Mathematical Biosciences and Engineering

http://www.aimspress.com/journal/MBE

MBE, 18(2): 1077–1120.
DOI: 10.3934/mbe.2021059
Received: 01 December 2020
Accepted: 28 December 2020
Published: 11 January 2021

Research article

Stability of HTLV/HIV dual infection model with mitosis and latency

A. M. Elaiw[1,2,*] **and N. H. AlShamrani**[1,3]

[1] Department of Mathematics, Faculty of Science, King Abdulaziz University, P.O. Box 80203, Jeddah 21589, Saudi Arabia

[2] Department of Mathematics, Faculty of Science, Al-Azhar University, Assiut Branch, Assiut 71452, Egypt

[3] Department of Mathematics, Faculty of Science, University of Jeddah, P.O. Box 80327, Jeddah 21589, Saudi Arabia

* **Correspondence:** Email: a_m_elaiw@yahoo.com.

Abstract: In this paper, we formulate and analyze an HTLV/HIV dual infection model taking into consideration the response of Cytotoxic T lymphocytes (CTLs). The model includes eight compartments, uninfected $CD4^+T$ cells, latent HIV-infected cells, active HIV-infected cells, free HIV particles, HIV-specific CTLs, latent HTLV-infected cells, active HTLV-infected cells and HTLV-specific CTLs. The HIV can enter and infect an uninfected $CD4^+T$ cell by two ways, free-to-cell and infected-to-cell. Infected-to-cell spread of HIV occurs when uninfected $CD4^+T$ cells are touched with active or latent HIV-infected cells. In contrast, there are two modes for HTLV-I transmission, (i) horizontal, via direct infected-to-cell touch, and (ii) vertical, by mitotic division of active HTLV-infected cells. We analyze the model by proving the nonnegativity and boundedness of the solutions, calculating all possible steady states, deriving a set of key threshold parameters, and proving the global stability of all steady states. The global asymptotic stability of all steady states is proven by using Lyapunov-LaSalle asymptotic stability theorem. We performed numerical simulations to support and illustrate the theoretical results. In addition, we compared between the dynamics of single and dual infections.

Keywords: HTLV/HIV dual infection; viral and cellular infections; global stability; mitotic transmission; latency; CTL-mediated immune response; Lyapunov function

1. Introduction

Since past decades humanity has been under attack by many viruses such as hepatitis C virus (HCV), human immunodeficiency virus (HIV), hepatitis B virus (HBV), human T-lymphotropic virus type I (HTLV-I), dengue virus and lastly coronavirus. During the last decade HTLV-I and HIV dual infection

has been extensively reported. It has been discovered that the simultaneous infection by the two viruses affects the pathogenic development and influences the outcomes for associated chronic diseases [1]. In fact, concurrent infections with HTLV-I and HIV have occurred frequently in areas where peoples living at high risk activities such as needle injection sharing and unprotected sexual relationships. In addition, HTLV/HIV dual infection has documented in specific geographic regions where both retroviruses become endemic [2], and among those who belonged to a specific ethnic as well. For instance, the dual infection rates in peoples living in some parts of Brazil have reached 16% of HIV-infected patients [3]. In a recent work, it has been estimated that the HIV single infected patients are more exposure to be dually infected with HTLV-I at a higher rate initiating from 100 to 500 times in comparison to the uninfected peoples [4]. Moreover, some seroepidemiologic studies have reported that HTLV-infected patients are at risk to have a concurrent infection with HIV, and vice versa compared to those who are infection-free from the general population [2]. HTLV-I and HIV are mainly attack the $CD4^+$T cells and lead to immune dysfunctional as well, however, they also conflict no doubt with respect to the etiology of their pathogenic and clinical outcomes [5]. HTLV-I and HIV dual infection appears to have an overlap on the course of associated clinical outcomes with both viruses [2]. Many researchers have reported that HIV infected individuals who are possibly dually infected with HTLV-I can potentially associated with clinical progression to AIDS. In contrast, HIV can modify HTLV-I expression in dual infected patients which leads them to a higher risk of developing HTLV-I related diseases such as HTLV-associated myelopathy/tropical spastic paraparesis (TSP/HAM) and adult T-cell leukemia (ATL) [2, 4].

Mathematical models

Viral infection models have become an indispensable tool to biological researchers, where they can improve the understanding of a within-host virus dynamics and help in predicting the effect of antiviral drug efficacy on disease's progression (see e.g., [6–17]).

- **HIV single infection model:** Nowak and Bangham [18] have constructed the following standard HIV infection model to describe the within-host interaction between uninfected $CD4^+$T cells, active HIV-infected cells, free HIV particles and Cytotoxic T lymphocytes (CTLs):

$$\begin{cases} \frac{dS}{dt} = \rho - \alpha S - \varkappa_1 S V, \\ \frac{dI}{dt} = \varkappa_1 S V - aI - \mu_1 C^I I, \\ \frac{dV}{dt} = bI - \varepsilon V, \\ \frac{dC^I}{dt} = \sigma_1 C^I I - \pi_1 C^I, \end{cases} \tag{1.1}$$

  where $S = S(t)$, $I = I(t)$, $V = V(t)$ and $C^I = C^I(t)$ are the concentrations of uninfected $CD4^+$T cells, active HIV-infected cells, free HIV particles and HIV-specific CTLs, respectively, and t is the time. The parameter ρ represents the creation rate of the uninfected $CD4^+$T cells. The HIV particles infect the uninfected $CD4^+$T cells at term $\varkappa_1 S V$ (free-to-cell infection). The free HIV particles are generated at rate bI. The expansion rate of effective HIV-specific CTLs is represented by $\sigma_1 C^I I$. The term $\mu_1 C^I I$ is the killing rate of active HIV-infected cells by their specific CTLs. The death rates of the uninfected $CD4^+$T cells, active HIV-infected cells, free HIV particles and HIV-specific CTLs are represented by αS, aI, εV and $\pi_1 C^I$, respectively. Since then several extensions of model (1.1) have been proposed and analyzed (see e.g., [19–21]).
- **HTLV-I single infection model**: Modeling and analysis of HTLV-I single infection have been addressed in several works [22–25]. The effect of CTLs on HTLV-I dynamics has been investi-

gated in many works (see e.g., [26–31]). Lim and Maini [32] have proposed an HTLV-I dynamics model with mitotic division of active HTLV-infected cells and CTL immunity as:

$$\begin{cases} \frac{dS}{dt} = \rho - \alpha S - \varkappa_4 S Y, \\ \frac{dE}{dt} = \varkappa_4 S Y + \kappa r^* Y - (\psi + \omega) E, \\ \frac{dY}{dt} = \psi E - \delta^* Y - \mu_2 C^Y Y, \\ \frac{dC^Y}{dt} = \sigma_2 Y - \pi_2 C^Y, \end{cases} \tag{1.2}$$

where $E = E(t)$, $Y = Y(t)$ and $C^Y = C^Y(t)$ are the concentrations of latent HTLV-infected cells, active HTLV-infected cells and HTLV-specific CTLs at time t, respectively. The uninfected CD4$^+$T cells become HTLV-infected cells due to infected-to-cell contact at rate $\varkappa_4 S Y$ (horizontal transmission). The term $\kappa r^* Y$ (vertical transmission) represents the rate at which active HTLV-infected cells become latent where $\kappa \in (0, 1)$. The terms ωE and $\delta^* Y$ denote the death rates of the latent and active HTLV-infected cells, respectively. The latent HTLV-infected cells are activated with rate ψE. The active HTLV-infected cells are killed by their specific CTLs at rate $\mu_2 C^Y Y$. The linear term $\sigma_2 Y$ represents the expansion rate of HTLV-specific CTLs. The HTLV-specific CTLs decay at rate $\pi_2 C^Y$. This model has been developed and extended in [33–35].

- **HTLV/HIV dual infection model**: In a very recent work [36], Elaiw and AlShamrani have formulated an HTLV/HIV dual infection model taking into account the following factors:

(F1) The uninfected CD4$^+$T cells are the main target of each of HTLV-I and HIV;

(F2) There exist latent HIV-infected and HTLV-infected cells;

(F3) Specific CTL immune response to each of HTLV-I and HIV;

(F4) The HIV can spread when an uninfected CD4$^+$T cell is contacted with free HIV particle (free-to-cell infection) or active HIV-infected cell (infected-to-cell infection);

(F5) HTLV-I can be transmitted via two routes, (i) horizontal transmission via direct infected-to-cell touch via virological synapse, and (ii) vertical transmission by mitotic division of active HTLV-infected cells.

$$\begin{cases} \frac{dS}{dt} = \rho - \alpha S - \varkappa_1 S V - \varkappa_3 S I - \varkappa_4 S Y, \\ \frac{dL}{dt} = \varkappa_1 S V + \varkappa_3 S I - (\lambda + \gamma) L, \\ \frac{dI}{dt} = \lambda L - aI - \mu_1 C^I I, \\ \frac{dE}{dt} = \varphi \varkappa_4 S Y + \kappa r^* Y - (\psi + \omega) E, \\ \frac{dY}{dt} = \psi E + (1 - \kappa) r^* Y - \delta^* Y - \mu_2 C^Y Y, \\ \frac{dV}{dt} = bI - \varepsilon V, \\ \frac{dC^I}{dt} = \sigma_1 C^I I - \pi_1 C^I, \\ \frac{dC^Y}{dt} = \sigma_2 C^Y Y - \pi_2 C^Y, \end{cases} \tag{1.3}$$

where $L = L(t)$ is the concentration of latent HIV-infected cells. The incidence between HIV-infected cells and uninfected CD4$^+$T cells is represented by $\varkappa_3 S I$. Latent HIV-infected cells are activated at rate λL. The term γL is the death rate of latent HIV-infected cells. The parameter $\varphi \in (0, 1)$ is the probability of new HTLV infections could be enter a latent period.

Model (1.3) assumes that the infected-to-cell HIV infection is only due to the active HIV-infected CD4$^+$T cells. It has been shown in [37] that latent HIV-infected CD4$^+$T cells can also infect the uninfected CD4$^+$T cells. In 2020, Wang et al. [38] have formulated a viral infection model by assuming that both latent and active infected cells can share in infected-to-cell transmission, but the effect of

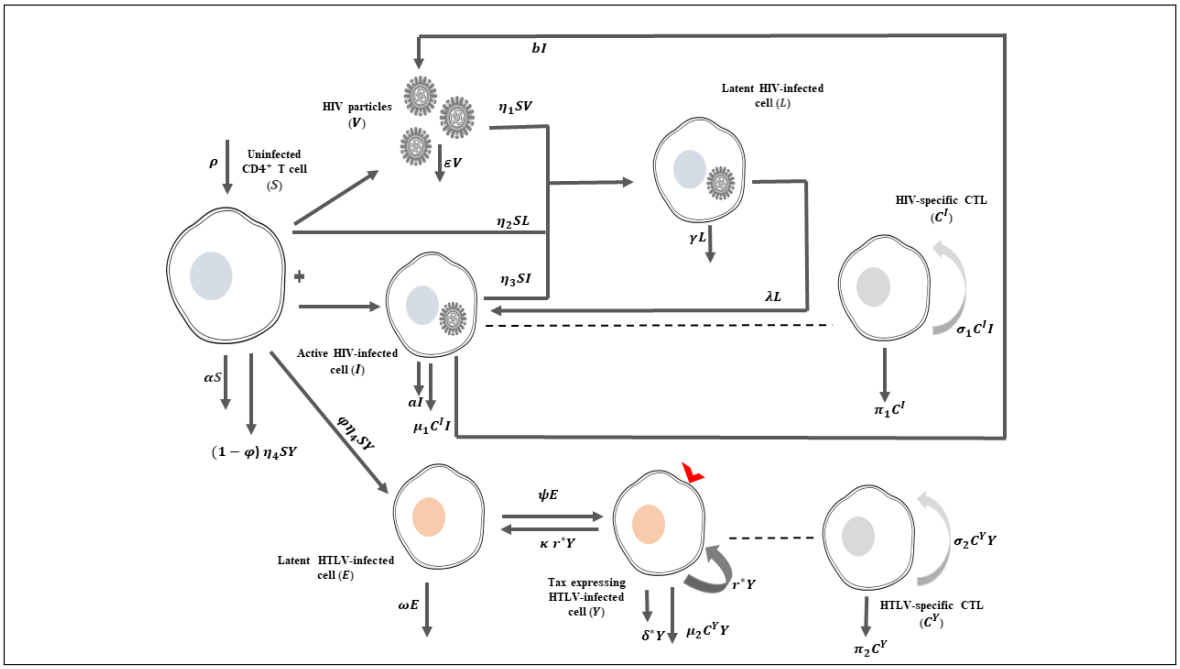


Figure 1. The schematic diagram of within host dynamics of HTLV/HIV dual infection.

immune response has been neglected. In 2020, Elaiw and AlShamrani [39] and Elaiw et al. [40] have investigated HIV single infection models with latent and active infected-to-cell infections and CTL immune response.

The aim of the present paper is to extend model (1.3) by assuming that both latent and active HIV-infected cells can share in infected-to-cell infection. We first address the basic and global properties of the model, then we perform numerical simulation and present some comparison results. The results of this work, such as dual infection model and its analysis will help clinicians in estimating the appropriate time for patients with dual infection to begin treatment. On the other hand, this study, from a certain point of view, illustrates the complexity of this dual infection model and the model is helpful to clinical treatment. Our model may also helpful to study different dual infections such as Coronavirus/Influenza, HIV/HCV, HIV/HBV and HIV/Malaria.

2. Model formulation

In this section, we introduce an HTLV/HIV dual infection by assuming that both latent and active infected cells can share in infected-to-cell HIV infection. The dynamics of HTLV/HIV dual infection is schematically shown in Figure 1. We propose the following model:

$$\frac{dS}{dt} = \rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y, \tag{2.1}$$

$$\frac{dL}{dt} = \varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda + \gamma) L, \tag{2.2}$$

$$\frac{dI}{dt} = \lambda L - aI - \mu_1 C^I I, \tag{2.3}$$

$$\frac{dE}{dt} = \varphi\varkappa_4 S\,Y + \kappa r^* Y - (\psi + \omega)\,E, \tag{2.4}$$

$$\frac{dY}{dt} = \psi E + (1-\kappa)\,r^* Y - \delta^* Y - \mu_2 C^Y Y, \tag{2.5}$$

$$\frac{dV}{dt} = bI - \varepsilon V, \tag{2.6}$$

$$\frac{dC^I}{dt} = \sigma_1 C^I I - \pi_1 C^I, \tag{2.7}$$

$$\frac{dC^Y}{dt} = \sigma_2 C^Y Y - \pi_2 C^Y. \tag{2.8}$$

The uninfected CD4$^+$T cells are contacted with latent HIV-infected cells and become infected due to infected-to-cell infection at rate $\varkappa_2 S\,L$. The expansion rate of HTLV-specific CTLs is represented by bilinear form $\sigma_2 C^Y Y$. In [32], it is assumed that $r^* < \upsilon^* = \min\{\alpha, \omega, \delta^*\}$. Since $r^* < \delta^*$ and $0 < \kappa < 1$, then $(1-\kappa)\,r^* < \delta^*$ and

$$\delta^* - (1-\kappa)\,r^* > 0.$$

Let $\delta = \delta^* - (1-\kappa)\,r^*$ and $r = \kappa r^*$. Therefore, model (2.1)–(2.8) becomes

$$\frac{dS}{dt} = \rho - \alpha S - \varkappa_1 S\,V - \varkappa_2 S\,L - \varkappa_3 S\,I - \varkappa_4 S\,Y, \tag{2.9}$$

$$\frac{dL}{dt} = \varkappa_1 S\,V + \varkappa_2 S\,L + \varkappa_3 S\,I - (\lambda + \gamma)\,L, \tag{2.10}$$

$$\frac{dI}{dt} = \lambda L - aI - \mu_1 C^I I, \tag{2.11}$$

$$\frac{dE}{dt} = \varphi\varkappa_4 S\,Y + rY - (\psi + \omega)\,E, \tag{2.12}$$

$$\frac{dY}{dt} = \psi E - \delta Y - \mu_2 C^Y Y, \tag{2.13}$$

$$\frac{dV}{dt} = bI - \varepsilon V, \tag{2.14}$$

$$\frac{dC^I}{dt} = \sigma_1 C^I I - \pi_1 C^I, \tag{2.15}$$

$$\frac{dC^Y}{dt} = \sigma_2 C^Y Y - \pi_2 C^Y. \tag{2.16}$$

In the next section we study the mathematical analysis of model (2.9)–(2.16).

3. Model analysis

Proposition 1. The solutions $(S, L, I, E, Y, V, C^I, C^Y)(t)$ of system (2.9)–(2.16) satisfy

$$0 \le S(t), L(t), I(t) \le \Omega_1,\ 0 \le E(t), Y(t) \le \Omega_2,\ 0 \le V(t) \le \Omega_3,$$
$$0 \le C^I(t) \le \Omega_4 \text{ and } 0 \le C^Y(t) \le \Omega_5,$$

where $\Omega_i > 0$, $i = 1, ..., 5$.

The proof is given in the Appendix.

3.1. Steady states

Now we calculate all possible steady states of system (2.9)–(2.16). The steady states of the system satisfying the following algebraic equations:

$$0 = \rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y, \tag{3.1}$$
$$0 = \varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda + \gamma) L, \tag{3.2}$$
$$0 = \lambda L - aI - \mu_1 C^I I, \tag{3.3}$$
$$0 = \varphi \varkappa_4 S Y + rY - (\psi + \omega) E, \tag{3.4}$$
$$0 = \psi E - \delta Y - \mu_2 C^Y Y, \tag{3.5}$$
$$0 = bI - \varepsilon V, \tag{3.6}$$
$$0 = (\sigma_1 I - \pi_1) C^I, \tag{3.7}$$
$$0 = (\sigma_2 Y - \pi_2) C^Y. \tag{3.8}$$

We find that system (2.9)–(2.16) has eight possible steady states.

(i) Infection-free steady state, $Ð_0 = (S_0, 0, 0, 0, 0, 0, 0, 0)$, where $S_0 = \rho/\alpha$. In this case the body is free from HIV and HTLV.

(ii) Persistent HIV single infection steady state with an ineffective immune response, $Ð_1 = (S_1, L_1, I_1, 0, 0, V_1, 0, 0)$, where

$$S_1 = \frac{S_0}{\Re_1}, \qquad L_1 = \frac{a\alpha\varepsilon}{a\varepsilon\varkappa_2 + \lambda(b\varkappa_1 + \varepsilon\varkappa_3)} (\Re_1 - 1),$$
$$I_1 = \frac{\alpha\varepsilon\lambda}{a\varepsilon\varkappa_2 + \lambda(b\varkappa_1 + \varepsilon\varkappa_3)} (\Re_1 - 1), \qquad V_1 = \frac{\alpha b\lambda}{a\varepsilon\varkappa_2 + \lambda(b\varkappa_1 + \varepsilon\varkappa_3)} (\Re_1 - 1).$$

The parameter $\Re_1$ represents the basic HIV single infection reproduction number for system (2.9)–(2.16) and is defined as:

$$\Re_1 = \frac{S_0 \lambda b \varkappa_1}{a\varepsilon(\gamma + \lambda)} + \frac{S_0 \varkappa_2}{\gamma + \lambda} + \frac{S_0 \lambda \varkappa_3}{a(\gamma + \lambda)}.$$

The parameter $\Re_1$ decides whether or not a persistent HIV infection can be established. It is clear that at the steady state $Ð_1$ the HIV single infection persists with ineffective immune response.

(iii) Persistent HTLV single infection steady state with an ineffective immune response, $Ð_2 = (S_2, 0, 0, E_2, Y_2, 0, 0, 0)$, where

$$S_2 = \frac{S_0}{\Re_2}, \quad E_2 = \frac{\alpha\delta}{\varkappa_4\psi} (\Re_2 - 1), \quad Y_2 = \frac{\alpha}{\varkappa_4} (\Re_2 - 1).$$

The parameter $\Re_2$ denotes the basic HTLV single infection reproduction number for system (2.9)–(2.16) and is defined as:

$$\Re_2 = \frac{\varphi \varkappa_4 \psi S_0}{(\delta - r)\psi + \delta\omega}.$$

The parameter $\Re_2$ decides whether or not a persistent HTLV infection can be established.

(iv) Persistent HIV single infection steady state with only effective HIV-specific CTL, $Ð_3 = (S_3, L_3, I_3, 0, 0, V_3, C_3^I, 0)$, where

$$S_3 = \frac{\rho\varepsilon\sigma_1}{b\pi_1\varkappa_1 + \varepsilon(\pi_1\varkappa_3 + \alpha\sigma_1 + \sigma_1\varkappa_2 L_3)}, \; I_3 = \frac{\pi_1}{\sigma_1}, \; V_3 = \frac{b}{\varepsilon} I_3 = \frac{b\pi_1}{\varepsilon\sigma_1}, \; C_3^I = \frac{a}{\mu_1}(\Re_3 - 1),$$

and L_3 satisfies the following equation

$$\tilde{A}L_3^2 + \tilde{B}L_3 + \tilde{C} = 0, \tag{3.9}$$

where

$$\begin{aligned}
\tilde{A} &= \varepsilon\varkappa_2\sigma_1(\gamma+\lambda) > 0,\\
\tilde{B} &= \pi_1(b\varkappa_1 + \varepsilon\varkappa_3)(\gamma+\lambda) + \varepsilon\sigma_1[\alpha(\gamma+\lambda) - \varkappa_2\rho],\\
\tilde{C} &= -\pi_1\rho(b\varkappa_1 + \varepsilon\varkappa_3) < 0.
\end{aligned} \tag{3.10}$$

Since $\tilde{B}^2 - 4\tilde{A}\tilde{C} > 0$ then Eq (3.9) has two different real solutions. The positive solution is

$$L_3 = \frac{-\tilde{B} + \sqrt{\tilde{B}^2 - 4\tilde{A}\tilde{C}}}{2\tilde{A}}.$$

It follows that $S_3 > 0$ and $C_3^I > 0$ only when $\mathfrak{R}_3 > 1$. We define the HIV-specific CTL-mediated immunity reproduction number in case of HIV single infection as follows:

$$\mathfrak{R}_3 = \frac{\lambda\sigma_1 L_3}{a\pi_1}.$$

The parameter $\mathfrak{R}_3$ determines whether or not the HIV-specific CTL-mediated immune response is effective in the absence of HTLV.

(v) Persistent HTLV single infection steady state with only effective HTLV-specific CTL, $Ð_4 = (S_4, 0, 0, E_4, Y_4, 0, 0, C_4^Y)$, where

$$\begin{aligned}
S_4 &= \frac{\sigma_2\rho}{\pi_2\varkappa_4 + \alpha\sigma_2}, \quad Y_4 = \frac{\pi_2}{\sigma_2},\\
E_4 &= \frac{\pi_2[r(\pi_2\varkappa_4 + \alpha\sigma_2) + \varkappa_4\rho\varphi\sigma_2]}{\sigma_2(\psi+\omega)(\pi_2\varkappa_4 + \alpha\sigma_2)},\\
C_4^Y &= \frac{(\delta - r)\psi + \delta\omega}{\mu_2(\psi+\omega)}(\mathfrak{R}_4 - 1).
\end{aligned}$$

The HTLV-specific CTL-mediated immunity reproduction number in case of HTLV single infection is stated as:

$$\mathfrak{R}_4 = \frac{\sigma_2\rho\varphi\varkappa_4\psi}{(\pi_2\varkappa_4 + \alpha\sigma_2)[(\delta - r)\psi + \delta\omega]}.$$

The parameter $\mathfrak{R}_4$ determines whether or not the HTLV-specific CTL-mediated immune response is effective in the absence of HIV.

