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Research article

Mathematical modeling of HIV/HTLV co-infection with CTL-mediated immunity

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

[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, Egypt

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

* **Correspondence:** E-mail: a_m_elaiw@yahoo.com.

Abstract: In the literature, a great number of HIV and HTLV-I mono-infection models has been formulated and analyzed. However, the within-host dynamics of HIV/HTLV-I co-infection has not been modeled. In the present paper we formulate and analyze a new HIV/HTLV-I co-infection model with latency and Cytotoxic T lymphocytes (CTLs) immune response. The model describes the interaction between susceptible CD4$^+$T cells, latently HIV-infected cells, actively HIV-infected cells, latently HTLV-infected cells, Tax-expressing HTLV-infected cells, free HIV particles, HIV-specific CTLs and HTLV-specific CTLs. The HIV can spread by virus-to-cell and cell-to-cell transmissions, while the HTLV-I can only spread via cell-to-cell transmission. The well-posedness of the model is established by showing that the solutions of the model are nonnegative and bounded. We derive the threshold parameters which govern the existence and stability of all equilibria of the model. We prove the global asymptotic stability of all equilibria by utilizing Lyapunov function and Lyapunov-LaSalle asymptotic stability theorem. We have presented numerical simulations to illustrate the effectiveness of our main results. In addition, we have discussed the effect of HTLV-I infection on the HIV-infected patients and vice versa. We have pointed out the influence of CTL immune response on the co-infection dynamics.

Keywords: HIV/HTLV-I co-infection; global stability; CTL-mediated immune response; Lyapunov function
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1. Introduction

During the last decades different dangerous viruses have been recognized which attack the human body and causes many fatal diseases. As an example of these viruses, the human immunodeficiency virus (HIV) which is the causative agent for acquired immunodeficiency syndrome (AIDS). According to global health observatory (GHO, 2018) data of HIV/AIDS published by WHO [1] that says, globally, about 37.9 million HIV-infected people in 2018, 1.7 million newly HIV-infected and 770,000 HIV-related death in the same year. HIV is a retrovirus that infects the susceptible CD4^{+}T cells which play a central role in immune system defence. During the last decades, mathematical modeling of within-host HIV infection has witnessed a significant development [2]. Nowak and Bangham [3] have introduced the basic HIV infection model which describes the interaction between three compartments, susceptible CD4^{+}T cells (S), actively HIV-infected cells (I) and free HIV particles (V). Latent viral reservoirs remain one of the major hurdles for eradicating the HIV by current antiviral therapy. Latently HIV-infected cells include HIV virions but do not produce them until they become activated. Mathematical modeling of HIV dynamics with latency can help in predicting the effect of antiviral drug efficacy on HIV progression [4]. Rong and Perelson [5] have incorporated the latently infected cells in the basic HIV model presented in [3] as:

$$\begin{cases} \dot{S} = \rho - \alpha S - \eta_1 S V, \\ \dot{L} = (1-\beta)\,\eta_1 S V - (\lambda + \gamma)\,L, \\ \dot{I} = \beta \eta_1 S V + \lambda L - aI, \\ \dot{V} = bI - \varepsilon V, \end{cases} \tag{1.1}$$

where $S = S(t)$, $L = L(t)$, $I = I(t)$ and $V = V(t)$ are the concentrations of susceptible CD4^{+}T cells, latently HIV-infected cells, actively HIV-infected cells and free HIV particles at time t, respectively. The susceptible CD4^{+}T cells are produced at specific constant rate ρ. The HIV virions can replicate using virus-to-cell (VTC) transmission. The term $\eta_1 S V$ refers to the rate at which new infectious appears by VTC contact between free HIV particles and susceptible CD4^{+}T cells. Latently HIV-infected cells are transmitted to be active at rate λL. The free HIV particles are generated at rate bI. The natural death rates of the susceptible CD4^{+}T cells, latently HIV-infected cells, actively HIV-infected cells and free HIV particles are given by αS, γL, aI and εV, respectively. A fraction $\beta \in (0, 1)$ of new HIV-infected cells will be active, and the remaining part $1 - \beta$ will be latent. During the last decades, mathematical modeling and analysis of HIV mono-infection with both latently and actively HIV-infected cells have witnessed a significant development [6–12].

Model (1.1) assumed that the HIV can only spread by VTC transmission. However, several works have reported that there is another mode of transmission called cell-to-cell (CTC) where the HIV can be transmitted directly from an infected cell to a healthy CD4^{+}T cell through the formation of virological synapses [13]. Sourisseau et al. [14] have shown that CTC transmission plays an efficient role in the HIV replication. Sigal et al. [15] have demonstrated the importance of CTC transmission in the HIV infection process during the antiviral treatment. Iwami et al. [13] have shown that about 60% of HIV infections are due to CTC transmission. In addition, CTC transmission can increase the HIV fitness by 3.9 times and decrease the production time of HIV particles by 0.9 times [16]. HIV dynamics model with latency and both VTC and CTC transmissions is given by [17, 18]:

$$
\begin{cases}
\dot{S} = \rho - \alpha S - \eta_1 S V - \eta_2 S I, \\
\dot{L} = (1-\beta)(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma) L, \\
\dot{I} = \beta(\eta_1 S V + \eta_2 S I) + \lambda L - a I, \\
\dot{V} = bI - \varepsilon V,
\end{cases}
\tag{1.2}
$$

where, the term $\eta_2 S I$ refers to the rate at which new infectious appears by CTC contact between HIV-infected cells and susceptible CD4$^+$T cells.

Another example of the dangerous human viruses is called Human T-lymphotropic virus type I (HTLV-I) which can lead to two diseases, adult T-cell leukemia (ATL) and HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP). The discovery of the first human retrovirus HTLV-I is back to 1980, and after 3 years the HIV was determined [19]. HTLV-I is global epidemic that infects about 10-25 million persons [20]. The infection is endemic in the Caribbean, southern Japan, the Middle East, South America, parts of Africa, Melanesia and Papua New Guinea [21]. HTLV-I is a provirus that targets the susceptible CD4$^+$T cells. HTLV-I can spread to susceptible CD4$^+$T cells from CTC through the virological synapse. HTLV-infected cells can be divided into two kinds based on the presence of Tax inside the cell or not: (i) Tax$^-$, or latently HTLV-infected cells are resting CD4$^+$T cells that contain a provirus and do not express Tax, and (ii) Tax$^+$, or actively HTLV-infected cells are activated provirus-carrying CD4$^+$T cells that do express Tax [22]. During the primary infection stage of HTLV-I, the proviral load can reach high level, approximately 30-50% [23]. Unlike in the case of HIV infection, however, only a small percentage of infected individuals develop the disease and 2-5% percent of HTLV-I carriers develop symptoms of ATL and another 0.25-3% develop HAM/TSP [24]. Stilianakis and Seydel [25] have formulated an HTLV-I model to describe the interaction of susceptible CD4$^+$T cells, latently HTLV-infected cells, Tax-expressing HTLV-infected cells (actively HTLV-infected cells) and leukemia cells (ATL cells) as:

$$
\begin{cases}
\dot{S} = \rho - \alpha S - \eta_3 S Y, \\
\dot{E} = \eta_3 S Y - (\psi + \omega) E, \\
\dot{Y} = \psi E - (\vartheta + \delta) Y, \\
\dot{Z} = \vartheta Y + \ell Z \left(1 - \frac{Z}{Z_{\max}}\right) - \theta Z,
\end{cases}
\tag{1.3}
$$

where $S = S(t)$, $E = E(t)$, $Y = Y(t)$ and $Z = Z(t)$ are the concentrations of susceptible CD4$^+$T cells, latently HTLV-infected cells, Tax-expressing HTLV-infected cells and ATL cells, at time t, respectively. In contrast of HIV, the transmission of HTLV-I can be only from CTC that is the HTLV virions can only survive inside the host CD4$^+$T cells and cannot be detectable in the plasma. The rate at which new infectious appears by CTC contact between Tax-expressing HTLV-infected cells and susceptible CD4$^+$T cells is assumed to be $\eta_3 S Y$. The natural death rate of the latently HTLV-infected cells, Tax-expressing HTLV-infected cells and ATL cells are represented by ωE, δY and θZ, respectively. The term ψE accounts for the rate of latently HTLV-infected cells that become Tax-expressing HTLV-infected cells. ϑY is the transmission rate at which Tax-expressing HTLV-infected cells convert to ATL cells. The logistic term $\ell Z \left(1 - \frac{Z}{Z_{\max}}\right)$ denotes the proliferation rate of the ATL cells, where $Z_{\max}$ is the maximal concentration that ATL cells can grow. The parameter ℓ is the maximum proliferation rate constant of ATL cells. Many researchers have been concerned to study mathematical modeling and analysis of HTLV-I mono-infection in several works [26–28].

Cytotoxic T lymphocytes (CTLs) are recognized as the significant component of the human immune response against viral infections. CTLs inhibit viral replication and kill the cells which are infected by viruses. In fact, CTLs are necessary and universal to control HIV infection [29]. During the recent years, great efforts have been made to formulate and analyze the within-host HIV mono-infection models under the influence of CTL immune response (see e.g. [2, 3]). In [30], latently HIV-infected cells have been included in the HIV dynamics models with CTL immune response. In case of HTLV-I infection, it has been reported in [31] that the CTLs play an effective role in controlling such infection. CTLs can recognize and kill the Tax-expressing HTLV-infected cells, moreover, they can reduce the proviral load. In the literature, several mathematical models have been proposed to describe the dynamics of HTLV-I under the effect of CTL immune response (see e.g. [21, 32–36]). In [20, 37, 38], HTLV-I dynamics models have been presented by incorporating latently HTLV-infected cells and CTL immune response.

Simultaneous infection by HIV and HTLV-I and the etiology of their pathogenic and disease outcomes have become a global health matter over the past 10 years [39]. It is commonly that HIV/HTLV-I co-infection can be endemic in areas where individuals experience high risk attitudes; such as unprotected sexual contact and unsafe injection practices; that cause transmission of contaminated body fluids between individuals. This shed a light on the importance of studying HIV/HTLV-I co-infection [40]. Although $CD4^{+}T$ cells are the major targets of both HIV and HTLV-I, however, these viruses present a different biological behavior that causes diverse impacts on host immunity and ultimately lead to numerous clinical diseases [41]. It has been reported that the HTLV-I co-infection rate among HIV infected patients as increase as 100 to 500 times in comparison with the general population [42]. In seroepidemiologic studies, it has been recorded that HIV-infected patients are more exposure to be co-infected with HTLV-I, and vice versa compared to the general population [43]. HIV/HTLV-I co-infection is usually found in individuals of specific ethnic or who belonged to geographic origins where these viruses are simultaneously endemic [44]. As an example, the co-infection rates in individuals living in Bahia have reached 16% of HIV-infected patients [45]. The prevalence of dual infection with HIV and HTLV-I has become more widely in several geographical regions throughout the world such as South America, Europe, the Caribbean, Bahia (Brazil), Mozambique (Africa), and Japan [39, 43, 45–47]. HIV and HTLV-I dual infection appears to have an overlap on the course of associated clinical outcomes with both viruses [43]. Several reports have concluded that HIV/HTLV-I co-infected patients were found to have an increase of $CD4^{+}T$ cells count in comparison with HIV mono-infected patients, although there is no evident to result in a better immune response [41, 48]. Indeed, simultaneous infected patients by both viruses with $CD4^{+}T$ counts greater than 200 cells/mm^3 are more exposure to have other opportunistic infections as compared with HIV mono-infected patients who have similar $CD4^{+}T$ counts [48]. Studies have reported that higher mortality and shortened survival rates were accompany with co-infected individuals more than mono-infected individuals [46]. Considering the natural history of HIV, many researchers have noted that co-infection with HIV and HTLV-I can accelerate the clinical progression to AIDS. On the other hand, HIV can adjust HTLV-I expression in co-infected individuals which leads them to a higher risk of developing HTLV-I related diseases such as ATL and TSP/HAM [42, 43, 46].

Great efforts have been made to develop and analyze mathematical models of HIV and HTLV-I mono-infections, however, modeling of HIV/HTLV-I co-infection has not been studied. In fact, such co-infection modeling and its analysis will be needed to help clinicians on estimating the appropriate

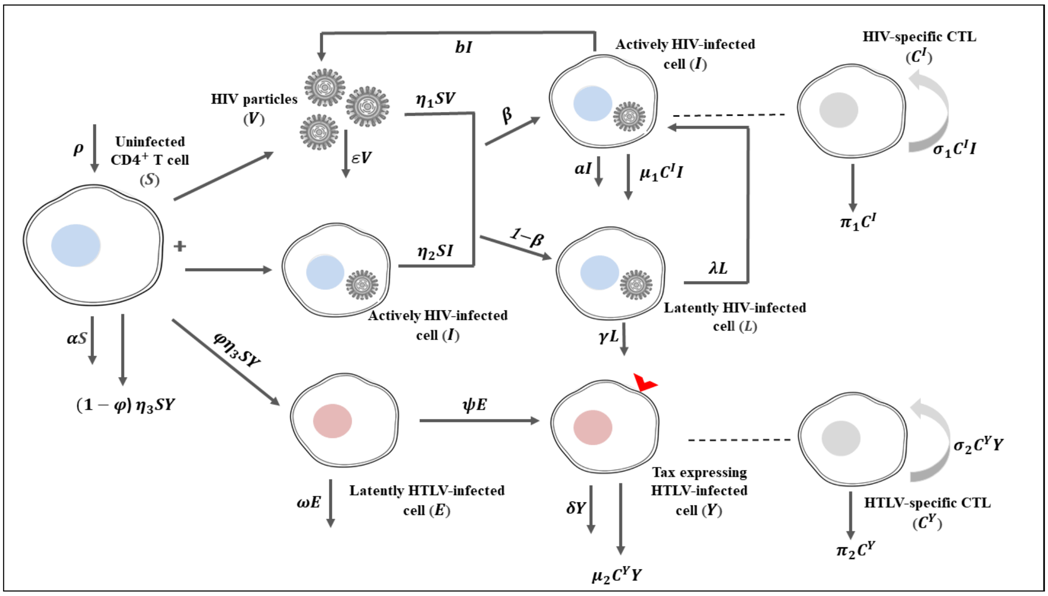


Figure 1. The schematic diagram of the HIV/HTLV-I co-infection dynamics in vivo.

time to initiate treatment in co-infected patients. Therefore, the aim of the present paper is to formulate a new HIV/HTLV-I co-infection model. We show that the model is well-posed by establishing that the solutions of the model are nonnegative and bounded. We derive a set of threshold parameters which govern the existence and stability of the equilibria of the model. Global stability of all equilibria is proven by constructing suitable Lyapunov functions and utilizing Lyapunov-LaSalle asymptotic stability theorem. We conduct some numerical simulations to illustrate the theoretical results.

The results of this work, such as co-infection model and its analysis will help clinicians estimate the appropriate time for patients with co-infection to begin treatment. On the other hand, this study, from a certain point of view, illustrate the complexity of this co-infection model and the model is helpful to clinic treatment. It is worth mentioning, if we look at research perspectives, that appropriate developments of the model presented in this paper can be focused on the within host modeling of the competition between COVID19 virus and the immune system by a complex dynamics described in [49]. This dynamics which occurs, in human lungs, once the virus, after contagion, has gone over the biological barriers which protect each individuals, see [47].

2. Model formulation

We set up an ordinary differential equation model that describes the change of concentrations of eight compartments with respect to time t; susceptible CD4$^+$T cells $S(t)$, latently HIV-infected cells $L(t)$, actively HIV-infected cells $I(t)$, latently HTLV-infected cells $E(t)$, Tax-expressing HTLV-infected cells $Y(t)$, free HIV particles $V(t)$, HIV-specific CTLs $C^I(t)$ and HTLV-specific CTLs $C^Y(t)$. The dynamics of HIV/HTLV-I co-infection is schematically shown in the transfer diagram given in Figure 1. Our proposed model is given by the following form:

$$\begin{cases} \dot{S} = \rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y, \\ \dot{L} = (1-\beta)(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma) L, \\ \dot{I} = \beta(\eta_1 S V + \eta_2 S I) + \lambda L - aI - \mu_1 C^I I, \\ \dot{E} = \varphi \eta_3 S Y - (\psi + \omega) E, \\ \dot{Y} = \psi E - \delta Y - \mu_2 C^Y Y, \\ \dot{V} = bI - \varepsilon V, \\ \dot{C}^I = \sigma_1 C^I I - \pi_1 C^I, \\ \dot{C}^Y = \sigma_2 C^Y Y - \pi_2 C^Y, \end{cases} \tag{2.1}$$

where $(S, L, I, E, Y, V, C^I, C^Y) = (S(t), L(t), I(t), E(t), Y(t), V(t), C^I(t), C^Y(t))$. The term $\mu_1 C^I I$ is the killing rate of actively HIV-infected cells due to their specific immunity. The term $\mu_2 C^Y Y$ is the killing rate of Tax-expressing HTLV-infected cells due to their specific immunity. The proliferation and death rates for both effective HIV-specific CTLs and HTLV-specific CTLs are given by $\sigma_1 C^I I$, $\sigma_2 C^Y Y$, $\pi_1 C^I$ and $\pi_2 C^Y$, respectively. All remaining parameters have the same biological meaning as explained in the previous section. All parameters and their definitions are summarized in Table 1.

Table 1. Parameter description.

