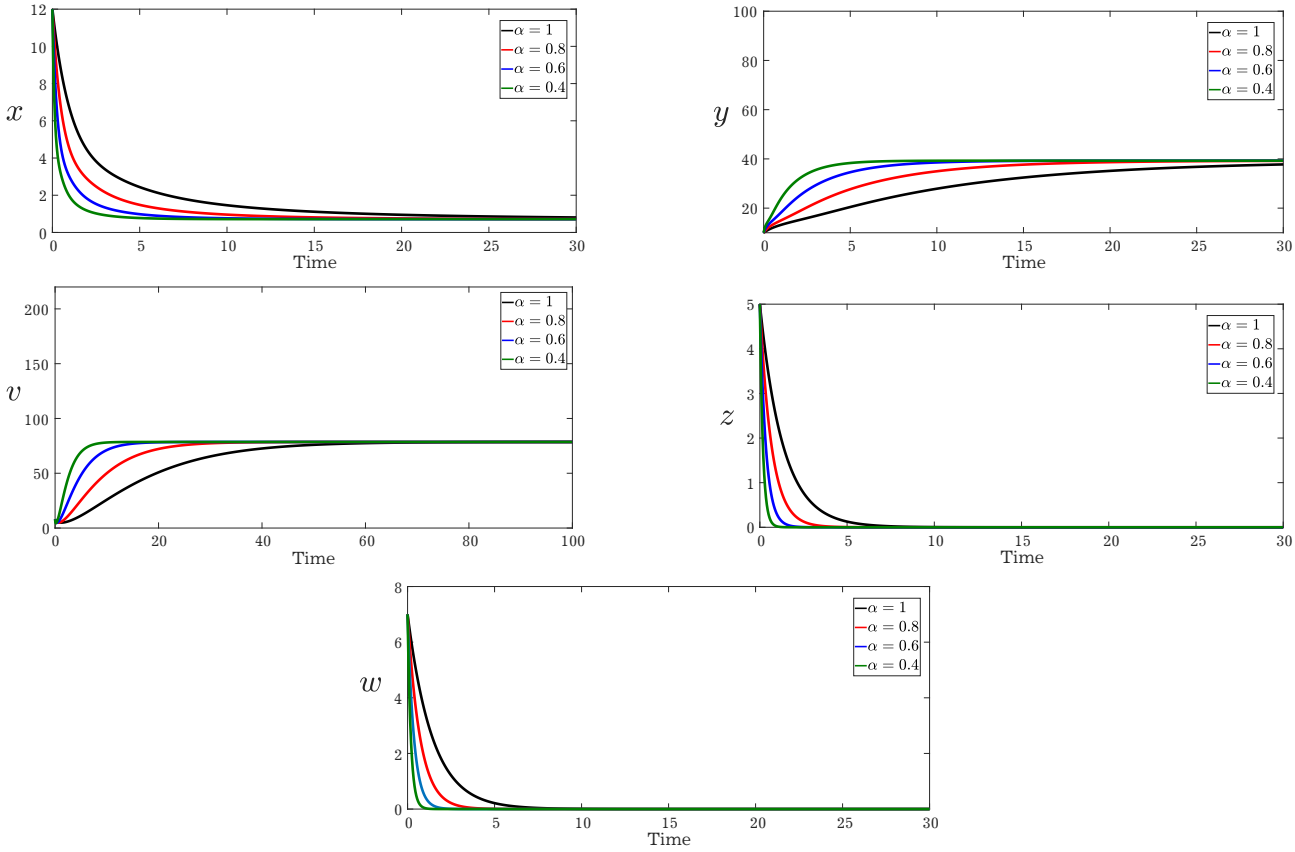

Fig. 3. Global stability of E_1 with the different value of fractional derivative order.