(vi) Persistent HTLV/HIV dual infection steady state with only effective HIV-specific CTL, $Ð_5 = (S_5, L_5, I_5, E_5, Y_5, V_5, C_5^I, 0)$, where

$$\begin{aligned}
S_5 &= \frac{(\delta - r)\psi + \delta\omega}{\varphi\varkappa_4\psi} = S_2, \quad I_5 = \frac{\pi_1}{\sigma_1} = I_3,\\
V_5 &= \frac{b\pi_1}{\varepsilon\sigma_1} = V_3, \quad L_5 = \frac{\pi_1(b\varkappa_1 + \varepsilon\varkappa_3)}{\varepsilon\sigma_1\varkappa_2(\mathfrak{R}_5^* - 1)},
\end{aligned}$$

$$E_5 = \frac{\delta\left[\pi_1\varkappa_4\psi\varphi(b\varkappa_1+\varepsilon\varkappa_3)(\gamma+\lambda)+\alpha\varepsilon\sigma_1\varkappa_2\left\{(\delta-r)\psi+\delta\omega\right\}(\mathfrak{R}_5^*-1)\right]}{\varepsilon\sigma_1\varkappa_4\psi\varkappa_2\left[(\delta-r)\psi+\delta\omega\right]}\left(\frac{\mathfrak{R}_5-1}{\mathfrak{R}_5^*-1}\right),$$

$$Y_5 = \frac{\pi_1\varphi\psi\varkappa_4(b\varkappa_1+\varepsilon\varkappa_3)(\gamma+\lambda)+\alpha\varepsilon\sigma_1\varkappa_2\left[(\delta-r)\psi+\delta\omega\right](\mathfrak{R}_5^*-1)}{\varepsilon\sigma_1\varkappa_4\varkappa_2\left[(\delta-r)\psi+\delta\omega\right]}\left(\frac{\mathfrak{R}_5-1}{\mathfrak{R}_5^*-1}\right),$$

$$C_5^I = \frac{a\varkappa_4\varphi\psi(\gamma+\lambda)}{\mu_1\varkappa_2\left[(\delta-r)\psi+\delta\omega\right]\left(\mathfrak{R}_5^*-1\right)}\left(\mathfrak{R}_1/\mathfrak{R}_2-1\right).$$

The HTLV infection reproduction number in the presence of HIV infection is stated as:

$$\mathfrak{R}_5 = \frac{\rho\varphi\psi\varepsilon\sigma_1\varkappa_4\varkappa_2(\mathfrak{R}_5^*-1)}{\pi_1\varphi\psi\varkappa_4(b\varkappa_1+\varepsilon\varkappa_3)(\gamma+\lambda)+\alpha\varepsilon\sigma_1\varkappa_2\left[(\delta-r)\psi+\delta\omega\right](\mathfrak{R}_5^*-1)},$$

where

$$\mathfrak{R}_5^* = \frac{\varkappa_4\varphi\psi(\gamma+\lambda)}{\varkappa_2\left[(\delta-r)\psi+\delta\omega\right]}.$$

It is obvious that the parameter $\mathfrak{R}_5$ determines whether or not HIV-infected patients could be dually infected with HTLV.

(vii) Persistent HTLV/HIV dual infection steady state with only effective HTLV-specific CTL, $\text{Đ}_6 = (S_6, L_6, I_6, E_6, Y_6, V_6, 0, C_6^Y)$, where

$$\begin{aligned}
S_6 &= \frac{a\varepsilon(\gamma+\lambda)}{a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)} = S_1,\\
L_6 &= \frac{a\varepsilon(\pi_2\varkappa_4+\alpha\sigma_2)}{\sigma_2\left[a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\right]}\left(\mathfrak{R}_6-1\right),\\
I_6 &= \frac{\lambda\varepsilon(\pi_2\varkappa_4+\alpha\sigma_2)}{\sigma_2\left[a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\right]}\left(\mathfrak{R}_6-1\right),\\
E_6 &= \frac{\pi_2\left[r\left\{a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\right\}+a\varepsilon\varkappa_4\varphi(\gamma+\lambda)\right]}{\sigma_2(\psi+\omega)\left[a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\right]},\\
Y_6 &= \frac{\pi_2}{\sigma_2} = Y_4,\\
V_6 &= \frac{b\lambda(\pi_2\varkappa_4+\alpha\sigma_2)}{\sigma_2\left[a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\right]}\left(\mathfrak{R}_6-1\right),\\
C_6^Y &= \frac{(\delta-r)\psi+\delta\omega}{\mu_2(\psi+\omega)}\left(\mathfrak{R}_2/\mathfrak{R}_1-1\right).
\end{aligned}$$

The HIV infection reproduction number in the presence of HTLV infection is stated as:

$$\mathfrak{R}_6 = \frac{\rho\sigma_2\left[a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\right]}{a\varepsilon(\gamma+\lambda)(\pi_2\varkappa_4+\alpha\sigma_2)}.$$

It is clear that the parameter $\mathfrak{R}_6$ determines whether or not HTLV-infected patients could be dually infected with HIV.

(viii) Persistent HTLV/HIV dual infection steady state with effective HIV-specific CTL and HTLV-specific CTL, $\text{Đ}_7 = (S_7, L_7, I_7, E_7, Y_7, V_7, C_7^I, C_7^Y)$, where

$$S_7 = \frac{\varepsilon\sigma_1\sigma_2\rho}{\pi_1\sigma_2(b\varkappa_1+\varepsilon\varkappa_3)+\varepsilon\sigma_1(\pi_2\varkappa_4+\alpha\sigma_2+\varkappa_2\sigma_2L_7)},$$

$$E_7 = \frac{\pi_2\varepsilon\varkappa_4\rho\sigma_1\sigma_2\varphi + \pi_2 r\left[\pi_1\sigma_2\left(b\varkappa_1+\varepsilon\varkappa_3\right)+\varepsilon\sigma_1(\pi_2\varkappa_4+\alpha\sigma_2+L_7\varkappa_2\sigma_2)\right]}{\sigma_2(\psi+\omega)\left[\pi_1\sigma_2\left(b\varkappa_1+\varepsilon\varkappa_3\right)+\varepsilon\sigma_1(\pi_2\varkappa_4+\alpha\sigma_2+\varkappa_2\sigma_2L_7)\right]},$$
$$I_7 = \frac{\pi_1}{\sigma_1} = I_3 = I_5, \quad Y_7 = \frac{\pi_2}{\sigma_2} = Y_4 = Y_6, \quad V_7 = \frac{b\pi_1}{\varepsilon\sigma_1} = V_3 = V_5,$$
$$C_7^I = \frac{a}{\mu_1}\left(\mathfrak{R}_7 - 1\right),$$
$$C_7^Y = \frac{(\delta-r)\psi+\delta\omega}{\mu_2(\psi+\omega)}\left(\mathfrak{R}_8 - 1\right),$$

and L_7 is given by

$$L_7 = \frac{-\bar{B} + \sqrt{\bar{B}^2 - 4\bar{A}\bar{C}}}{2\bar{A}},$$

where

$$\begin{aligned}
&\bar{A} = \varepsilon\varkappa_2\sigma_1\sigma_2(\gamma+\lambda),\\
&\bar{B} = \pi_2\varepsilon\varkappa_4\sigma_1(\gamma+\lambda) + \pi_1\sigma_2(b\varkappa_1+\varepsilon\varkappa_3)(\gamma+\lambda) + \alpha\varepsilon\sigma_1\sigma_2(\gamma+\lambda) - \varepsilon\varkappa_2\rho\sigma_1\sigma_2,\\
&\bar{C} = -\pi_1\rho\sigma_2(b\varkappa_1+\varepsilon\varkappa_3).
\end{aligned} \tag{3.11}$$

Now we define

$$\mathfrak{R}_7 = \frac{\lambda\sigma_1 L_7}{a\pi_1},$$
$$\mathfrak{R}_8 = \frac{\pi_2\varepsilon\varkappa_4\rho\sigma_1\sigma_2\varphi\psi}{\pi_2\left[\pi_1\sigma_2\left(b\varkappa_1+\varepsilon\varkappa_3\right)+\varepsilon\sigma_1(\pi_2\varkappa_4+\alpha\sigma_2+\varkappa_2\sigma_2L_7)\right]\left((\delta-r)\psi+\delta\omega\right)}.$$

The parameter $\mathfrak{R}_7$ is the competed HIV-specific CTL-mediated immunity reproduction number in case of HTLV/HIV dual infection. The parameter $\mathfrak{R}_8$ is the competed HTLV-specific CTL-mediated immunity reproduction number in case of HTLV/HIV dual infection. Clearly, $Ð_7$ exists when $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$.

3.2. Global stability analysis

In this subsection, we analyze the global asymptotic stability of all steady states by Lyapunov method. We construct Lyapunov functions which were first used for Lotka–Volterra predator–prey systems [41, 42] and extended for virus dynamics systems [43–46].

Theorem 1. If $\mathfrak{R}_1 \le 1$ and $\mathfrak{R}_2 \le 1$, then $Ð_0$ is globally asymptotically stable (G.A.S).

Lemma 1. If $\mathfrak{R}_3 \le 1$, then $I_1 \le I_3$.

Theorem 2. Let $\mathfrak{R}_1 > 1$, $\mathfrak{R}_2/\ \mathfrak{R}_1 \le 1$ and $\mathfrak{R}_3 \le 1$, then $Ð_1$ is G.A.S.

Theorem 3. If $\mathfrak{R}_2 > 1$, $\mathfrak{R}_1/\ \mathfrak{R}_2 \le 1$ and $\mathfrak{R}_4 \le 1$, then $Ð_2$ is G.A.S.

Theorem 4. Let $\mathfrak{R}_3 > 1$ and $\mathfrak{R}_5 \le 1$, then $Ð_3$ is G.A.S.

Theorem 5. If $\mathfrak{R}_4 > 1$ and $\mathfrak{R}_6 \le 1$, then $Ð_4$ is G.A.S.

Theorem 6. If $\mathfrak{R}_5 > 1$, $\mathfrak{R}_5^* > 1$, $\mathfrak{R}_8 \le 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 > 1$, then $Ð_5$ is G.A.S.

Lemma 2. If $\mathfrak{R}_7 \le 1$, then $I_6 \le I_7$.

Theorem 7. If $\mathfrak{R}_6 > 1$, $\mathfrak{R}_7 \le 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 > 1$, then $Ð_6$ is G.A.S.

Theorem 8. If $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$, then $Ð_7$ is G.A.S.

The proofs of Lemmas 1–2 and Theorems 1–8 are given in the Appendix.

4. Numerical simulations

In this section, we numerically illustrate the global stability of steady states using the values of the parameters given in Table 1. Moreover, we present comparison between single and dual infections.

Table 1. The values of parameters of model (2.1)–(2.8).

Parameter	Value	Parameter	Value	Parameter	Value
ρ	10	κ	0.9	ε	2
α	0.01	r^*	0.008	γ	0.02
$\varkappa_1$	Varied	δ^*	0.2	σ_1	Varied
$\varkappa_2$	Varied	b	5	σ_2	Varied
$\varkappa_3$	Varied	π_1	0.1	λ	0.2
$\varkappa_4$	Varied	π_2	0.1	ω	0.01
a	0.5	μ_1	0.2	ψ	0.003
φ	0.2	μ_2	0.2		

4.1. Stability of the steady states

In this subsection, we numerically solve system (2.1)–(2.8) with the following three different initial states $(S, L, I, E, Y, V, C^I, C^Y)(0)$ as:

Initial-1 : $(700, 15, 1.5, 30, 0.2, 5, 3, 3)$,

Initial-2: $(600, 10, 1, 20, 0.18, 2, 2, 2)$,

Initial-3: $(400, 5, 0.5, 10, 0.16, 1.5, 1, 1)$.

We choose the values of $\varkappa_1, \varkappa_2, \varkappa_3, \varkappa_4, \sigma_1$ and σ_2 according to the following sets:

Set 1 (**Stability of Đ_0**): $\varkappa_1 = 0.00006$, $\varkappa_2 = 0.00005$, $\varkappa_3 = 0.00007$, $\varkappa_4 = 0.001$, $\sigma_1 = 0.3$ and $\sigma_2 = 0.5$. For this set of parameters, we have $\mathfrak{R}_1 = 0.63 < 1$ and $\mathfrak{R}_2 = 0.23 < 1$. Figure 2 displays that the trajectories initiating with Initial-1, Initial-2 and Initial-3 reach the steady state $\text{Đ}_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$. This shows that Đ_0 is G.A.S according to Theorem 1. In this situation both HIV and HTLV will be died out.

Set 2 (Stability of Đ_1): $\varkappa_1 = 0.0001$, $\varkappa_2 = 0.0002$, $\varkappa_3 = 0.0003$, $\varkappa_4 = 0.0005$, $\sigma_1 = 0.003$ and $\sigma_2 = 0.2$. With such choice we get $\mathfrak{R}_2 = 0.12 < 1 < 1.91 = \mathfrak{R}_1$, $\mathfrak{R}_3 = 0.39 < 1$ and hence $\mathfrak{R}_2/\mathfrak{R}_1 = 0.06 < 1$. The steady state Đ_1 exists with $\text{Đ}_1 = (523.81, 21.65, 8.66, 0, 0, 21.65, 0, 0)$. Figure 3 shows the stability of the system around Đ_1 initiating from different states. Thus, the numerical simulations support the result obtained in Theorem 2. This will lead to the situation of persistent HIV single infection but with an ineffective CTL-mediated immune response.

Set 3 (Stability of Đ_2): $\varkappa_1 = 0.0001$, $\varkappa_2 = 0.00005$, $\varkappa_3 = 0.00007$, $\varkappa_4 = 0.006$, $\sigma_1 = 0.001$ and $\sigma_2 = 0.05$. Then, we calculate $\mathfrak{R}_1 = 0.81 < 1 < 1.4 = \mathfrak{R}_2$, $\mathfrak{R}_4 = 0.64 < 1$ and then $\mathfrak{R}_1/\mathfrak{R}_2 = 0.58 < 1$ and $\text{Đ}_2 = (713.33, 0, 0, 44.47, 0.67, 0, 0, 0)$. Figure 4 declares that the solutions of the system starting from different states tend to the steady state Đ_2. This shows the consistency between the numerical results and theoretical result of Theorem 3. It means that, a persistent HTLV single infection with an ineffective CTL-mediated immune response will be reached.

Set 4 (Stability of Đ_3): $\varkappa_1 = 0.001$, $\varkappa_2 = 0.0001$, $\varkappa_3 = 0.0003$, $\varkappa_4 = 0.001$, $\sigma_1 = 0.05$ and $\sigma_2 = 0.005$. Then, we calculate $\mathfrak{R}_3 = 3.91 > 1$ and $\mathfrak{R}_5 = 0.22 < 1$. Figure 5 shows that the

trajectories starting with different states tend to $Đ_3 = (569.59, 19.56, 2, 0, 0, 5, 7.28, 0)$. Therefore, $Đ_3$ is G.A.S and this is compatible with Theorem 4. Hence, a persistent HIV single infection with effective HIV-specific CTL-mediated immune response is attained.

Set 5 (Stability of $Đ_4$): $\varkappa_1 = \varkappa_2 = 0.0001$, $\varkappa_3 = 0.0002$, $\varkappa_4 = 0.035$, $\sigma_1 = 0.05$ and $\sigma_2 = 0.4$. Then, we calculate $\Re_4 = 4.35 > 1$ and $\Re_6 = 0.68 < 1$ and $Đ_4$ exists with $Đ_4 = (533.33, 0, 0, 71.93, 0.25, 0, 0, 3.32)$. In Figure 6, we draw the trajectories of the system with three different initial states. It is clear that $Đ_4$ is G.A.S which supports Theorem 5. In this case, a persistent HTLV single infection with effective HTLV-specific CTL-mediated immunity is reached.

Set 6 (Stability of $Đ_5$): $\varkappa_1 = 0.001$, $\varkappa_2 = 0.0001$, $\varkappa_3 = 0.0002$, $\varkappa_4 = 0.011$, $\sigma_1 = 0.1$ and $\sigma_2 = 0.01$. Then, we calculate $\Re_5^* = 5.64 > 1$, $\Re_5 = 1.93 > 1$, $\Re_8 = 0.21 < 1$ and $\Re_1/\Re_2 = 2.09 > 1$. The numerical results demonstrated in Figure 7 show that $Đ_5 = (389.09, 5.80, 1, 74.98, 1.13, 2.5, 3.30, 0)$ exists and based on Theorem 6, $Đ_5$ is G.A.S. This case leads to a persistent dual infection with HTLV and HIV where the HIV-specific CTL-mediated immunity is effective and the HTLV-specific CTL-mediated immunity is ineffective.

Set 7 (Stability of $Đ_6$): $\varkappa_1 = 0.0006$, $\varkappa_2 = 0.0001$, $\varkappa_3 = 0.0002$, $\varkappa_4 = 0.04$, $\sigma_1 = 0.001$ and $\sigma_2 = 0.7$. We compute $\Re_6 = 2.26 > 1$, $\Re_7 = 0.17 < 1$ and $\Re_2/\Re_1 = 2.63 > 1$. Based on this set of values we get $Đ_6 = (282.05, 25.31, 10.12, 24.87, 0.143, 25.31, 0, 1.62)$. In Figure 8, we plot the numerical solutions of the system and show that $Đ_6$ is G.A.S (Theorem 7). This situation leads to a persistent dual infection with HTLV and HIV where the HTLV-specific CTL-mediated immunity is effective and the HIV-specific CTL-mediated immunity is not working.

Set 8 (Stability of $Đ_7$): $\varkappa_1 = 0.0006$, $\varkappa_2 = 0.0001$, $\varkappa_3 = 0.0002$, $\varkappa_4 = 0.03$, $\sigma_1 = 0.04$ and $\sigma_2 = 0.5$. These data give $\Re_7 = 1.83 > 1$ and $\Re_8 = 3.27 > 1$. According to these values the steady state $Đ_7 = (467.37, 11.46, 2.5, 43.25, 0.2, 6.25, 2.09, 2.25)$ exists. Figure 9 illustrates that the solutions of the system initiating with three different states tend to $Đ_7$. In this case, a persistent dual infection with HTLV and HIV is reached where both immune responses are well working.

To further confirmation, we study the local stability of the system's steady states. We first calculate the Jacobian matrix $J = J(S, L, I, E, Y, V, C^I, C^Y)$ of system (2.1)–(2.8) as:

$$J = \begin{pmatrix} J_{11} & -\varkappa_2 S & -\varkappa_3 S & 0 & -\varkappa_4 S & -\varkappa_1 S & 0 & 0 \\ \varkappa_1 V + \varkappa_2 L + \varkappa_3 I & J_{22} & \varkappa_3 S & 0 & 0 & \varkappa_1 S & 0 & 0 \\ 0 & \lambda & J_{33} & 0 & 0 & 0 & -\mu_1 I & 0 \\ \varphi\varkappa_4 Y & 0 & 0 & J_{44} & \varphi\varkappa_4 S + \kappa r^* & 0 & 0 & 0 \\ 0 & 0 & 0 & \psi & J_{55} & 0 & 0 & -\mu_2 Y \\ 0 & 0 & b & 0 & 0 & J_{66} & 0 & 0 \\ 0 & 0 & \sigma_1 C^I & 0 & 0 & 0 & J_{77} & 0 \\ 0 & 0 & 0 & 0 & \sigma_2 C^Y & 0 & 0 & J_{88} \end{pmatrix},$$

where $J_{11} = -(\alpha + \varkappa_1 V + \varkappa_2 L + \varkappa_3 I + \varkappa_4 Y)$, $J_{22} = \varkappa_2 S - (\gamma + \lambda)$, $J_{33} = -\left(a + \mu_1 C^I\right)$, $J_{44} = -(\psi + \omega)$, $J_{55} = (1 - \kappa) r^* - \left(\delta^* + \mu_2 C^Y\right)$, $J_{66} = -\varepsilon$, $J_{77} = \sigma_1 I - \pi_1$, and $J_{88} = \sigma_2 Y - \pi_2$. Then, we compute the eigenvalues λ_i, $i = 1, 2, ..., 8$ of J at each steady state. The steady state is locally stable if the eigenvalues satisfy $\mathrm{Re}(\lambda_i) < 0$, for all $i = 1, 2, ..., 8$. We use the values of the parameters $\varkappa_1$, $\varkappa_2$, $\varkappa_3$, $\varkappa_4$, σ_1 and σ_2 given in Sets 1-8 and compute all nonnegative steady states and the corresponding real parts of the eigenvalues (see Table 2). The local stability results agree with the global stability results given in Theorems 1–8.

Table 2. Local stability of steady states.