Parameter	Description
ρ	Recruitment rate for the susceptible CD4$^+$T cells
α	Natural mortality rate constant for the susceptible CD4$^+$T cells
η_1	Virus-cell incidence rate constant between free HIV particles and susceptible CD4$^+$T cells
η_2	Cell-cell incidence rate constant between HIV-infected cells and susceptible CD4$^+$T cells
η_3	Cell-cell incidence rate constant between Tax-expressing HTLV-infected cells and susceptible CD4$^+$T cells
$\beta \in (0, 1)$	Fraction coefficient accounts for the probability of new HIV-infected cells could be active, and the remaining part $1-\beta$ will be latent
γ	Death rate constant of latently HIV-infected cells
a	Death rate constant of actively HIV-infected cells
μ_1	Killing rate constant of actively HIV-infected cells due to HIV-specific CTLs
μ_2	Killing rate constant of Tax-expressing HTLV-infected cells due to HTLV-specific CTLs
$\varphi \in (0, 1)$	Probability of new HTLV infections could be enter a latent period
λ	Transmission rate constant of latently HIV-infected cells that become actively HIV-infected cells
ψ	Transmission rate constant of latently HTLV-infected cells that become Tax-expressing HTLV-infected cells
ω	Death rate constant of latently HTLV-infected cells
δ	Death rate constant of Tax-expressing HTLV-infected cells
b	Generation rate constant of new HIV particles
ε	Death rate constant of free HIV particles
σ_1	Proliferation rate constant of HIV-specific CTLs
σ_2	Proliferation rate constant of HTLV-specific CTLs
π_1	Decay rate constant of HIV-specific CTLs
π_2	Decay rate constant of HTLV-specific CTLs

3. Preliminaries

Let $\Omega_j > 0$, $j = 1, ..., 5$ and define

$$\Theta = \Big\{(S, L, I, E, Y, V, C^I, C^Y) \in \mathbb{R}^8_{\geq 0} : 0 \leq S(t), L(t), I(t) \leq \Omega_1,$$

$$0 \le E(t), Y(t) \le \Omega_2,\ 0 \le V(t) \le \Omega_3,\ 0 \le C^I(t) \le \Omega_4,\ 0 \le C^Y(t) \le \Omega_5 \Big\}.$$

Proposition 1. The compact set Θ is positively invariant for system (2.1).
Proof. We have

$$\begin{aligned}
&\dot{S}\ |_{S=0}= \rho > 0, \quad \dot{L}\ |_{L=0}= (1-\beta)\,(\eta_1 S V + \eta_2 S I) \ge 0 \text{ for all } S, V, I \ge 0,\\
&\dot{I}\ |_{I=0}= \beta\eta_1 S V + \lambda L \ge 0 \text{ for all } S, V, L \ge 0,\\
&\dot{E}\ |_{E=0}= \varphi\eta_3 S Y \text{ for all } S, Y \ge 0, \quad \dot{Y}\ |_{Y=0}= \psi E \ge 0 \text{ for all } E \ge 0,\\
&\dot{V}\ |_{V=0}= bI \ge 0 \text{ for all } I \ge 0, \quad \dot{C}^I\ |_{C^I=0}= 0, \quad \dot{C}^Y\ |_{C^Y=0}= 0.
\end{aligned}$$

This ensures that, $(S(t), L(t), I(t), E(t), Y(t), V(t), C^I(t), C^Y(t)) \in \mathbb{R}^8_{\ge 0}$ for all $t \ge 0$ when $(S(0), L(0), I(0), E(0), Y(0), V(0), C^I(0), C^Y(0)) \in \mathbb{R}^8_{\ge 0}$. To show the boundedness of all state variables, 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

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

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

4. Equilibria

In this section, we derive eight threshold parameters which guarantee the existence of the equilibria of the model. Let $(S, L, I, E, Y, V, C^I, C^Y)$ be any equilibrium of system (2.1) satisfying the following equations:

$$0 = \rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y, \tag{4.1}$$
$$0 = (1-\beta)\,(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma)\,L, \tag{4.2}$$
$$0 = \beta\,(\eta_1 S V + \eta_2 S I) + \lambda L - aI - \mu_1 C^I I, \tag{4.3}$$
$$0 = \varphi\eta_3 S Y - (\psi + \omega)\,E, \tag{4.4}$$
$$0 = \psi E - \delta Y - \mu_2 C^Y Y, \tag{4.5}$$
$$0 = bI - \varepsilon V, \tag{4.6}$$
$$0 = (\sigma_1 I - \pi_1)\,C^I, \tag{4.7}$$
$$0 = (\sigma_2 Y - \pi_2)\,C^Y. \tag{4.8}$$

The straightforward calculation finds that system (2.1) admits eight equilibria.

(i) Infection-free equilibrium, $Đ_0 = (S_0, 0, 0, 0, 0, 0, 0, 0)$, where $S_0 = \rho/\alpha$. This case describes the situation of healthy state where both HIV and HTLV are absent.

(ii) Chronic HIV mono-infection equilibrium with inactive immune response, $Đ_1 = (S_1, L_1, I_1, 0, 0, V_1, 0, 0)$, where

$$S_1 = \frac{a\varepsilon(\gamma+\lambda)}{(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)},\ L_1 = \frac{a\varepsilon\alpha(1-\beta)}{(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}\left[\frac{S_0(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)}-1\right],$$
$$I_1 = \frac{\varepsilon\alpha}{\eta_1 b+\eta_2\varepsilon}\left[\frac{S_0(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)}-1\right],\ V_1 = \frac{\alpha b}{\eta_1 b+\eta_2\varepsilon}\left[\frac{S_0(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)}-1\right].$$

Therefore, $Đ_1$ exists when

$$\frac{S_0(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)} > 1.$$

At the equilibrium $Đ_1$ the chronic HIV mono-infection persists while the immune response is unstimulated. The basic HIV mono-infection reproductive ratio for system (2.1) is defined as:

$$\Re_1 = \frac{S_0(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)} = \Re_{11} + \Re_{12},$$

where

$$\Re_{11} = \frac{S_0\eta_1 b(\beta\gamma+\lambda)}{a\varepsilon(\gamma+\lambda)}, \qquad \Re_{12} = \frac{S_0\eta_2(\beta\gamma+\lambda)}{a(\gamma+\lambda)}.$$

The parameter $\Re_1$ determines whether or not a chronic HIV infection can be established. In fact, $\Re_{11}$ measures the average number of secondary HIV infected generation caused by an existing free HIV particles, while $\Re_{12}$ measures the average number of secondary HIV infected generation caused by an HIV-infected cell. Therefore, $\Re_{11}$ and $\Re_{12}$ are the basic HIV mono-infection reproductive ratio corresponding to VTC and CTC infections, respectively. In terms of $\Re_1$, we can write

$$S_1 = \frac{S_0}{\Re_1},\ L_1 = \frac{a\varepsilon\alpha(1-\beta)}{(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}(\Re_1-1),\ I_1 = \frac{\varepsilon\alpha}{\eta_1 b+\eta_2\varepsilon}(\Re_1-1),\ V_1 = \frac{\alpha b}{\eta_1 b+\eta_2\varepsilon}(\Re_1-1).$$

(iii) Chronic HTLV mono-infection equilibrium with inactive immune response, $Đ_2 = (S_2, 0, 0, E_2, Y_2, 0, 0, 0)$, where

$$S_2 = \frac{\delta(\psi+\omega)}{\varphi\eta_3\psi}, \quad E_2 = \frac{\alpha\delta}{\eta_3\psi}\left[\frac{\varphi\eta_3\psi S_0}{\delta(\psi+\omega)}-1\right], \quad Y_2 = \frac{\alpha}{\eta_3}\left[\frac{\varphi\eta_3\psi S_0}{\delta(\psi+\omega)}-1\right].$$

Therefore, $Đ_2$ exists when

$$\frac{\varphi\eta_3\psi S_0}{\delta(\psi+\omega)} > 1.$$

At the equilibrium $Đ_2$ the chronic HTLV mono-infection persists while the immune response is unstimulated. The basic HTLV mono-infection reproductive ratio for system (2.1) is defined as:

$$\Re_2 = \frac{\varphi\eta_3\psi S_0}{\delta(\psi+\omega)}.$$

The parameter $\Re_2$ decides whether or not a chronic HTLV infection can be established. In terms of $\Re_2$, we can write

$$S_2 = \frac{S_0}{\Re_2}, \quad E_2 = \frac{\alpha\delta}{\eta_3\psi}(\Re_2-1), \quad Y_2 = \frac{\alpha}{\eta_3}(\Re_2-1).$$

Remark 1. We note that both $\Re_1$ and $\Re_2$ does not depend of parameters σ_i, π_i and μ_i, $i = 1,2$. Therefore, without treatment CTLs will not able to clear HIV or HTLV-I from the body.

(iv) Chronic HIV mono-infection equilibrium with only active HIV-specific CTL, $Đ_3 = (S_3, L_3, I_3, 0, 0, V_3, C_3^I, 0)$, where

$$S_3 = \frac{\varepsilon\sigma_1\rho}{\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1}, \quad L_3 = \frac{\rho\pi_1(1-\beta)(\eta_1 b + \eta_2\varepsilon)}{(\gamma+\lambda)[\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1]}, \quad I_3 = \frac{\pi_1}{\sigma_1},$$
$$V_3 = \frac{b}{\varepsilon}I_3 = \frac{b\pi_1}{\varepsilon\sigma_1}, \quad C_3^I = \frac{a}{\mu_1}\left[\frac{\sigma_1\rho(\beta\gamma+\lambda)(\eta_1 b + \eta_2\varepsilon)}{a(\gamma+\lambda)\{\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1\}} - 1\right].$$

We note that $Đ_3$ exists when $\dfrac{\sigma_1\rho(\beta\gamma+\lambda)(\eta_1 b + \eta_2\varepsilon)}{a(\gamma+\lambda)[\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1]} > 1$. The HIV-specific CTL-mediated immunity reproductive ratio in case of HIV mono-infection is stated as:

$$\Re_3 = \frac{\sigma_1\rho(\beta\gamma+\lambda)(\eta_1 b + \eta_2\varepsilon)}{a(\gamma+\lambda)[\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1]}.$$

Thus, $C_3^I = \dfrac{a}{\mu_1}(\Re_3 - 1)$. The parameter $\Re_3$ determines whether or not the HIV-specific CTL-mediated immune response is stimulated in the absent of HTLV infection.

(v) Chronic HTLV mono-infection equilibrium with only active HTLV-specific CTL, $Đ_4 = (S_4, 0, 0, E_4, Y_4, 0, 0, C_4^Y)$, where

$$S_4 = \frac{\sigma_2\rho}{\pi_2\eta_3 + \alpha\sigma_2}, \quad Y_4 = \frac{\pi_2}{\sigma_2}, \quad E_4 = \frac{\pi_2\eta_3\rho\varphi}{(\psi+\omega)(\pi_2\eta_3 + \alpha\sigma_2)},$$
$$C_4^Y = \frac{\delta}{\mu_2}\left[\frac{\sigma_2\rho\varphi\eta_3\psi}{\delta(\psi+\omega)(\pi_2\eta_3 + \alpha\sigma_2)} - 1\right].$$

We note that $Đ_4$ exists when $\dfrac{\sigma_2\rho\varphi\eta_3\psi}{\delta(\psi+\omega)(\pi_2\eta_3 + \alpha\sigma_2)} > 1$. The HTLV-specific CTL-mediated immunity reproductive ratio in case of HTLV mono-infection is stated as:

$$\Re_4 = \frac{\sigma_2\rho\varphi\eta_3\psi}{\delta(\psi+\omega)(\pi_2\eta_3 + \alpha\sigma_2)}.$$

Thus, $C_4^Y = \dfrac{\delta}{\mu_2}(\Re_4 - 1)$. The parameter $\Re_4$ determines whether or not the HTLV-specific CTL-mediated immune response is stimulated in the absent of HIV infection.

(vi) Chronic HIV/HTLV co-infection equilibrium with only active HIV-specific CTL, $Đ_5 = (S_5, L_5, I_5, E_5, Y_5, V_5, C_5^I, 0)$, where

$$S_5 = \frac{\delta(\psi+\omega)}{\varphi\eta_3\psi} = S_2, \quad I_5 = \frac{\pi_1}{\sigma_1} = I_3,$$
$$V_5 = \frac{b\pi_1}{\varepsilon\sigma_1} = V_3, \quad L_5 = \frac{\delta\pi_1(1-\beta)(\psi+\omega)(\eta_1 b + \eta_2\varepsilon)}{\varepsilon\eta_3\sigma_1\varphi\psi(\gamma+\lambda)},$$
$$E_5 = \frac{\delta[\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1]}{\varepsilon\eta_3\sigma_1\psi}\left[\frac{\rho\varphi\varepsilon\eta_3\sigma_1\psi}{\delta(\psi+\omega)\{\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1\}} - 1\right],$$

$$Y_5=\frac{\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1}{\varepsilon\eta_3\sigma_1}\left[\frac{\rho\varphi\varepsilon\eta_3\sigma_1\psi}{\delta(\psi+\omega)\{\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1\}}-1\right],$$
$$C_5^I=\frac{a}{\mu_1}\left[\frac{\delta(\eta_1 b+\eta_2\varepsilon)(\beta\gamma+\lambda)(\psi+\omega)}{a\varepsilon\varphi\eta_3\psi(\gamma+\lambda)}-1\right]=\frac{a}{\mu_1}(\Re_1/\Re_2-1).$$

We note that $Đ_5$ exists when $\Re_1/\Re_2>1$ and $\frac{\rho\varphi\varepsilon\eta_3\sigma_1\psi}{\delta(\psi+\omega)[\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1]}>1$. The HTLV infection reproductive ratio in the presence of HIV infection is stated as:

$$\Re_5=\frac{\rho\varphi\varepsilon\eta_3\sigma_1\psi}{\delta(\psi+\omega)[\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1]}.$$

Thus, $E_5=\frac{\delta[\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1]}{\varepsilon\eta_3\sigma_1\psi}(\Re_5-1)$, $Y_5=\frac{\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1}{\varepsilon\eta_3\sigma_1}(\Re_5-1)$. The parameter $\Re_5$ determines whether or not HIV-infected patients could be co-infected with HTLV.

(vii) Chronic HIV/HTLV co-infection equilibrium with only active HTLV-specific CTL, $Đ_6=(S_6,L_6,I_6,E_6,Y_6,V_6,0,C_6^Y)$, where

$$S_6=\frac{a\varepsilon(\gamma+\lambda)}{(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}=S_1,\quad L_6=\frac{a\varepsilon(1-\beta)(\pi_2\eta_3+\alpha\sigma_2)}{\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}\left[\frac{\rho\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)(\pi_2\eta_3+\alpha\sigma_2)}-1\right],$$
$$I_6=\frac{\varepsilon(\pi_2\eta_3+\alpha\sigma_2)}{\sigma_2(\eta_1 b+\eta_2\varepsilon)}\left[\frac{\rho\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)(\pi_2\eta_3+\alpha\sigma_2)}-1\right],\quad E_6=\frac{a\varepsilon\varphi\pi_2\eta_3(\gamma+\lambda)}{\sigma_2(\beta\gamma+\lambda)(\psi+\omega)(\eta_1 b+\eta_2\varepsilon)},$$
$$Y_6=\frac{\pi_2}{\sigma_2}=Y_4,\quad V_6=\frac{b(\pi_2\eta_3+\alpha\sigma_2)}{\sigma_2(\eta_1 b+\eta_2\varepsilon)}\left[\frac{\rho\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)(\pi_2\eta_3+\alpha\sigma_2)}-1\right],$$
$$C_6^Y=\frac{\delta}{\mu_2}\left[\frac{a\varepsilon\varphi\eta_3\psi(\gamma+\lambda)}{\delta(\beta\gamma+\lambda)(\psi+\omega)(\eta_1 b+\eta_2\varepsilon)}-1\right]=\frac{\delta}{\mu_2}(\Re_2/\Re_1-1).$$

We note that $Đ_6$ exists when $\Re_2/\Re_1>1$ and $\frac{\rho\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)(\pi_2\eta_3+\alpha\sigma_2)}>1$. The HIV infection reproductive ratio in the presence of HTLV infection is stated as:

$$\Re_6=\frac{\rho\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)(\pi_2\eta_3+\alpha\sigma_2)}.$$

Thus, $L_6=\frac{a\varepsilon(1-\beta)(\pi_2\eta_3+\alpha\sigma_2)}{\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}(\Re_6-1)$, $I_6=\frac{\varepsilon(\pi_2\eta_3+\alpha\sigma_2)}{\sigma_2(\eta_1 b+\eta_2\varepsilon)}(\Re_6-1)$, $V_6=\frac{b(\pi_2\eta_3+\alpha\sigma_2)}{\sigma_2(\eta_1 b+\eta_2\varepsilon)}(\Re_6-1)$. The parameter $\Re_6$ determines whether or not HTLV-infected patients could be co-infected with HIV.

(viii) Chronic HIV/HTLV co-infection equilibrium with active HIV-specific CTL and HTLV-specific CTL, $Đ_7=(S_7,L_7,I_7,E_7,Y_7,V_7,C_7^I,C_7^Y)$, where

$$S_7=\frac{\varepsilon\sigma_1\sigma_2\rho}{\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2},\quad L_7=\frac{\pi_1\sigma_2\rho(1-\beta)(\eta_1 b+\eta_2\varepsilon)}{(\gamma+\lambda)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]},$$
$$E_7=\frac{\pi_2\eta_3\varepsilon\sigma_1\rho\varphi}{(\psi+\omega)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]},\quad I_7=\frac{\pi_1}{\sigma_1}=I_3=I_5,\quad Y_7=\frac{\pi_2}{\sigma_2}=Y_4=Y_6,$$
$$V_7=\frac{b\pi_1}{\varepsilon\sigma_1}=V_3=V_5,\quad C_7^I=\frac{a}{\mu_1}\left[\frac{\sigma_1\sigma_2\rho(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a(\gamma+\lambda)\{\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2\}}-1\right],$$

$$C_7^Y = \frac{\delta}{\mu_2}\left[\frac{\varphi\eta_3\varepsilon\sigma_1\sigma_2\rho\psi}{\delta(\psi+\omega)\{\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2\}}-1\right].$$

It is obvious that $Ð_7$ exists when $\dfrac{\sigma_1\sigma_2\rho(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a(\gamma+\lambda)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]} > 1$ and $\dfrac{\varphi\eta_3\varepsilon\sigma_1\sigma_2\rho\psi}{\delta(\psi+\omega)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]} > 1$. Now we define

$$\begin{aligned}
\Re_7 &= \frac{\sigma_1\sigma_2\rho(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a(\gamma+\lambda)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]},\\
\Re_8 &= \frac{\varphi\eta_3\varepsilon\sigma_1\sigma_2\rho\psi}{\delta(\psi+\omega)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]}.
\end{aligned}$$

Clearly, $Ð_7$ exists when $\Re_7 > 1$ and $\Re_8 > 1$ and we can write $C_7^I = \dfrac{a}{\mu_1}(\Re_7 - 1)$ and $C_7^Y = \dfrac{\delta}{\mu_2}(\Re_8 - 1)$. The parameter $\Re_7$ refers to the competed HIV-specific CTL-mediated immunity reproductive ratio in case of HIV/HTLV co-infection. On the other hand, the parameter $\Re_8$ refers to the competed HTLV-specific CTL-mediated immunity reproductive ratio case of HIV/HTLV co-infection.

The eight threshold parameters are given as follows:

$$\begin{aligned}
\Re_1 &= \frac{S_0(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)}, \quad \Re_2 = \frac{\varphi\eta_3\psi S_0}{\delta(\psi+\omega)},\\
\Re_3 &= \frac{\sigma_1\rho(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a(\gamma+\lambda)[\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1]}, \quad \Re_4 = \frac{\sigma_2\rho\varphi\eta_3\psi}{\delta(\psi+\omega)(\pi_2\eta_3+\alpha\sigma_2)},\\
\Re_5 &= \frac{\rho\varphi\varepsilon\eta_3\sigma_1\psi}{\delta(\psi+\omega)[\pi_1(\eta_1 b+\eta_2\varepsilon)+\alpha\varepsilon\sigma_1]}, \quad \Re_6 = \frac{\rho\sigma_2(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a\varepsilon(\gamma+\lambda)(\pi_2\eta_3+\alpha\sigma_2)},\\
\Re_7 &= \frac{\sigma_1\sigma_2\rho(\beta\gamma+\lambda)(\eta_1 b+\eta_2\varepsilon)}{a(\gamma+\lambda)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]},\\
\Re_8 &= \frac{\varphi\eta_3\varepsilon\sigma_1\sigma_2\rho\psi}{\delta(\psi+\omega)[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2]}. \ \square
\end{aligned}$$

According to the above discussion, we sum up the existence conditions for all equilibria in Table 2.

5. Global stability analysis

In this section we prove the global asymptotic stability of all equilibria by constructing Lyapunov functional following the method presented in [50]. We will use the arithmetic-geometric mean inequality

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

which yields

$$\frac{S_j}{S} + \frac{SIL_j}{S_j I_j L} + \frac{LI_j}{L_j I} \geq 3, \quad j = 1, 3, 5, 6, 7, \tag{5.1}$$

Table 2. Model (2.1) equilibria and their existence conditions.