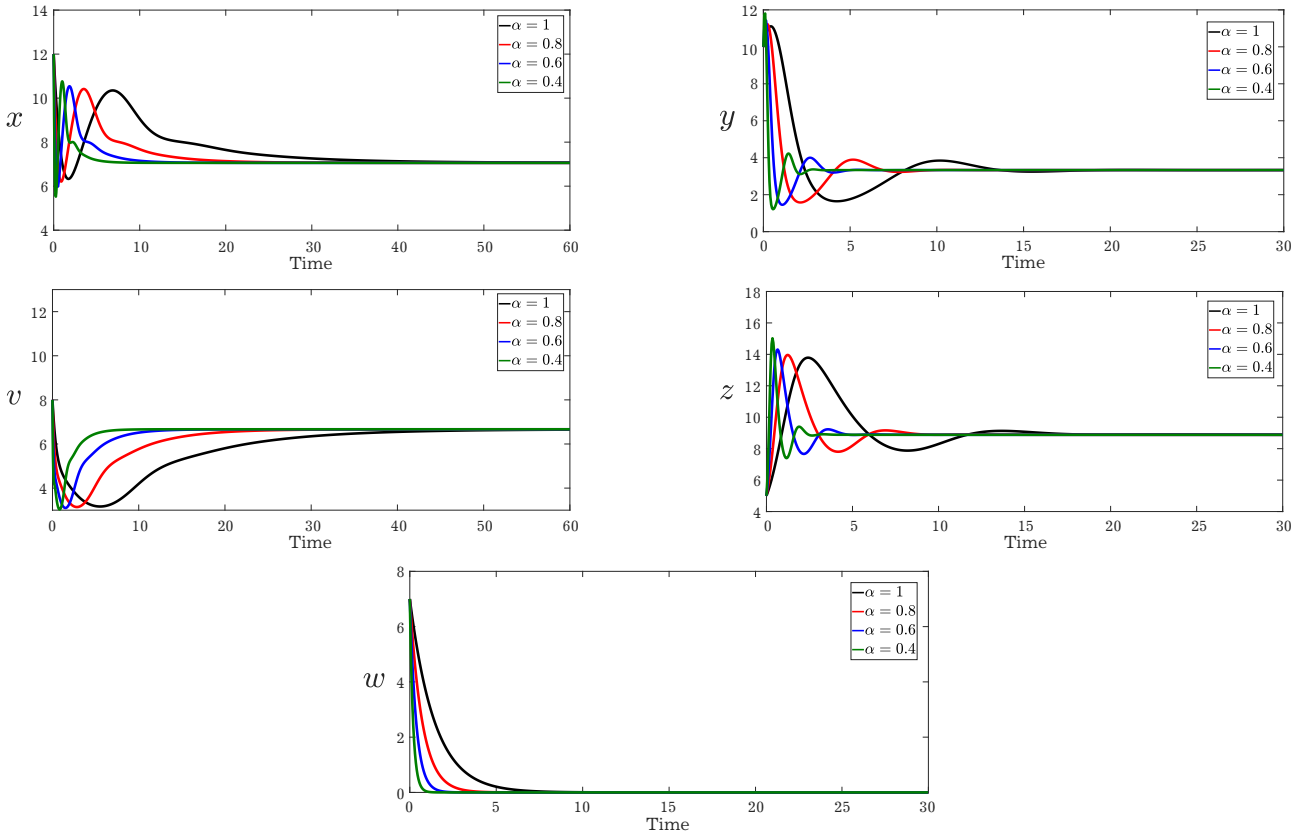

Fig. 4. Global stability of E_2 with the different value of fractional derivative order.