Set	The steady state	(Re(λ_i), $i = 1, 2, ..., 8$)	Stability
1	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.98, -0.63, -0.2, -0.1, -0.1, -0.07, -0.01, -0.01)$	stable
2	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.96, -0.7, -0.2, 0.15, -0.1, -0.1, -0.01, -0.01)$	unstable
	$Ð_1 = (523.81, 21.65, 8.66, 0, 0, 21.65, 0, 0)$	$(-1.98, -0.64, -0.2, -0.1, -0.07, -0.01, -0.01, -0.01)$	stable
3	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.96, -0.68, -0.22, -0.1, -0.1, -0.03, -0.01, 0.004)$	unstable
	$Ð_2 = (713.33, 0, 0, 44.47, 0.67, 0, 0, 0)$	$(-1.97, -0.64, -0.21, -0.1, -0.07, -0.07, -0.01, -0.01)$	stable
4	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.51, -1.51, 0.41, -0.2, -0.1, -0.1, -0.01, -0.01)$	unstable
	$Ð_1 = (180.33, 37.26, 14.9, 0, 0, 37.26, 0, 0)$	$(-1.92, -0.79, 0.65, -0.2, -0.1, -0.02, -0.02, -0.01)$	unstable
	$Ð_3 = (569.59, 19.56, 2, 0, 0, 5, 7.28, 0)$	$(-2.03, -2.03, -0.2, -0.03, -0.03, -0.1, -0.02, -0.01)$	stable
5	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.96, -0.7, -0.28, -0.1, -0.1, 0.07, 0.04, -0.01)$	unstable
	$Ð_1 = (785.71, 9.74, 3.9, 0, 0, 9.74, 0, 0)$	$(-1.97, -0.67, -0.26, -0.1, 0.09, 0.05, -0.01, -0.01)$	unstable
	$Ð_2 = (122.29, 0, 0, 136.17, 2.05, 0, 0, 0)$	$(-2, 0.72, -0.54, -0.22, -0.17, -0.1, -0.06, -0.01)$	unstable
	$Ð_3 = (870.39, 5.89, 2, 0, 0, 5, 0.45, 0)$	$(-1.97, -0.75, -0.27, -0.1, 0.06, -0.01, -0.01, -0.01)$	unstable
	$Ð_4 = (533.33, 0, 0, 71.93, 0.25, 0, 0, 3.32)$	$(-1.98, -0.79, -0.63, -0.1, -0.06, -0.06, -0.03, -0.01)$	stable
6	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.51, -1.51, 0.39, -0.23, -0.1, -0.1, 0.02, -0.01)$	unstable
	$Ð_1 = (186.44, 36.98, 14.79, 0, 0, 36.98, 0, 0)$	$(-1.92, 1.38, -0.79, -0.21, -0.1, -0.02, -0.02, -0.01)$	unstable
	$Ð_2 = (389.09, 0, 0, 94.78, 1.43, 0, 0, 0)$	$(-1.81, -0.99, -0.21, 0.13, -0.1, -0.09, -0.01, -0.01)$	unstable
	$Ð_3 = (714.37, 12.98, 1, 0, 0, 2.5, 10.48, 0)$	$(-2.34, -2.34, -0.22, -0.03, -0.03, -0.1, -0.01, 0.01)$	unstable
	$Ð_5 = (389.09, 5.8, 1, 74.98, 1.13, 2.5, 3.3, 0)$	$(-1.65, -1.65, -0.21, -0.02, -0.02, -0.09, -0.01, -0.01)$	stable
7	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.65, -1.24, -0.29, 0.27, -0.1, -0.1, 0.07, -0.01)$	unstable
	$Ð_1 = (282.05, 32.63, 13.05, 0, 0, 32.63, 0, 0)$	$(-1.93, -0.77, -0.23, -0.1, -0.09, -0.01, -0.01, 0.02)$	unstable
	$Ð_2 = (107, 0, 0, 138.54, 2.09, 0, 0, 0)$	$(-1.98, 1.36, -0.62, -0.22, -0.11, -0.1, -0.07, -0.01)$	unstable
	$Ð_4 = (636.36, 0, 0, 56.02, 0.14, 0, 0, 4.89)$	$(-1.83, -1.1, -0.98, 0.15, -0.1, -0.07, -0.02, -0.01)$	unstable
	$Ð_6 = (282.05, 25.31, 10.12, 24.87, 0.14, 25.31, 0, 1.62)$	$(-1.93, -0.77, -0.47, -0.09, -0.02, -0.02, -0.05, -0.02)$	stable
8	$Ð_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-1.65, -1.24, 0.27, -0.27, -0.1, -0.1, 0.06, -0.01)$	unstable
	$Ð_1 = (282.05, 32.63, 13.05, 0, 0, 32.63, 0, 0)$	$(-1.93, -0.77, 0.42, -0.22, -0.1, -0.01, -0.01, 0.01)$	unstable
	$Ð_2 = (142.67, 0, 0, 133.01, 2, 0, 0, 0)$	$(-1.97, 0.9, -0.65, -0.22, -0.1, -0.08, -0.05, -0.01)$	unstable
	$Ð_3 = (627.17, 16.95, 2.5, 0, 0, 6.25, 4.28, 0)$	$(-1.73, -1.73, -0.25, -0.1, -0.02, -0.02, 0.04, -0.02)$	unstable
	$Ð_4 = (625, 0, 0, 57.8, 0.2, 0, 0, 3.34)$	$(-1.83, -0.98, -0.8, 0.15, -0.1, -0.06, -0.02, -0.01)$	unstable
	$Ð_6 = (282.05, 24.94, 9.98, 26.15, 0.2, 24.94, 0, 0.96)$	$(-1.93, -0.77, -0.35, 0.3, -0.02, -0.02, -0.03, -0.03)$	unstable
	$Ð_7 = (467.37, 11.46, 2.5, 43.25, 0.2, 6.25, 2.09, 2.25)$	$(-1.81, -1.25, -0.59, -0.02, -0.02, -0.05, -0.03, -0.01)$	stable

4.2. Comparison study

In this subsection, we compare between single and dual infections dynamics

4.2.1. Influence of HTLV infection on the dynamics of HIV single infection

To study the effect of HTLV infection on the dynamics of HIV single infection, we make a comparison between model (2.1)–(2.8) and the following HIV single infection model:

$$\frac{dS}{dt} = \rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I, \tag{4.1}$$

$$\frac{dL}{dt} = \varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda + \gamma) L, \tag{4.2}$$

$$\frac{dI}{dt} = \lambda L - aI - \mu_1 C^I I, \tag{4.3}$$

$$\frac{dV}{dt} = bI - \varepsilon V, \tag{4.4}$$

$$\frac{dC^I}{dt} = \sigma_1 C^I I - \pi_1 C^I. \tag{4.5}$$

We select $\varkappa_1 = 0.0006$, $\varkappa_2 = 0.0002$, $\varkappa_3 = 0.0004$, $\varkappa_4 = 0.07$, $\sigma_1 = 0.05$, and $\sigma_2 = 0.5$ and take the following initial state:

Initial-4: $(450, 12, 2, 70, 0.2, 5, 4, 4.5)$.

Figure 10 shows that when an individual who has only HIV infection is dually infected with HTLV then the concentrations of uninfected CD4$^+$T cells, latent HIV-infected cells and HIV-specific CTLs are decreased. While, the concentration of free HIV particles reaches the same value in both HIV single infection and HTLV/HIV dual infection. In fact, this observation is consistent with the recent study [47], where it has found that there is no worthy differences in the concentration of HIV particles in comparison between HIV single infected and HTLV/HIV dual infected patients.

4.2.2. Influence of HIV infection on the dynamics of HTLV single infection

To see the effect of HIV infection on the dynamics of HTLV single infection, we perform a comparison between model (2.1)–(2.8) and the following HTLV single infection model:

$$\frac{dS}{dt} = \rho - \alpha S - \varkappa_4 S Y, \tag{4.6}$$

$$\frac{dE}{dt} = \varphi \varkappa_4 S Y + \kappa r^* Y - (\psi + \omega) E, \tag{4.7}$$

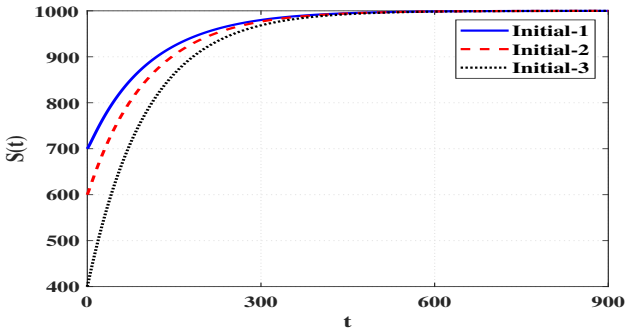
$$\frac{dY}{dt} = \psi E + (1 - \kappa) r^* Y - \delta^* Y - \mu_2 C^Y Y, \tag{4.8}$$

$$\frac{dC^Y}{dt} = \sigma_2 C^Y Y - \pi_2 C^Y. \tag{4.9}$$

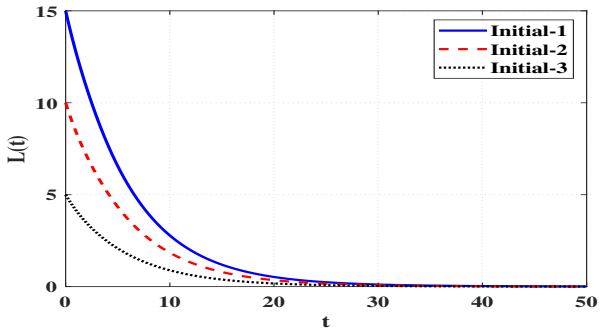
We select the values $\varkappa_1 = 0.0005$, $\varkappa_2 = 0.0002$, $\varkappa_3 = 0.0003$, $\varkappa_4 = 0.01$, $\sigma_1 = 0.05$, and $\sigma_2 = 0.2$ and take the following initial state:

Initial-5: $(550, 12, 2, 45, 0.5, 5, 3.5, 0.4)$.

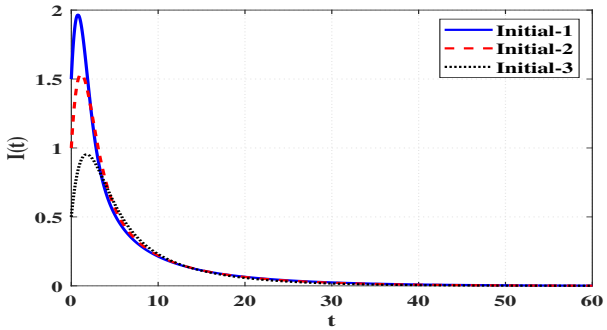
Figure 11 displays the solutions of two systems (2.1)–(2.8) and (4.6)–(4.9). We observe that the concentrations of uninfected CD4$^+$T cells, latent HTLV-infected cells and HTLV-specific CTLs are smaller in case of dual infection than that of HTLV single infection. In contrast, the concentration of active HTLV-infected cells reaches the same value in both HTLV single and HTLV/HIV dual infections.



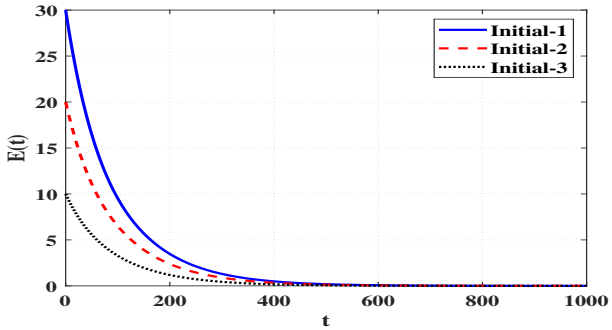
(a) Uninfected CD4$^+$T cells



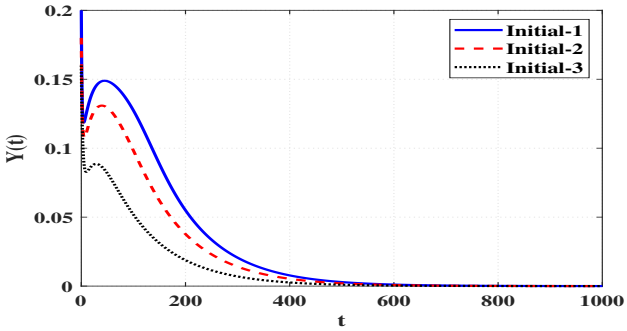
(b) Latent HIV-infected cells



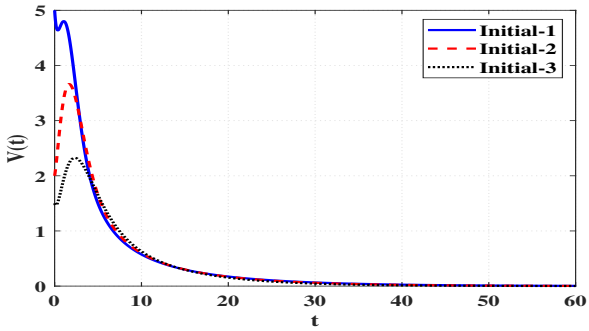
(c) Active HIV-infected cells



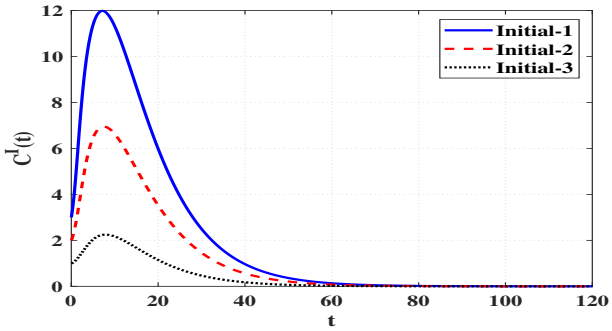
(d) Latent HTLV-infected cells



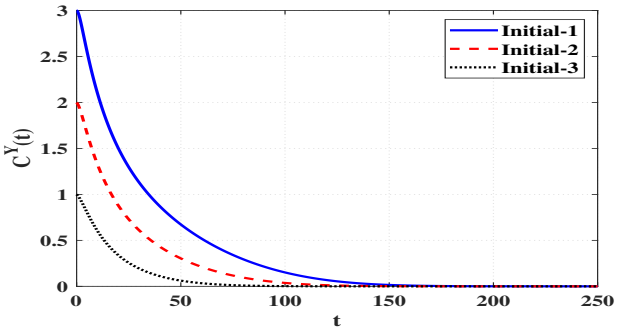
(e) Active HTLV-infected cells



(f) Free HIV particles

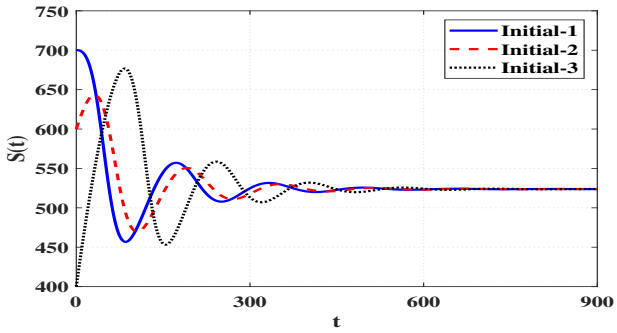


(g) HIV-specific CTLs

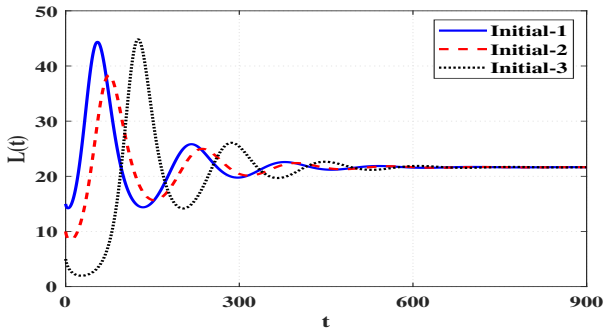


(h) HTLV-specific CTLs

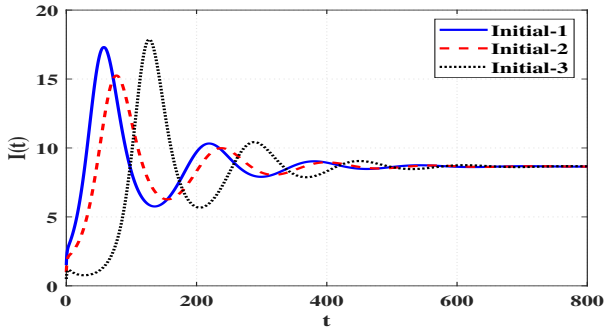
Figure 2. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$.



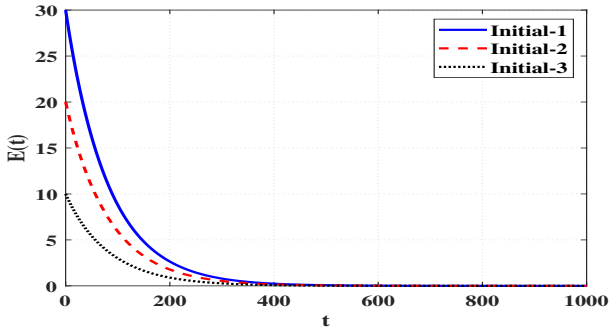
(a) Uninfected CD4$^+$T cells



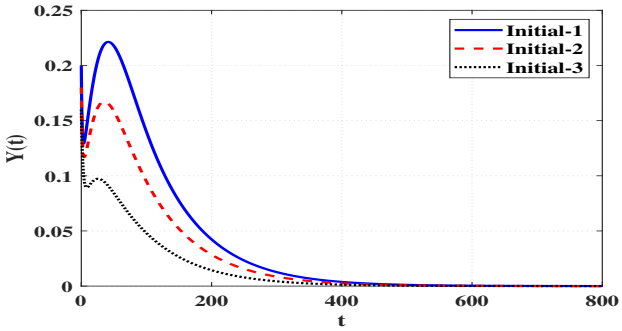
(b) Latent HIV-infected cells



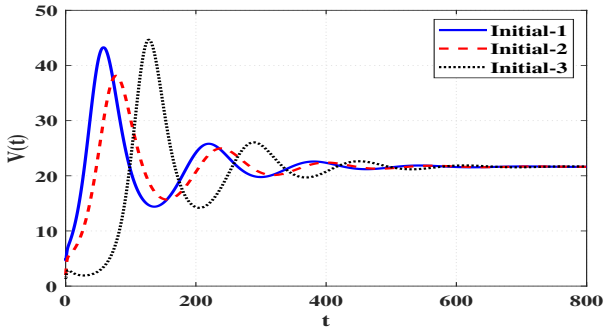
(c) Active HIV-infected cells



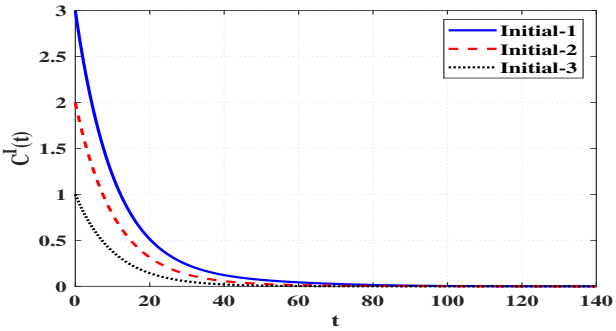
(d) Latent HTLV-infected cells



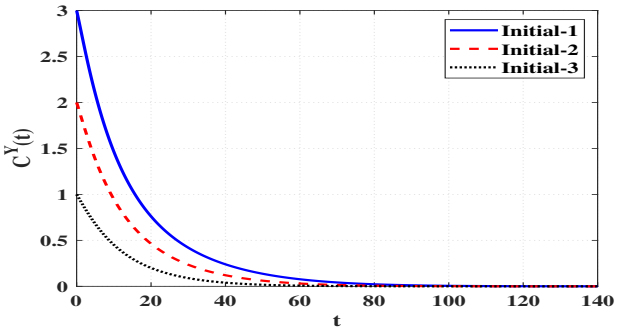
(e) Active HTLV-infected cells



(f) Free HIV particles

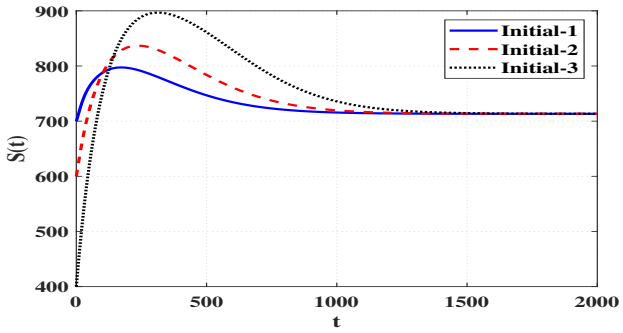


(g) HIV-specific CTLs

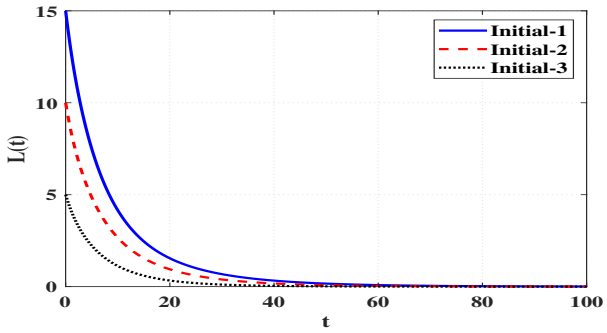


(h) HTLV-specific CTLs

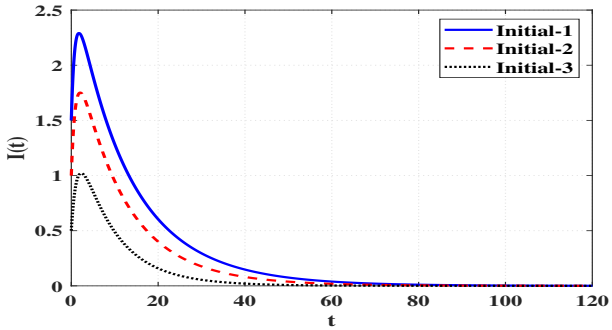
Figure 3. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_1 > 1$, $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_3 \leq 1$.



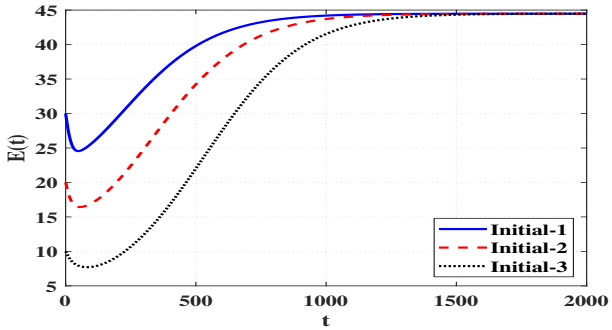
(a) Uninfected CD4$^+$T cells



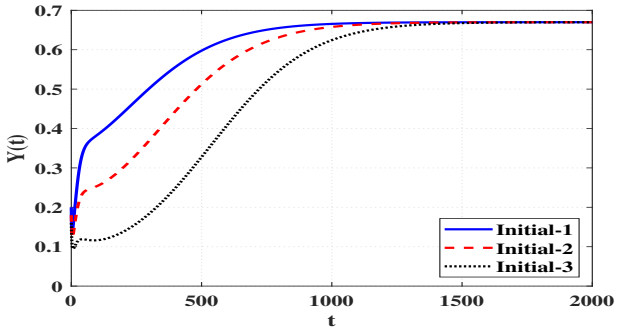
(b) Latent HIV-infected cells



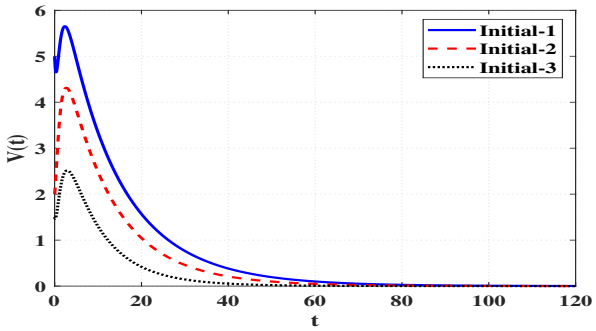
(c) Active HIV-infected cells



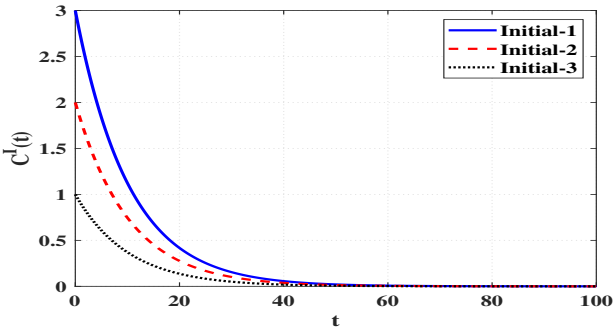
(d) Latent HTLV-infected cells



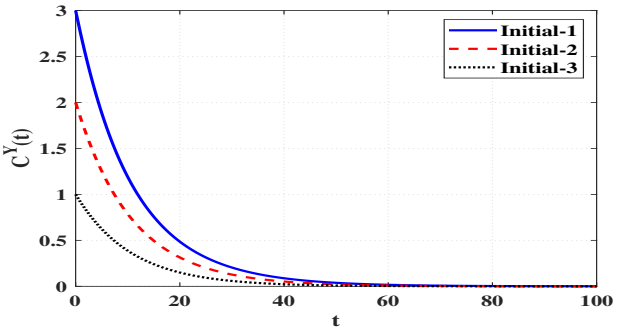
(e) Active HTLV-infected cells



(f) Free HIV particles

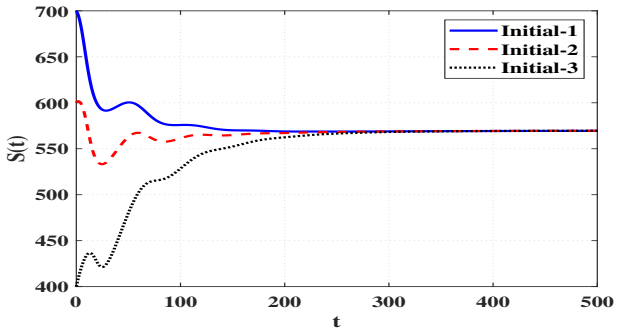


(g) HIV-specific CTLs

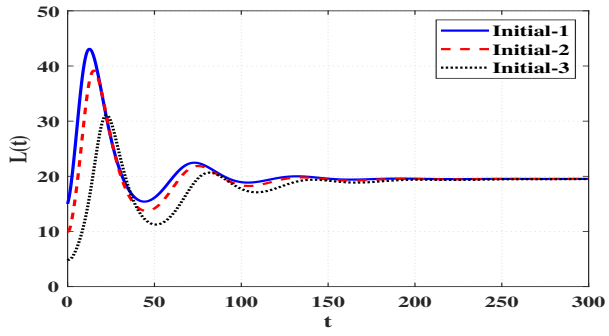


(h) HTLV-specific CTLs

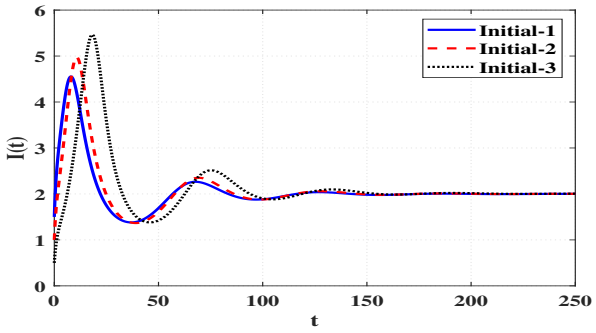
Figure 4. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_2 > 1$, $\mathfrak{R}_1/\mathfrak{R}_2 \leq 1$ and $\mathfrak{R}_4 \leq 1$.