Equilibrium point	Definition	Existence conditions
$Ð_0 = (S_0, 0, 0, 0, 0, 0, 0, 0)$	Infection-free equilibrium	None
$Ð_1 = (S_1, L_1, I_1, 0, 0, V_1, 0, 0)$	Chronic HIV mono-infection equilibrium with inactive immune response	$\Re_1 > 1$
$Ð_2 = (S_2, 0, 0, E_2, Y_2, 0, 0, 0)$	Chronic HTLV mono-infection equilibrium with inactive immune response	$\Re_2 > 1$
$Ð_3 = (S_3, L_3, I_3, 0, 0, V_3, C^I_3, 0)$	Chronic HIV mono-infection equilibrium with only active HIV-specific CTL	$\Re_3 > 1$
$Ð_4 = (S_4, 0, 0, E_4, Y_4, 0, 0, C^Y_4)$	Chronic HTLV mono-infection equilibrium with only active HTLV-specific CTL	$\Re_4 > 1$
$Ð_5 = (S_5, L_5, I_5, E_5, Y_5, V_5, C^I_5, 0)$	Chronic HIV/HTLV co-infection equilibrium with only active HIV-specific CTL	$\Re_5 > 1$ and $\Re_1/\Re_2 > 1$
$Ð_6 = (S_6, L_6, I_6, E_6, Y_6, V_6, 0, C^Y_6)$	Chronic HIV/HTLV co-infection equilibrium with only active HTLV-specific CTL	$\Re_6 > 1$ and $\Re_2/\Re_1 > 1$
$Ð_7 = (S_7, L_7, I_7, E_7, Y_7, V_7, C^I_7, C^Y_7)$	Chronic HIV/HTLV co-infection equilibrium with active HIV-specific CTL and HTLV-specific CTL	$\Re_7 > 1$ and $\Re_8 > 1$

$$\frac{S_j}{S} + \frac{SVI_j}{S_jV_jI} + \frac{IV_j}{I_jV} \geq 3, \quad j = 1, 3, 5, 6, 7, \tag{5.2}$$

$$\frac{S_j}{S} + \frac{SVL_j}{S_jV_jL} + \frac{LI_j}{L_jI} + \frac{IV_j}{I_jV} \geq 4, \quad j = 1, 3, 5, 6, 7, \tag{5.3}$$

$$\frac{S_j}{S} + \frac{SYE_j}{S_jY_jE} + \frac{EY_j}{E_jY} \geq 3, \quad j = 2, 4, 5, 6, 7. \tag{5.4}$$

Theorem 1. If $\Re_1 \leq 1$ and $\Re_2 \leq 1$, then $Ð_0$ is globally asymptotically stable (G.A.S).
Proof. We construct a Lyapunov function $\Phi_0(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\Phi_0 = S_0F\left(\frac{S}{S_0}\right) + \frac{\lambda}{\beta\gamma + \lambda}L + \frac{\gamma + \lambda}{\beta\gamma + \lambda}I + \frac{1}{\varphi}E + \frac{\psi + \omega}{\varphi\psi}Y + \frac{\eta_1 S_0}{\varepsilon}V + \frac{\mu_1(\gamma + \lambda)}{\sigma_1(\beta\gamma + \lambda)}C^I + \frac{\mu_2(\psi + \omega)}{\varphi\psi\sigma_2}C^Y,$$

where,

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

Clearly, $\Phi_0(S, L, I, E, Y, V, C^I, C^Y) > 0$ for all $S, L, I, E, Y, V, C^I, C^Y > 0$, and $\Phi_0(S_0, 0, 0, 0, 0, 0, 0, 0) = 0$. Calculating $\frac{d\Phi_0}{dt}$ along the solutions of system (2.1) as:

$$\begin{aligned}\frac{d\Phi_0}{dt} &= \left(1 - \frac{S_0}{S}\right)[\rho - \alpha S - \eta_1 SV - \eta_2 SI - \eta_3 SY] + \frac{\lambda}{\beta\gamma + \lambda}[(1 - \beta)(\eta_1 SV + \eta_2 SI) - (\lambda + \gamma)L] \\ &+ \frac{\gamma + \lambda}{\beta\gamma + \lambda}\left[\beta(\eta_1 SV + \eta_2 SI) + \lambda L - aI - \mu_1 C^I I\right] + \frac{1}{\varphi}[\varphi\eta_3 SY - (\psi + \omega)E] \\ &+ \frac{\psi + \omega}{\varphi\psi}\left[\psi E - \delta Y - \mu_2 C^Y Y\right] + \frac{\eta_1 S_0}{\varepsilon}(bI - \varepsilon V) + \frac{\mu_1(\gamma + \lambda)}{\sigma_1(\beta\gamma + \lambda)}\left[\sigma_1 C^I I - \pi_1 C^I\right] \\ &+ \frac{\mu_2(\psi + \omega)}{\varphi\psi\sigma_2}\left[\sigma_2 C^Y Y - \pi_2 C^Y\right]\end{aligned}$$

$$= \left(1 - \frac{S_0}{S}\right)(\rho - \alpha S) + \eta_2 S_0 I + \eta_3 S_0 Y - \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda} I - \frac{\delta(\psi+\omega)}{\varphi\psi} Y + \frac{\eta_1 b S_0}{\varepsilon} I$$
$$- \frac{\mu_1 \pi_1 (\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)} C^I - \frac{\mu_2 \pi_2 (\psi+\omega)}{\varphi\psi\sigma_2} C^Y.$$

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

$$\frac{d\Phi_0}{dt} = -\alpha \frac{(S - S_0)^2}{S} + \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}(\Re_1 - 1) I + \frac{\delta(\psi+\omega)}{\varphi\psi}(\Re_2 - 1) Y$$
$$- \frac{\mu_1 \pi_1 (\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)} C^I - \frac{\mu_2 \pi_2 (\psi+\omega)}{\varphi\psi\sigma_2} C^Y.$$

Therefore, $\frac{d\Phi_0}{dt} \leq 0$ for all $S, I, Y, C^I, C^Y > 0$ and $\frac{d\Phi_0}{dt} = 0$ when $S = S_0$ and $I = Y = C^I = C^Y = 0$. Define $\Upsilon_0 = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_0}{dt} = 0\right\}$ and let Υ_0' be the largest invariant subset of Υ_0. The solutions of system (2.1) converge to Υ_0'. The set Υ_0' includes elements with $S = S_0$ and $I = Y = C^I = C^Y = 0$, and hence $\dot{S} = \dot{Y} = 0$. The first and fifth equations of system (2.1) yield

$$0 = \dot{S} = \rho - \alpha S_0 - \eta_1 S_0 V,$$
$$0 = \dot{Y} = \psi E.$$

Thus, $V(t) = E(t) = 0$ for all t. In addition, we have $\dot{I} = 0$ and from the third equation of system (2.1) we obtain

$$0 = \dot{I} = \lambda L,$$

which yields $L(t) = 0$ for all t. Therefore, $\Upsilon_0' = \{Đ_0\}$ and by applying Lyapunov-LaSalle asymptotic stability theorem [51–53] we get that $Đ_0$ is G.A.S. □

Theorem 2. Let $\Re_1 > 1$, $\Re_2/\Re_1 \leq 1$ and $\Re_3 \leq 1$, then $Đ_1$ is G.A.S.

Proof. Define a function $\Phi_1(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\Phi_1 = S_1 F\left(\frac{S}{S_1}\right) + \frac{\lambda}{\beta\gamma+\lambda} L_1 F\left(\frac{L}{L_1}\right) + \frac{\gamma+\lambda}{\beta\gamma+\lambda} I_1 F\left(\frac{I}{I_1}\right) + \frac{1}{\varphi} E$$
$$+ \frac{\psi+\omega}{\varphi\psi} Y + \frac{\eta_1 S_1}{\varepsilon} V_1 F\left(\frac{V}{V_1}\right) + \frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)} C^I + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2} C^Y.$$

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

$$\frac{d\Phi_1}{dt} = \left(1 - \frac{S_1}{S}\right)[\rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y]$$
$$+ \frac{\lambda}{\beta\gamma+\lambda}\left(1 - \frac{L_1}{L}\right)[(1-\beta)(\eta_1 S V + \eta_2 S I) - (\lambda+\gamma) L]$$
$$+ \frac{\gamma+\lambda}{\beta\gamma+\lambda}\left(1 - \frac{I_1}{I}\right)\left[\beta(\eta_1 S V + \eta_2 S I) + \lambda L - a I - \mu_1 C^I I\right]$$
$$+ \frac{1}{\varphi}[\varphi\eta_3 S Y - (\psi+\omega) E] + \frac{\psi+\omega}{\varphi\psi}\left[\psi E - \delta Y - \mu_2 C^Y Y\right]$$
$$+ \frac{\eta_1 S_1}{\varepsilon}\left(1 - \frac{V_1}{V}\right)[b I - \varepsilon V] + \frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}\left[\sigma_1 C^I I - \pi_1 C^I\right]$$

$$
\begin{aligned}
&+ \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left[\sigma_2 C^Y Y - \pi_2 C^Y\right] \\
&= \left(1-\frac{S_1}{S}\right)(\rho-\alpha S) + \eta_2 S_1 I + \eta_3 S_1 Y - \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 SV + \eta_2 SI)\frac{L_1}{L} \\
&+ \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_1 - \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I - \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}(\eta_1 SV + \eta_2 SI)\frac{I_1}{I} - \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L\frac{I_1}{I} \\
&+ \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_1 + \frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C^I I_1 - \frac{\delta(\psi+\omega)}{\varphi\psi}Y + \eta_1 S_1\frac{bI}{\varepsilon} - \eta_1 S_1\frac{bI}{\varepsilon}\frac{V_1}{V} \\
&+ \eta_1 S_1 V_1 - \frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I - \frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}
$$

Using the equilibrium conditions for $Đ_1$, we get

$$
\begin{aligned}
&\rho = \alpha S_1 + \eta_1 S_1 V_1 + \eta_2 S_1 I_1, \quad \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_1 V_1 + \eta_2 S_1 I_1) = \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_1, \\
&\eta_1 S_1 V_1 + \eta_2 S_1 I_1 = \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_1, \quad V_1 = \frac{bI_1}{\varepsilon}.
\end{aligned}
$$

Then, we obtain

$$
\begin{aligned}
\frac{d\Phi_1}{dt} &= \left(1-\frac{S_1}{S}\right)(\alpha S_1 - \alpha S) + (\eta_1 S_1 V_1 + \eta_2 S_1 I_1)\left(1-\frac{S_1}{S}\right) + \eta_3 S_1 Y - \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_1 V_1\frac{SVL_1}{S_1V_1L} \\
&- \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_1 I_1\frac{SIL_1}{S_1I_1L} + \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_1 V_1 + \eta_2 S_1 I_1) - \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_1 V_1\frac{SVI_1}{S_1V_1I} \\
&- \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2 S_1 I_1\frac{S}{S_1} - \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_1 V_1 + \eta_2 S_1 I_1)\frac{LI_1}{L_1I} + \eta_1 S_1 V_1 + \eta_2 S_1 I_1 + \frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C^I I_1 \\
&- \frac{\delta(\psi+\omega)}{\varphi\psi}Y - \eta_1 S_1 V_1\frac{IV_1}{I_1V} + \eta_1 S_1 V_1 - \frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I - \frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y \\
&= -\alpha\frac{(S-S_1)^2}{S} + \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_1 V_1\left(4-\frac{S_1}{S}-\frac{SVL_1}{S_1V_1L}-\frac{LI_1}{L_1I}-\frac{IV_1}{I_1V}\right) \\
&+ \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_1 I_1\left(3-\frac{S_1}{S}-\frac{SIL_1}{S_1I_1L}-\frac{LI_1}{L_1I}\right) + \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_1 V_1\left(3-\frac{S_1}{S}-\frac{SVI_1}{S_1V_1I}-\frac{IV_1}{I_1V}\right) \\
&+ \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2 S_1 I_1\left(2-\frac{S_1}{S}-\frac{S}{S_1}\right) + \frac{\delta(\psi+\omega)}{\varphi\psi}\left(\frac{\varphi\eta_3\psi S_1}{\delta(\psi+\omega)}-1\right)Y \\
&+ \frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}\left(I_1-\frac{\pi_1}{\sigma_1}\right)C^I - \frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y. \qquad (5.5)
\end{aligned}
$$

Therefore, Eq (5.5) becomes

$$
\begin{aligned}
\frac{d\Phi_1}{dt} &= -\left(\alpha + \frac{\beta\eta_2 I_1(\gamma+\lambda)}{\beta\gamma+\lambda}\right)\frac{(S-S_1)^2}{S} + \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_1 V_1\left(4-\frac{S_1}{S}-\frac{SVL_1}{S_1V_1L}-\frac{LI_1}{L_1I}-\frac{IV_1}{I_1V}\right) \\
&+ \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_1 I_1\left(3-\frac{S_1}{S}-\frac{SIL_1}{S_1I_1L}-\frac{LI_1}{L_1I}\right) + \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_1 V_1\left(3-\frac{S_1}{S}-\frac{SVI_1}{S_1V_1I}-\frac{IV_1}{I_1V}\right) \\
&+ \frac{\delta(\psi+\omega)}{\varphi\psi}(\Re_2/\Re_1 - 1)Y + \frac{\mu_1(\gamma+\lambda)\left[\pi_1(\eta_1 b + \eta_2\varepsilon) + \alpha\varepsilon\sigma_1\right]}{\sigma_1(\beta\gamma+\lambda)(\eta_1 b + \eta_2\varepsilon)}(\Re_3 - 1)C^I - \frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y. \\
&\qquad (5.6)
\end{aligned}
$$

Since $\Re_2/\Re_1 \leq 1$ and $\Re_3 \leq 1$, then using inequalities (5.1)–(5.3) we get $\frac{d\Phi_1}{dt} \leq 0$ for all $S, L, I, Y, V, C^I, C^Y > 0$. Moreover, $\frac{d\Phi_1}{dt} = 0$ when $S = S_1$, $L = L_1$, $I = I_1$, $V = V_1$ and $Y = C^I = C^Y = 0$. The solutions of system (2.1) converge to Υ_1' the largest invariant subset of $\Upsilon_1 = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_1}{dt} = 0\right\}$. The set Υ_1' includes $Y = 0$, and then $\dot{Y} = 0$. The fifth equation of system (2.1) implies

$$0 = \dot{Y} = \psi E,$$

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. □

Theorem 3. If $\Re_2 > 1$, $\Re_1/\Re_2 \leq 1$ and $\Re_4 \leq 1$, then $Đ_2$ is G.A.S.

Proof. We define $\Phi_2(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\begin{aligned}\Phi_2 = {} & S_2 F\left(\frac{S}{S_2}\right) + \frac{\lambda}{\beta\gamma + \lambda} L + \frac{\gamma + \lambda}{\beta\gamma + \lambda} I + \frac{1}{\varphi} E_2 F\left(\frac{E}{E_2}\right) \\ & + \frac{\psi + \omega}{\varphi\psi} Y_2 F\left(\frac{Y}{Y_2}\right) + \frac{\eta_1 S_2}{\varepsilon} V + \frac{\mu_1(\gamma + \lambda)}{\sigma_1(\beta\gamma + \lambda)} C^I + \frac{\mu_2(\psi + \omega)}{\varphi\psi\sigma_2} C^Y.\end{aligned}$$

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

$$\begin{aligned}\frac{d\Phi_2}{dt} = {} & \left(1 - \frac{S_2}{S}\right)[\rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y] + \frac{\lambda}{\beta\gamma + \lambda}[(1 - \beta)(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma) L] \\ & + \frac{\gamma + \lambda}{\beta\gamma + \lambda}\left[\beta(\eta_1 S V + \eta_2 S I) + \lambda L - aI - \mu_1 C^I I\right] + \frac{1}{\varphi}\left(1 - \frac{E_2}{E}\right)[\varphi\eta_3 S Y - (\psi + \omega) E] \\ & + \frac{\psi + \omega}{\varphi\psi}\left(1 - \frac{Y_2}{Y}\right)\left[\psi E - \delta Y - \mu_2 C^Y Y\right] + \frac{\eta_1 S_2}{\varepsilon}[bI - \varepsilon V] + \frac{\mu_1(\gamma + \lambda)}{\sigma_1(\beta\gamma + \lambda)}\left[\sigma_1 C^I I - \pi_1 C^I\right] \\ & + \frac{\mu_2(\psi + \omega)}{\varphi\psi\sigma_2}\left[\sigma_2 C^Y Y - \pi_2 C^Y\right] \\ = {} & \left(1 - \frac{S_2}{S}\right)(\rho - \alpha S) + \eta_2 S_2 I + \eta_3 S_2 Y - \frac{a(\gamma + \lambda)}{\beta\gamma + \lambda} I - \eta_3 S Y \frac{E_2}{E} + \frac{\psi + \omega}{\varphi} E_2 \\ & - \frac{\delta(\psi + \omega)}{\varphi\psi} Y - \frac{\psi + \omega}{\varphi} E \frac{Y_2}{Y} + \frac{\delta(\psi + \omega)}{\varphi\psi} Y_2 + \frac{\mu_2(\psi + \omega)}{\varphi\psi} C^Y Y_2 + \eta_1 S_2 \frac{bI}{\varepsilon} \\ & - \frac{\mu_1\pi_1(\gamma + \lambda)}{\sigma_1(\beta\gamma + \lambda)} C^I - \frac{\mu_2\pi_2(\psi + \omega)}{\varphi\psi\sigma_2} C^Y.\end{aligned}$$

Using the equilibrium conditions for $Đ_2$:

$$\rho = \alpha S_2 + \eta_3 S_2 Y_2, \quad \eta_3 S_2 Y_2 = \frac{\psi + \omega}{\varphi} E_2 = \frac{\delta(\psi + \omega)}{\varphi\psi} Y_2, \tag{5.7}$$

we obtain

$$\begin{aligned}\frac{d\Phi_2}{dt} = {} & \left(1 - \frac{S_2}{S}\right)(\alpha S_2 - \alpha S) + \eta_3 S_2 Y_2\left(1 - \frac{S_2}{S}\right) + \eta_2 S_2 I - \frac{a(\gamma + \lambda)}{\beta\gamma + \lambda} I - \eta_3 S_2 Y_2 \frac{S Y E_2}{S_2 Y_2 E} + \eta_3 S_2 Y_2 \\ & - \eta_3 S_2 Y_2 \frac{E Y_2}{E_2 Y} + \eta_3 S_2 Y_2 + \frac{\mu_2(\psi + \omega)}{\varphi\psi} C^Y Y_2 + \eta_1 S_2 \frac{bI}{\varepsilon} - \frac{\mu_1\pi_1(\gamma + \lambda)}{\sigma_1(\beta\gamma + \lambda)} C^I - \frac{\mu_2\pi_2(\psi + \omega)}{\varphi\psi\sigma_2} C^Y \\ = {} & -\alpha\frac{(S - S_2)^2}{S} + \eta_3 S_2 Y_2\left(3 - \frac{S_2}{S} - \frac{S Y E_2}{S_2 Y_2 E} - \frac{E Y_2}{E_2 Y}\right) + \frac{a(\gamma + \lambda)}{\beta\gamma + \lambda}\left(\frac{(\eta_1 b + \eta_2\varepsilon)(\beta\gamma + \lambda) S_2}{a\varepsilon(\gamma + \lambda)} - 1\right) I\end{aligned}$$

$$
\begin{aligned}
&-\frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I+\frac{\mu_2(\psi+\omega)}{\varphi\psi}\left(Y_2-\frac{\pi_2}{\sigma_2}\right)C^Y\\
&=-\alpha\frac{(S-S_2)^2}{S}+\eta_3S_2Y_2\left(3-\frac{S_2}{S}-\frac{SYE_2}{S_2Y_2E}-\frac{EY_2}{E_2Y}\right)+\frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}(\Re_1/\Re_2-1)I\\
&-\frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I+\frac{\mu_2(\psi+\omega)(\alpha\sigma_2+\eta_3\pi_2)}{\varphi\psi\eta_3\sigma_2}(\Re_4-1)C^Y.
\end{aligned}
$$

Since $\Re_1/\Re_2\le 1$ and $\Re_4\le 1$, then using inequality (5.4) we get $\frac{d\Phi_2}{dt}\le 0$ for all $S,L,I,E,Y,V,C^I,C^Y>0$. In addition, $\frac{d\Phi_2}{dt}=0$ when $S=S_2$, $E=E_2$, $Y=Y_2$ and $I=C^I=C^Y=0$. Define $\Upsilon_2=\left\{(S,L,I,E,Y,V,C^I,C^Y):\frac{d\Phi_2}{dt}=0\right\}$ and let Υ_2' be the largest invariant subset of Υ_2. The solutions of system (2.1) converge to Υ_2' which includes elements with $S=S_2$, $Y=Y_2$, $I=0$, then $\dot{S}=0$. The first equation of system (2.1) gives

$$0=\dot{S}=\rho-\alpha S_2-\eta_1S_2V-\eta_3S_2Y_2.$$

From conditions (5.7) we get $V(t)=0$ for all t. Moreover, we have $\dot{I}=0$ and from the third equation of system (2.1) we obtain

$$0=\dot{I}=\lambda L,$$

which yields $L(t)=0$ for all t. Therefore, $\Upsilon_2'=\{Đ_2\}$. By applying Lyapunov-LaSalle asymptotic stability theorem we get that $Đ_2$ is G.A.S. □

Theorem 4. Let $\Re_3>1$ and $\Re_5\le 1$, then $Đ_3$ is G.A.S.