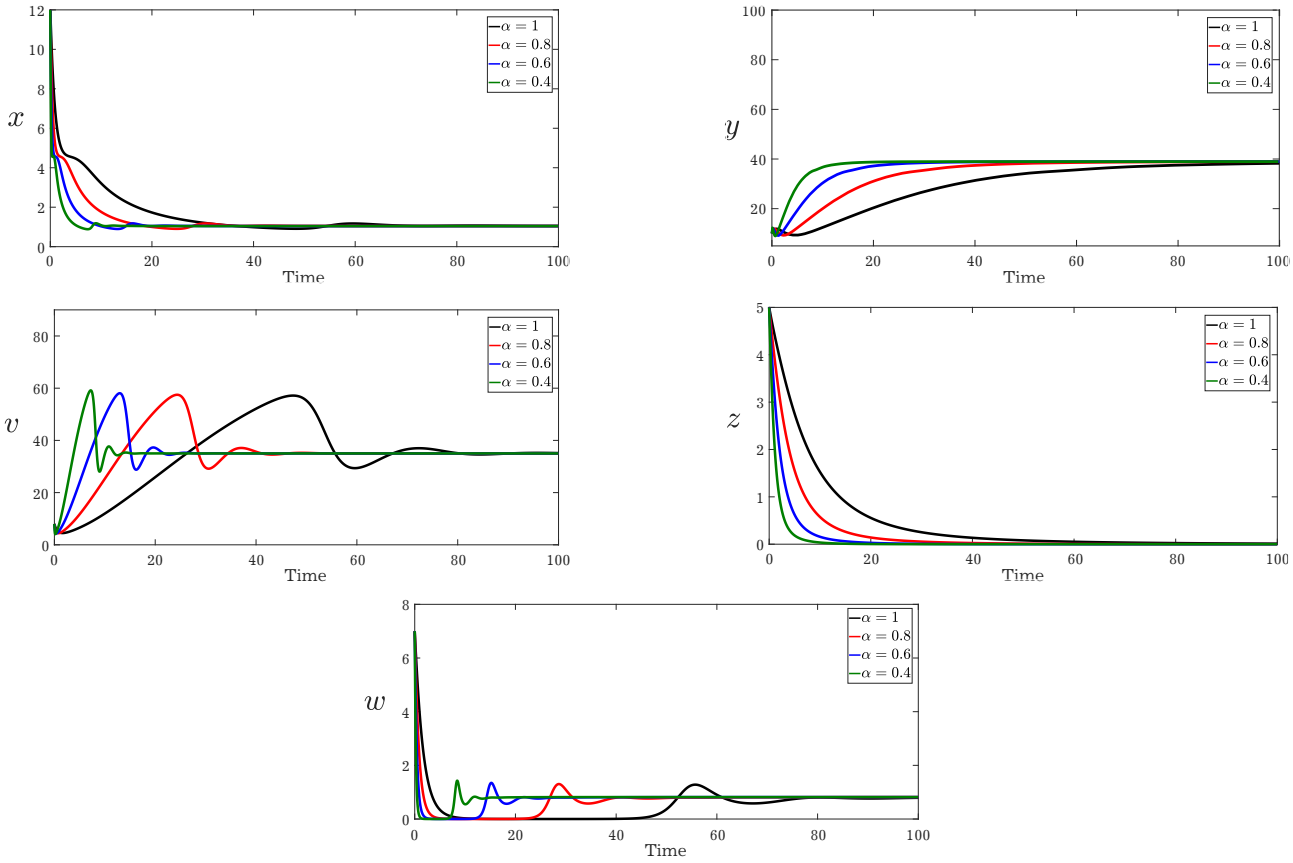

Fig. 5. Global stability of E_3 with the different value of fractional derivative order.