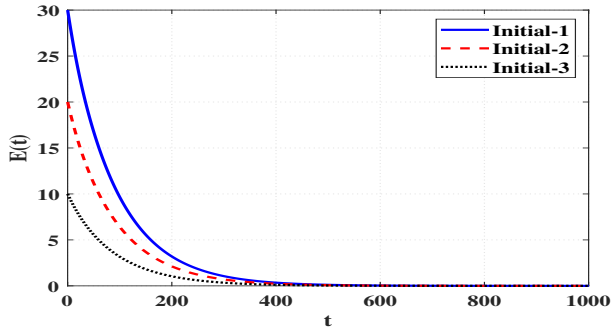
(a) Uninfected CD4$^+$T cells



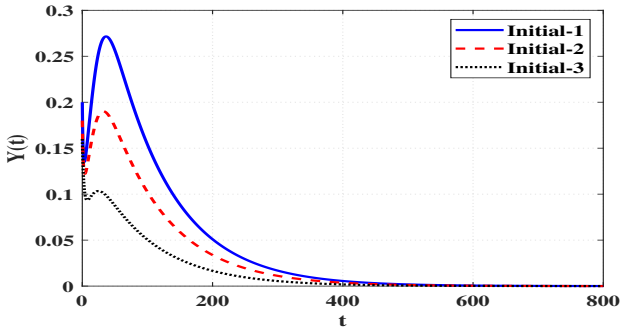
(b) Latent HIV-infected cells



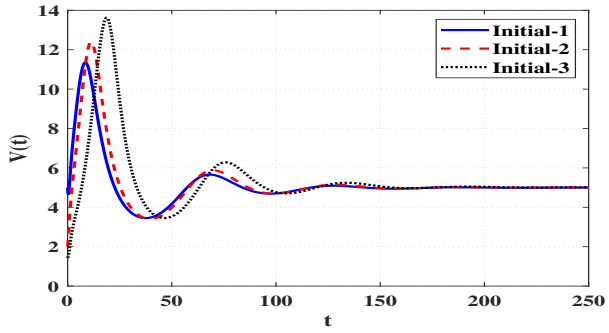
(c) Active HIV-infected cells



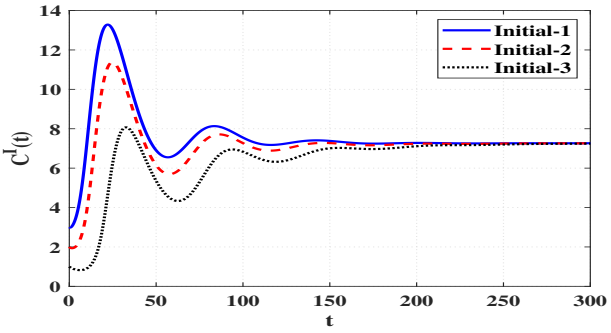
(d) Latent HTLV-infected cells



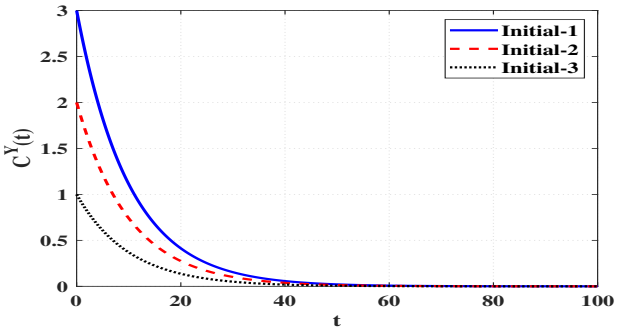
(e) Active HTLV-infected cells



(f) Free HIV particles

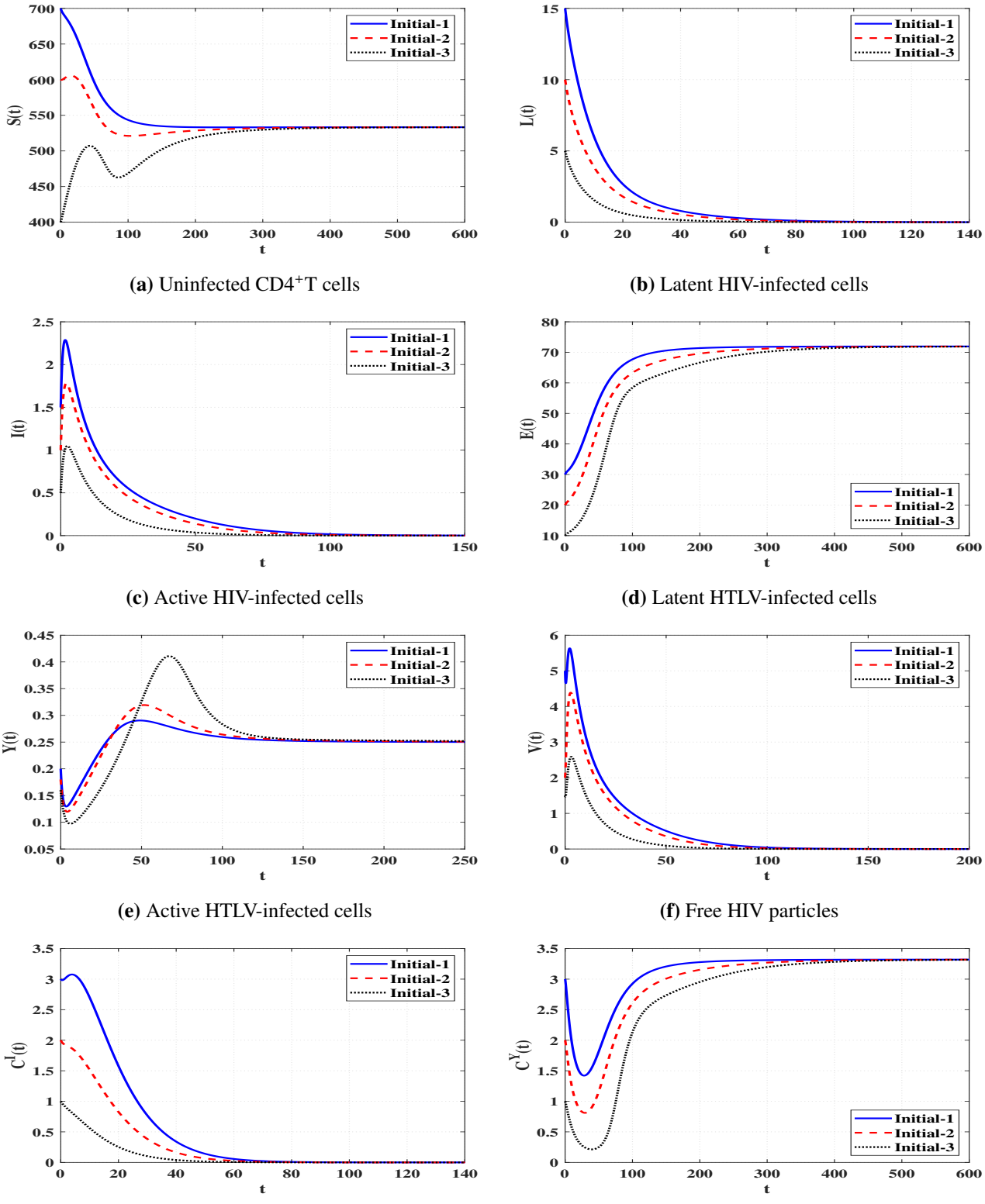


(g) HIV-specific CTLs



(h) HTLV-specific CTLs

Figure 5. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_3 > 1$ and $\mathfrak{R}_5 \leq 1$.



(a) Uninfected CD4$^+$T cells

(b) Latent HIV-infected cells

(c) Active HIV-infected cells

(d) Latent HTLV-infected cells

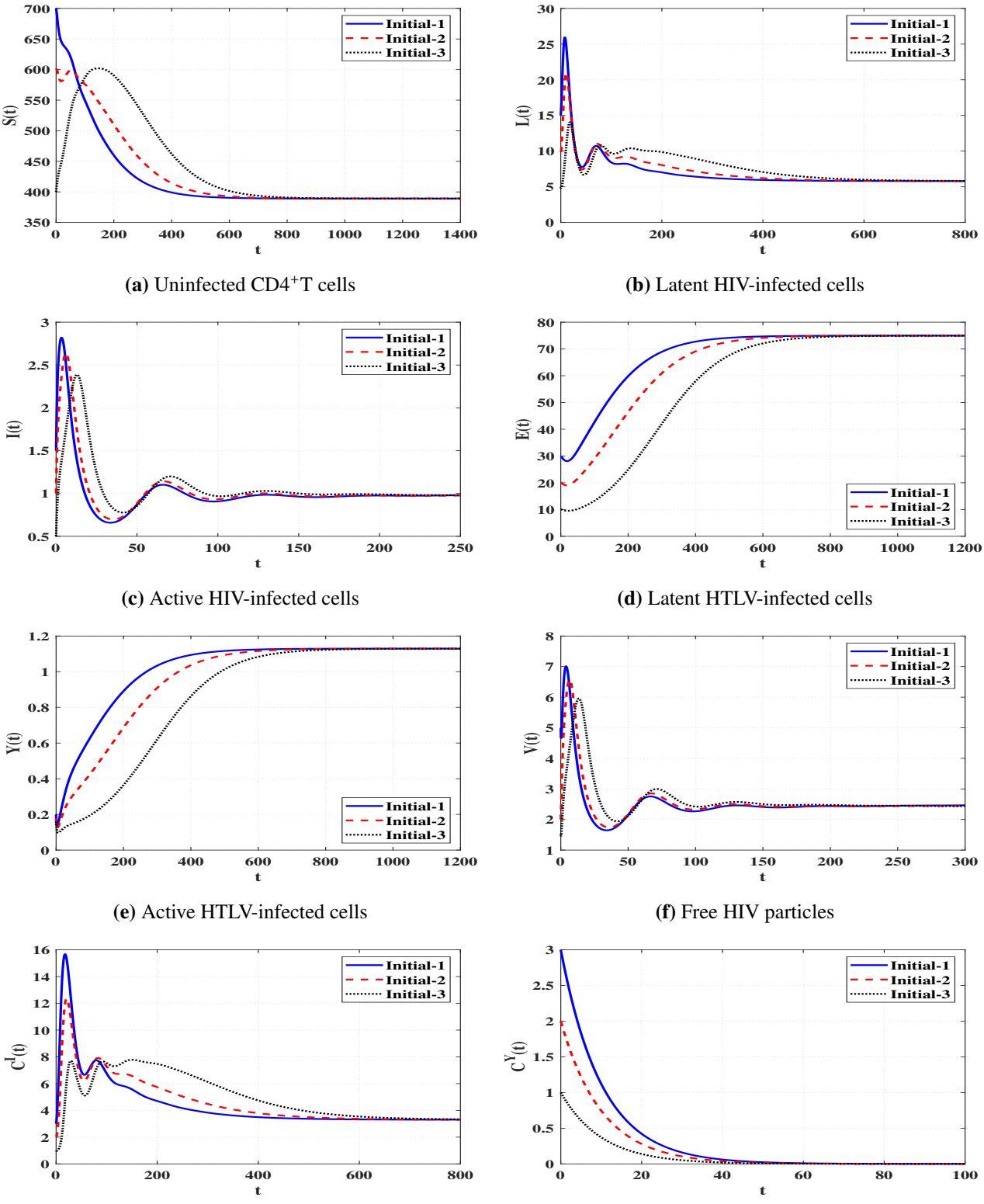
(e) Active HTLV-infected cells

(f) Free HIV particles

(g) HIV-specific CTLs

(h) HTLV-specific CTLs

Figure 6. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_4 > 1$ and $\mathfrak{R}_6 \leq 1$.



(a) Uninfected CD4$^+$T cells

(b) Latent HIV-infected cells

(c) Active HIV-infected cells

(d) Latent HTLV-infected cells

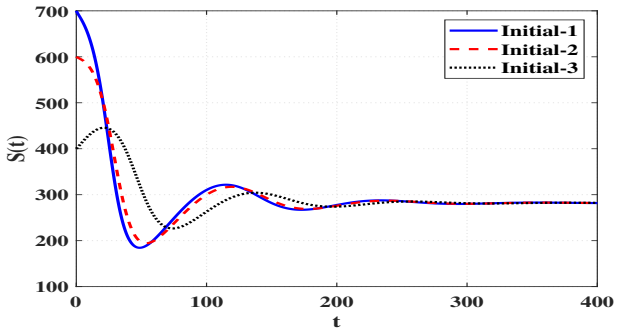
(e) Active HTLV-infected cells

(f) Free HIV particles

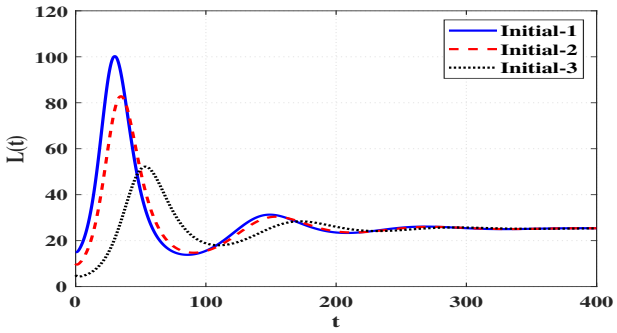
(g) HIV-specific CTLs

(h) HTLV-specific CTLs

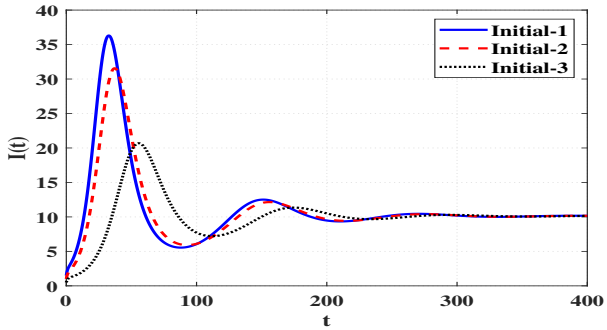
Figure 7. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_5^* > 1$, $\mathfrak{R}_5 > 1$, $\mathfrak{R}_8 \leq 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 > 1$.



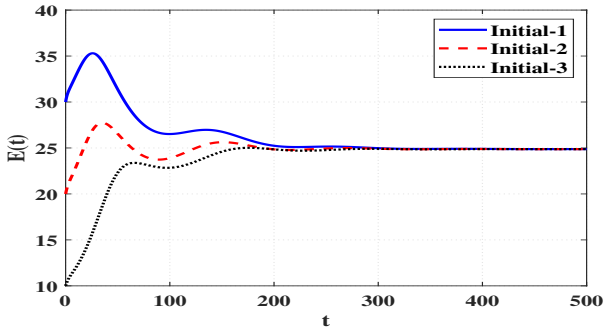
(a) Uninfected CD4$^+$T cells



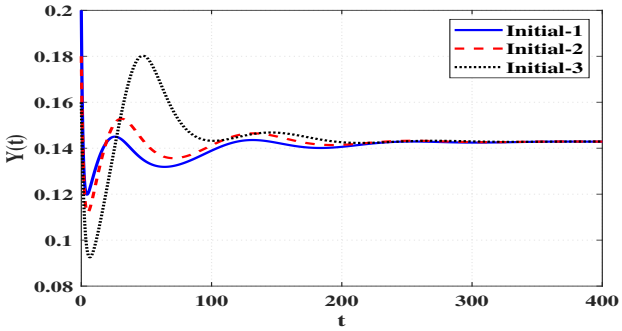
(b) Latent HIV-infected cells



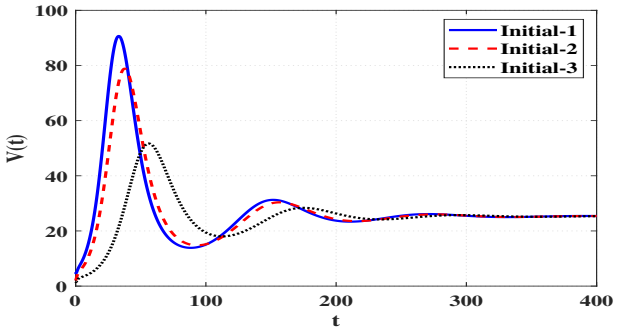
(c) Active HIV-infected cells



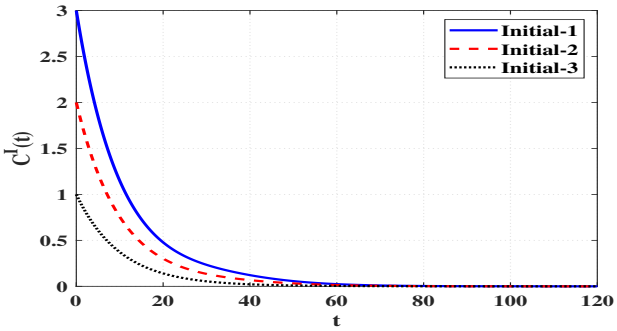
(d) Latent HTLV-infected cells



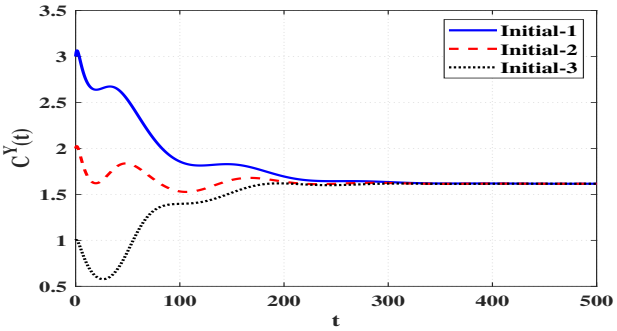
(e) Active HTLV-infected cells



(f) Free HIV particles

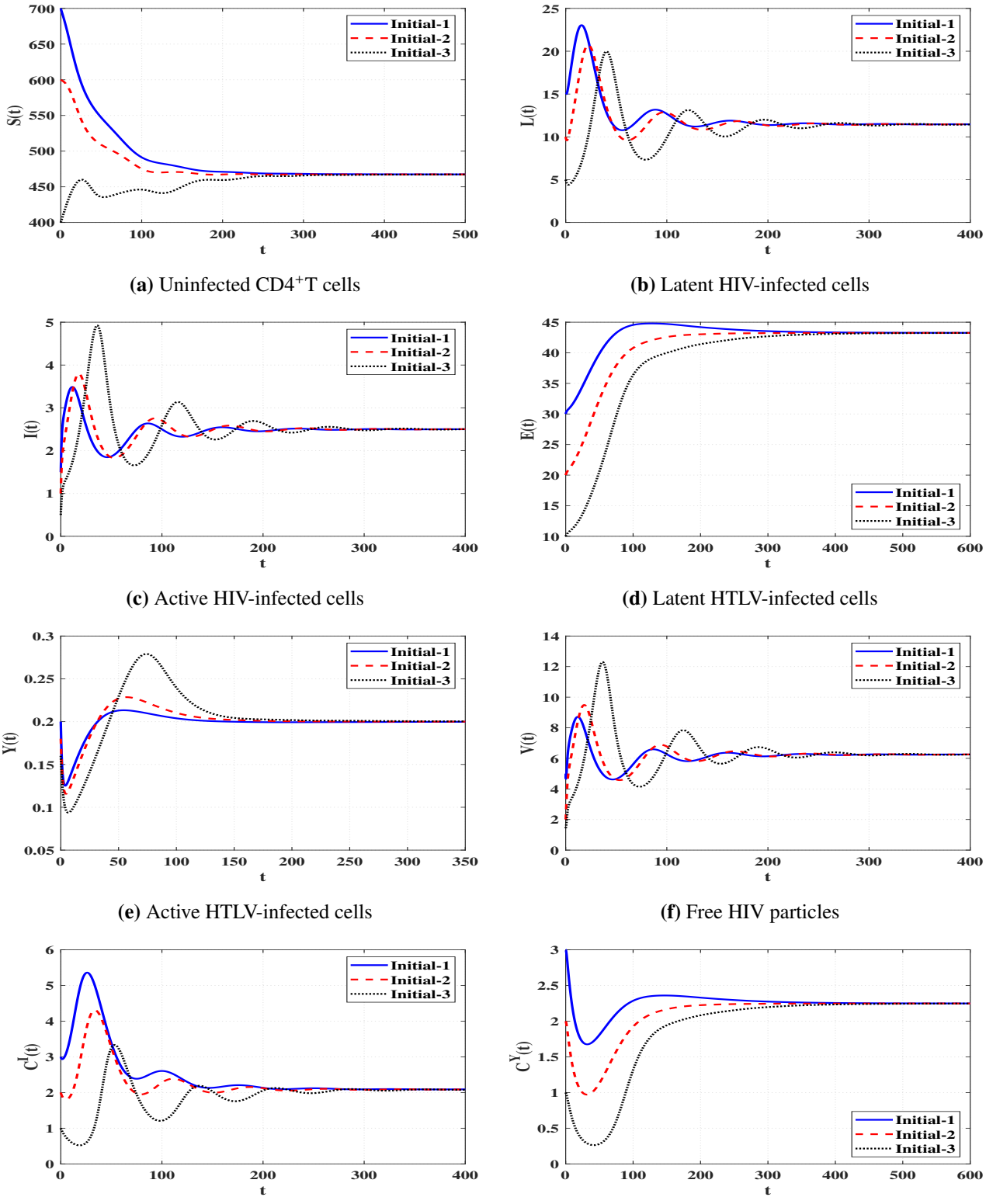


(g) HIV-specific CTLs



(h) HTLV-specific CTLs

Figure 8. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_6 > 1$, $\mathfrak{R}_7 \leq 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 > 1$.