Proof. Define a function $\Phi_3(S,L,I,E,Y,V,C^I,C^Y)$ as:

$$
\begin{aligned}
\Phi_3&=S_3F\left(\frac{S}{S_3}\right)+\frac{\lambda}{\beta\gamma+\lambda}L_3F\left(\frac{L}{L_3}\right)+\frac{\gamma+\lambda}{\beta\gamma+\lambda}I_3F\left(\frac{I}{I_3}\right)+\frac{1}{\varphi}E+\frac{\psi+\omega}{\varphi\psi}Y\\
&+\frac{\eta_1S_3}{\varepsilon}V_3F\left(\frac{V}{V_3}\right)+\frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C_3^IF\left(\frac{C^I}{C_3^I}\right)+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}
$$

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

$$
\begin{aligned}
\frac{d\Phi_3}{dt}&=\left(1-\frac{S_3}{S}\right)[\rho-\alpha S-\eta_1SV-\eta_2SI-\eta_3SY]\\
&+\frac{\lambda}{\beta\gamma+\lambda}\left(1-\frac{L_3}{L}\right)[(1-\beta)(\eta_1SV+\eta_2SI)-(\lambda+\gamma)L]\\
&+\frac{\gamma+\lambda}{\beta\gamma+\lambda}\left(1-\frac{I_3}{I}\right)\left[\beta(\eta_1SV+\eta_2SI)+\lambda L-aI-\mu_1C^II\right]+\frac{1}{\varphi}[\varphi\eta_3SY-(\psi+\omega)E]\\
&+\frac{\psi+\omega}{\varphi\psi}\left[\psi E-\delta Y-\mu_2C^YY\right]+\frac{\eta_1S_3}{\varepsilon}\left(1-\frac{V_3}{V}\right)[bI-\varepsilon V]\\
&+\frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}\left(1-\frac{C_3^I}{C^I}\right)\left[\sigma_1C^II-\pi_1C^I\right]+\frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left[\sigma_2C^YY-\pi_2C^Y\right]\\
&=\left(1-\frac{S_3}{S}\right)(\rho-\alpha S)+\eta_2S_3I+\eta_3S_3Y-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1SV+\eta_2SI)\frac{L_3}{L}+\frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_3\\
&-\frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}(\eta_1SV+\eta_2SI)\frac{I_3}{I}-\frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L\frac{I_3}{I}+\frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_3
\end{aligned}
$$

$$+\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C^I I_3-\frac{\delta(\psi+\omega)}{\varphi\psi}Y+\frac{\eta_1 S_3}{\varepsilon}bI-\frac{\eta_1 S_3}{\varepsilon}bI\frac{V_3}{V}+\eta_1 S_3 V_3$$
$$-\frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I-\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C_3^I I+\frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C_3^I-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.$$

Using the equilibrium conditions for $Đ_3$:

$$\rho=\alpha S_3+\eta_1 S_3 V_3+\eta_2 S_3 I_3,\quad \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_3 V_3++\eta_2 S_3 I_3)=\frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_3,$$
$$\eta_1 S_3 V_3+\eta_2 S_3 I_3=\frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_3+\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C_3^I I_3,\quad I_3=\frac{\pi_1}{\sigma_1},\quad V_3=\frac{b}{\varepsilon}I_3,$$

we obtain

$$\begin{aligned}
\frac{d\Phi_3}{dt}&=\left(1-\frac{S_3}{S}\right)(\alpha S_3-\alpha S)+(\eta_1 S_3 V_3+\eta_2 S_3 I_3)\left(1-\frac{S_3}{S}\right)+\left(\eta_3 S_3-\frac{\delta(\psi+\omega)}{\varphi\psi}\right)Y\\
&-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_3 V_3\frac{SVL_3}{S_3V_3L}-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_3 I_3\frac{SIL_3}{S_3I_3L}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_3 V_3+\eta_2 S_3 I_3)\\
&-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_3 V_3\frac{SVI_3}{S_3V_3I}-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2 S_3 I_3\frac{S}{S_3}-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_3 V_3+\eta_2 S_3 I_3)\frac{LI_3}{L_3I}\\
&+\eta_1 S_3 V_3+\eta_2 S_3 I_3-\eta_1 S_3 V_3\frac{IV_3}{I_3V}+\eta_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}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_3 V_3\left(4-\frac{S_3}{S}-\frac{SVL_3}{S_3V_3L}-\frac{LI_3}{L_3I}-\frac{IV_3}{I_3V}\right)\\
&+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_3 I_3\left(3-\frac{S_3}{S}-\frac{SIL_3}{S_3I_3L}-\frac{LI_3}{L_3I}\right)+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_3 V_3\left(3-\frac{S_3}{S}-\frac{SVI_3}{S_3V_3I}-\frac{IV_3}{I_3V}\right)\\
&+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2 S_3 I_3\left(2-\frac{S_3}{S}-\frac{S}{S_3}\right)+\frac{\delta(\psi+\omega)}{\varphi\psi}\left(\frac{\varphi\psi\eta_3 S_3}{\delta(\psi+\omega)}-1\right)Y-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y\\
&=-\left(\alpha+\frac{\beta\eta_2 I_3(\gamma+\lambda)}{\beta\gamma+\lambda}\right)\frac{(S-S_3)^2}{S}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_3 V_3\left(4-\frac{S_3}{S}-\frac{SVL_3}{S_3V_3L}-\frac{LI_3}{L_3I}-\frac{IV_3}{I_3V}\right)\\
&+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_3 I_3\left(3-\frac{S_3}{S}-\frac{SIL_3}{S_3I_3L}-\frac{LI_3}{L_3I}\right)+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_3 V_3\left(3-\frac{S_3}{S}-\frac{SVI_3}{S_3V_3I}-\frac{IV_3}{I_3V}\right)\\
&+\frac{\delta(\psi+\omega)}{\varphi\psi}(\Re_5-1)Y-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}$$

Hence, if $\Re_5\le 1$, then using inequalities (5.1)–(5.3) we get $\frac{d\Phi_3}{dt}\le 0$ for all $S,L,I,E,Y,V,C^I,C^Y>0$. Moreover, $\frac{d\Phi_3}{dt}=0$ at $S=S_3$, $L=L_3$, $I=I_3$, $V=V_3$ and $Y=C^Y=0$. The solutions of system (2.1) converge to Υ_3' the largest invariant subset of $\Upsilon_3=\left\{(S,L,I,E,Y,V,C^I,C^Y):\frac{d\Phi_3}{dt}=0\right\}$. The set Υ_3' contains elements with $S=S_3$, $L=L_3$, $I=I_3$, $V=V_3$, $Y=0$, and then $\dot I=\dot Y=0$. The third and fifth equations of system (2.1) give

$$\begin{aligned}
0&=\dot I=\beta(\eta_1 S_3 V_3+\eta_2 S_3 I_3)+\lambda L_3-aI_3-\mu_1 C^I I_3,\\
0&=\dot Y=\psi E,
\end{aligned}$$

which yield $C^I(t) = C^I_3$ and $E(t) = 0$ for all t. Therefore, $\Upsilon'_3 = \{Đ_3\}$. By applying Lyapunov-LaSalle asymptotic stability theorem we get that $Đ_3$ is G.A.S. □

Theorem 5. If $\Re_4 > 1$ and $\Re_6 \leq 1$, then $Đ_4$ is G.A.S.

Proof. Define $\Phi_4(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\Phi_4 = S_4 F\left(\frac{S}{S_4}\right) + \frac{\lambda}{\beta\gamma + \lambda} L + \frac{\gamma + \lambda}{\beta\gamma + \lambda} I + \frac{1}{\varphi} E_4 F\left(\frac{E}{E_4}\right) + \frac{\psi + \omega}{\varphi\psi} Y_4 F\left(\frac{Y}{Y_4}\right)$$
$$+ \frac{\eta_1 S_4}{\varepsilon} V + \frac{\mu_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C^I + \frac{\mu_2 (\psi + \omega)}{\varphi\psi\sigma_2} C^Y_4 F\left(\frac{C^Y}{C^Y_4}\right).$$

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

$$\frac{d\Phi_4}{dt} = \left(1 - \frac{S_4}{S}\right)[\rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y] + \frac{\lambda}{\beta\gamma + \lambda}[(1 - \beta)(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma) L]$$
$$+ \frac{\gamma + \lambda}{\beta\gamma + \lambda}\left[\beta(\eta_1 S V + \eta_2 S I) + \lambda L - aI - \mu_1 C^I I\right] + \frac{1}{\varphi}\left(1 - \frac{E_4}{E}\right)[\varphi\eta_3 S Y - (\psi + \omega) E]$$
$$+ \frac{\psi + \omega}{\varphi\psi}\left(1 - \frac{Y_4}{Y}\right)\left[\psi E - \delta Y - \mu_2 C^Y Y\right] + \frac{\eta_1 S_4}{\varepsilon}[bI - \varepsilon V]$$
$$+ \frac{\mu_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)}\left[\sigma_1 C^I I - \pi_1 C^I\right] + \frac{\mu_2 (\psi + \omega)}{\varphi\psi\sigma_2}\left(1 - \frac{C^Y_4}{C^Y}\right)\left[\sigma_2 C^Y Y - \pi_2 C^Y\right]$$
$$= \left(1 - \frac{S_4}{S}\right)(\rho - \alpha S) + \eta_2 S_4 I + \eta_3 S_4 Y - \frac{a(\gamma + \lambda)}{\beta\gamma + \lambda} I - \eta_3 S Y \frac{E_4}{E} + \frac{\psi + \omega}{\varphi} E_4$$
$$- \frac{\delta(\psi + \omega)}{\varphi\psi} Y - \frac{\psi + \omega}{\varphi} E \frac{Y_4}{Y} + \frac{\delta(\psi + \omega)}{\varphi\psi} Y_4 + \frac{\mu_2 (\psi + \omega)}{\varphi\psi} C^Y Y_4 + \eta_1 S_4 \frac{bI}{\varepsilon}$$
$$- \frac{\mu_1 \pi_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C^I - \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi\psi\sigma_2} C^Y - \frac{\mu_2 (\psi + \omega)}{\varphi\psi} C^Y_4 Y + \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi\psi\sigma_2} C^Y_4.$$

Using the equilibrium conditions for $Đ_4$:

$$\rho = \alpha S_4 + \eta_3 S_4 Y_4, \quad Y_4 = \frac{\pi_2}{\sigma_2},$$
$$\eta_3 S_4 Y_4 = \frac{\psi + \omega}{\varphi} E_4 = \frac{\delta(\psi + \omega)}{\varphi\psi} Y_4 + \frac{\mu_2 (\psi + \omega)}{\varphi\psi} C^Y_4 Y_4.$$

We obtain

$$\frac{d\Phi_4}{dt} = \left(1 - \frac{S_4}{S}\right)(\alpha S_4 - \alpha S) + \eta_3 S_4 Y_4 \left(1 - \frac{S_4}{S}\right) + \eta_2 S_4 I - \frac{a(\gamma + \lambda)}{\beta\gamma + \lambda} I$$
$$- \eta_3 S_4 Y_4 \frac{S Y E_4}{S_4 Y_4 E} + \eta_3 S_4 Y_4 - \eta_3 S_4 Y_4 \frac{E Y_4}{E_4 Y} + \eta_3 S_4 Y_4 + \eta_1 S_4 \frac{bI}{\varepsilon}$$
$$- \frac{\mu_1 \pi_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C^I$$
$$= -\alpha \frac{(S - S_4)^2}{S} + \eta_3 S_4 Y_4 \left(3 - \frac{S_4}{S} - \frac{S Y E_4}{S_4 Y_4 E} - \frac{E Y_4}{E_4 Y}\right)$$
$$+ \frac{a(\gamma + \lambda)}{\beta\gamma + \lambda}\left(\frac{(\eta_1 b + \eta_2 \varepsilon)(\beta\gamma + \lambda) S_4}{a\varepsilon(\gamma + \lambda)} - 1\right) I - \frac{\mu_1 \pi_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C^I$$

$$
\begin{aligned}
&= -\alpha\frac{(S-S_4)^2}{S} + \eta_3 S_4 Y_4\left(3 - \frac{S_4}{S} - \frac{SYE_4}{S_4Y_4E} - \frac{EY_4}{E_4Y}\right)\\
&+ \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}(\Re_6 - 1)I - \frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I.
\end{aligned}
$$

If $\Re_6 \leq 1$, then using inequality (5.4) we get $\frac{d\Phi_4}{dt} \leq 0$ for all $S, L, I, E, Y, V, C^I, C^Y > 0$, where $\frac{d\Phi_4}{dt} = 0$ at $S = S_4$, $E = E_4$, $Y = Y_4$ and $I = C^I = 0$. The solutions of system (2.1) converge to Υ_4' the largest invariant subset of $\Upsilon_4 = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_4}{dt} = 0\right\}$. The set Υ_4' contains elements with $S = S_4$, $E = E_4$, $Y = Y_4$, $I = 0$, and then $\dot{S} = \dot{Y} = 0$. The first and fifth equations of system (2.1) imply

$$
\begin{aligned}
0 &= \dot{S} = \rho - \alpha S_4 - \eta_1 S_4 V - \eta_3 S_4 Y_4,\\
0 &= \dot{Y} = \psi E_4 - \delta Y_4 - \mu_2 C^Y Y_4,
\end{aligned}
$$

which yield $V(t) = 0$ and $C^Y(t) = C_4^Y$ for all t. Since $\dot{I} = 0$, then from the third equation of system (2.1) we obtain

$$
0 = \dot{I} = \lambda L,
$$

which yields $L(t) = 0$ for all t. Therefore, $\Upsilon_4' = \{Đ_4\}$. By applying Lyapunov-LaSalle asymptotic stability theorem we obtain that $Đ_4$ is G.A.S. □

Theorem 6. If $\Re_5 > 1$, $\Re_8 \leq 1$ and $\Re_1/\Re_2 > 1$, then $Đ_5$ is G.A.S.

Proof. Define $\Phi_5(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$
\begin{aligned}
\Phi_5 &= S_5 F\left(\frac{S}{S_5}\right) + \frac{\lambda}{\beta\gamma+\lambda}L_5F\left(\frac{L}{L_5}\right) + \frac{\gamma+\lambda}{\beta\gamma+\lambda}I_5F\left(\frac{I}{I_5}\right) + \frac{1}{\varphi}E_5F\left(\frac{E}{E_5}\right)\\
&+ \frac{\psi+\omega}{\varphi\psi}Y_5F\left(\frac{Y}{Y_5}\right) + \frac{\eta_1 S_5}{\varepsilon}V_5F\left(\frac{V}{V_5}\right) + \frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C_5^IF\left(\frac{C^I}{C_5^I}\right) + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}
$$

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

$$
\begin{aligned}
\frac{d\Phi_5}{dt} &= \left(1 - \frac{S_5}{S}\right)[\rho - \alpha S - \eta_1 SV - \eta_2 SI - \eta_3 SY]\\
&+ \frac{\lambda}{\beta\gamma+\lambda}\left(1 - \frac{L_5}{L}\right)[(1-\beta)(\eta_1 SV + \eta_2 SI) - (\lambda+\gamma)L]\\
&+ \frac{\gamma+\lambda}{\beta\gamma+\lambda}\left(1 - \frac{I_5}{I}\right)\left[\beta(\eta_1 SV + \eta_2 SI) + \lambda L - aI - \mu_1 C^I I\right]\\
&+ \frac{1}{\varphi}\left(1 - \frac{E_5}{E}\right)[\varphi\eta_3 SY - (\psi+\omega)E] + \frac{\psi+\omega}{\varphi\psi}\left(1 - \frac{Y_5}{Y}\right)\left[\psi E - \delta Y - \mu_2 C^Y Y\right]\\
&+ \frac{\eta_1 S_5}{\varepsilon}\left(1 - \frac{V_5}{V}\right)[bI - \varepsilon V] + \frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}\left(1 - \frac{C_5^I}{C^I}\right)\left[\sigma_1 C^I I - \pi_1 C^I\right]\\
&+ \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left[\sigma_2 C^Y Y - \pi_2 C^Y\right]\\
&= \left(1 - \frac{S_5}{S}\right)(\rho - \alpha S) + \eta_2 S_5 I + \eta_3 S_5 Y - \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 SV + \eta_2 SI)\frac{L_5}{L} + \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_5\\
&- \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I - \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}(\eta_1 SV + \eta_2 SI)\frac{I_5}{I} - \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L\frac{I_5}{I} + \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_5
\end{aligned}
$$

$$
\begin{aligned}
&+\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C^I I_5-\eta_3 S Y\frac{E_5}{E}+\frac{\psi+\omega}{\varphi}E_5-\frac{\delta(\psi+\omega)}{\varphi\psi}Y-\frac{\psi+\omega}{\varphi}E\frac{Y_5}{Y}\\
&+\frac{\delta(\psi+\omega)}{\varphi\psi}Y_5+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C^Y Y_5+\eta_1 S_5\frac{bI}{\varepsilon}-\eta_1 S_5 V_5\frac{bI}{\varepsilon V}+\eta_1 S_5 V_5\\
&-\frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I-\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C^I_5 I+\frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}C^I_5-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y.
\end{aligned}
$$

Using the equilibrium conditions for Đ$_5$:

$$
\begin{aligned}
\rho&=\alpha S_5+\eta_1 S_5 V_5+\eta_2 S_5 I_5+\eta_3 S_5 Y_5,\\
\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_5 V_5+\eta_2 S_5 I_5)&=\frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_5,\\
\eta_1 S_5 V_5+\eta_2 S_5 I_5&=\frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_5+\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}C^I_5 I_5,\\
\eta_3 S_5 Y_5&=\frac{\psi+\omega}{\varphi}E_5=\frac{\delta(\psi+\omega)}{\varphi\psi}Y_5,\quad I_5=\frac{\pi_1}{\sigma_1},\quad V_5=\frac{bI_5}{\varepsilon}.
\end{aligned}
$$