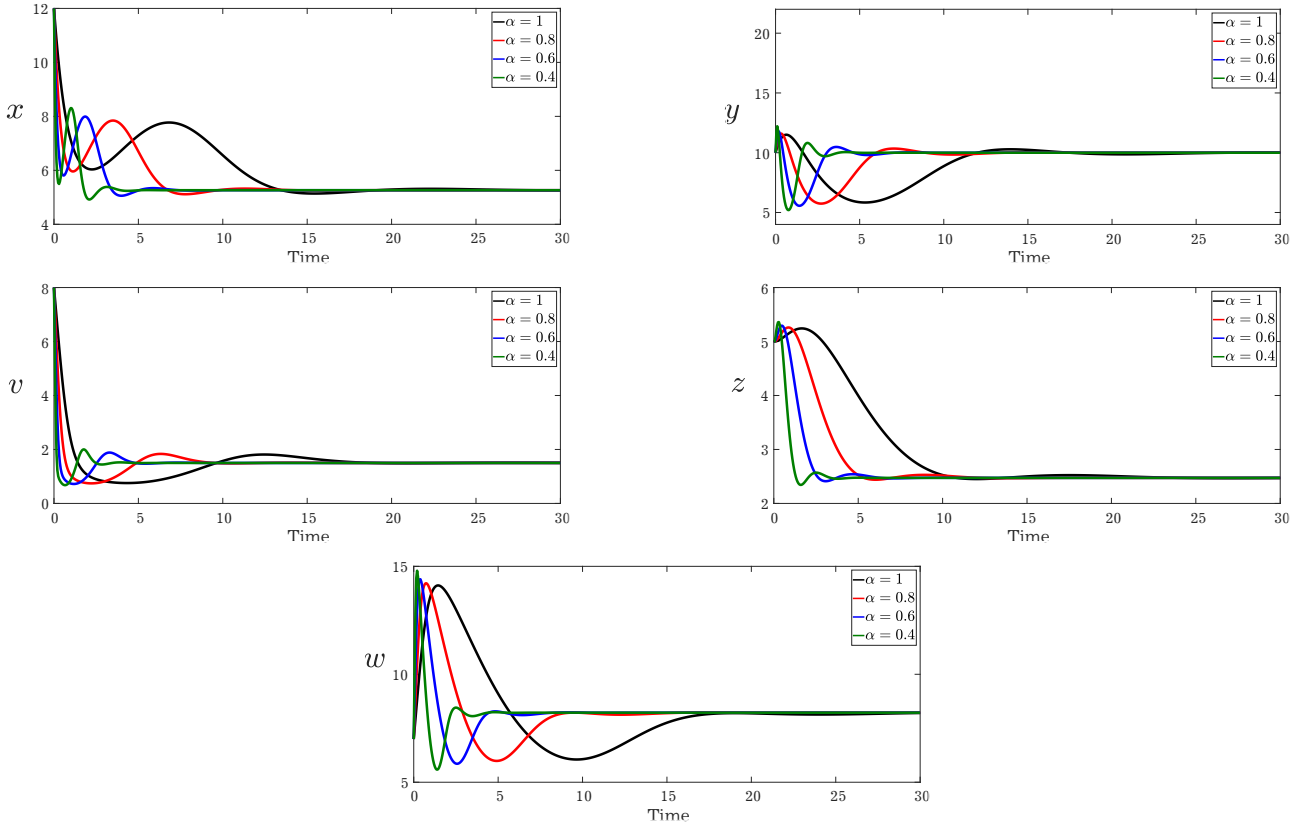

Fig. 6. Global stability of E_4 with the different value of fractional derivative order.

We observe the same thing in Figure 5, all curves converge toward the point $(1.042, 38.957, 35, 0.818, 0)$ for the different values of the fractional order derivative parameter. The value of the humoral immune reproductive number R^W and the CTL immune competitive number $R_2^{CTLs,W}$ are given by $R^W = 2.24$, $R_2^{CTLs,W} = 0.78$ (see the fourth column of Table 2). These values satisfy the conditions of the Theorem 6 concerning the global stability of E_3.

The last Figure 6 shows the behavior of HCV infection. In this figure, we can see that all curves converge toward the point $(5.263, 10, 1.5, 8.22, 2.473)$ for the different values of the fractional order derivative parameter. The humoral immune reproductive number $R_1^{CTLs,W}$ and he CTL immune competitive number $R_2^{CTLs,W}$ are given by $R_1^{CTLs,W} = 1.33$ and $R_2^{CTLs,W} = 2$ (see the column four of Table 2). These value check the Theorem 7 conditions concerning the global stability of E_4. All previous numerical findings confirm our theoretical results about the global stability of steady states. We can deduce that for a smaller value of fractional derivative order the curves representing the variables of the model converge more quickly to the equilibria and for a higher value α, the variables of the model converge more slowly to the steady states. So, the fractional order derivative has no effect on the global stability but on the speed of the convergence toward the equilibrium points.

6. Effect of the treatment parameters on HCV infection

In this subsection, we show the effect of the parameters of the treatment u_1 and u_2 to reduce de HCV infection using the value of the parameter presented in Table 1.