(a) Uninfected CD4$^+$T cells

(b) Latent HIV-infected cells

(c) Active HIV-infected cells

(d) Latent HTLV-infected cells

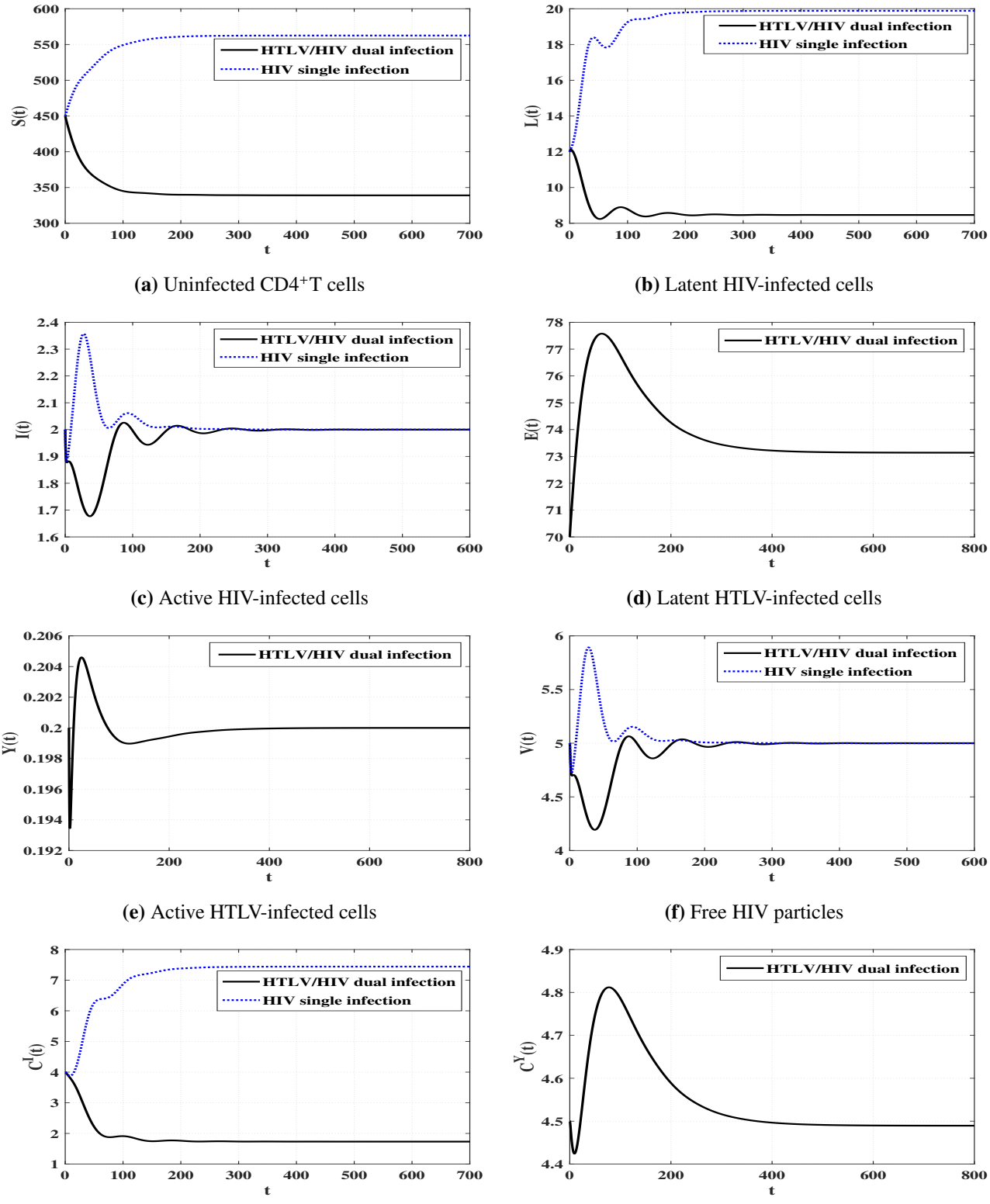
(e) Active HTLV-infected cells

(f) Free HIV particles

(g) HIV-specific CTLs

(h) HTLV-specific CTLs

Figure 9. Solutions of system (2.1)–(2.8) when $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$.



(a) Uninfected CD4$^+$T cells

(b) Latent HIV-infected cells

(c) Active HIV-infected cells

(d) Latent HTLV-infected cells

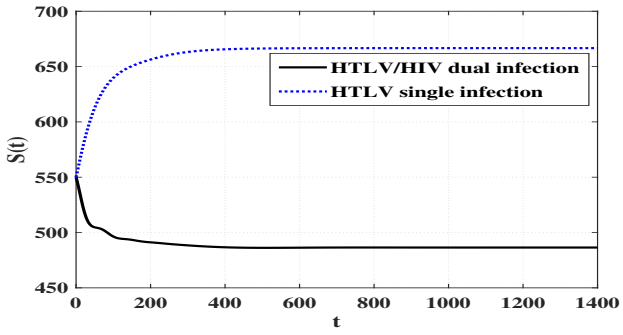
(e) Active HTLV-infected cells

(f) Free HIV particles

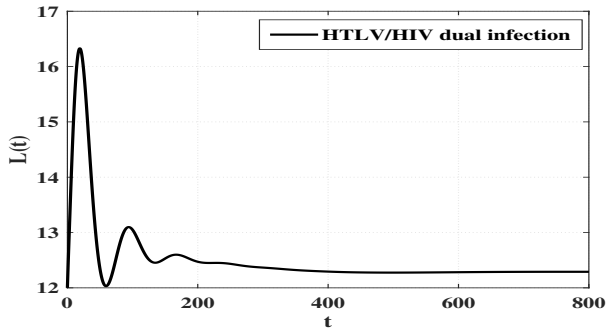
(g) HIV-specific CTLs

(h) HTLV-specific CTLs

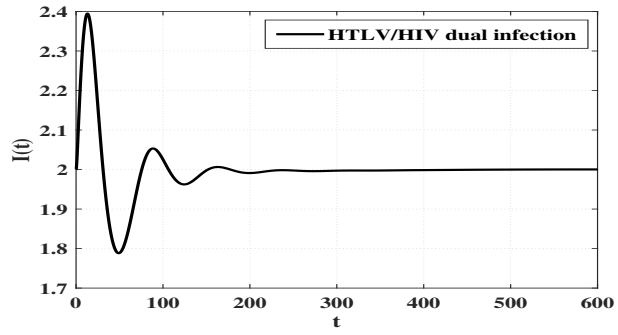
Figure 10. Comparison between the dynamics of HIV single infection and HTLV/HIV dual infection.



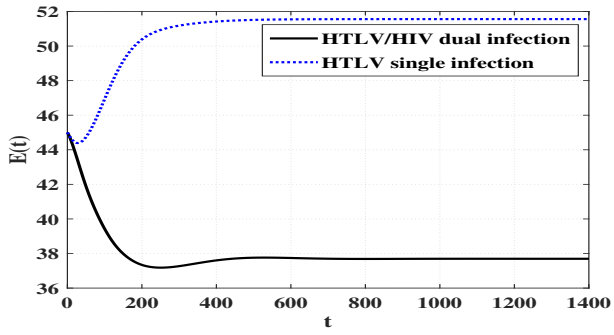
(a) Uninfected CD4$^+$T cells



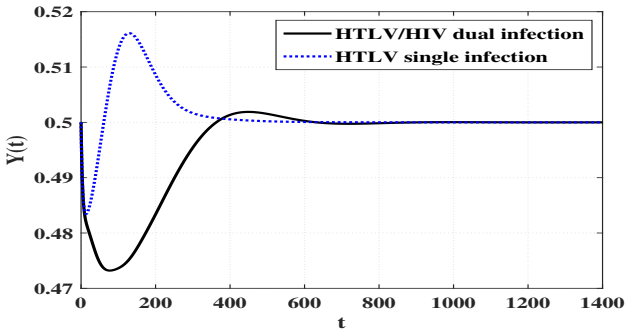
(b) Latent HIV-infected cells



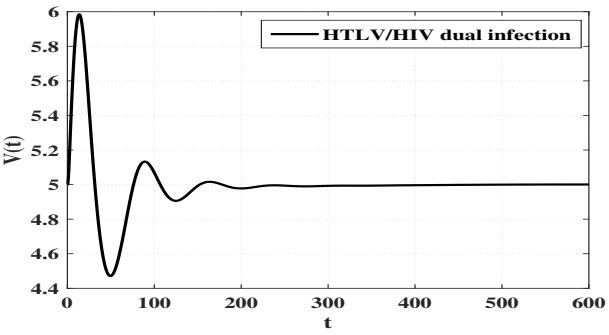
(c) Active HIV-infected cells



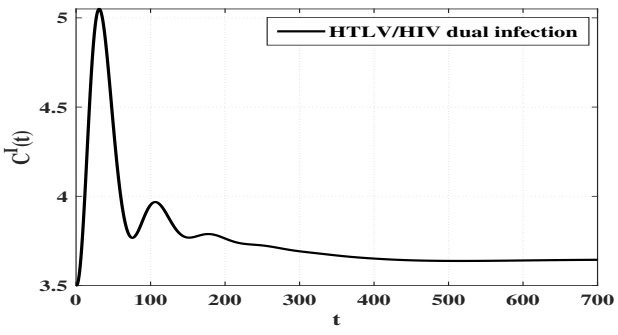
(d) Latent HTLV-infected cells



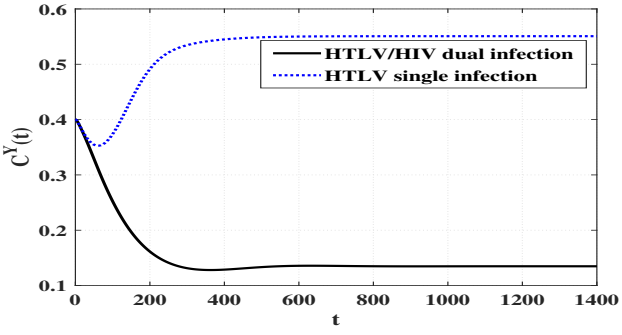
(e) Active HTLV-infected cells



(f) Free HIV particles



(g) HIV-specific CTLs



(h) HTLV-specific CTLs

Figure 11. Comparison between the dynamics of HTLV single infection and HTLV/HIV dual infection.

5. Conclusions and discussions

This work formulates and analyzes a within host HTLV/HIV dual infection model. The model includes eight compartments, uninfected CD4$^+$T cells, active HIV-infected cells, latent HIV-infected cells, free HIV particles, HIV-specific CTLs, active HTLV-infected cells, latent HTLV-infected cells and HTLV-specific CTLs. HIV has two predominant infection modes: the classical free-to-cell infection and infected-to-cell spread. Infected-to-cell spread of HIV occurs when uninfected CD4$^+$T cells are touched with active or latent HIV-infected cells. The HTLV has two ways of transmission, (i) horizontal transmission via direct infected-to-cell touch, and (ii) vertical transmission by mitotic division of active HTLV-infected cells. We first proved that the model is well-posed by showing that the solutions are nonnegative and bounded. We derived eight threshold parameters that governed the existence and stability of the eight steady states of the model. We constructed appropriate Lyapunov functions and applied Lyapunov-LaSalle asymptotic stability theorem to prove the global asymptotic stability of all steady states. We conducted numerical simulations to clarify and support our theoretical results (Theorems 1–8). We compared between the dynamics of single and dual infections. The model analysis suggested that dual infected individuals with both viruses will have smaller number of uninfected CD4$^+$T cells in comparison with HIV or HTLV single infected individuals.

Our model can be extended in many directions:

- In model (2.9)–(2.16), we supposed that uninfected CD4$^+$T cells are created at a constant rate ρ and die at linear rate αS. In fact, it would be more acceptable to examine the density dependent creation rate. One possibility is to consider a logistic growth for the uninfected CD4$^+$T cells. Moreover, the model assumed bilinear incidence rate of infection. However, such bilinear form may not describe the virus dynamics during the full course of infection. Therefore, it is reasonable to consider other forms of the incidence rate such as: saturated incidence, Beddington-DeAngelis incidence and general incidence [48].
- Model (2.9)–(2.16) assumed that once uninfected CD4$^+$T cell is contacted by HIV particles or HIV-infected cells or HTLV-infected cells it becomes latent or active infected instantaneously. However, such process needs time. The effect of intracellular time delay on the dynamics of dual infection has a significant importance. Delayed single virus infection models have been formulated and analyzed in many articles (see, e.g., [49–51]).
- Model (2.9)–(2.16) supposed that the viruses and cells are equally distributed in the domain with no spatial variations. Taking into account spatial variations in the case of HTLV/HIV dual infection will be significant [52].

We leave these extensions as a future project.

As we discussed in section 1 that CTLs have a significant importance in controlling HTLV and HIV single infections by killing infected cells. Model (2.9)–(2.16) in the absence of CTL immunity leads to a model with competition between HTLV and HIV on CD4$^+$T cells:

$$\frac{dS}{dt} = \rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y, \tag{5.1}$$

$$\frac{dL}{dt} = \varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda + \gamma) L, \tag{5.2}$$

$$\frac{dI}{dt} = \lambda L - aI, \tag{5.3}$$

$$\frac{dE}{dt} = \varphi\varkappa_4 S\,Y + rY - (\psi + \omega)\,E, \tag{5.4}$$

$$\frac{dY}{dt} = \psi E - \delta Y, \tag{5.5}$$

$$\frac{dV}{dt} = bI - \varepsilon V. \tag{5.6}$$

This system has only three steady states, infection-free steady state, $\overline{\mathrm{D}}_0 = (S_0, 0, 0, 0, 0, 0)$, persistent HIV single infection steady state, $\overline{\mathrm{D}}_1 = (S_1, L_1, I_1, 0, 0, V_1)$ and persistent HTLV single infection steady state, $\overline{\mathrm{D}}_2 = (S_2, 0, 0, E_2, Y_2, 0)$, where S_0, S_1, L_1, I_1, V_1, S_2, E_2 and Y_2 are given in section 3. The existence of these three steady states is determined by two threshold parameters $\mathfrak{R}_1$ and $\mathfrak{R}_2$ which are also defined in section 3.

Corollary 1. For system (5.1)–(5.6), the following statements hold true.

(i) If $\mathfrak{R}_1 \leq 1$ and $\mathfrak{R}_2 \leq 1$, then $\overline{\mathrm{D}}_0$ is G.A.S.

(ii) If $\mathfrak{R}_1 > 1$ and $\mathfrak{R}_2/\mathfrak{R}_1 \leq 1$, then $\overline{\mathrm{D}}_1$ is G.A.S.

(iii) If $\mathfrak{R}_2 > 1$ and $\mathfrak{R}_1/\mathfrak{R}_2 \leq 1$, then $\overline{\mathrm{D}}_2$ is G.A.S.

Therefore, the system will tend to one of the three steady states $\overline{\mathrm{D}}_0$, $\overline{\mathrm{D}}_1$ and $\overline{\mathrm{D}}_2$. The above result says that in the absence of CTL immunity, the competition between HTLV and HIV consuming common resources, only one type of viruses with maximum basic reproduction number can survive. However, in our proposed model (2.9)–(2.16) involving HIV- and HTLV-specific CTLs, HTLV and HIV coexist at a steady state. We can consider this situation as follows. Since CTL immune responses suppress viral progression, the competition between HTLV and HIV is also suppressed and the coexistence of HTLV and HIV is occurred [53].

It has been reported in [54] that, HIV has two classes of target cells, $CD4^+T$ cells and macrophages. In this case, HIV has two resources and then coexistence of HTLV and HIV can be occurred even when the immune system workless. HIV single infection models with two classes of target cells have been studied in several works, (see e.g., [45, 55]) Therefore, our model can be extended to take into account the second class of target cells for HIV, macrophages. We leave this extension for future works.

Acknowledgment

Not applicable.

Conflict of interest

The authors declare that they have no conflict interests.

References

1. C. Casoli, E. Pilotti, U. Bertazzoni, Molecular and cellular interactions of HIV-1/HTLV coinfection and impact on AIDS progression, *AIDS Rev.*, **9** (2007), 140–149.
2. M. Tulius Silva, O. de Melo Espíndola, A. C. Bezerra Leite, A. Araújo, Neurological aspects of HIV/human T lymphotropic virus coinfection, *AIDS Rev.*, **11** (2009), 71–78.

3. C. Brites, J. Sampalo, A. Oliveira, HIV/human T-cell lymphotropic virus coinfection revisited: impact on AIDS progression, *AIDS Rev.*, **11** (2009), 8–16.
4. C. Isache, M. Sands, N. Guzman, D. Figueroa, HTLV-1 and HIV-1 co-infection: A case report and review of the literature, *IDCases*, **4** (2016), 53–55.
5. M. A. Beilke, K. P. Theall, M. O'Brien, J. L. Clayton, S. M. Benjamin, E. L. Winsor, et al., Clinical outcomes and disease progression among patients coinfected with HIV and human T lymphotropic virus types 1 and 2, *Clin. Infect. Dis.*, **39** (2004), 256–263.
6. K. D. Pedro, A. J. Henderson, L. M. Agosto, Mechanisms of HIV-1 cell-to-cell transmission and the establishment of the latent reservoir, *Virus Res.*, **265** (2019), 115–121.
7. L. Wang, M. Y. Li, Mathematical analysis of the global dynamics of a model for HIV infection of $CD4^+$ T cells, *Math. Biosci.*, **200** (2006), 44–57.
8. J. Wang, C. Qin, Y. Chen, X. Wang, Hopf bifurcation in a CTL-inclusive HIV-1 infection model with two time delays, *Math. Biosci. Eng.*, **16** (2019), 2587–2612.
9. K. Hattaf, N. Yousfi, Dynamics of SARS-CoV-2 infection model with two modes of transmission and immune response, *Math. Biosci. Eng.*, **17** (2020), 5326–5340.
10. G. Huang, X. Liu, Y. Takeuchi, Lyapunov functions and global stability for age-structured HIV infection model,*SIAM J. Appl. Math.*, **72** (2012), 25–38.
11. M. Y. Li, A. G. Lim, Modelling the role of Tax expression in HTLV-1 persisence *in vivo*, *Bull. Math. Biol.*, **73** (2011), 3008–3029.
12. Y. Gao, J. Wang, Threshold dynamics of a delayed nonlocal reaction-diffusion HIV infection model with both cell-free and cell-to-cell transmissions, *J. Math. Anal. Appl.*, **488** (2020).
13. A. U. Neumann, N. P. Lam, H. Dahari, D. R. Gretch, T. E. Wiley, T. J, Layden, et al., Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy, *Science*, **282** (1998), 103–107.
14. S. Zhang, X. Xu, Dynamic analysis and optimal control for a model of hepatitis C with treatment, *Commun. Nonlinear Sci. Numer. Simul.*, **46** (2017), 14–25.
15. K. Wang, A. Fan, A. Torres, Global properties of an improved hepatitis B virus model, *Nonlinear Anal. Real World Appl.*, **11** (2010), 3131–3138.
16. S. Perera, S. S. N. Perera, Mathematical modeling and analysis of innate and humoral immune responses to dengue infections, *Int. J. Biomath.*, **12** (2019).
17. M. A. Nowak, R. M. May, *Virus dynamics: Mathematical Principles of Immunology and Virology*, Oxford University Press, (2000).
18. M. A. Nowak, C. R. M. Bangham, Population dynamics of immune responses to persistent viruses, *Science*, **272** (1996), 74–79.
19. X. Shi, X. Zhou, X. Song, Dynamical behavior of a delay virus dynamics model with CTL immune response, *Nonlinear Anal. Real World Appl.*, **11** (2010), 1795–1809.
20. T. Guo, Z. Qiu, The effects of CTL immune response on HIV infection model with potent therapy, latently infected cells and cell-to-cell viral transmission, *Math. Biosci. Eng.*, **16** (2019), 6822–6841.

21. H. Shu, L. Wang, J. Watmough, Global stability of a nonlinear viral infection model with infinitely distributed intracellular delays and CTL imune responses, *SIAM J. Appl. Math.*, **73** (2013), 1280–1302.
22. N. I. Stilianakis and J. Seydel, Modeling the T-cell dynamics and pathogenesis of HTLV-I infection, *Bull. Math. Biol.*, **61** (1999), 935–947.
23. H. Gomez-Acevedo, M. Y. Li, Backward bifurcation in a model for HTLV-I infection of $CD4^+$T cells, *Bull. Math. Biol.*, **67** (2005), 101–114.
24. C. Vargas-De-Leon, The complete classification for global dynamics of amodel for the persistence of HTLV-1 infection, *Appl. Math. Comput.*, **237** (2014), 489–493.
25. L. Wang, M. Y. Li, D. Kirschner, Mathematical analysis of the global dynamics of a model for HTLV-I infection and ATL progression, *Math. Biosci.*, **179** (2002), 207–217.
26. X. Pan, Y. Chen, H. Shu, Rich dynamics in a delayed HTLV-I infection model: Stability switch, multiple stable cycles, and torus, *J. Math. Anal. Appl.*, **479** (2019), 2214–2235.
27. H. Gomez-Acevedo, M. Y. Li, S. Jacobson, Multi-stability in a model for CTL response to HTLV-I infection and its consequences in HAM/TSP development, and prevention, *Bull. Math. Biol.*, **72** (2010), 681–696.
28. J. Lang, M. Y. Li, Stable and transient periodic oscillations in a mathematical model for CTL response to HTLV-I infection, *J. Math. Biol.*, **65** (2012), 181–199.
29. M. Y. Li, H. Shu, Multiple stable periodic oscillations in a mathematical model of CTL response to HTLV-I infection, *Bull. Math. Biol.*, **73** (2011), 1774–1793.
30. L. Wang, Z. Liu, Y. Li, D. Xu, Complete dynamical analysis for a nonlinear HTLV-I infection model with distributed delay, CTL response and immune impairment, *Discrete Continuous Dyn. Syst. Ser. B*, **25** (2020), 917–933.
31. Y. Wang, J. Liu, J. M. Heffernan, Viral dynamics of an HTLV-I infection model with intracellular delay and CTL immune response delay, *J. Math. Anal. Appl.*, **459** (2018), 506–527.
32. A. G. Lim, P. K. Maini, HTLV-Iinfection: A dynamic struggle between viral persistence and host immunity, *J. Theor. Biol.*, **352** (2014), 92–108.
33. F. Li, W. Ma, Dynamics analysis of an HTLV-1 infection model with mitotic division of actively infected cells and delayed CTL immune response, *Math. Methods Appl. Sci.*, **41** (2018), 3000–3017.
34. S. Li, Y. Zhou, Backward bifurcation of an HTLV-I model with immune response, *Discrete Continuous Dyn. Syst. Ser. B*, **21** (2016), 863–881.
35. W. Wang, W. Ma, Global dynamics of a reaction and diffusion model for an HTLV-I infection with mitotic division of actively infected cells, *J. Appl. Anal. Comput.*, **7** (2017), 899–930.
36. A. M. Elaiw, N. H. AlShamrani, Analysis of a within-host HIV/HTLV-I co-infection model with immunity, *Virus Res.*, (2020), Forthcoming.
37. L. Agosto, M. Herring, W. Mothes, A. Henderson, HIV-1-infected $CD4^+$ T cells facilitate latent infection of resting $CD4^+$ T cells through cell-cell contact, *Cell*, **24** (2018), 2088–2100.

38. W. Wang, X. Wang, K. Guo, W. Ma, Global analysis of a diffusive viral model with cell-to-cell infection and incubation period, *Math. Methods Appl. Sci.*, **43** (2020), 5963–5978.
39. A. M. Elaiw, N. H. AlShamrani, Stability of a general CTL-mediated immunity HIV infection model with latent infected cell-to-cell spread, *Adv. Differ. Equations*, **2020** (2020).
40. A. M. Elaiw, N. H. AlShamrani, A. D. Hobiny, Stability of an adaptive immunity delayed HIV infection model with active and latent cell-to-cell spread, *Math. Biosci. Eng.*, **17** (2020), 6401–6458.
41. B. S. Goh, *Management and Analysis of Biological Populations*, Elsevier, (1980).
42. Y. Takeuchi, *Global Dynamical Properties of Lotka–Volterra Systems*, World Scientific, (1996).
43. A. Korobeinikov, Global properties of basic virus dynamics models, *Bull. Math. Biol.*, **66** (2004), 879–883.
44. A. Korobeinikov, Global properties of infectious disease models with nonlinear incidence, *Bull. Math. Biol.*, **69** (2007), 1871–1886.
45. A. M. Elaiw, Global properties of a class of HIV models, *Nonlinear Anal. Real World Appl.*, **11** (2010), 2253–2263.
46. A. M. Elaiw, Global properties of a class of virus infection models with multitarget cells, *Nonlinear Dyn.*, **69** (2012), 423–435.
47. A. Vandormael, F. Rego, S. Danaviah, L. Carlos Junior Alcantara, D. R. Boulware, et al., $CD4^+$ T-cell count may not be a useful strategy to monitor antiretroviral therapy response in HTLV-1/HIV co-infected patients, *Curr. HIV Res.*, **15** (2017), 225–231.
48. G. Huang, Y. Takeuchi, W. Ma, Lyapunov functionals for delay differential equations model of viral infections, *SIAM J. Appl. Math.*, **70** (2010), 2693–2708.
49. P. W. Nelson, J. D. Murray, A. S. Perelson, A model of HIV-1 pathogenesis that includes an intracellular delay, *Math. Biosci.*, **163** (2000), 201–215.
50. A. M. Elaiw, N. H. AlShamrani, Global stability of a delayed adaptive immunity viral infection with two routes of infection and multi-stages of infected cells, *Commun. Nonlinear Sci. Numer. Simul.*, **86** (2020).
51. R. V. Culshaw, S. Ruan, G. Webb, A mathematical model of cell-to-cell spread of HIV-1 that includes a time delay, *J. Math. Biol.*, **46** (2003), 425–444.
52. N. Bellomo, K. J. Painter, Y. Tao, M. Winkler, Occurrence vs. Absence of taxis-driven instabilities in a May-Nowak model for virus infection, *SIAM J. Appl. Math.*, **79** (2019), 1990–2010.
53. T. Inoue, T. Kajiwara, T. Saski, Global stability of models of humoral immunity against multiple viral strains, *J. Biol. Dyn.*, **4** (2010), 282–295.
54. A. S. Perelson, P. Essunger, Y. Cao, M. Vesanen, A. Hurley, K. Saksela, et al., Decay characteristics of HIV-1-infected compartments during combination therapy, *Nature*, **387** (1997), 188–191.
55. D. S. Callaway, A.S. Perelson, HIV-1 infection and low steady state viral loads, *Bull. Math. Biol.*, **64** (2002), 29–64.
56. E. A. Barbashin, *Introduction to the theory of stability*, Wolters-Noordhoff, (1970).