We obtain

$$
\begin{aligned}
\frac{d\Phi_5}{dt}&=\left(1-\frac{S_5}{S}\right)(\alpha S_5-\alpha S)+(\eta_1 S_5 V_5+\eta_2 S_5 I_5+\eta_3 S_5 Y_5)\left(1-\frac{S_5}{S}\right)-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_5 V_5\frac{SVL_5}{S_5 V_5 L}\\
&-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_5 I_5\frac{SIL_5}{S_5 I_5 L}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_5 V_5+\eta_2 S_5 I_5)-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_5 V_5\frac{SVI_5}{S_5 V_5 I}\\
&-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2 S_5 I_5\frac{S}{S_5}-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S_5 V_5+\eta_2 S_5 I_5)\frac{LI_5}{L_5 I}+\eta_1 S_5 V_5+\eta_2 S_5 I_5-\eta_3 S_5 Y_5\frac{SYE_5}{S_5 Y_5 E}\\
&+\eta_3 S_5 Y_5-\eta_3 S_5 Y_5\frac{EY_5}{E_5 Y}+\eta_3 S_5 Y_5-\eta_1 S_5 V_5\frac{IV_5}{I_5 V}+\eta_1 S_5 V_5+\frac{\mu_2(\psi+\omega)}{\varphi\psi}\left(Y_5-\frac{\pi_2}{\sigma_2}\right)C^Y\\
&=-\alpha\frac{(S-S_5)^2}{S}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_5 V_5\left(4-\frac{S_5}{S}-\frac{SVL_5}{S_5 V_5 L}-\frac{LI_5}{L_5 I}-\frac{IV_5}{I_5 V}\right)\\
&+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_5 I_5\left(3-\frac{S_5}{S}-\frac{SIL_5}{S_5 I_5 L}-\frac{LI_5}{L_5 I}\right)+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_5 V_5\left(3-\frac{S_5}{S}-\frac{SVI_5}{S_5 V_5 I}-\frac{IV_5}{I_5 V}\right)\\
&+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2 S_5 I_5\left(2-\frac{S_5}{S}-\frac{S}{S_5}\right)+\eta_3 S_5 Y_5\left(3-\frac{S_5}{S}-\frac{SYE_5}{S_5 Y_5 E}-\frac{EY_5}{E_5 Y}\right)\\
&+\frac{\mu_2(\psi+\omega)}{\varphi\psi}\left(Y_5-\frac{\pi_2}{\sigma_2}\right)C^Y. \qquad (5.8)
\end{aligned}
$$

Then, Eq (5.8) will be reduced to the form

$$
\begin{aligned}
\frac{d\Phi_5}{dt}&=-\left(\alpha+\frac{\beta\eta_2 I_5(\gamma+\lambda)}{\beta\gamma+\lambda}\right)\frac{(S-S_5)^2}{S}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_5 V_5\left(4-\frac{S_5}{S}-\frac{SVL_5}{S_5 V_5 L}-\frac{LI_5}{L_5 I}-\frac{IV_5}{I_5 V}\right)\\
&+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_5 I_5\left(3-\frac{S_5}{S}-\frac{SIL_5}{S_5 I_5 L}-\frac{LI_5}{L_5 I}\right)\\
&+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_5 V_5\left(3-\frac{S_5}{S}-\frac{SVI_5}{S_5 V_5 I}-\frac{IV_5}{I_5 V}\right)+\eta_3 S_5 Y_5\left(3-\frac{S_5}{S}-\frac{SYE_5}{S_5 Y_5 E}-\frac{EY_5}{E_5 Y}\right)
\end{aligned}
$$

$$+\frac{\mu_2(\psi+\omega)\left[\pi_1\sigma_2(\eta_1 b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2\right]}{\varphi\psi\eta_3\varepsilon\sigma_1\sigma_2}(\Re_8-1)C^Y.$$

If $\Re_8 \le 1$, then using inequalities (5.1)–(5.4) we get $\frac{d\Phi_5}{dt} \le 0$ for all $S, L, I, E, Y, V, C^I, C^Y > 0$, where $\frac{d\Phi_5}{dt} = 0$ at $S = S_5$, $L = L_5$, $I = I_5$, $E = E_5$, $Y = Y_5$, $V = V_5$ and $C^Y = 0$. The solutions of system (2.1) converge to Υ_5' the largest invariant subset of $\Upsilon_5 = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_5}{dt} = 0\right\}$. The set Υ_5' contains elements with $S = S_5$, $L = L_5$, $I = I_5$, $V = V_5$, and then $\dot{I} = 0$. Third equation of system (2.1) implies

$$0 = \dot{I} = \beta(\eta_1 S_5 V_5 + \eta_2 S_5 I_5) + \lambda L_5 - a I_5 - \mu_1 C^I I_5,$$

which gives $C^I(t) = C_5^I$ for all t. Therefore, $\Upsilon_5' = \{Đ_5\}$. Applying Lyapunov-LaSalle asymptotic stability theorem we get $Đ_5$ is G.A.S. □

Theorem 7. If $\Re_6 > 1$, $\Re_7 \le 1$ and $\Re_2/\Re_1 > 1$, then $Đ_6$ is G.A.S.

Proof. Define $\Phi_6(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\Phi_6 = S_6 F\left(\frac{S}{S_6}\right) + \frac{\lambda}{\beta\gamma+\lambda} L_6 F\left(\frac{L}{L_6}\right) + \frac{\gamma+\lambda}{\beta\gamma+\lambda} I_6 F\left(\frac{I}{I_6}\right) + \frac{1}{\varphi} E_6 F\left(\frac{E}{E_6}\right) + \frac{\psi+\omega}{\varphi\psi} Y_6 F\left(\frac{Y}{Y_6}\right)$$
$$+ \frac{\eta_1 S_6}{\varepsilon} V_6 F\left(\frac{V}{V_6}\right) + \frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)} C^I + \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2} C_6^Y F\left(\frac{C^Y}{C_6^Y}\right).$$

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

$$\begin{aligned}
\frac{d\Phi_6}{dt} &= \left(1-\frac{S_6}{S}\right)\left[\rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y\right] \\
&+ \frac{\lambda}{\beta\gamma+\lambda}\left(1-\frac{L_6}{L}\right)\left[(1-\beta)(\eta_1 S V + \eta_2 S I) - (\lambda+\gamma)L\right] \\
&+ \frac{\gamma+\lambda}{\beta\gamma+\lambda}\left(1-\frac{I_6}{I}\right)\left[\beta(\eta_1 S V + \eta_2 S I) + \lambda L - a I - \mu_1 C^I I\right] \\
&+ \frac{1}{\varphi}\left(1-\frac{E_6}{E}\right)\left[\varphi\eta_3 S Y - (\psi+\omega)E\right] \\
&+ \frac{\psi+\omega}{\varphi\psi}\left(1-\frac{Y_6}{Y}\right)\left[\psi E - \delta Y - \mu_2 C^Y Y\right] + \frac{\eta_1 S_6}{\varepsilon}\left(1-\frac{V_6}{V}\right)\left[b I - \varepsilon V\right] \\
&+ \frac{\mu_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)}\left[\sigma_1 C^I I - \pi_1 C^I\right] \\
&+ \frac{\mu_2(\psi+\omega)}{\varphi\psi\sigma_2}\left(1-\frac{C_6^Y}{C^Y}\right)\left[\sigma_2 C^Y Y - \pi_2 C^Y\right] \\
&= \left(1-\frac{S_6}{S}\right)(\rho - \alpha S) + \eta_2 S_6 I + \eta_3 S_6 Y - \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1 S V + \eta_2 S I)\frac{L_6}{L} + \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda} L_6 \\
&- \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda} I - \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}(\eta_1 S V + \eta_2 S I)\frac{I_6}{I} - \frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda} L\frac{I_6}{I} + \frac{a(\gamma+\lambda)}{\beta\gamma+\lambda} I_6 \\
&+ \frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda} C^I I_6 - \eta_3 S Y\frac{E_6}{E} + \frac{\psi+\omega}{\varphi} E_6 - \frac{\delta(\psi+\omega)}{\varphi\psi} Y - \frac{\psi+\omega}{\varphi} E\frac{Y_6}{Y} + \frac{\delta(\psi+\omega)}{\varphi\psi} Y_6 \\
&+ \frac{\mu_2(\psi+\omega)}{\varphi\psi} C^Y Y_6 + \eta_1 S_6\frac{bI}{\varepsilon} - \eta_1 S_6 V_6\frac{bI}{\varepsilon V} + \eta_1 S_6 V_6 - \frac{\mu_1\pi_1(\gamma+\lambda)}{\sigma_1(\beta\gamma+\lambda)} C^I
\end{aligned}$$

$$-\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C^Y-\frac{\mu_2(\psi+\omega)}{\varphi\psi}C_6^YY+\frac{\mu_2\pi_2(\psi+\omega)}{\varphi\psi\sigma_2}C_6^Y.$$

Using the equilibrium conditions for Đ$_6$:

$$\begin{aligned}&\rho=\alpha S_6+\eta_1S_6V_6+\eta_2S_6I_6+\eta_3S_6Y_6,\\&\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1S_6V_6+\eta_2S_6I_6)=\frac{\lambda(\gamma+\lambda)}{\beta\gamma+\lambda}L_6,\quad Y_6=\frac{\pi_2}{\sigma_2},\quad V_6=\frac{bI_6}{\varepsilon},\\&\eta_1S_6V_6+\eta_2S_6I_6=\frac{a(\gamma+\lambda)}{\beta\gamma+\lambda}I_6,\\&\eta_3S_6Y_6=\frac{\psi+\omega}{\varphi}E_6=\frac{\delta(\psi+\omega)}{\varphi\psi}Y_6+\frac{\mu_2(\psi+\omega)}{\varphi\psi}C_6^YY_6.\end{aligned}$$

We obtain

$$\begin{aligned}\frac{d\Phi_6}{dt}&=\left(1-\frac{S_6}{S}\right)(\alpha S_6-\alpha S)+(\eta_1S_6V_6+\eta_2S_6I_6+\eta_3S_6Y_6)\left(1-\frac{S_6}{S}\right)-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1S_6V_6\frac{SVL_6}{S_6V_6L}\\&-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2S_6I_6\frac{SIL_6}{S_6I_6L}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1S_6V_6+\eta_2S_6I_6)-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1S_6V_6\frac{SVI_6}{S_6V_6I}\\&-\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2S_6I_6\frac{S}{S_6}-\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}(\eta_1S_6V_6+\eta_2S_6I_6)\frac{LI_6}{L_6I}+\eta_1S_6V_6+\eta_2S_6I_6-\eta_3S_6Y_6\frac{SYE_6}{S_6Y_6E}\\&+\eta_3S_6Y_6-\eta_3S_6Y_6\frac{EY_6}{E_6Y}+\eta_3S_6Y_6-\eta_1S_6V_6\frac{IV_6}{I_6V}+\eta_1S_6V_6+\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}\left(I_6-\frac{\pi_1}{\sigma_1}\right)C^I\\&=-\alpha\frac{(S-S_6)^2}{S}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1S_6V_6\left(4-\frac{S_6}{S}-\frac{SVL_6}{S_6V_6L}-\frac{LI_6}{L_6I}-\frac{IV_6}{I_6V}\right)\\&+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2S_6I_6\left(3-\frac{S_6}{S}-\frac{SIL_6}{S_6I_6L}-\frac{LI_6}{L_6I}\right)+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1S_6V_6\left(3-\frac{S_6}{S}-\frac{SVI_6}{S_6V_6I}-\frac{IV_6}{I_6V}\right)\\&+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_2S_6I_6\left(2-\frac{S_6}{S}-\frac{S}{S_6}\right)+\eta_3S_6Y_6\left(3-\frac{S_6}{S}-\frac{SYE_6}{S_6Y_6E}-\frac{EY_6}{E_6Y}\right)\\&+\frac{\mu_1(\gamma+\lambda)}{\beta\gamma+\lambda}\left(I_6-\frac{\pi_1}{\sigma_1}\right)C^I.\end{aligned}\tag{5.9}$$

Then, Eq (5.9) will be reduced to the form

$$\begin{aligned}\frac{d\Phi_6}{dt}&=-\left(\alpha+\frac{\beta\eta_2I_6(\gamma+\lambda)}{\beta\gamma+\lambda}\right)\frac{(S-S_6)^2}{S}+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1S_6V_6\left(4-\frac{S_6}{S}-\frac{SVL_6}{S_6V_6L}-\frac{LI_6}{L_6I}-\frac{IV_6}{I_6V}\right)\\&+\frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2S_6I_6\left(3-\frac{S_6}{S}-\frac{SIL_6}{S_6I_6L}-\frac{LI_6}{L_6I}\right)+\frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1S_6V_6\left(3-\frac{S_6}{S}-\frac{SVI_6}{S_6V_6I}-\frac{IV_6}{I_6V}\right)\\&+\eta_3S_6Y_6\left(3-\frac{S_6}{S}-\frac{SYE_6}{S_6Y_6E}-\frac{EY_6}{E_6Y}\right)\\&+\frac{\mu_1(\gamma+\lambda)\left[\pi_1\sigma_2(\eta_1b+\eta_2\varepsilon)+\pi_2\eta_3\varepsilon\sigma_1+\alpha\varepsilon\sigma_1\sigma_2\right]}{\sigma_1\sigma_2(\beta\gamma+\lambda)(\eta_1b+\eta_2\varepsilon)}(\Re_7-1)C^I.\end{aligned}$$

Therefore, if $\Re_7\le1$, then using inequalities (5.1)–(5.4) we get $\frac{d\Phi_6}{dt}\le0$ for all $S,L,I,E,Y,V,C^I,C^Y>0$, where $\frac{d\Phi_6}{dt}=0$ at $S=S_6$, $L=L_6$, $I=I_6$, $E=E_6$, $Y=Y_6$, $V=V_6$ and $C^I=0$. Define

$\Upsilon_6 = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_6}{dt} = 0\right\}$ and let Υ_6' be the largest invariant subset of Υ_6. The solutions of system (2.1) tend to Υ_6' which includes elements with $E = E_6$, $Y = Y_6$, and then $\dot{Y} = 0$. The fifth equation of system (2.1) implies

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

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

Theorem 8. If $\mathfrak{R}_7 > 1$ and $\mathfrak{R}_8 > 1$, then Đ_7 is G.A.S.

Proof. Define $\Phi_7(S, L, I, E, Y, V, C^I, C^Y)$ as:

$$\Phi_7 = S_7 F\left(\frac{S}{S_7}\right) + \frac{\lambda}{\beta\gamma + \lambda} L_7 F\left(\frac{L}{L_7}\right) + \frac{\gamma + \lambda}{\beta\gamma + \lambda} I_7 F\left(\frac{I}{I_7}\right) + \frac{1}{\varphi} E_7 F\left(\frac{E}{E_7}\right) + \frac{\psi + \omega}{\varphi\psi} Y_7 F\left(\frac{Y}{Y_7}\right)$$
$$+ \frac{\eta_1 S_7}{\varepsilon} V_7 F\left(\frac{V}{V_7}\right) + \frac{\mu_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C_7^I F\left(\frac{C^I}{C_7^I}\right) + \frac{\mu_2 (\psi + \omega)}{\varphi\psi\sigma_2} C_7^Y F\left(\frac{C^Y}{C_7^Y}\right).$$

Calculating $\frac{d\Phi_7}{dt}$ and after collecting terms we get

$$\frac{d\Phi_7}{dt} = \left(1 - \frac{S_7}{S}\right)(\rho - \alpha S) + \eta_2 S_7 I + \eta_3 S_7 Y - \frac{\lambda (1 - \beta)}{\beta\gamma + \lambda} (\eta_1 S V + \eta_2 S I) \frac{L_7}{L} + \frac{\lambda (\gamma + \lambda)}{\beta\gamma + \lambda} L_7$$
$$- \frac{a (\gamma + \lambda)}{\beta\gamma + \lambda} I - \frac{\beta (\gamma + \lambda)}{\beta\gamma + \lambda} (\eta_1 S V + \eta_2 S I) \frac{I_7}{I} - \frac{\lambda (\gamma + \lambda)}{\beta\gamma + \lambda} L \frac{I_7}{I} + \frac{a (\gamma + \lambda)}{\beta\gamma + \lambda} I_7 + \frac{\mu_1 (\gamma + \lambda)}{\beta\gamma + \lambda} C^I I_7$$
$$- \eta_3 S Y \frac{E_7}{E} + \frac{\psi + \omega}{\varphi} E_7 - \frac{\delta (\psi + \omega)}{\varphi\psi} Y - \frac{\psi + \omega}{\varphi} E \frac{Y_7}{Y} + \frac{\delta (\psi + \omega)}{\varphi\psi} Y_7 + \frac{\mu_2 (\psi + \omega)}{\varphi\psi} C^Y Y_7$$
$$+ \eta_1 S_7 \frac{bI}{\varepsilon} - \eta_1 S_7 V_7 \frac{bI}{\varepsilon V} + \eta_1 S_7 V_7 - \frac{\mu_1 \pi_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C^I - \frac{\mu_1 (\gamma + \lambda)}{\beta\gamma + \lambda} C_7^I I + \frac{\mu_1 \pi_1 (\gamma + \lambda)}{\sigma_1 (\beta\gamma + \lambda)} C_7^I$$
$$- \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi\psi\sigma_2} C^Y - \frac{\mu_2 (\psi + \omega)}{\varphi\psi} C_7^Y Y + \frac{\mu_2 \pi_2 (\psi + \omega)}{\varphi\psi\sigma_2} C_7^Y.$$

Using the equilibrium conditions for Đ_7:

$$\rho = \alpha S_7 + \eta_1 S_7 V_7 + \eta_2 S_7 I_7 + \eta_3 S_7 Y_7, \quad \frac{\lambda (1 - \beta)}{\beta\gamma + \lambda} (\eta_1 S_7 V_7 + \eta_2 S_7 I_7) = \frac{\lambda (\gamma + \lambda)}{\beta\gamma + \lambda} L_7,$$
$$\eta_1 S_7 V_7 + \eta_2 S_7 I_7 = \frac{a (\gamma + \lambda)}{\beta\gamma + \lambda} I_7 + \frac{\mu_1 (\gamma + \lambda)}{\beta\gamma + \lambda} C_7^I I_7, \quad I_7 = \frac{\pi_1}{\sigma_1}, \quad Y_7 = \frac{\pi_2}{\sigma_2}, \quad V_7 = \frac{bI_7}{\varepsilon}$$
$$\eta_3 S_7 Y_7 = \frac{\psi + \omega}{\varphi} E_7 = \frac{\delta (\psi + \omega)}{\varphi\psi} Y_7 + \frac{\mu_2 (\psi + \omega)}{\varphi\psi} C_7^Y Y_7.$$