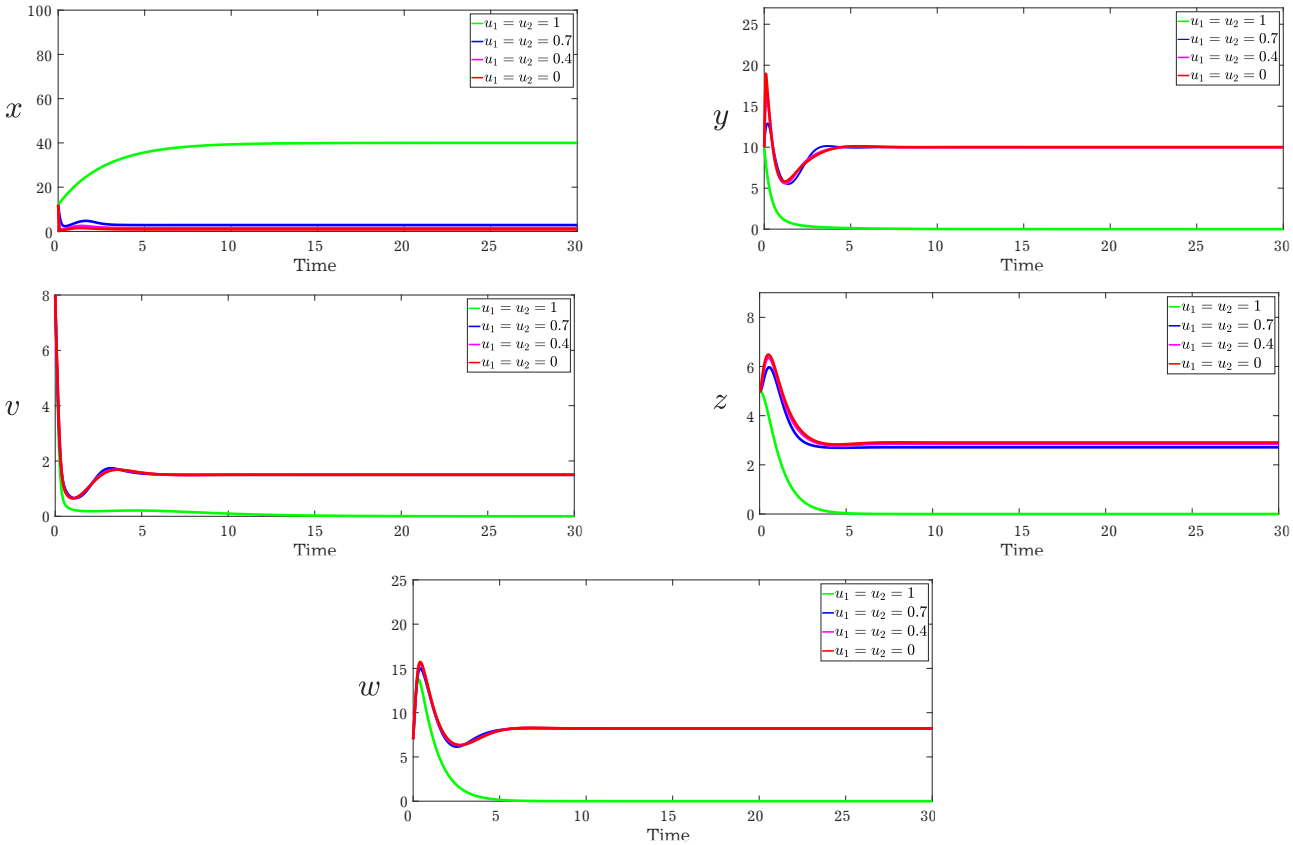

Fig. 7. Effect of u_1 and u_2 on the HCV infection.

This figure shows the effect of the parameters of the treatment u_1 and u_2 to eliminate HCV infection. In this figure, we can notice that in the existence of the treatment the number of infected cells and the number of free viruses diminished, also we can see that the number of susceptible cells increased. Moreover, we also note the absence of an adaptive immune response because the existence of treatment

helps fight the infection. Otherwise, we can notice a reduction of susceptible cells and an increase in infected cells, free viruses, and the adaptive immune.

7. Conclusion

In this work, we have analyzed a fractional order HCV model cell-to-cell and virus-to-cell and treatment. In our suggested model, the antibody and cytotoxic T-lymphocyte immune responses are taken into consideration. The presented model has one basic reproduction number R_0 that was obtained by using the next generation matrix method and other four basic reproductive numbers are R^{CTLs} the CTL immune reproductive number, R^w the humoral immune reproductive number, $R_1^{CTLs,W}$ the humoral competitive number and R_2^W the CTL immune competitive number. These reproductive numbers depend on the chosen parameters of treatment. By using Lyapunov's functional and LaSalle's invariance principle, we gave the theorems of global stability of the equilibria, this stability depends on the different reproductive numbers. Finally, some numerical simulations are given in the last part of this paper to value our theoretical results concerning the global stability of steady states, and to show the effect of fractional derivative order and the parameters of treatment on the stability. We notice that the values of the fractional derivative have no effect on the stability of steady States but only on the speed of the convergence toward the corresponding equilibrium points, for the effect of parameters of treatment we deduce that in the presence of these parameters, the infection diminished.

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Дробова модель HCV-інфекції з адаптивним імунітетом і лікуванням

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У цій статті запропоновано та досліджено дробову модель HCV-інфекції з адаптивним імунітетом і лікуванням. Адаптивний імунітет включає відповідь CTL й антитіла. Ця модель містить п'ять звичайних диференціальних рівнянь. Дослідження починаються з доведення існування, єдиності та обмеженості додатних розв'язків. Модель має точки вільної рівноваги та інші ендемічні рівноваги. Використовуючи функцію Ляпунова та принцип інваріантності Ласаля, показано глобальну стійкість цих точок рівноваги. Під кінець, проведено декілька чисельних симуляцій, щоб перевірити отримані теоретичні результати та показати вплив параметра порядку дробової похідної та інших параметрів лікування.

Ключові слова: *дробовий порядок; HCV; від клітини до клітини; від вірусу до клітини; глобальна стійкість; чисельне моделювання.*