57. J. P. LaSalle, The Stability of Dynamical Systems, *SIAM*, (1976).

58. A. M. Lyapunov, *The general problem of the stability of motion*, Taylor & Francis, Ltd., (1992).

Appendix

Proof of Proposition 1. We have

$$\begin{aligned}
&\frac{dS}{dt}\,|_{S=0}=\rho>0, \quad \frac{dL}{dt}\,|_{L=0}=\varkappa_1 SV+\varkappa_3 SI\geq 0 \text{ for all } S,V,I\geq 0,\\
&\frac{dI}{dt}\,|_{I=0}=\lambda L\geq 0 \text{ for all } L\geq 0, \quad \frac{dE}{dt}\,|_{E=0}=\varphi\varkappa_4 SY+rY \text{ for all } S,Y\geq 0,\\
&\frac{dY}{dt}\,|_{Y=0}=\psi E\geq 0 \text{ for all } E\geq 0, \quad \frac{dV}{dt}\,|_{V=0}=bI\geq 0 \text{ for all } I\geq 0,\\
&\frac{dC^I}{dt}\,|_{C^I=0}=0, \quad \frac{dC^Y}{dt}\,|_{C^Y=0}=0.
\end{aligned}$$

This shows that, if $(S(0),L(0),I(0),E(0),Y(0),V(0),C^I(0),C^Y(0)) \in \mathbb{R}^8_{\geq 0}$ then $(S(t),L(t),I(t),E(t),Y(t),V(t),C^I(t),C^Y(t)) \in \mathbb{R}^8_{\geq 0}$ for all $t \geq 0$. To show the boundedness of solution, we let

$$\Psi = S + L + I + \frac{1}{\varphi}(E+Y) + \frac{a}{2b}V + \frac{\mu_1}{\sigma_1}C^I + \frac{\mu_2}{\varphi\sigma_2}C^Y.$$

Then

$$\dot{\Psi} = \rho - \alpha S - \gamma L - \frac{a}{2}I - \frac{\omega}{\varphi}E - \frac{\delta - r}{\varphi}Y - \frac{a\varepsilon}{2b}V - \frac{\mu_1\pi_1}{\sigma_1}C^I - \frac{\mu_2\pi_2}{\varphi\sigma_2}C^Y.$$

We have $\delta - r = \delta^* - r^* > 0$. Hence,

$$\begin{aligned}
\dot{\Psi} &= \rho - \alpha S - \gamma L - \frac{a}{2}I - \frac{\omega}{\varphi}E - \frac{\delta^* - r^*}{\varphi}Y - \frac{a\varepsilon}{2b}V - \frac{\mu_1\pi_1}{\sigma_1}C^I - \frac{\mu_2\pi_2}{\varphi\sigma_2}C^Y\\
&\leq \rho - \phi\left[S + L + I + \frac{1}{\varphi}(E+Y) + \frac{a}{2b}V + \frac{\mu_1}{\sigma_1}C^I + \frac{\mu_2}{\varphi\sigma_2}C^Y\right] = \rho - \phi\Psi,
\end{aligned}$$

where $\phi = \min\{\alpha, \gamma, \frac{a}{2}, \omega, \delta^* - r^*, \varepsilon, \pi_1, \pi_2\}$. If $\Psi(0) \leq \Omega_1$, then $0 \leq \Psi(t) \leq \Omega_1$ for $t \geq 0$, where $\Omega_1 = \frac{\rho}{\phi}$. Since S, L, I, E, Y, V, C^I, and C^Y are all nonnegative then $0 \leq S(t), L(t), I(t) \leq \Omega_1$, $0 \leq E(t), Y(t) \leq \Omega_2$, $0 \leq V(t) \leq \Omega_3$, $0 \leq C^I(t) \leq \Omega_4$, $0 \leq C^Y(t) \leq \Omega_5$ if $S(0) + L(0) + I(0) + \frac{1}{\varphi}(E(0) + Y(0)) + \frac{a}{2b}V(0) + \frac{\mu_1}{\sigma_1}C^I(0) + \frac{\mu_2}{\varphi\sigma_2}C^Y(0) \leq \Omega_1$, where $\Omega_2 = \varphi\Omega_1$, $\Omega_3 = \frac{2b\Omega_1}{a}$, $\Omega_4 = \frac{\sigma_1\Omega_1}{\mu_1}$ and $\Omega_5 = \frac{\varphi\sigma_2\Omega_1}{\mu_2}$. □

To prove Theorems 1–8 we need the arithmetic-geometric mean inequality

$$\sqrt[n]{\prod_{i=1}^{n}\chi_i} \leq \frac{1}{n}\sum_{i=1}^{n}\chi_i, \quad \chi_i \geq 0,\ i = 1,2,...$$

which yields

$$3 \leq \frac{S_j}{S} + \frac{SIL_j}{S_jI_jL} + \frac{LI_j}{L_jI}, \quad j = 1,3,5,6,7, \tag{1}$$

$$4 \leq \frac{S_j}{S} + \frac{SVL_j}{S_jV_jL} + \frac{LI_j}{L_jI} + \frac{IV_j}{I_jV}, \quad j = 1,3,5,6,7, \tag{2}$$

$$3 \leq \frac{S_j}{S} + \frac{SYE_j}{S_jY_jE} + \frac{EY_j}{E_jY}, \quad j = 2,4,5,6,7. \tag{3}$$

Define a function $\Phi_j(S, L, I, E, Y, V, C^I, C^Y)$ and $\Upsilon_j^{'}$ is the largest invariant subset of

$$\Upsilon_j = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_j}{dt} = 0\right\}, \quad j = 0, 1, 2, ..., 7.$$

We define a function

$$F(\upsilon) = \upsilon - 1 - \ln \upsilon.$$

Proof of Theorem 1. We construct a Lyapunov function candidate Φ_0 as:

$$\Phi_0 = S_0 F\left(\frac{S}{S_0}\right) + L + \frac{S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon} I + \frac{1}{\varphi}E + \frac{\psi+\omega}{\varphi\psi}Y + \frac{\varkappa_1 S_0}{\varepsilon}V + \frac{\mu_1 S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y$$

Clearly, $\Phi_0(S_0, 0, 0, 0, 0, 0, 0, 0) = 0$ and $\Phi_0(S, L, I, E, Y, V, C^I, C^Y) > 0$ for all $S, L, I, E, Y, V, C^I, C^Y > 0$. We calculate $\frac{d\Phi_0}{dt}$ along the solutions of model (2.9)–(2.16) as:

$$\begin{aligned}
\frac{d\Phi_0}{dt} &= \left(1 - \frac{S_0}{S}\right)(\rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y) + \varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda+\gamma) L \\
&+ \frac{S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon}\left(\lambda L - aI - \mu_1 C^I I\right) + \frac{1}{\varphi}(\varphi\varkappa_4 S Y + rY - (\psi+\omega)E) + \frac{\psi+\omega}{\varphi\psi}\left(\psi E - \delta Y - \mu_2 C^Y Y\right) \\
&+ \frac{\varkappa_1 S_0}{\varepsilon}(bI - \varepsilon V) + \frac{\mu_1 S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon\sigma_1}\left(\sigma_1 C^I I - \pi_1 C^I\right) + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(\sigma_2 C^Y Y - \pi_2 C^Y\right) \\
&= \left(1 - \frac{S_0}{S}\right)(\rho - \alpha S) + \varkappa_2 S_0 L + \varkappa_4 S_0 Y - (\lambda+\gamma) L + \frac{\lambda S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon} L + \frac{r}{\varphi}Y - \frac{\delta(\psi+\omega)}{\varphi\psi}Y \\
&- \frac{\mu_1\pi_1 S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I - \frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}$$

Using $S_0 = \rho/\alpha$, we obtain

$$\begin{aligned}
\frac{d\Phi_0}{dt} &= -\alpha\frac{(S - S_0)^2}{S} + (\gamma+\lambda)(\Re_1 - 1) L + \frac{(\delta - r)\psi + \delta\omega}{\varphi\psi}(\Re_2 - 1) Y \\
&- \frac{\mu_1\pi_1 S_0(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I - \frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}$$

Therefore, $\frac{d\Phi_0}{dt} \leq 0$ for all $S, L, Y, C^I, C^Y > 0$ with equality holding when $(S, L, Y, C^I, C^Y) = (S_0, 0, 0, 0, 0)$. The solutions of system (2.9)–(2.16) converge to $\Upsilon_0^{'}$. The elements of $\Upsilon_0^{'}$ satisfy $Y = C^Y = 0$ and then $\frac{dY}{dt} = 0$. Eq (2.13) implies

$$0 = \frac{dY}{dt} = \psi E,$$

which gives that $E(t) = 0$ for all $t > 0$. From Eqs (2.11) and (2.14), we obtain

$$\begin{cases} \frac{dI}{dt} = -aI, \\ \frac{dV}{dt} = bI - \varepsilon V. \end{cases} \tag{4}$$

For system (4) we define a Lyapunov function

$$\tilde{\Phi}_0 = I + \frac{a}{2b}V.$$

Therefore, we calculate $\frac{d\tilde{\Phi}_0}{dt}$ along the solutions of system (4) as:

$$\frac{d\tilde{\Phi}_0}{dt} = -\frac{a}{2}\tilde{\Phi}_0 \leq 0.$$

Clearly $\frac{d\tilde{\Phi}_0}{dt} = 0$ when $I = V = 0$ for all t. Let

$$\Upsilon_0^{''} = \left\{(S, L, I, E, Y, V, C^I, C^Y) \in \Upsilon_0^{'} : \frac{d\tilde{\Phi}_0}{dt} = 0\right\}.$$

Thus

$$\Upsilon_0^{''} = \left\{(S, L, I, E, Y, V, C^I, C^Y) \in \Upsilon_0^{'} : S = S_0, L = I = E = Y = V = C^I = C^Y = 0\right\} = \{\text{Đ}_0\}.$$

Applying Lyapunov-LaSalle asymptotic stability theorem [56–58] we obtain that Đ_0 is G.A.S. □

Proof of Lemma 1. Let $\mathfrak{R}_3 \leq 1$, hence $\frac{\lambda\sigma_1 L_3}{a\pi_1} \leq 1$ and therefore

$$\begin{aligned}
&L_3 \leq \frac{a\pi_1}{\lambda\sigma_1} \Longrightarrow \frac{-\tilde{B} + \sqrt{\tilde{B}^2 - 4\tilde{A}\tilde{C}}}{2\tilde{A}} \leq \frac{a\pi_1}{\lambda\sigma_1} \\
&\Longrightarrow \sqrt{\tilde{B}^2 - 4\tilde{A}\tilde{C}} \leq \frac{2\tilde{A}a\pi_1 + \lambda\sigma_1\tilde{B}}{\lambda\sigma_1} \\
&\Longrightarrow \left(\frac{2\tilde{A}a\pi_1 + \lambda\sigma_1\tilde{B}}{\lambda\sigma_1}\right)^2 + 4\tilde{A}\tilde{C} - \tilde{B}^2 \geq 0.
\end{aligned}$$

Using Eq (3.10), we obtain

$$\frac{4a\pi_1\varepsilon\varkappa_2\sigma_1(\gamma+\lambda)^2\left[a\varepsilon\varkappa_2 + \lambda\left(b\varkappa_1 + \varepsilon\varkappa_3\right)\right]}{\lambda^2}\left(I_3 - I_1\right) \geq 0.$$

Hence, $I_1 \leq I_3$. □

Proof of Theorem 2. Define a function Φ_1 as:

$$\begin{aligned}
\Phi_1 = {} & S_1 F\left(\frac{S}{S_1}\right) + L_1 F\left(\frac{L}{L_1}\right) + \frac{S_1\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon} I_1 F\left(\frac{I}{I_1}\right) + \frac{1}{\varphi}E \\
& + \frac{\psi+\omega}{\varphi\psi}Y + \frac{\varkappa_1 S_1}{\varepsilon}V_1 F\left(\frac{V}{V_1}\right) + \frac{\mu_1 S_1\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}C^I + \frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}$$

Calculating $\frac{d\Phi_1}{dt}$ as:

$$\begin{aligned}
\frac{d\Phi_1}{dt} = {} & \left(1 - \frac{S_1}{S}\right)\left(\rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y\right) \\
& + \left(1 - \frac{L_1}{L}\right)\left(\varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda+\gamma) L\right)
\end{aligned}$$

$$
\begin{aligned}
&+\frac{S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}\left(1-\frac{I_1}{I}\right)\left(\lambda L-aI-\mu_1C^II\right)+\frac{1}{\varphi}\left(\varphi\varkappa_4SY+rY-(\psi+\omega)E\right)\\
&+\frac{\psi+\omega}{\varphi\psi}\left(\psi E-\delta Y-\mu_2C^YY\right)+\frac{\varkappa_1S_1}{\varepsilon}\left(1-\frac{V_1}{V}\right)(bI-\varepsilon V)\\
&+\frac{\mu_1S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}\left(\sigma_1C^II-\pi_1C^I\right)+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(\sigma_2C^YY-\pi_2C^Y\right)\\
&=\left(1-\frac{S_1}{S}\right)(\rho-\alpha S)+\varkappa_2S_1L+\varkappa_4S_1Y-(\lambda+\gamma)L-\varkappa_1SV\frac{L_1}{L}-\varkappa_2SL_1\\
&-\varkappa_3SI\frac{L_1}{L}+(\lambda+\gamma)L_1+\frac{\lambda S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}L-\frac{\lambda S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}L\frac{I_1}{I}\\
&+\frac{S_1(b\varkappa_1+\varepsilon\varkappa_3)}{\varepsilon}I_1+\frac{\mu_1S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}C^II_1+\frac{r}{\varphi}Y-\frac{\delta(\psi+\omega)}{\varphi\psi}Y\\
&-\varkappa_1S_1\frac{bI}{\varepsilon}\frac{V_1}{V}+\varkappa_1S_1V_1-\frac{\mu_1\pi_1S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}
$$

The steady state conditions for $Đ_1$ are given by

$$
\begin{aligned}
&\rho=\alpha S_1+\varkappa_1S_1V_1+\varkappa_2S_1L_1+\varkappa_3S_1I_1,\\
&\varkappa_1S_1V_1+\varkappa_2S_1L_1+\varkappa_3S_1I_1=(\lambda+\gamma)L_1,\\
&\frac{\lambda L_1}{a}=I_1,\quad V_1=\frac{bI_1}{\varepsilon}.
\end{aligned}
$$

Then, we get

$$
\varkappa_1S_1V_1+\varkappa_3S_1I_1=\frac{S_1(b\varkappa_1+\varepsilon\varkappa_3)}{\varepsilon}I_1=\frac{\lambda S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}L_1.
$$

Further, we obtain

$$
\begin{aligned}
\frac{d\Phi_1}{dt}&=\left(1-\frac{S_1}{S}\right)(\alpha S_1-\alpha S)+(\varkappa_1S_1V_1+\varkappa_2S_1L_1+\varkappa_3S_1I_1)\left(1-\frac{S_1}{S}\right)+\varkappa_4S_1Y\\
&-\varkappa_1S_1V_1\frac{SVL_1}{S_1V_1L}-\varkappa_2S_1L_1\frac{S}{S_1}-\varkappa_3S_1I_1\frac{SIL_1}{S_1I_1L}+\varkappa_1S_1V_1+\varkappa_2S_1L_1+\varkappa_3S_1I_1\\
&-\frac{\delta(\psi+\omega)}{\varphi\psi}Y-\varkappa_1S_1V_1\frac{IV_1}{I_1V}+\varkappa_1S_1V_1-(\varkappa_1S_1V_1+\varkappa_3S_1I_1)\frac{LI_1}{L_1I}+\varkappa_1S_1V_1+\varkappa_3S_1I_1\\
&+\frac{\mu_1S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}C^II_1+\frac{r}{\varphi}Y-\frac{\mu_1\pi_1S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y\\
&=-\alpha\frac{(S-S_1)^2}{S}+\varkappa_1S_1V_1\left(4-\frac{S_1}{S}-\frac{SVL_1}{S_1V_1L}-\frac{IV_1}{I_1V}-\frac{LI_1}{L_1I}\right)\\
&+\varkappa_2S_1L_1\left(2-\frac{S_1}{S}-\frac{S}{S_1}\right)+\varkappa_3S_1I_1\left(3-\frac{S_1}{S}-\frac{SIL_1}{S_1I_1L}-\frac{LI_1}{L_1I}\right)\\
&+\frac{(\delta-r)\psi+\delta\omega}{\varphi\psi}\left(\frac{\varphi\varkappa_4\psi S_1}{(\delta-r)\psi+\delta\omega}-1\right)Y\\
&+\frac{\mu_1S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}\left(I_1-\frac{\pi_1}{\sigma_1}\right)C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}
\tag{5}
$$

Therefore, Eq (5) becomes

$$\begin{aligned}\frac{d\Phi_1}{dt} &= -(\alpha+\varkappa_2 L_1)\frac{(S-S_1)^2}{S}+\varkappa_1 S_1 V_1\left(4-\frac{S_1}{S}-\frac{SVL_1}{S_1V_1L}-\frac{IV_1}{I_1V}-\frac{LI_1}{L_1I}\right)\\ &+\varkappa_3 S_1 I_1\left(3-\frac{S_1}{S}-\frac{SIL_1}{S_1I_1L}-\frac{LI_1}{L_1I}\right)+\frac{(\delta-r)\psi+\delta\omega}{\varphi\psi}\left(\mathfrak{R}_2/\mathfrak{R}_1-1\right)Y\\ &+\frac{\mu_1 S_1(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}(I_1-I_3)C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y. \end{aligned} \tag{6}$$

Using Lemma 1 we get that $I_1 \le I_3$ whenever $\mathfrak{R}_3 \le 1$. We have $\mathfrak{R}_2/\ \mathfrak{R}_1 \le 1$ and using inequalities (1)-(2) we get that for all $S, L, I, Y, V, C^I, C^Y > 0$, then $\frac{d\Phi_1}{dt} \le 0$. In addition $\frac{d\Phi_1}{dt} = 0$ when $(S, L, I, V, Y, C^I, C^Y) = (S_1, L_1, I_1, V_1, 0, 0, 0)$. The solutions of system (2.9)–(2.16) converge to Υ_1' which includes elements with $Y = 0$ and then $\frac{dY}{dt} = 0$. Eq (2.13) implies that

$$0 = \frac{dY}{dt} = \psi E,$$

which yields $E(t) = 0$ for all t. Hence, $\Upsilon_1' = \{Đ_1\}$ and $Đ_1$ is G.A.S using Lyapunov-LaSalle asymptotic stability theorem. □

Proof of Theorem 3. Let Φ_2 be defined as:

$$\begin{aligned}\Phi_2 &= S_2 F\left(\frac{S}{S_2}\right)+L+\frac{S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}I+\frac{1}{\varphi}E_2F\left(\frac{E}{E_2}\right)+\frac{\psi+\omega}{\varphi\psi}Y_2F\left(\frac{Y}{Y_2}\right)\\ &+\frac{\varkappa_1 S_2}{\varepsilon}V+\frac{\mu_1 S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.\end{aligned}$$

We calculate $\frac{d\Phi_2}{dt}$ as:

$$\begin{aligned}\frac{d\Phi_2}{dt} &= \left(1-\frac{S_2}{S}\right)(\rho-\alpha S-\varkappa_1 SV-\varkappa_2 SL-\varkappa_3 SI-\varkappa_4 SY)+\varkappa_1 SV+\varkappa_2 SL+\varkappa_3 SI\\ &-(\lambda+\gamma)L+\frac{S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}\left(\lambda L-aI-\mu_1 C^I I\right)+\frac{1}{\varphi}\left(1-\frac{E_2}{E}\right)(\varphi\varkappa_4 SY+rY-(\psi+\omega)E)\\ &+\frac{\psi+\omega}{\varphi\psi}\left(1-\frac{Y_2}{Y}\right)\left(\psi E-\delta Y-\mu_2 C^Y Y\right)+\frac{\varkappa_1 S_2}{\varepsilon}(bI-\varepsilon V)\\ &+\frac{\mu_1 S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}\left(\sigma_1 C^I I-\pi_1 C^I\right)+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(\sigma_2 C^Y Y-\pi_2 C^Y\right)\\ &=\left(1-\frac{S_2}{S}\right)(\rho-\alpha S)+\varkappa_2 S_2 L+\varkappa_4 S_2 Y-(\gamma+\lambda)L+\frac{\lambda S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}L\\ &+\frac{r}{\varphi}Y-\varkappa_4 SY\frac{E_2}{E}-\frac{r}{\varphi}Y\frac{E_2}{E}+\frac{\psi+\omega}{\varphi}E_2-\frac{\delta(\psi+\omega)}{\varphi\psi}Y-\frac{\psi+\omega}{\varphi}E\frac{Y_2}{Y}\\ &+\frac{\delta(\psi+\omega)}{\varphi\psi}Y_2+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C^Y Y_2-\frac{\mu_1\pi_1 S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.\end{aligned}$$

Using the steady state conditions for $Đ_2$:

$$\rho=\alpha S_2+\varkappa_4 S_2 Y_2,\quad \varkappa_4 S_2 Y_2+\frac{r}{\varphi}Y_2=\frac{\psi+\omega}{\varphi}E_2=\frac{\delta(\psi+\omega)}{\varphi\psi}Y_2, \tag{7}$$

we obtain

$$\begin{aligned}
\frac{d\Phi_2}{dt} &= \left(1-\frac{S_2}{S}\right)(\alpha S_2-\alpha S)+\varkappa_4 S_2 Y_2\left(1-\frac{S_2}{S}\right)+\varkappa_2 S_2 L-(\gamma+\lambda)L\\
&+\frac{\lambda S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}L-\varkappa_4 S_2 Y_2\frac{SYE_2}{S_2Y_2E}-\frac{r}{\varphi}Y_2\frac{YE_2}{Y_2E}+\varkappa_4 S_2Y_2+\frac{r}{\varphi}Y_2\\
&-\varkappa_4 S_2 Y_2\frac{EY_2}{E_2Y}-\frac{r}{\varphi}Y_2\frac{EY_2}{E_2Y}+\varkappa_4 S_2Y_2+\frac{r}{\varphi}Y_2+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C^YY_2\\
&-\frac{\mu_1\pi_1 S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y\\
&=-\alpha\frac{(S-S_2)^2}{S}+\varkappa_4 S_2Y_2\left(3-\frac{S_2}{S}-\frac{SYE_2}{S_2Y_2E}-\frac{EY_2}{E_2Y}\right)\\
&+\frac{r}{\varphi}Y_2\left(2-\frac{YE_2}{Y_2E}-\frac{EY_2}{E_2Y}\right)+(\gamma+\lambda)\left[\frac{S_2\{a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\}}{a\varepsilon(\gamma+\lambda)}-1\right]L\\
&-\frac{\mu_1\pi_1 S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I+\frac{\mu_2(\psi+\omega)}{\varphi\psi}\left(Y_2-\frac{\pi_2}{\sigma_2}\right)C^Y\\
&=-\alpha\frac{(S-S_2)^2}{S}-\frac{r}{\varphi}\frac{(YE_2-EY_2)^2}{EE_2Y}\\
&+\varkappa_4 S_2Y_2\left(3-\frac{S_2}{S}-\frac{SYE_2}{S_2Y_2E}-\frac{EY_2}{E_2Y}\right)+(\gamma+\lambda)(\mathfrak{R}_1/\mathfrak{R}_2-1)L\\
&-\frac{\mu_1\pi_1 S_2(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I+\frac{\mu_2(\psi+\omega)(\alpha\sigma_2+\varkappa_4\pi_2)}{\varphi\psi\varkappa_4\sigma_2}(\mathfrak{R}_4-1)C^Y. \qquad (8)
\end{aligned}$$