We obtain

$$\frac{d\Phi_7}{dt} = \left(1 - \frac{S_7}{S}\right)(\alpha S_7 - \alpha S) + (\eta_1 S_7 V_7 + \eta_2 S_7 I_7 + \eta_3 S_7 Y_7)\left(1 - \frac{S_7}{S}\right) - \frac{\lambda (1 - \beta)}{\beta\gamma + \lambda} \eta_1 S_7 V_7 \frac{S V L_7}{S_7 V_7 L}$$
$$- \frac{\lambda (1 - \beta)}{\beta\gamma + \lambda} \eta_2 S_7 I_7 \frac{S I L_7}{S_7 I_7 L} + \frac{\lambda (1 - \beta)}{\beta\gamma + \lambda} (\eta_1 S_7 V_7 + \eta_2 S_7 I_7) - \frac{\beta (\gamma + \lambda)}{\beta\gamma + \lambda} \eta_1 S_7 V_7 \frac{S V I_7}{S_7 V_7 I}$$
$$- \frac{\beta (\gamma + \lambda)}{\beta\gamma + \lambda} \eta_2 S_7 I_7 \frac{S}{S_7} - \frac{\lambda (1 - \beta)}{\beta\gamma + \lambda} (\eta_1 S_7 V_7 + \eta_2 S_7 I_7) \frac{L I_7}{L_7 I} + \eta_1 S_7 V_7 + \eta_2 S_7 I_7$$

$$
\begin{aligned}
&-\eta_3 S_7 Y_7 \frac{SYE_7}{S_7 Y_7 E} + \eta_3 S_7 Y_7 - \eta_3 S_7 Y_7 \frac{EY_7}{E_7 Y} + \eta_3 S_7 Y_7 - \eta_1 S_7 V_7 \frac{IV_7}{I_7 V} + \eta_1 S_7 V_7 \\
&= -\left(\alpha + \frac{\beta\eta_2 I_7 (\gamma+\lambda)}{\beta\gamma+\lambda}\right)\frac{(S-S_7)^2}{S} + \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_1 S_7 V_7 \left(4 - \frac{S_7}{S} - \frac{SVL_7}{S_7 V_7 L} - \frac{LI_7}{L_7 I} - \frac{IV_7}{I_7 V}\right) \\
&+ \frac{\lambda(1-\beta)}{\beta\gamma+\lambda}\eta_2 S_7 I_7 \left(3 - \frac{S_7}{S} - \frac{SIL_7}{S_7 I_7 L} - \frac{LI_7}{L_7 I}\right) + \frac{\beta(\gamma+\lambda)}{\beta\gamma+\lambda}\eta_1 S_7 V_7 \left(3 - \frac{S_7}{S} - \frac{SVI_7}{S_7 V_7 I} - \frac{IV_7}{I_7 V}\right) \\
&+ \eta_3 S_7 Y_7 \left(3 - \frac{S_7}{S} - \frac{SYE_7}{S_7 Y_7 E} - \frac{EY_7}{E_7 Y}\right).
\end{aligned}
$$

Therefore, using inequalities (5.1)–(5.4) we get $\frac{d\Phi_7}{dt} \leq 0$ for all $S, L, I, E, Y, V, C^I, C^Y > 0$. In addition we have $\frac{d\Phi_7}{dt} = 0$ at $S = S_7$, $L = L_7$, $I = I_7$, $E = E_7$, $Y = Y_7$ and $V = V_7$. The solutions of system (2.1) converge to Υ_7' the largest invariant subset of $\Upsilon_7 = \left\{(S, L, I, E, Y, V, C^I, C^Y) : \frac{d\Phi_7}{dt} = 0\right\}$. The set Υ_7' contains elements with $S = S_7$, $L = L_7$, $I = I_7$, $E = E_7$, $Y = Y_7$ and $V = V_7$. Then $\dot{I} = \dot{Y} = 0$ and from the third and fifth equations of system (2.1) we get

$$
\begin{aligned}
0 = \dot{I} &= \beta(\eta_1 S_7 V_7 + \eta_2 S_7 I_7) + \lambda L_7 - aI_7 - \mu_1 C^I I_7, \\
0 = \dot{Y} &= \psi E_7 - \delta Y_7 - \mu_2 C^Y Y_7,
\end{aligned}
$$

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

In Table 3, we summarize the global stability results given in Theorems 1–8.

Table 3. Global stability conditions of the equilibria of model (2.1).

Equilibrium point	Global stability conditions
$Đ_0 = (S_0, 0, 0, 0, 0, 0, 0, 0)$	$\Re_1 \leq 1$ and $\Re_2 \leq 1$
$Đ_1 = (S_1, L_1, I_1, 0, 0, V_1, 0, 0)$	$\Re_1 > 1$, $\Re_2/\Re_1 \leq 1$ and $\Re_3 \leq 1$
$Đ_2 = (S_2, 0, 0, E_2, Y_2, 0, 0, 0)$	$\Re_2 > 1$, $\Re_1/\Re_2 \leq 1$ and $\Re_4 \leq 1$
$Đ_3 = (S_3, L_3, I_3, 0, 0, V_3, C_3^I, 0)$	$\Re_3 > 1$ and $\Re_5 \leq 1$
$Đ_4 = (S_4, 0, 0, E_4, Y_4, 0, 0, C_4^Y)$	$\Re_4 > 1$ and $\Re_6 \leq 1$
$Đ_5 = (S_5, L_5, I_5, E_5, Y_5, V_5, C_5^I, 0)$	$\Re_5 > 1$, $\Re_8 \leq 1$ and $\Re_1/\Re_2 > 1$
$Đ_6 = (S_6, L_6, I_6, E_6, Y_6, V_6, 0, C_6^Y)$	$\Re_6 > 1$, $\Re_7 \leq 1$ and $\Re_2/\Re_1 > 1$
$Đ_7 = (S_7, L_7, I_7, E_7, Y_7, V_7, C_7^I, C_7^Y)$	$\Re_7 > 1$ and $\Re_8 > 1$

6. Numerical results and discussions

In this section, we illustrate the results of Theorems 1–8 by performing numerical simulations. Moreover, we study the effect of HTLV-I infection on the HIV mono-infected individuals by making a comparison between the dynamics of HIV mono-infection and HIV/HTLV-I co-infection. Otherwise, we investigate the influence of HIV infection on the HTLV-I mono-infected individuals by conducting a comparison between the dynamics of HTLV-I mono-infection and HIV/HTLV-I co-infection.

To solve system (2.1) numerically we fix the values of some parameters (see Table 4) and the others will be varied.

6.1. Stability of the equilibria

In this subsection, we choose the following three different initial conditions for system (2.1):

Table 4. The data of model (2.1).

Parameter	Value	Parameter	Value	Parameter	Value
ρ	10	δ	0.2	β	0.7
α	0.01	b	5	γ	0.02
η_1	Varied	π_1	0.1	σ_1	Varied
η_2	Varied	π_2	0.1	σ_2	Varied
η_3	Varied	μ_1	0.2	λ	0.2
a	0.5	μ_2	0.2	ω	0.01
φ	0.2	ε	2	ψ	0.003

Initial-1 : $(S(0), L(0), I(0), E(0), Y(0), V(0), C^I(0), C^Y(0)) = (600, 1.5, 1.5, 30, 0.3, 5, 1, 3)$,
Initial-2: $(S(0), L(0), I(0), E(0), Y(0), V(0), C^I(0), C^Y(0)) = (500, 1, 1, 20, 0.2, 2, 2, 2)$,
Initial-3: $(S(0), L(0), I(0), E(0), Y(0), V(0), C^I(0), C^Y(0)) = (300, 0.5, 0.5, 10, 0.1, 1.5, 3, 1)$.

Choosing selected values of η_1, η_2, η_3, σ_1 and σ_2 under the above initial conditions leads to the following scenarios:

Scenario 1 (Stability of Đ$_0$): $\eta_1 = \eta_2 = 0.0001$, $\eta_3 = 0.001$ and $\sigma_1 = \sigma_2 = 0.2$. For this set of parameters, we have $\Re_1 = 0.68 < 1$ and $\Re_2 = 0.23 < 1$. Figure 2 displays that the trajectories initiating with Initial-1, Initial-2 and Initial-3 reach the equilibrium 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.

Scenario 2 (Stability of Đ$_1$): $\eta_1 = 0.0005$, $\eta_2 = 0.0003$, $\eta_3 = 0.0005$, $\sigma_1 = 0.003$ and $\sigma_2 = 0.2$. With such choice we get $\Re_2 = 0.12 < 1 < 3.02 = \Re_1$, $\Re_3 = 0.49 < 1$ and hence $\Re_2/\Re_1 = 0.04 < 1$. Therefore, the conditions in Table 2 is verified. In fact, the equilibrium point Đ$_1$ exists with Đ$_1 = (331.63, 9.11, 13, 0, 0, 32.51, 0, 0)$. Figure 3 displays that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to Đ$_1$. Therefore, the numerical results support Theorem 2. This case corresponds to a chronic HIV mono-infection but with unstimulated CTL-mediated immune response.

Scenario 3 (Stability of Đ$_2$): $\eta_1 = 0.0001$, $\eta_2 = 0.0002$, $\eta_3 = 0.01$, $\sigma_1 = 0.001$ and $\sigma_2 = 0.05$. Then, we calculate $\Re_1 = 0.88 < 1 < 2.31 = \Re_2$, $\Re_4 = 0.77 < 1$ and then $\Re_1/\Re_2 = 0.38 < 1$. Hence, the conditions in Table 2 is satisfied. The numerical results show that Đ$_2 = (433.33, 0, 0, 87.18, 1.31, 0, 0, 0)$ exists. Figure 4 illustrates that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to Đ$_2$. Thus, the numerical results consistent with Theorem 3. This situation leads to a persistent HTLV mono-infection with unstimulated CTL-mediated immune response.

Scenario 4 (Stability of Đ$_3$): $\eta_1 = 0.001$, $\eta_2 = 0.0001$, $\eta_3 = 0.005$ and $\sigma_1 = \sigma_2 = 0.01$. Then, we calculate $\Re_3 = 1.41 > 1$ and $\Re_5 = 0.32 < 1$. Table 2 and Figure 5 show that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to Đ$_3 = (277.78, 9.85, 10, 0, 0, 25, 1.01, 0)$. Therefore, Đ$_3$ is G.A.S and this agrees with Theorem 4. Hence, a chronic HIV mono-infection with HIV-specific CTL-mediated immune response is attained.

Scenario 5 (Stability of Đ$_4$): $\eta_1 = 0.0007$, $\eta_2 = 0.0001$, $\eta_3 = 0.1$, $\sigma_1 = 0.05$ and $\sigma_2 = 0.3$. Then, we calculate $\Re_4 = 5.33 > 1$ and $\Re_6 = 0.83 < 1$. According to Table 2, Đ$_4$ exists with Đ$_4 = (230.77, 0, 0, 118.34, 0.33, 0, 0, 4.33)$. In Figure 6, we show that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to Đ$_4$ and then it is G.A.S which agrees with Theorem 5. Hence, a chronic HTLV mono-infection with HTLV-specific CTL-mediated immune response is attained.

Scenario 6 (Stability of Đ$_5$): $\eta_1 = 0.001$, $\eta_2 = 0.0001$, $\eta_3 = 0.01$, $\sigma_1 = 0.05$ and $\sigma_2 = 0.08$. Then, we calculate $\Re_5 = 1.52 > 1$, $\Re_8 = 0.83 < 1$ and $\Re_1/\Re_2 = 2.19 > 1$. Table 2 and the numerical results demonstrated in Figure 7 show that $Đ_5 = (433.33, 3.07, 2, 52.51, 0.79, 5, 2.98, 0)$ exists and it is G.A.S and this agrees with Theorem 6. As a result, a chronic co-infection with HIV and HTLV is attained where the HIV-specific CTL-mediated immune response is active and the HTLV-specific CTL-mediated immune response is unstimulated.

Scenario 7 (Stability of $Đ_6$): $\eta_1 = 0.0006$, $\eta_2 = 0.0001$, $\eta_3 = 0.04$, $\sigma_1 = 0.01$ and $\sigma_2 = 0.5$. We compute $\Re_6 = 1.73 > 1$, $\Re_7 = 0.92 < 1$ and $\Re_2/\Re_1 = 2.97 > 1$. Based on the conditions in Table 2, the equilibrium $Đ_6 = (321.26, 5.75, 8.2, 39.54, 0.2, 20.51, 0, 1.97)$ exists. Moreover, the numerical results plotted in Figure 8 show that $Đ_6$ is G.A.S and this illustrates Theorem 7. As a result, a chronic co-infection with HIV and HTLV is attained where the HTLV-specific CTL-mediated immune response is active and the HIV-specific CTL-mediated immune response is unstimulated.

Scenario 8 (Stability of $Đ_7$): $\eta_1 = 0.0006$, $\eta_2 = 0.0002$, $\eta_3 = 0.04$, $\sigma_1 = 0.05$ and $\sigma_2 = 0.5$. These data give $\Re_7 = 1.55 > 1$ and $\Re_8 = 4.31 > 1$. According to Table 2, the equilibrium $Đ_7$ exists. Figure 9 illustrates that the trajectories initiating with Initial-1, Initial-2 and Initial-3 tend to $Đ_7 = (467.29, 2.17, 2, 57.51, 0.2, 5, 1.36, 3.31)$. The numerical results displayed in Figure 9 show that $Đ_7$ is G.A.S based on Theorem 8. In this case, a chronic co-infection with HIV and HTLV is attained where both HIV-specific CTL-mediated and HTLV-specific CTL-mediated immune responses are working.

To further confirmation, we calculate the Jacobian matrix $J = J(S, L, I, E, Y, V, C^I, C^Y)$ of system (2.1) as in the following form:

$$J = \begin{pmatrix} -(\alpha+\eta_1 V+\eta_2 I+\eta_3 Y) & 0 & -\eta_2 S & 0 & -\eta_3 S & -\eta_1 S & 0 & 0 \\ (1-\beta)(\eta_1 V+\eta_2 I) & -(\gamma+\lambda) & (1-\beta)\eta_2 S & 0 & 0 & (1-\beta)\eta_1 S & 0 & 0 \\ \beta(\eta_1 V+\eta_2 I) & \lambda & \beta\eta_2 S-\left(a+\mu_1 C^I\right) & 0 & 0 & \beta\eta_1 S & -\mu_1 I & 0 \\ \varphi\eta_3 Y & 0 & 0 & -(\psi+\omega) & \varphi\eta_3 S & 0 & 0 & 0 \\ 0 & 0 & 0 & \psi & -\left(\delta+\mu_2 C^Y\right) & 0 & 0 & -\mu_2 Y \\ 0 & 0 & b & 0 & 0 & -\varepsilon & 0 & 0 \\ 0 & 0 & \sigma_1 C^I & 0 & 0 & 0 & \sigma_1 I-\pi_1 & 0 \\ 0 & 0 & 0 & 0 & \sigma_2 C^Y & 0 & 0 & \sigma_2 Y-\pi_2 \end{pmatrix}.$$

Then, we calculate the eigenvalues λ_i, $i = 1, 2, ..., 8$ of the matrix J at each equilibrium. The examined steady will be locally stable if all its eigenvalues satisfy the following condition:

$$\mathrm{Re}(\lambda_i) < 0, \; i = 1, 2, ..., 8.$$

We use the parameters η_1, η_2, η_3, σ_1 and σ_2 the same as given above to compute all positive equilibria and the corresponding eigenvalues. From the scenarios 1–8, we present in Table 5 the positive equilibria, the real parts of the eigenvalues and whether the equilibrium is locally stable or unstable.

6.2. Comparison results

In this subsection, we study the influence of HTLV-I infection on HIV mono-infection dynamics, and how affect the HIV infection on the dynamics of HTLV-I mono-infection as well.

6.2.1. Impact of HTLV-I infection on HIV mono-infection dynamics

To investigate the effect of HTLV-I infection on HIV mono-infection dynamics, we make a comparison between model (2.1) and the following HIV mono-infection model:

$$\begin{cases} \dot{S} = \rho - \alpha S - \eta_1 S V - \eta_2 S I, \\ \dot{L} = (1-\beta)(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma) L, \\ \dot{I} = \beta\eta_1 (\eta_1 S V + \eta_2 S I) + \lambda L - a I - \mu_1 C^I I, \\ \dot{V} = b I - \varepsilon V, \\ \dot{C^I} = \sigma_1 C^I I - \pi_1 C^I. \end{cases} \tag{6.1}$$

Table 5. Local stability of positive equilibria Đ$_i$, $i = 0, 1, ..., 7$.

Scenario	The equilibria	$(\mathrm{Re}(\lambda_i), i = 1, 2, ..., 6)$	Stability
1	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-2.19, -0.37, -0.2, -0.1, -0.1, -0.09, -0.01, -0.01)$	stable
2	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-2.7, 0.51, -0.32, -0.2, -0.1, -0.1, -0.01, -0.01)$	unstable
	Đ$_1 = (331.63, 9.11, 13, 0, 0, 32.51, 0, 0)$	$(-2.3, -0.35, -0.2, -0.1, -0.02, -0.02, -0.06, -0.01)$	stable
3	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-2.18, -0.36, -0.23, -0.1, -0.1, -0.03, 0.01, -0.01)$	unstable
	Đ$_2 = (433.33, 0, 0, 87.18, 1.31, 0, 0, 0)$	$(-2.09, -0.41, -0.21, -0.16, -0.1, -0.03, -0.01, -0.01)$	stable
4	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-3.22, 0.88, -0.31, -0.21, -0.1, -0.1, -0.01, 0.002)$	unstable
	Đ$_1 = (197.7, 10.94, 15.61, 0, 0, 39.02, 0, 0)$	$(-2.36, -0.35, -0.2, -0.03, -0.03, -0.1, 0.06, -0.01)$	unstable
	Đ$_2 = (866.67, 0, 0, 20.51, 0.31, 0, 0, 0)$	$(-3.1, 0.76, -0.32, -0.21, -0.1, -0.1, -0.01, -0.002)$	unstable
	Đ$_3 = (277.78, 9.85, 10, 0, 0, 25, 1.01, 0)$	$(-2.51, -0.37, -0.2, -0.02, -0.02, -0.1, -0.02, -0.01)$	stable
5	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-2.94, 0.61, -0.37, -0.32, 0.16, -0.1, -0.1, -0.01)$	unstable
	Đ$_1 = (277.85, 9.85, 14.05, 0, 0, 35.12, 0, 0)$	$(-2.35, 0.6, -0.35, -0.27, -0.1, -0.02, -0.02, 0.05)$	unstable
	Đ$_2 = (43.33, 0, 0, 147.18, 2.21, 0, 0, 0)$	$(-2.06, 0.56, -0.45, -0.27, -0.2, -0.16, -0.1, -0.01)$	unstable
	Đ$_3 = (729.93, 3.68, 2, 0, 0, 5, 4.07, 0)$	$(-2.99, -0.43, -0.34, -0.03, -0.03, 0.12, -0.1, -0.01)$	unstable
	Đ$_4 = (230.77, 0, 0, 118.34, 0.33, 0, 0, 4.33)$	$(-2.3, -0.99, -0.36, -0.1, -0.06, -0.06, -0.05, -0.01)$	stable
6	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-3.22, 0.88, -0.31, -0.23, -0.1, -0.1, 0.01, -0.01)$	unstable
	Đ$_1 = (197.7, 10.94, 15.61, 0, 0, 39.02, 0, 0)$	$(-2.36, 0.68, -0.35, -0.21, -0.03, -0.03, -0.1, -0.01)$	unstable
	Đ$_2 = (433.33, 0, 0, 87.18, 1.31, 0, 0, 0)$	$(-2.67, -0.33, 0.3, -0.21, -0.1, -0.01, -0.01, 0.005)$	unstable
	Đ$_3 = (657.89, 4.67, 2, 0, 0, 5, 5.82, 0)$	$(-3.3, -0.45, -0.22, -0.05, -0.05, -0.1, -0.01, 0.01)$	unstable
	Đ$_4 = (444.44, 0, 0, 85.47, 1.25, 0, 0, 0.03)$	$(-2.68, -0.32, 0.32, -0.22, -0.1, -0.01, -0.01, -0.005)$	unstable
	Đ$_5 = (433.33, 3.07, 2, 52.51, 0.79, 5, 2.98, 0)$	$(-2.83, -0.41, -0.21, -0.03, -0.03, -0.04, -0.01, -0.01)$	stable
7	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-2.84, 0.51, -0.32, -0.29, -0.1, -0.1, 0.07, -0.01)$	unstable
	Đ$_1 = (321.26, 9.26, 13.2, 0, 0, 33.01, 0, 0)$	$(-2.35, -0.35, -0.23, -0.1, -0.02, -0.02, 0.03, 0.02)$	unstable
	Đ$_2 = (108.33, 0, 0, 137.18, 2.06, 0, 0, 0)$	$(-2.13, 0.93, -0.42, -0.22, -0.16, -0.1, -0.07, -0.01)$	unstable
	Đ$_3 = (384.62, 8.39, 10, 0, 0, 25, 0.49, 0)$	$(-2.42, -0.36, -0.24, -0.1, -0.01, -0.01, 0.03, -0.01)$	unstable
	Đ$_4 = (555.56, 0, 0, 68.38, 0.2, 0, 0, 4.13)$	$(-2.54, -0.95, -0.33, 0.19, -0.1, -0.07, -0.03, -0.01)$	unstable
	Đ$_6 = (321.26, 5.75, 8.2, 39.54, 0.2, 20.51, 0, 1.97)$	$(-2.35, -0.53, -0.35, -0.02, -0.02, -0.05, -0.02, -0.02)$	stable
8	Đ$_0 = (1000, 0, 0, 0, 0, 0, 0, 0)$	$(-2.83, 0.56, -0.32, -0.29, -0.1, -0.1, 0.07, -0.01)$	unstable
	Đ$_1 = (302.36, 9.51, 13.57, 0, 0, 33.93, 0, 0)$	$(-2.33, 0.58, -0.35, -0.23, -0.1, -0.02, -0.02, 0.02)$	unstable
	Đ$_2 = (108.33, 0, 0, 137.18, 2.06, 0, 0, 0)$	$(-2.13, 0.93, -0.41, -0.22, -0.16, -0.1, -0.07, -0.01)$	unstable
	Đ$_3 = (746.27, 3.46, 2, 0, 0, 5, 3.67, 0)$	$(-2.86, -0.42, -0.27, -0.03, -0.03, -0.1, 0.06, -0.01)$	unstable
	Đ$_4 = (555.56, 0, 0, 68.38, 0.2, 0, 0, 4.13)$	$(-2.53, -0.95, -0.33, 0.22, -0.1, -0.07, -0.03, -0.01)$	unstable
	Đ$_6 = (302.36, 6.21, 8.87, 37.21, 0.2, 22.17, 0, 1.79)$	$(-2.33, -0.5, -0.35, 0.34, -0.02, -0.02, -0.05, -0.02)$	unstable
	Đ$_7 = (467.29, 2.17, 2, 57.51, 0.2, 5, 1.36, 3.31)$	$(-2.52, -0.79, -0.38, -0.01, -0.01, -0.06, -0.03, -0.01)$	stable

We fix parameters $\eta_1 = 0.0006$, $\eta_2 = 0.0001$, $\sigma_1 = 0.05$, and $\sigma_2 = 0.5$ and consider the following initial condition:

Initial-4: $(S(0), L(0), I(0), E(0), Y(0), V(0), C^I(0), C^Y(0)) = (600, 2.4, 1.8, 60, 0.2, 4.5, 1.8, 3.5)$.

We choose two values of the parameter η_3 as $\eta_3 = 0.04$ (HIV/HTLV-I co-infection), and $\eta_3 = 0.0$ (HIV mono-infection). It can be seen from Figure 10 that when the HIV mono-infected individual is co-infected with HTLV-I then the concentrations of susceptible CD4$^+$T cells, latently HIV-infected cells and HIV-specific CTLs are decreased. Although, the concentration of free HIV particles tend to the same value in both HIV mono-infection and HIV/HTLV-I co-infection. Indeed, such observation are compatible with the study that has been performed by Vandormael et al. in 2017 [54]. The researchers have not found any worthy differences in the concentration of HIV virus particles in comparison between HIV mono-infected and HIV/HTLV-I co-infected patients.

6.2.2. Impact of HIV infection on HTLV-I mono-infection dynamics

To investigate the effect of HIV infection on HTLV-I mono-infection dynamics, we make a comparison between model (2.1) and the following HTLV-I mono-infection model:

$$\begin{cases} \dot{S} = \rho - \alpha S - \eta_2 S Y, \\ \dot{E} = \varphi \eta_2 S Y - (\psi + \omega) E, \\ \dot{Y} = \psi E - \delta Y - \mu_2 C^Y Y, \\ \dot{C}^Y = \sigma_2 C^Y Y - \pi_2 C^Y. \end{cases} \tag{6.2}$$

We fix parameters $\eta_3 = 0.01$; $\sigma_1 = 0.05$, and $\sigma_2 = 0.5$ and consider the following initial condition:

Initial-5: $(S(0), L(0), I(0), E(0), Y(0), V(0), C^I(0), C^Y(0)) = (700, 4, 2, 21, 0.198, 5, 4.5, 0.6)$.

We choose two values of the parameters η_1, η_2 as $\eta_1 = 0.001$, $\eta_2 = 0.0002$ (HIV/HTLV-I co-infection), and $\eta_1 = \eta_2 = 0.0$ (HTLV-I mono-infection). It can be seen from Figure 11 that when the HTLV-I mono-infected individual is co-infected with HIV then the concentrations of susceptible CD4$^+$T cells, latently HTLV-infected cells and HTLV-specific CTLs are decreased. Although, the concentration of Tax-expressing HTLV-infected cells tend to the same value in both HTLV-I mono-infection and HIV/HTLV-I co-infection.

6.2.3. Effect of CTL immnue response

As we discussed in Section 1 that CTLs have significant important in controlling HIV and HTLV-I mono-infections by killing infected cells. Model (2.1) in the absence of CTL immune response leads to a model with competition between HIV and HTLV-I on CD4$^+$T cells:

$$\begin{cases} \dot{S} = \rho - \alpha S - \eta_1 S V - \eta_2 S I - \eta_3 S Y, \\ \dot{L} = (1-\beta)(\eta_1 S V + \eta_2 S I) - (\lambda + \gamma) L, \\ \dot{I} = \beta (\eta_1 S V + \eta_2 S I) + \lambda L - a I, \\ \dot{E} = \varphi \eta_3 S Y - (\psi + \omega) E, \\ \dot{Y} = \psi E - \delta Y, \\ \dot{V} = b I - \varepsilon V. \end{cases} \tag{6.3}$$

The system has only three equilibria, infection-free equilibrium, $\overline{Đ}_0 = (S_0, 0, 0, 0, 0, 0)$, chronic HIV mono-infection equilibrium, $\overline{Đ}_1 = (S_1, L_1, I_1, 0, 0, V_1)$ and chronic HTLV mono-infection equilibrium, $\overline{Đ}_2 = (S_2, 0, 0, E_2, Y_2, 0)$, where S_0, S_1, L_1, I_1, V_1, S_2, E_2 and Y_2 are given in Section 4. The existence of the these three equilibria is determined by two threshold parameters $\Re_1$ and $\Re_2$ which are defined in Section 4.

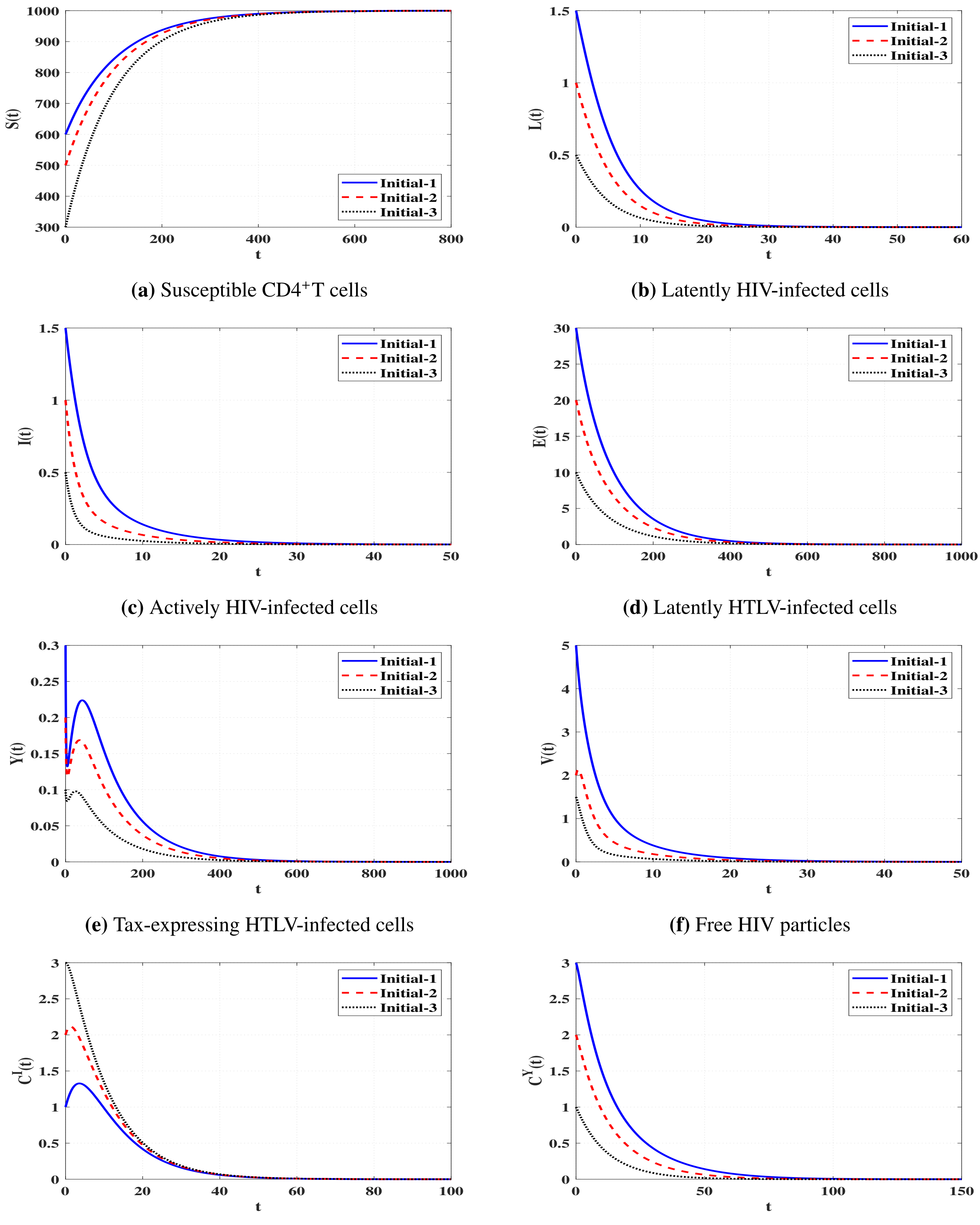
Corollary 1. For system (6.3), the following statements hold true.

(i) If $\Re_1 \le 1$ and $\Re_2 \le 1$, then $\overline{Đ}_0$ is G.A.S.

(ii) If $\Re_1 > 1$ and $\Re_2/\Re_1 \le 1$, then $\overline{Đ}_1$ is G.A.S.

(iii) If $\Re_2 > 1$ and $\Re_1/\Re_2 \le 1$, then $\overline{Đ}_2$ is G.A.S.

Therefore, the system will tend to one of the three equilibria $\overline{Đ}_0$, $\overline{Đ}_1$ and $\overline{Đ}_2$. The above result says that in the absence of immune response, the competition between HIV and HTLV-I consuming common resources, only one type of viruses with maximum basic reproductive ratio can survive. However, in our proposed model (2.1) involving HIV- and HTLV-specific CTLs, HIV and HTLV-I coexist at equilibrium. We can consider this situation as follows. Since CTL immune responses suppress viral progression, the competition between HIV and HTLV-I is also suppressed and the coexistence of HIV and HTLV-I is occurred [55].



(a) Susceptible CD4$^+$T cells

(b) Latently HIV-infected cells

(c) Actively HIV-infected cells

(d) Latently HTLV-infected cells

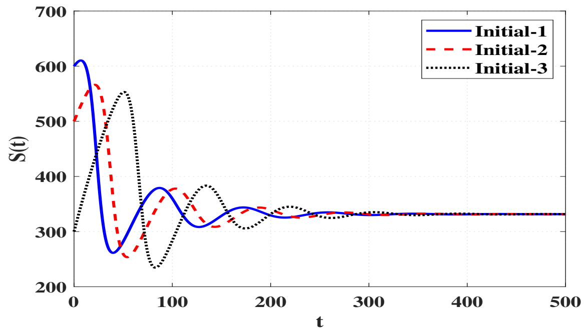
(e) Tax-expressing HTLV-infected cells

(f) Free HIV particles

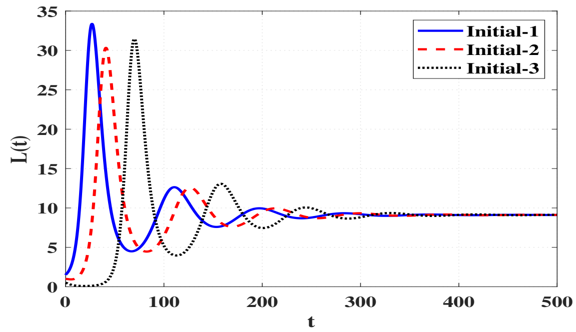
(g) HIV-specific CTLs

(h) HTLV-specific CTLs

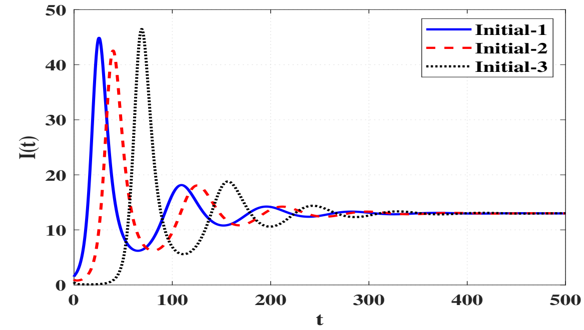
Figure 2. The behavior of solution trajectories of system (2.1) when $\Re_1 \leq 1$ and $\Re_2 \leq 1$.



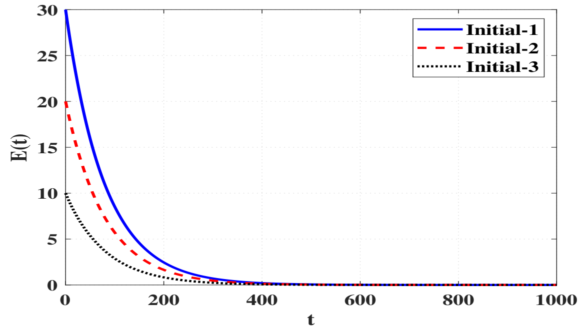
(a) Susceptible CD4^{+}T cells



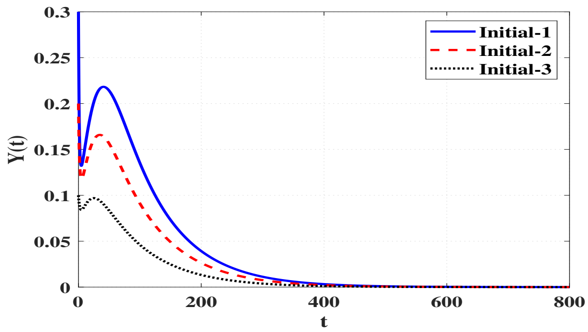
(b) Latently HIV-infected cells



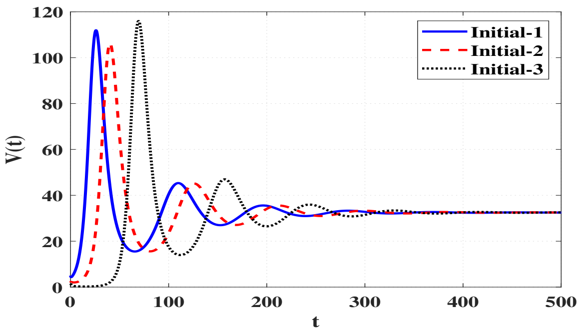
(c) Actively HIV-infected cells



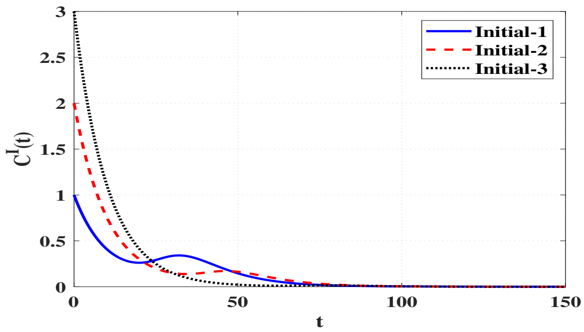
(d) Latently HTLV-infected cells



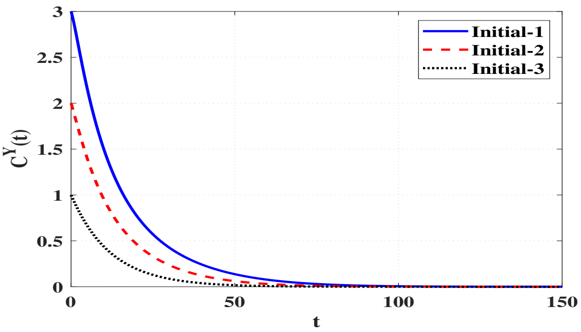
(e) Tax-expressing HTLV-infected cells



(f) Free HIV particles

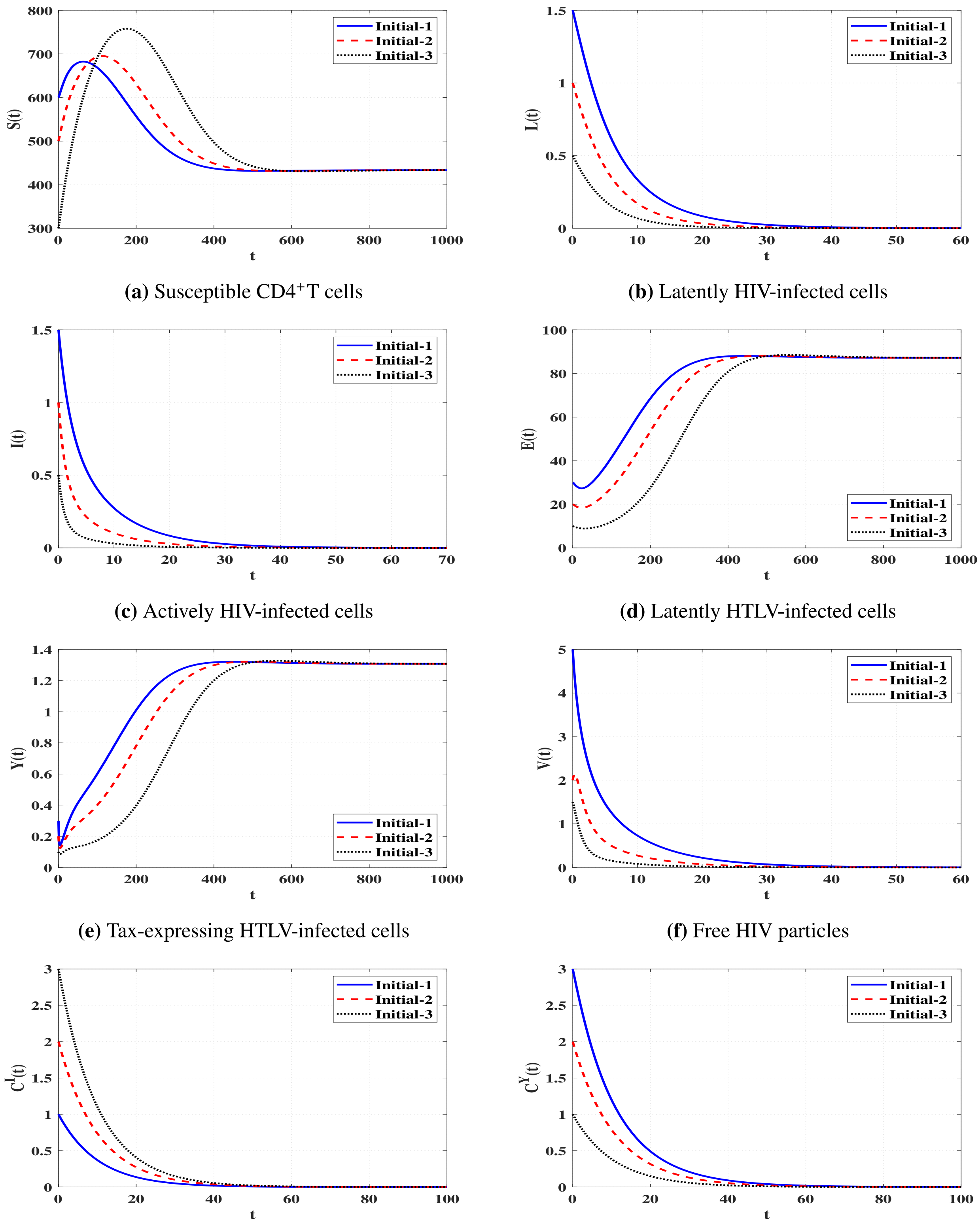


(g) HIV-specific CTLs



(h) HTLV-specific CTLs

Figure 3. The behavior of solution trajectories of system (2.1) when $\Re_1 > 1$, $\Re_2/\Re_1 \leq 1$ and $\Re_3 \leq 1$.