Thus, if $\mathfrak{R}_1/\ \mathfrak{R}_2 \le 1$ and $\mathfrak{R}_4 \le 1$, then using inequality (3) we obtain $\frac{d\Phi_2}{dt} \le 0$ with equality holding when $(S, E, Y, L, C^I, C^Y) = (S_2, E_2, Y_2, 0, 0, 0)$. Similar to the proof of Theorem 1 one can show that Đ_2 is G.A.S. □

Proof of Theorem 4. Define a function Φ_3 as:

$$\begin{aligned}
\Phi_3 &= S_3F\left(\frac{S}{S_3}\right)+L_3F\left(\frac{L}{L_3}\right)+\frac{S_3(b\varkappa_1+\varepsilon\varkappa_3)}{\varepsilon\left(a+\mu_1C_3^I\right)}I_3F\left(\frac{I}{I_3}\right)+\frac{1}{\varphi}E+\frac{\psi+\omega}{\varphi\psi}Y\\
&+\frac{\varkappa_1S_3}{\varepsilon}V_3F\left(\frac{V}{V_3}\right)+\frac{\mu_1S_3(b\varkappa_1+\varepsilon\varkappa_3)}{\varepsilon\sigma_1\left(a+\mu_1C_3^I\right)}C_3^IF\left(\frac{C^I}{C_3^I}\right)+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}$$

We calculate $\frac{d\Phi_3}{dt}$ as:

$$\begin{aligned}
\frac{d\Phi_3}{dt} &= \left(1-\frac{S_3}{S}\right)(\rho-\alpha S-\varkappa_1SV-\varkappa_2SL-\varkappa_3SI-\varkappa_4SY)\\
&+\left(1-\frac{L_3}{L}\right)(\varkappa_1SV+\varkappa_2SL+\varkappa_3SI-(\lambda+\gamma)L)\\
&+\frac{S_3(b\varkappa_1+\varepsilon\varkappa_3)}{\varepsilon\left(a+\mu_1C_3^I\right)}\left(1-\frac{I_3}{I}\right)\left(\lambda L-aI-\mu_1C^II\right)+\frac{1}{\varphi}(\varphi\varkappa_4SY+rY-(\psi+\omega)E)\\
&+\frac{\psi+\omega}{\varphi\psi}\left(\psi E-\delta Y-\mu_2C^YY\right)+\frac{\varkappa_1S_3}{\varepsilon}\left(1-\frac{V_3}{V}\right)(bI-\varepsilon V)
\end{aligned}$$

$$+\frac{\mu_1 S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_3^I\right)}\left(1-\frac{C_3^I}{C^I}\right)\left(\sigma_1 C^I I-\pi_1 C^I\right)+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(\sigma_2 C^Y Y-\pi_2 C^Y\right). \tag{9}$$

Equation (9) can be simplified as:

$$\begin{aligned}\frac{d\Phi_3}{dt}=&\left(1-\frac{S_3}{S}\right)(\rho-\alpha S)+\varkappa_2 S_3 L+\varkappa_3 S_3 I+\varkappa_4 S_3 Y-(\lambda+\gamma)L-\varkappa_1 S V\frac{L_3}{L}\\&-\varkappa_2 S L_3-\varkappa_3 S I\frac{L_3}{L}+(\lambda+\gamma)L_3+\frac{\lambda S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}L-\frac{aS_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}I\\&-\frac{\lambda S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}L\frac{I_3}{I}+\frac{aS_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}I_3+\frac{\mu_1 S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}C^I I_3+\frac{r}{\varphi}Y\\&-\frac{\delta(\psi+\omega)}{\varphi\psi}Y+\frac{\varkappa_1 S_3}{\varepsilon}bI-\frac{\varkappa_1 S_3}{\varepsilon}bI\frac{V_3}{V}+\varkappa_1 S_3 V_3-\frac{\mu_1\pi_1 S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_3^I\right)}C^I\\&-\frac{\mu_1 S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}C_3^I I+\frac{\mu_1\pi_1 S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_3^I\right)}C_3^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.\end{aligned}$$

Using the steady state conditions for $Đ_3$:

$$\begin{aligned}&\rho=\alpha S_3+\varkappa_1 S_3 V_3+\varkappa_2 S_3 L_3+\varkappa_3 S_3 I_3,\\&\varkappa_1 S_3 V_3+\varkappa_2 S_3 L_3+\varkappa_3 S_3 I_3=(\gamma+\lambda)L_3,\\&\lambda L_3=\left(a+\mu_1 C_3^I\right)I_3,\quad I_3=\frac{\pi_1}{\sigma_1},\quad V_3=\frac{b}{\varepsilon}I_3,\end{aligned}$$

we get

$$\varkappa_1 S_3 V_3+\varkappa_3 S_3 I_3=\frac{S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon}I_3=\frac{\lambda S_3\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_3^I\right)}L_3.$$

Further, we obtain

$$\begin{aligned}\frac{d\Phi_3}{dt}=&\left(1-\frac{S_3}{S}\right)(\alpha S_3-\alpha S)+\left(\varkappa_1 S_3 V_3+\varkappa_2 S_3 L_3+\varkappa_3 S_3 I_3\right)\left(1-\frac{S_3}{S}\right)\\&+\varkappa_4 S_3 Y-\varkappa_1 S_3 V_3\frac{S V L_3}{S_3 V_3 L}-\varkappa_2 S_3 L_3\frac{S}{S_3}-\varkappa_3 S_3 I_3\frac{S I L_3}{S_3 I_3 L}+\varkappa_1 S_3 V_3\\&+\varkappa_2 S_3 L_3+\varkappa_3 S_3 I_3-\left(\varkappa_1 S_3 V_3+\varkappa_3 S_3 I_3\right)\frac{L I_3}{L_3 I}+\varkappa_1 S_3 V_3+\varkappa_3 S_3 I_3\\&-\frac{(\delta-r)\psi+\delta\omega}{\varphi\psi}Y-\varkappa_1 S_3 V_3\frac{I V_3}{I_3 V}+\varkappa_1 S_3 V_3-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y\\=&-\alpha\frac{(S-S_3)^2}{S}+\varkappa_1 S_3 V_3\left(4-\frac{S_3}{S}-\frac{S V L_3}{S_3 V_3 L}-\frac{L I_3}{L_3 I}-\frac{I V_3}{I_3 V}\right)\\&+\varkappa_2 S_3 L_3\left(2-\frac{S_3}{S}-\frac{S}{S_3}\right)+\varkappa_3 S_3 I_3\left(3-\frac{S_3}{S}-\frac{S I L_3}{S_3 I_3 L}-\frac{L I_3}{L_3 I}\right)\\&+\varkappa_4\left(S_3-\frac{(\delta-r)\psi+\delta\omega}{\varkappa_4\varphi\psi}\right)Y-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y\end{aligned}$$

$$= -(\alpha + \varkappa_2 L_3)\frac{(S - S_3)^2}{S} + \varkappa_1 S_3 V_3\left(4 - \frac{S_3}{S} - \frac{SVL_3}{S_3 V_3 L} - \frac{LI_3}{L_3 I} - \frac{IV_3}{I_3 V}\right)$$
$$+ \varkappa_3 S_3 I_3\left(3 - \frac{S_3}{S} - \frac{SIL_3}{S_3 I_3 L} - \frac{LI_3}{L_3 I}\right) + \varkappa_4 (S_3 - S_5) Y - \frac{\mu_2\pi_2(\psi + \omega)}{\varphi\psi\sigma_2} C^Y.$$

Hence, if $\mathfrak{R}_5 \leq 1$, then $Đ_5$ does not exist since $E_5 \leq 0$ and $Y_5 \leq 0$. In this case

$$\frac{dE}{dt} = \varphi\varkappa_4 S Y + rY - (\psi + \omega) E \leq 0,$$
$$\frac{dY}{dt} = \psi E - \delta Y - \mu_2 C^Y Y \leq 0.$$

Now we want to find the value $\bar{S}$ with $0 < S(t) \leq \bar{S}$ such that $\frac{dE}{dt} \leq 0$ and $\frac{dY}{dt} \leq 0$. Let us consider

$$\frac{dE}{dt} + \frac{\psi + \omega}{\psi}\frac{dY}{dt} = \varphi\varkappa_4 S Y - \frac{(\delta - r)\psi + \delta\omega}{\psi} Y - \frac{\mu_2(\psi + \omega)}{\psi} C^Y Y$$
$$= \varphi\varkappa_4\left(S - \frac{(\delta - r)\psi + \delta\omega}{\varkappa_4\varphi\psi}\right) Y - \frac{\mu_2(\psi + \omega)}{\psi} C^Y Y \leq 0 \text{ for all } C^Y, Y > 0.$$

This happens when $S_3 \leq \bar{S} = \frac{(\delta - r)\psi + \delta\omega}{\varkappa_4\varphi\psi} = S_5$. Then using inequalities (1)–(2) we obtain $\frac{d\Phi_3}{dt} \leq 0$ for all $S, L, I, Y, V, C^Y > 0$ with equality holding when $(S, L, I, V, Y, C^Y) = (S_3, L_3, I_3, V_3, 0, 0)$. The solutions of system (2.9)–(2.16) converge to Υ_3' which contains elements with $(S, L, I, V, Y, C^Y) = (S_3, L_3, I_3, V_3, 0, 0)$. It follows that $\frac{dI}{dt} = 0$ and $\frac{dY}{dt} = 0$. Eqs (2.11) and (2.13) become

$$0 = \frac{dI}{dt} = \lambda L_3 - a I_3 - \mu_1 C^I I_3,$$
$$0 = \frac{dY}{dt} = \psi E,$$

which give $C^I(t) = C_3^I$ and $E(t) = 0$ for all t and then $\Upsilon_3' = \{Đ_3\}$. Applying Lyapunov-LaSalle asymptotic stability theorem we get $Đ_3$ is G.A.S. □

Proof of Theorem 5. Define Φ_4 as:

$$\Phi_4 = S_4 F\left(\frac{S}{S_4}\right) + L + \frac{S_4(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon} I + \frac{1}{\varphi} E_4 F\left(\frac{E}{E_4}\right) + \frac{\psi + \omega}{\varphi\psi} Y_4 F\left(\frac{Y}{Y_4}\right)$$
$$+ \frac{\varkappa_1 S_4}{\varepsilon} V + \frac{\mu_1 S_4(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon\sigma_1} C^I + \frac{\mu_2(\psi + \omega)}{\varphi\psi\sigma_2} C_4^Y F\left(\frac{C^Y}{C_4^Y}\right).$$

Calculating $\frac{d\Phi_4}{dt}$ as:

$$\frac{d\Phi_4}{dt} = \left(1 - \frac{S_4}{S}\right)(\rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y) + \varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda + \gamma) L$$
$$+ \frac{S_4(b\varkappa_1 + \varepsilon\varkappa_3)}{a\varepsilon}\left(\lambda L - a I - \mu_1 C^I I\right) + \frac{1}{\varphi}\left(1 - \frac{E_4}{E}\right)(\varphi\varkappa_4 S Y + rY - (\psi + \omega) E)$$
$$+ \frac{\psi + \omega}{\varphi\psi}\left(1 - \frac{Y_4}{Y}\right)\left(\psi E - \delta Y - \mu_2 C^Y Y\right) + \frac{\varkappa_1 S_4}{\varepsilon}(bI - \varepsilon V)$$

$$
\begin{aligned}
&+\frac{\mu_1 S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}\left(\sigma_1 C^I I-\pi_1 C^I\right)+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(1-\frac{C_4^Y}{C^Y}\right)\left(\sigma_2 C^Y Y-\pi_2 C^Y\right)\\
&=\left(1-\frac{S_4}{S}\right)(\rho-\alpha S)+\varkappa_2 S_4 L+\varkappa_4 S_4 Y-(\gamma+\lambda)L+\frac{\lambda S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon}L\\
&+\frac{r}{\varphi}Y-\varkappa_4 S Y\frac{E_4}{E}-\frac{r}{\varphi}Y\frac{E_4}{E}+\frac{\psi+\omega}{\varphi}E_4-\frac{\delta(\psi+\omega)}{\varphi\psi}Y-\frac{\psi+\omega}{\varphi}E\frac{Y_4}{Y}\\
&+\frac{\delta(\psi+\omega)}{\varphi\psi}Y_4+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C^Y Y_4-\frac{\mu_1\pi_1 S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}C^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y\\
&-\frac{\mu_2(\psi+\omega)}{\varphi\psi}C_4^Y Y+\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C_4^Y.
\end{aligned}
$$

Using the steady state conditions for Đ_4:

$$
\begin{aligned}
\rho&=\alpha S_4+\varkappa_4 S_4 Y_4,\quad Y_4=\frac{\pi_2}{\sigma_2},\\
\varkappa_4 S_4 Y_4+\frac{r}{\varphi}Y_4&=\frac{\psi+\omega}{\varphi}E_4=\frac{\delta(\psi+\omega)}{\varphi\psi}Y_4+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C_4^Y Y_4.
\end{aligned}
$$

We obtain

$$
\begin{aligned}
\frac{d\Phi_4}{dt}&=\left(1-\frac{S_4}{S}\right)(\alpha S_4-\alpha S)+\varkappa_4 S_4 Y_4\left(1-\frac{S_4}{S}\right)+\varkappa_2 S_4 L-(\gamma+\lambda)L+\frac{\lambda S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon}L\\
&-\varkappa_4 S_4 Y_4\frac{S Y E_4}{S_4 Y_4 E}-\frac{r}{\varphi}Y_4\frac{Y E_4}{Y_4 E}+\varkappa_4 S_4 Y_4+\frac{r}{\varphi}Y_4-\varkappa_4 S_4 Y_4\frac{E Y_4}{E_4 Y}-\frac{r}{\varphi}Y_4\frac{E Y_4}{E_4 Y}+\varkappa_4 S_4 Y_4\\
&+\frac{r}{\varphi}Y_4-\frac{\mu_1\pi_1 S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}C^I\\
&=-\alpha\frac{(S-S_4)^2}{S}+\varkappa_4 S_4 Y_4\left(3-\frac{S_4}{S}-\frac{S Y E_4}{S_4 Y_4 E}-\frac{E Y_4}{E_4 Y}\right)+\frac{r}{\varphi}Y_4\left(2-\frac{Y E_4}{Y_4 E}-\frac{E Y_4}{E_4 Y}\right)\\
&+(\gamma+\lambda)\left[\frac{S_4\{a\varepsilon\varkappa_2+\lambda(b\varkappa_1+\varepsilon\varkappa_3)\}}{a\varepsilon(\gamma+\lambda)}-1\right]L-\frac{\mu_1\pi_1 S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}C^I\\
&=-\alpha\frac{(S-S_4)^2}{S}-\frac{r}{\varphi}\frac{(Y E_4-E Y_4)^2}{E E_4 Y}+\varkappa_4 S_4 Y_4\left(3-\frac{S_4}{S}-\frac{S Y E_4}{S_4 Y_4 E}-\frac{E Y_4}{E_4 Y}\right)\\
&+(\gamma+\lambda)\left(\Re_6-1\right)L-\frac{\mu_1\pi_1 S_4\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}C^I.
\end{aligned}
$$

Clearly, for all $S, L, I, E, Y, V, C^I > 0$ we have $\frac{d\Phi_4}{dt} \leq 0$. Moreover, $\frac{d\Phi_4}{dt} = 0$ when $(S, E, Y, L, C^I) = (S_4, E_4, Y_4, 0, 0)$. The system's solutions tend to Υ_4' which includes elements satisfying $E = E_4$ and $Y = Y_4$. This gives $\frac{dY}{dt} = 0$ and from Eq (2.13) we obtain

$$
0=\frac{dY}{dt}=\psi E_4-\delta Y_4-\mu_2 C^Y Y_4,
$$

which yields $C^Y(t) = C_4^Y$ for all t. Similar to the proof of Theorem 1 one can show that Đ_4 is G.A.S. □

Proof of Theorem 6. Define Φ_5 as:

$$
\Phi_5=S_5 F\left(\frac{S}{S_5}\right)+L_5 F\left(\frac{L}{L_5}\right)+\frac{S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_5^I\right)}I_5 F\left(\frac{I}{I_5}\right)+\frac{1}{\varphi}E_5 F\left(\frac{E}{E_5}\right)
$$

$$+\frac{\psi+\omega}{\varphi\psi}Y_5F\left(\frac{Y}{Y_5}\right)+\frac{\varkappa_1S_5}{\varepsilon}V_5F\left(\frac{V}{V_5}\right)+\frac{\mu_1S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1C_5^I\right)}C_5^IF\left(\frac{C^I}{C_5^I}\right)+\frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}C^Y.$$

Calculating $\frac{d\Phi_5}{dt}$ as:

$$\begin{aligned}\frac{d\Phi_5}{dt}&=\left(1-\frac{S_5}{S}\right)\left(\rho-\alpha S-\varkappa_1SV-\varkappa_2SL-\varkappa_3SI-\varkappa_4SY\right)\\&+\left(1-\frac{L_5}{L}\right)\left(\varkappa_1SV+\varkappa_2SL+\varkappa_3SI-\left(\lambda+\gamma\right)L\right)\\&+\frac{S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}\left(1-\frac{I_5}{I}\right)\left(\lambda L-aI-\mu_1C^II\right)+\frac{1}{\varphi}\left(1-\frac{E_5}{E}\right)\left(\varphi\varkappa_4SY+rY-\left(\psi+\omega\right)E\right)\\&+\frac{\psi+\omega}{\varphi\psi}\left(1-\frac{Y_5}{Y}\right)\left(\psi E-\delta Y-\mu_2C^YY\right)+\frac{\varkappa_1S_5}{\varepsilon}\left(1-\frac{V_5}{V}\right)\left(bI-\varepsilon V\right)\\&+\frac{\mu_1S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1C_5^I\right)}\left(1-\frac{C_5^I}{C^I}\right)\left(\sigma_1C^II-\pi_1C^I\right)+\frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}\left(\sigma_2C^YY-\pi_2C^Y\right).\end{aligned}\tag{10}$$

Equation (10) can be simplified as:

$$\begin{aligned}\frac{d\Phi_5}{dt}&=\left(1-\frac{S_5}{S}\right)\left(\rho-\alpha S\right)+\varkappa_2S_5L+\varkappa_3S_5I+\varkappa_4S_5Y-\left(\gamma+\lambda\right)L-\varkappa_1SV\frac{L_5}{L}\\&-\varkappa_2SL_5-\varkappa_3SI\frac{L_5}{L}+\left(\gamma+\lambda\right)L_5+\frac{\lambda S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}L-\frac{aS_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}I\\&-\frac{\lambda S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}L\frac{I_5}{I}+\frac{aS_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}I_5+\frac{\mu_1S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}C^II_5+\frac{r}{\varphi}Y\\&-\varkappa_4SY\frac{E_5}{E}-\frac{r}{\varphi}Y\frac{E_5}{E}+\frac{\psi+\omega}{\varphi}E_5-\frac{\delta\left(\psi+\omega\right)}{\varphi\psi}Y-\frac{\psi+\omega}{\varphi}E\frac{Y_5}{Y}+\frac{\delta\left(\psi+\omega\right)}{\varphi\psi}Y_5\\&+\frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi}C^YY_5+\varkappa_1S_5\frac{bI}{\varepsilon}-\varkappa_1S_5V_5\frac{bI}{\varepsilon V}+\varkappa_1S_5V_5-\frac{\mu_1\pi_1S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1C_5^I\right)}C^I\\&-\frac{\mu_1S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}C_5^II+\frac{\mu_1\pi_1S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1C_5^I\right)}C_5^I-\frac{\mu_2\pi_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}C^Y.\end{aligned}$$

Using the steady state conditions for $Ð_5$:

$$\begin{aligned}&\rho=\alpha S_5+\varkappa_1S_5V_5+\varkappa_2S_5L_5+\varkappa_3S_5I_5+\varkappa_4S_5Y_5,\\&\varkappa_1S_5V_5+\varkappa_2S_5L_5+\varkappa_3S_5I_5=\left(\gamma+\lambda\right)L_5,\\&\lambda L_5=\left(a+\mu_1C_5^I\right)I_5,\quad I_5=\frac{\pi_1}{\sigma_1},\quad V_5=\frac{b}{\varepsilon}I_5,\\&\varkappa_4S_5Y_5+\frac{r}{\varphi}Y_5=\frac{\psi+\omega}{\varphi}E_5=\frac{\delta\left(\psi+\omega\right)}{\varphi\psi}Y_5.\end{aligned}$$

We obtain

$$\varkappa_1S_5V_5+\varkappa_3S_5I_5=\frac{S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon}I_5=\frac{\lambda S_5\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1C_5^I\right)}L_5.$$

Further, we get

$$\begin{aligned}
\frac{d\Phi_5}{dt} &= \left(1-\frac{S_5}{S}\right)(\alpha S_5-\alpha S)+(\varkappa_1 S_5V_5+\varkappa_2 S_5L_5+\varkappa_3 S_5I_5+\varkappa_4 S_5Y_5)\left(1-\frac{S_5}{S}\right)\\
&-\varkappa_1 S_5V_5\frac{SVL_5}{S_5V_5L}-\varkappa_2 S_5L_5\frac{S}{S_5}-\varkappa_3 S_5I_5\frac{SIL_5}{S_5I_5L}+\varkappa_1 S_5V_5+\varkappa_2 S_5L_5+\varkappa_3 S_5I_5\\
&-(\varkappa_1 S_5V_5+\varkappa_3 S_5I_5)\frac{LI_5}{L_5I}+\varkappa_1 S_5V_5+\varkappa_3 S_5I_5-\varkappa_4 S_5Y_5\frac{SYE_5}{S_5Y_5E}-\frac{r}{\varphi}Y_5\frac{YE_5}{Y_5E}\\
&+\varkappa_4 S_5Y_5+\frac{r}{\varphi}Y_5-\varkappa_4 S_5Y_5\frac{EY_5}{E_5Y}-\frac{r}{\varphi}Y_5\frac{EY_5}{E_5Y}+\varkappa_4 S_5Y_5+\frac{r}{\varphi}Y_5-\varkappa_1 S_5V_5\frac{IV_5}{I_5V}\\
&+\varkappa_1 S_5V_5+\frac{\mu_2(\psi+\omega)}{\varphi\psi}\left(Y_5-\frac{\pi_2}{\sigma_2}\right)C^Y\\
&=-\alpha\frac{(S-S_5)^2}{S}+\varkappa_1 S_5V_5\left(4-\frac{S_5}{S}-\frac{SVL_5}{S_5V_5L}-\frac{LI_5}{L_5I}-\frac{IV_5}{I_5V}\right)\\
&+\varkappa_2 S_5L_5\left(2-\frac{S_5}{S}-\frac{S}{S_5}\right)+\varkappa_3 S_5I_5\left(3-\frac{S_5}{S}-\frac{SIL_5}{S_5I_5L}-\frac{LI_5}{L_5I}\right)\\
&+\varkappa_4 S_5Y_5\left(3-\frac{S_5}{S}-\frac{SYE_5}{S_5Y_5E}-\frac{EY_5}{E_5Y}\right)+\frac{r}{\varphi}Y_5\left(2-\frac{YE_5}{Y_5E}-\frac{EY_5}{E_5Y}\right)\\
&+\frac{\mu_2(\psi+\omega)}{\varphi\psi}\left(Y_5-\frac{\pi_2}{\sigma_2}\right)C^Y. \qquad (11)
\end{aligned}$$

Then, Eq (11) will be reduced to the form

$$\begin{aligned}
\frac{d\Phi_5}{dt} &= -(\alpha+\varkappa_2L_5)\frac{(S-S_5)^2}{S}-\frac{r}{\varphi}\frac{(YE_5-EY_5)^2}{EE_5Y}\\
&+\varkappa_1 S_5V_5\left(4-\frac{S_5}{S}-\frac{SVL_5}{S_5V_5L}-\frac{LI_5}{L_5I}-\frac{IV_5}{I_5V}\right)\\
&+\varkappa_3 S_5I_5\left(3-\frac{S_5}{S}-\frac{SIL_5}{S_5I_5L}-\frac{LI_5}{L_5I}\right)+\varkappa_4 S_5Y_5\left(3-\frac{S_5}{S}-\frac{SYE_5}{S_5Y_5E}-\frac{EY_5}{E_5Y}\right)\\
&+\frac{\mu_2(\psi+\omega)}{\varphi\psi}(Y_5-Y_7)C^Y.
\end{aligned}$$

Hence, if $\mathfrak{R}_8 \leq 1$, then Đ_7 does not exists since $C_7^Y = \frac{(\delta-r)\psi+\delta\omega}{\mu_2(\psi+\omega)}(\mathfrak{R}_8-1) \leq 0$. This implies that, $\frac{dC^Y}{dt} = \sigma_2\left(Y-\frac{\pi_2}{\sigma_2}\right)C^Y \leq 0$ for all $C^Y > 0$. This yields, $Y_5 \leq \frac{\pi_2}{\sigma_2} = Y_7$. It is obvious that for all $S, L, I, E, Y, V, C^Y > 0$ we have $\frac{d\Phi_5}{dt} \leq 0$. We also have $\frac{d\Phi_5}{dt} = 0$ when $(S, L, I, E, Y, V, C^Y) = (S_5, L_5, I_5, E_5, Y_5, V_5, 0)$. The system's solutions tend to Υ_5' which includes elements satisfying $L = L_5$ and $I = I_5$, and this implies that $\frac{dI}{dt} = 0$. Eq (2.11) becomes

$$0 = \frac{dI}{dt} = \lambda L_5 - aI_5 - \mu_1 C^I I_5,$$

which provides that $C^I(t) = C_5^I$ for all t and therefore $\Upsilon_5' = \{\text{Đ}_5\}$. Applying Lyapunov-LaSalle asymptotic stability theorem we get Đ_5 is G.A.S. □

Proof of Lemma 2. Let $\mathfrak{R}_7 \leq 1$, hence $\dfrac{\lambda\sigma_1 L_7}{a\pi_1} \leq 1$ and therefore

$$\begin{aligned} L_7 \leq \frac{a\pi_1}{\lambda\sigma_1} &\Longrightarrow \frac{-\bar{B} + \sqrt{\bar{B}^2 - 4\bar{A}\bar{C}}}{2\bar{A}} \leq \frac{a\pi_1}{\lambda\sigma_1} \\ &\Longrightarrow \sqrt{\bar{B}^2 - 4\bar{A}\bar{C}} \leq \frac{2\bar{A}a\pi_1 + \lambda\sigma_1\bar{B}}{\lambda\sigma_1} \\ &\Longrightarrow \left(\frac{2\bar{A}a\pi_1 + \lambda\sigma_1\bar{B}}{\lambda\sigma_1}\right)^2 + 4\bar{A}\bar{C} - \bar{B}^2 \geq 0. \end{aligned}$$

Using Eq (3.11), we obtain

$$\frac{4a\pi_1\varepsilon\varkappa_2\sigma_1\sigma_2^2(\gamma+\lambda)^2\left[a\varepsilon\varkappa_2 + \lambda\left(b\varkappa_1 + \varepsilon\varkappa_3\right)\right]}{\lambda^2}\left(I_7 - I_6\right) \geq 0.$$

Hence, $I_6 \leq I_7$. □

Proof of Theorem 7. Define Φ_6 as:

$$\begin{aligned} \Phi_6 = {} & S_6 F\left(\frac{S}{S_6}\right) + L_6 F\left(\frac{L}{L_6}\right) + \frac{S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon} I_6 F\left(\frac{I}{I_6}\right) + \frac{1}{\varphi} E_6 F\left(\frac{E}{E_6}\right) + \frac{\psi+\omega}{\varphi\psi} Y_6 F\left(\frac{Y}{Y_6}\right) \\ & + \frac{\varkappa_1 S_6}{\varepsilon} V_6 F\left(\frac{V}{V_6}\right) + \frac{\mu_1 S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1} C^I + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2} C_6^Y F\left(\frac{C^Y}{C_6^Y}\right). \end{aligned}$$

Calculating $\frac{d\Phi_6}{dt}$ as:

$$\begin{aligned} \frac{d\Phi_6}{dt} = {} & \left(1 - \frac{S_6}{S}\right)\left(\rho - \alpha S - \varkappa_1 S V - \varkappa_2 S L - \varkappa_3 S I - \varkappa_4 S Y\right) \\ & + \left(1 - \frac{L_6}{L}\right)\left(\varkappa_1 S V + \varkappa_2 S L + \varkappa_3 S I - (\lambda+\gamma) L\right) \\ & + \frac{S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon}\left(1 - \frac{I_6}{I}\right)\left(\lambda L - aI - \mu_1 C^I I\right) + \frac{1}{\varphi}\left(1 - \frac{E_6}{E}\right)\left(\varphi\varkappa_4 S Y + rY - (\psi+\omega) E\right) \\ & + \frac{\psi+\omega}{\varphi\psi}\left(1 - \frac{Y_6}{Y}\right)\left(\psi E - \delta Y - \mu_2 C^Y Y\right) + \frac{\varkappa_1 S_6}{\varepsilon}\left(1 - \frac{V_6}{V}\right)\left(bI - \varepsilon V\right) \\ & + \frac{\mu_1 S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon\sigma_1}\left(\sigma_1 C^I I - \pi_1 C^I\right) + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(1 - \frac{C_6^Y}{C^Y}\right)\left(\sigma_2 C^Y Y - \pi_2 C^Y\right). \end{aligned} \tag{12}$$

Simplifying Eq (12), we get

$$\begin{aligned} \frac{d\Phi_6}{dt} = {} & \left(1 - \frac{S_6}{S}\right)\left(\rho - \alpha S\right) + \varkappa_2 S_6 L + \varkappa_3 S_6 I + \varkappa_4 S_6 Y - (\gamma+\lambda) L - \varkappa_1 S V \frac{L_6}{L} \\ & - \varkappa_2 S L_6 - \varkappa_3 S I \frac{L_6}{L} + (\gamma+\lambda) L_6 + \frac{\lambda S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon} L - \frac{S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{\varepsilon} I \\ & - \frac{\lambda S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon} L\frac{I_6}{I} + \frac{S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{\varepsilon} I_6 + \frac{\mu_1 S_6\left(b\varkappa_1 + \varepsilon\varkappa_3\right)}{a\varepsilon} C^I I_6 + \frac{r}{\varphi} Y \\ & - \varkappa_4 S Y\frac{E_6}{E} - \frac{r}{\varphi} Y\frac{E_6}{E} + \frac{\psi+\omega}{\varphi} E_6 - \frac{\delta(\psi+\omega)}{\varphi\psi} Y - \frac{\psi+\omega}{\varphi} E\frac{Y_6}{Y} + \frac{\delta(\psi+\omega)}{\varphi\psi} Y_6 \end{aligned}$$

$$+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C^Y Y_6+\varkappa_1 S_6\frac{bI}{\varepsilon}-\varkappa_1 S_6 V_6\frac{bI}{\varepsilon V}+\varkappa_1 S_6 V_6-\frac{\mu_1\pi_1 S_6(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon\sigma_1}C^I$$
$$-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y-\frac{\mu_2(\psi+\omega)}{\varphi\psi}C_6^Y Y+\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C_6^Y.$$

Using the steady state conditions for $Đ_6$:

$$\rho=\alpha S_6+\varkappa_1 S_6 V_6+\varkappa_2 S_6 L_6+\varkappa_3 S_6 I_6+\varkappa_4 S_6 Y_6,$$
$$\varkappa_1 S_6 V_6+\varkappa_2 S_6 L_6+\varkappa_3 S_6 I_6=(\gamma+\lambda)L_6,$$
$$Y_6=\frac{\pi_2}{\sigma_2},\quad V_6=\frac{bI_6}{\varepsilon},\quad \frac{\lambda}{a}L_6=I_6,$$
$$\varkappa_4 S_6 Y_6+\frac{r}{\varphi}Y_6=\frac{\psi+\omega}{\varphi}E_6=\frac{\delta(\psi+\omega)}{\varphi\psi}Y_6+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C_6^Y Y_6.$$

It follows that

$$\varkappa_1 S_6 V_6+\varkappa_3 S_6 I_6=\frac{S_6(b\varkappa_1+\varepsilon\varkappa_3)}{\varepsilon}I_6=\frac{\lambda S_6(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}L_6.$$

Then, we obtain

$$\begin{aligned}\frac{d\Phi_6}{dt}&=\left(1-\frac{S_6}{S}\right)(\alpha S_6-\alpha S)+(\varkappa_1 S_6 V_6+\varkappa_2 S_6 L_6+\varkappa_3 S_6 I_6+\varkappa_4 S_6 Y_6)\left(1-\frac{S_6}{S}\right)\\
&-\varkappa_1 S_6 V_6\frac{S V L_6}{S_6 V_6 L}-\varkappa_2 S_6 L_6\frac{S}{S_6}-\varkappa_3 S_6 I_6\frac{S I L_6}{S_6 I_6 L}+\varkappa_1 S_6 V_6+\varkappa_2 S_6 L_6+\varkappa_3 S_6 I_6\\
&-(\varkappa_1 S_6 V_6+\varkappa_3 S_6 I_6)\frac{L I_6}{L_6 I}+\varkappa_1 S_6 V_6+\varkappa_3 S_6 I_6-\varkappa_4 S_6 Y_6\frac{S Y E_6}{S_6 Y_6 E}-\frac{r}{\varphi}Y_6\frac{Y E_6}{Y_6 E}\\
&+\varkappa_4 S_6 Y_6+\frac{r}{\varphi}Y_6-\varkappa_4 S_6 Y_6\frac{E Y_6}{E_6 Y}-\frac{r}{\varphi}Y_6\frac{E Y_6}{E_6 Y}+\varkappa_4 S_6 Y_6+\frac{r}{\varphi}Y_6\\
&-\varkappa_1 S_6 V_6\frac{I V_6}{I_6 V}+\varkappa_1 S_6 V_6+\frac{\mu_1 S_6(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}\left(I_6-\frac{\pi_1}{\sigma_1}\right)C^I\\
&=-\alpha\frac{(S-S_6)^2}{S}+\varkappa_1 S_6 V_6\left(4-\frac{S_6}{S}-\frac{S V L_6}{S_6 V_6 L}-\frac{L I_6}{L_6 I}-\frac{I V_6}{I_6 V}\right)\\
&+\varkappa_2 S_6 L_6\left(2-\frac{S_6}{S}-\frac{S}{S_6}\right)+\varkappa_3 S_6 I_6\left(3-\frac{S_6}{S}-\frac{S I L_6}{S_6 I_6 L}-\frac{L I_6}{L_6 I}\right)\\
&+\varkappa_4 S_6 Y_6\left(3-\frac{S_6}{S}-\frac{S Y E_6}{S_6 Y_6 E}-\frac{E Y_6}{E_6 Y}\right)+\frac{r}{\varphi}Y_6\left(2-\frac{Y E_6}{Y_6 E}-\frac{E Y_6}{E_6 Y}\right)\\
&+\frac{\mu_1 S_6(b\varkappa_1+\varepsilon\varkappa_3)}{a\varepsilon}\left(I_6-\frac{\pi_1}{\sigma_1}\right)C^I.\end{aligned}\tag{13}$$

Then, Eq (13) will be reduced to the form

$$\frac{d\Phi_6}{dt}=-(\alpha+\varkappa_2 L_6)\frac{(S-S_6)^2}{S}-\frac{r}{\varphi}\frac{(Y E_6-E Y_6)^2}{E E_6 Y}$$
$$+\varkappa_1 S_6 V_6\left(4-\frac{S_6}{S}-\frac{S V L_6}{S_6 V_6 L}-\frac{L I_6}{L_6 I}-\frac{I V_6}{I_6 V}\right)$$

$$+\varkappa_3 S_6 I_6\left(3-\frac{S_6}{S}-\frac{SIL_6}{S_6 I_6 L}-\frac{LI_6}{L_6 I}\right)+\varkappa_4 S_6 Y_6\left(3-\frac{S_6}{S}-\frac{SYE_6}{S_6 Y_6 E}-\frac{EY_6}{E_6 Y}\right)$$
$$+\frac{\mu_1 S_6\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{a\varepsilon}\left(I_6-I_7\right)C^I.$$

Hence, if $\Re_7 \leq 1$, then using Lemma 2 we get $I_6 \leq I_7$. Therefore, $\frac{d\Phi_6}{dt} \leq 0$ for all $S, L, I, E, Y, V, C^I > 0$ and $\frac{d\Phi_6}{dt} = 0$ when $(S, L, I, E, Y, V, C^I) = (S_6, L_6, I_6, E_6, Y_6, V_6, 0)$. The system's solutions tend to Υ_6' which includes elements satisfying $E = E_6$ and $Y = Y_6$. Then, $\frac{dY}{dt} = 0$ and from Eq (2.13) we obtain

$$0 = \frac{dY}{dt} = \psi E_6 - \delta Y_6 - \mu_2 C^Y Y_6,$$

which provides that $C^Y(t) = C_6^Y$ for all t and hence $\Upsilon_6' = \{\text{Đ}_6\}$. Applying Lyapunov-LaSalle asymptotic stability theorem we get Đ_6 is G.A.S. □

Proof of Theorem 8. Define Φ_7 as:

$$\Phi_7 = S_7 F\left(\frac{S}{S_7}\right)+L_7 F\left(\frac{L}{L_7}\right)+\frac{S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}I_7 F\left(\frac{I}{I_7}\right)+\frac{1}{\varphi}E_7 F\left(\frac{E}{E_7}\right)+\frac{\psi+\omega}{\varphi\psi}Y_7 F\left(\frac{Y}{Y_7}\right)$$
$$+\frac{\varkappa_1 S_7}{\varepsilon}V_7 F\left(\frac{V}{V_7}\right)+\frac{\mu_1 S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_7^I\right)}C_7^I F\left(\frac{C^I}{C_7^I}\right)+\frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}C_7^Y F\left(\frac{C^Y}{C_7^Y}\right).$$

Calculating $\frac{d\Phi_7}{dt}$ as:

$$\frac{d\Phi_7}{dt} = \left(1-\frac{S_7}{S}\right)\left(\rho-\alpha S-\varkappa_1 S V-\varkappa_2 S L-\varkappa_3 S I-\varkappa_4 S Y\right)$$
$$+\left(1-\frac{L_7}{L}\right)\left(\varkappa_1 S V+\varkappa_2 S L+\varkappa_3 S I-(\lambda+\gamma)L\right)$$
$$+\frac{S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}\left(1-\frac{I_7}{I}\right)\left(\lambda L-aI-\mu_1 C^I I\right)+\frac{1}{\varphi}\left(1-\frac{E_7}{E}\right)\left(\varphi\varkappa_4 S Y+rY-(\psi+\omega)E\right)$$
$$+\frac{\psi+\omega}{\varphi\psi}\left(1-\frac{Y_7}{Y}\right)\left(\psi E-\delta Y-\mu_2 C^Y Y\right)+\frac{\varkappa_1 S_7}{\varepsilon}\left(1-\frac{V_7}{V}\right)(bI-\varepsilon V)$$
$$+\frac{\mu_1 S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_7^I\right)}\left(1-\frac{C_7^I}{C^I}\right)\left(\sigma_1 C^I I-\pi_1 C^I\right)+\frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}\left(1-\frac{C_7^Y}{C^Y}\right)\left(\sigma_2 C^Y Y-\pi_2 C^Y\right). \quad (14)$$

Simplifying Eq (14), we get

$$\frac{d\Phi_7}{dt} = \left(1-\frac{S_7}{S}\right)\left(\rho-\alpha S\right)+\varkappa_2 S_7 L+\varkappa_3 S_7 I+\varkappa_4 S_7 Y-(\gamma+\lambda)L-\varkappa_1 S V\frac{L_7}{L}-\varkappa_2 S L_7$$
$$-\varkappa_3 S I\frac{L_7}{L}+(\gamma+\lambda)L_7+\frac{\lambda S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}L-\frac{aS_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}I-\frac{\lambda S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}L\frac{I_7}{I}$$
$$+\frac{aS_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}I_7+\frac{\mu_1 S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}C^I I_7+\frac{r}{\varphi}Y-\varkappa_4 S Y\frac{E_7}{E}-\frac{r}{\varphi}Y\frac{E_7}{E}+\frac{\psi+\omega}{\varphi}E_7$$
$$-\frac{\delta\left(\psi+\omega\right)}{\varphi\psi}Y-\frac{\psi+\omega}{\varphi}E\frac{Y_7}{Y}+\frac{\delta\left(\psi+\omega\right)}{\varphi\psi}Y_7+\frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi}C^Y Y_7+\varkappa_1 S_7\frac{bI}{\varepsilon}-\varkappa_1 S_7 V_7\frac{bI}{\varepsilon V}$$

$$+\varkappa_1 S_7 V_7 - \frac{\mu_1\pi_1 S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_7^I\right)}C^I - \frac{\mu_1 S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}C_7^I I + \frac{\mu_1\pi_1 S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\sigma_1\left(a+\mu_1 C_7^I\right)}C_7^I$$
$$-\frac{\mu_2\pi_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}C^Y - \frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi}C_7^Y Y + \frac{\mu_2\pi_2\left(\psi+\omega\right)}{\varphi\psi\sigma_2}C_7^Y.$$

The steady state conditions for $Đ_7$ give

$$\begin{aligned}
&\rho = \alpha S_7 + \varkappa_1 S_7 V_7 + \varkappa_2 S_7 L_7 + \varkappa_3 S_7 I_7 + \varkappa_4 S_7 Y_7,\\
&\varkappa_1 S_7 V_7 + \varkappa_2 S_7 L_7 + \varkappa_3 S_7 I_7 = \left(\gamma+\lambda\right)L_7,\\
&\lambda L_7 = \left(a+\mu_1 C_7^I\right)I_7,\quad I_7 = \frac{\pi_1}{\sigma_1},\quad Y_7 = \frac{\pi_2}{\sigma_2},\quad V_7 = \frac{bI_7}{\varepsilon}\\
&\varkappa_4 S_7 Y_7 + \frac{r}{\varphi}Y_7 = \frac{\psi+\omega}{\varphi}E_7 = \frac{\delta\left(\psi+\omega\right)}{\varphi\psi}Y_7 + \frac{\mu_2\left(\psi+\omega\right)}{\varphi\psi}C_7^Y Y_7.
\end{aligned}$$

From the above conditions, we have

$$\varkappa_1 S_7 V_7 + \varkappa_3 S_7 I_7 = \frac{S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon}I_7 = \frac{\lambda S_7\left(b\varkappa_1+\varepsilon\varkappa_3\right)}{\varepsilon\left(a+\mu_1 C_7^I\right)}L_7.$$

Moreover,

$$\begin{aligned}
\frac{d\Phi_7}{dt} &= \left(1-\frac{S_7}{S}\right)\left(\alpha S_7 - \alpha S\right) + \left(\varkappa_1 S_7 V_7 + \varkappa_2 S_7 L_7 + \varkappa_3 S_7 I_7 + \varkappa_4 S_7 Y_7\right)\left(1-\frac{S_7}{S}\right)\\
&\quad - \varkappa_1 S_7 V_7 \frac{S V L_7}{S_7 V_7 L} - \varkappa_2 S_7 L_7 \frac{S}{S_7} - \varkappa_3 S_7 I_7 \frac{S I L_7}{S_7 I_7 L} + \varkappa_1 S_7 V_7 + \varkappa_2 S_7 L_7 + \varkappa_3 S_7 I_7\\
&\quad - \left(\varkappa_1 S_7 V_7 + \varkappa_3 S_7 I_7\right)\frac{L I_7}{L_7 I} + \varkappa_1 S_7 V_7 + \varkappa_3 S_7 I_7 - \varkappa_4 S_7 Y_7 \frac{S Y E_7}{S_7 Y_7 E} - \frac{r}{\varphi}Y_7\frac{Y E_7}{Y_7 E}\\
&\quad + \varkappa_4 S_7 Y_7 + \frac{r}{\varphi}Y_7 - \varkappa_4 S_7 Y_7 \frac{E Y_7}{E_7 Y} - \frac{r}{\varphi}Y_7\frac{E Y_7}{E_7 Y} + \varkappa_4 S_7 Y_7 + \frac{r}{\varphi}Y_7\\
&\quad - \varkappa_1 S_7 V_7 \frac{I V_7}{I_7 V} + \varkappa_1 S_7 V_7\\
&= -\left(\alpha+\varkappa_2 L_7\right)\frac{\left(S-S_7\right)^2}{S} - \frac{r}{\varphi}\frac{\left(Y E_7 - E Y_7\right)^2}{E E_7 Y}\\
&\quad + \varkappa_1 S_7 V_7\left(4 - \frac{S_7}{S} - \frac{S V L_7}{S_7 V_7 L} - \frac{L I_7}{L_7 I} - \frac{I V_7}{I_7 V}\right)\\
&\quad + \varkappa_3 S_7 I_7\left(3 - \frac{S_7}{S} - \frac{S I L_7}{S_7 I_7 L} - \frac{L I_7}{L_7 I}\right) + \varkappa_4 S_7 Y_7\left(3 - \frac{S_7}{S} - \frac{S Y E_7}{S_7 Y_7 E} - \frac{E Y_7}{E_7 Y}\right).
\end{aligned}$$

Clearly, $\frac{d\Phi_7}{dt} \le 0$ for all $S, L, I, E, Y, V > 0$ where $\frac{d\Phi_7}{dt} = 0$ occurs at $(S, L, I, E, Y, V) = (S_7, L_7, I_7, E_7, Y_7, V_7)$. The system's solutions (2.9)–(2.16) tend to Υ_7' which includes elements satisfying $(S, L, I, E, Y, V) = (S_7, L_7, I_7, E_7, Y_7, V_7)$, and then $\frac{dI}{dt} = \frac{dY}{dt} = 0$. Eqs (2.11) and (2.13) become

$$\begin{aligned}
0 &= \frac{dI}{dt} = \lambda L_7 - a I_7 - \mu_1 C^I I_7,\\
0 &= \frac{dY}{dt} = \psi E_7 - \delta Y_7 - \mu_2 C^Y Y_7,
\end{aligned}$$

which yield that $C^I(t) = C_7^I$ and $C^Y(t) = C_7^Y$ for all t and hence $\Upsilon_7' = \{Đ_7\}$. Applying Lyapunov-LaSalle asymptotic stability theorem we get $Đ_7$ is G.A.S. □

AIMS Press