(a) Susceptible CD4$^+$T cells

(b) Latently HIV-infected cells

(c) Actively HIV-infected cells

(d) Latently HTLV-infected cells

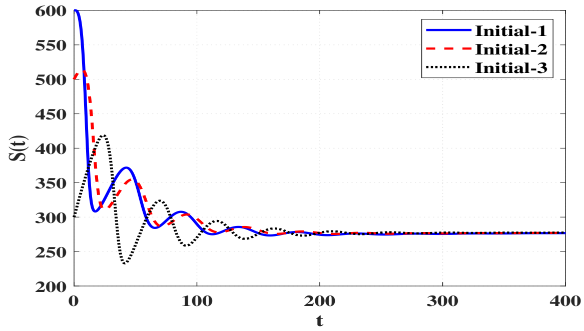
(e) Tax-expressing HTLV-infected cells

(f) Free HIV particles

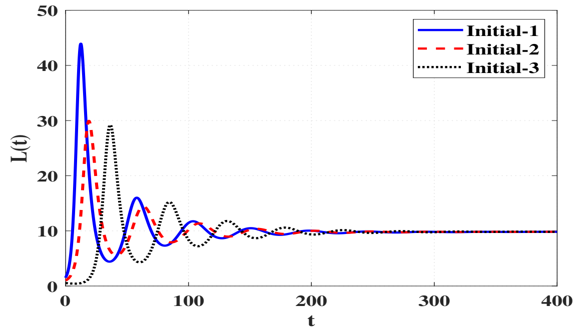
(g) HIV-specific CTLs

(h) HTLV-specific CTLs

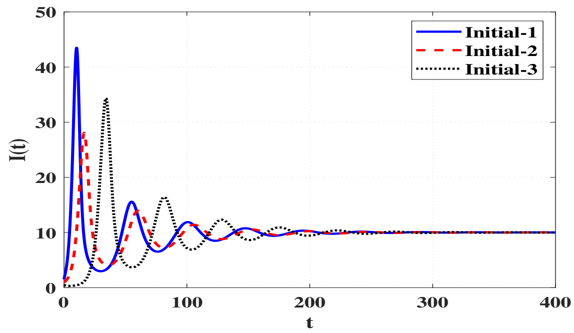
Figure 4. The behavior of solution trajectories of system (2.1) when $\Re_2 > 1$, $\Re_1/\Re_2 \le 1$ and $\Re_4 \le 1$



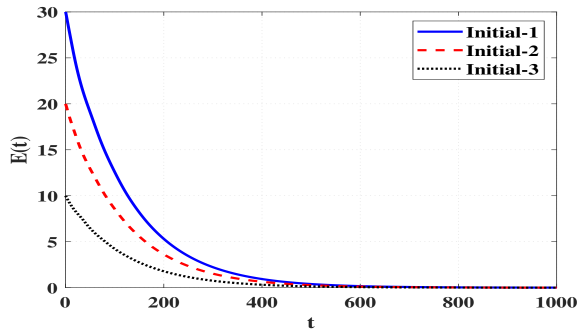
(a) Susceptible CD4$^+$T cells



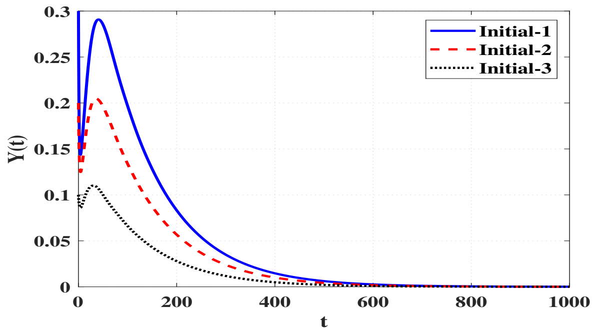
(b) Latently HIV-infected cells



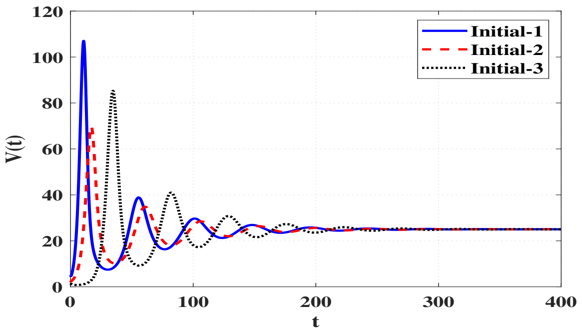
(c) Actively HIV-infected cells



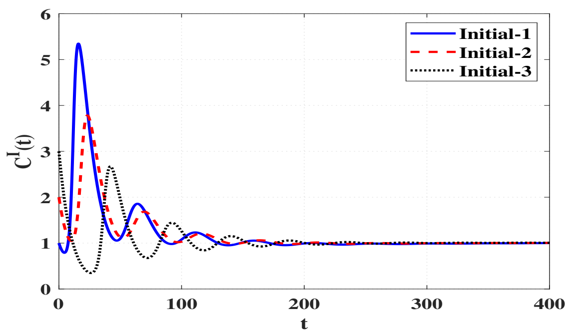
(d) Latently HTLV-infected cells



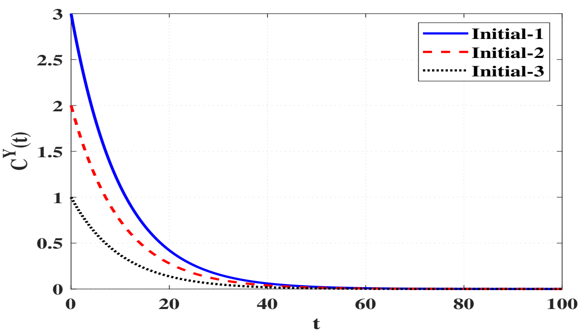
(e) Tax-expressing HTLV-infected cells



(f) Free HIV particles

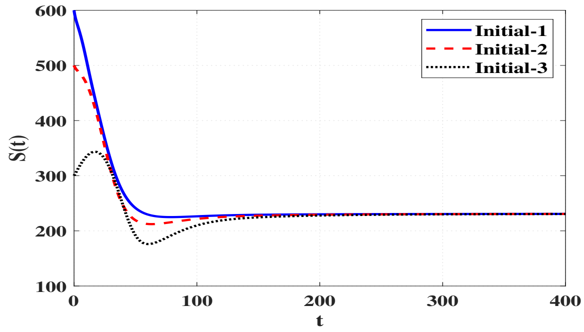


(g) HIV-specific CTLs

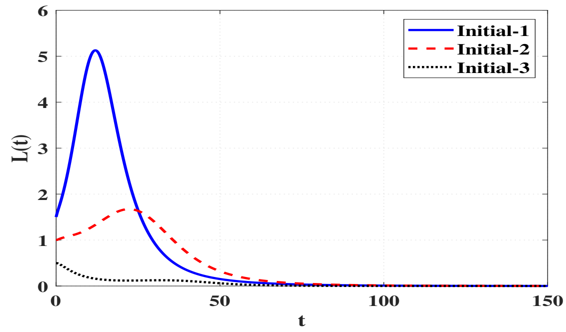


(h) HTLV-specific CTLs

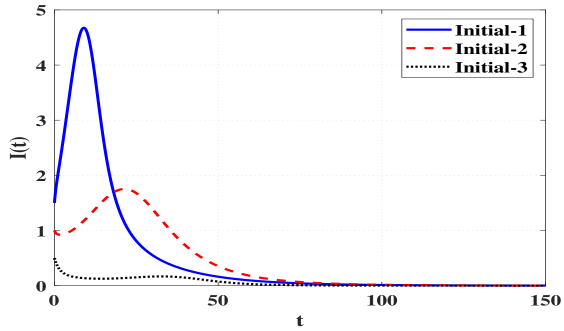
Figure 5. The behavior of solution trajectories of system (2.1) when $\Re_3 > 1$ and $\Re_5 \leq 1$.



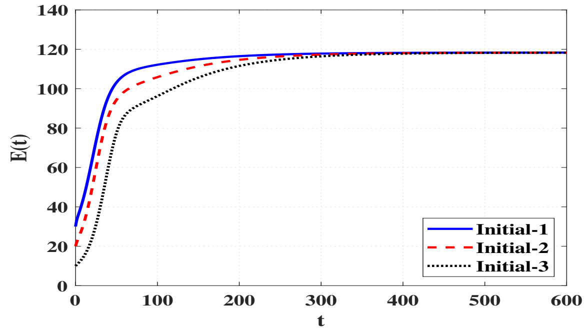
(a) Susceptible CD4$^+$T cells



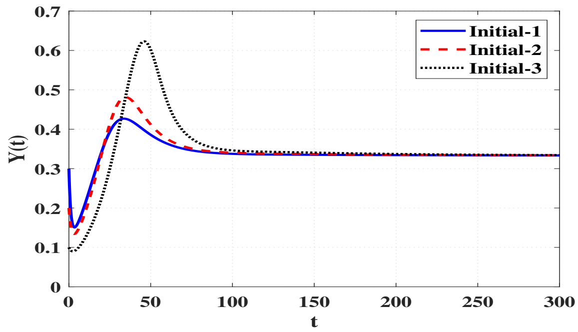
(b) Latently HIV-infected cells



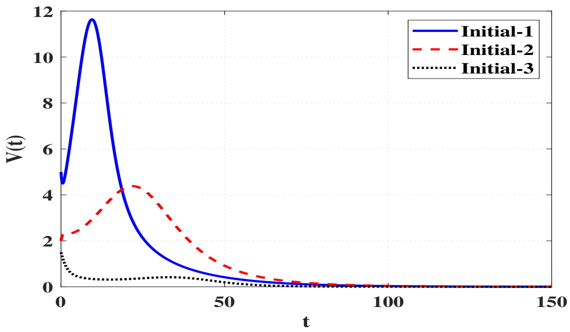
(c) Actively HIV-infected cells



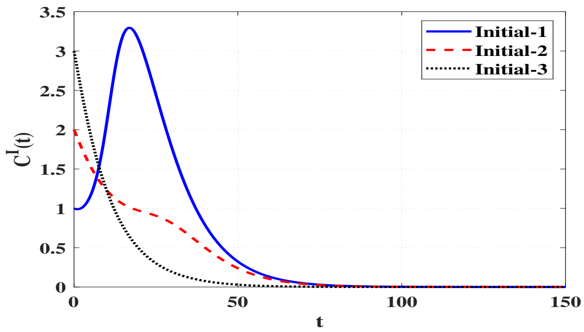
(d) Latently HTLV-infected cells



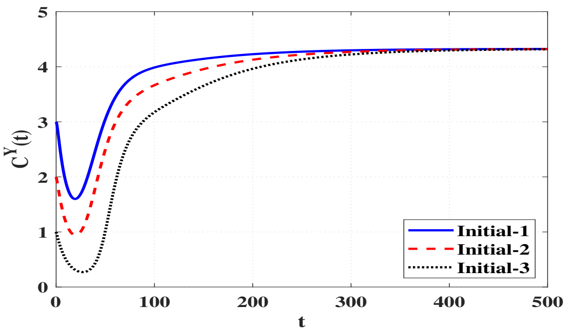
(e) Tax-expressing HTLV-infected cells



(f) Free HIV particles

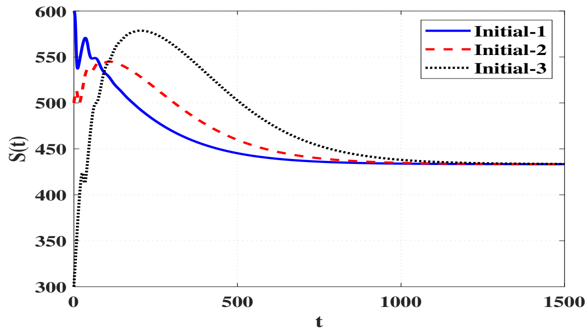


(g) HIV-specific CTLs

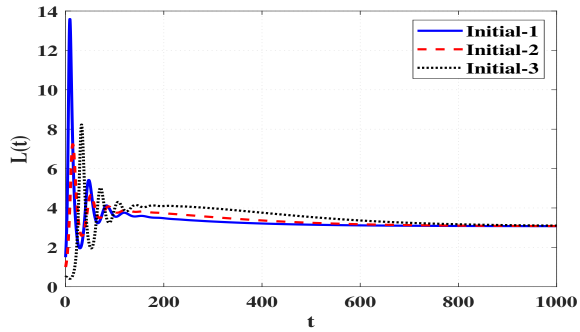


(h) HTLV-specific CTLs

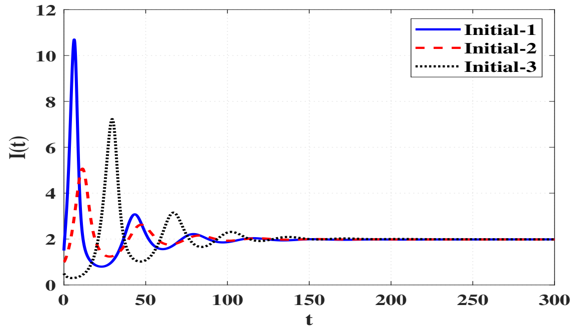
Figure 6. The behavior of solution trajectories of system (2.1) when $\Re_4 > 1$ and $\Re_6 \leq 1$.



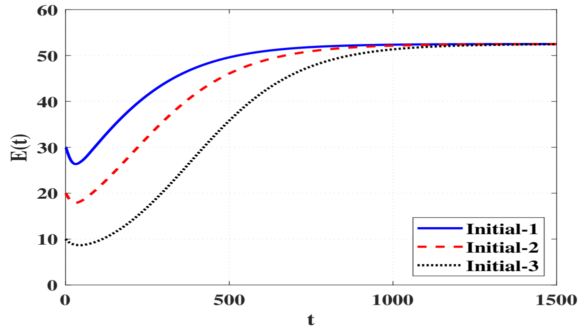
(a) Susceptible CD4^{+}T cells



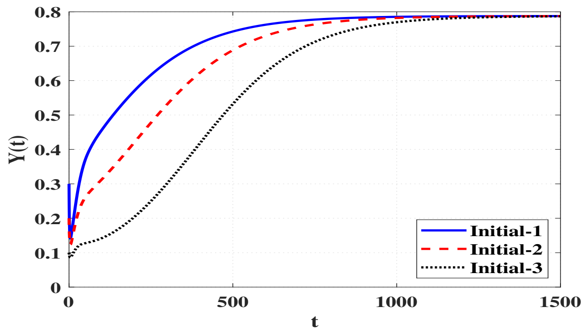
(b) Latently HIV-infected cells



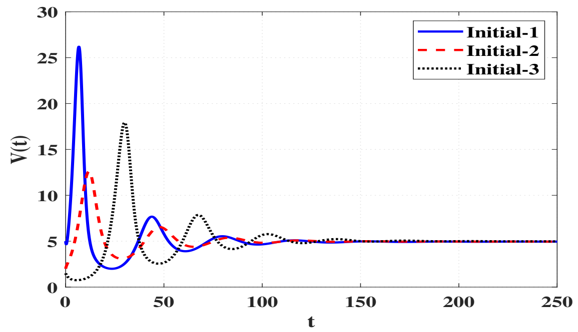
(c) Actively HIV-infected cells



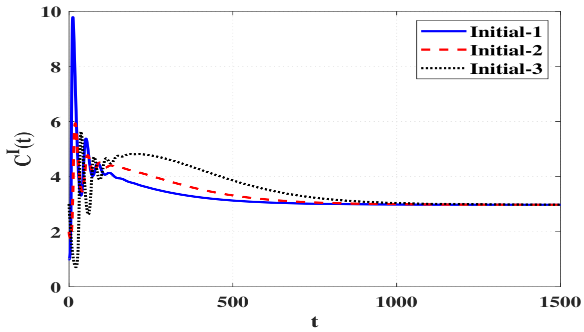
(d) Latently HTLV-infected cells



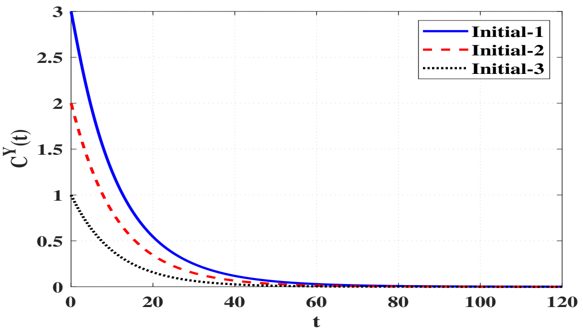
(e) Tax-expressing HTLV-infected cells



(f) Free HIV particles

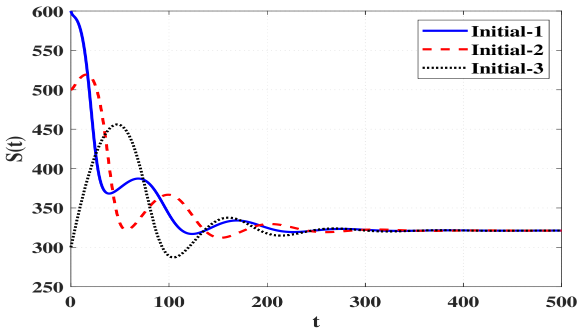


(g) HIV-specific CTLs

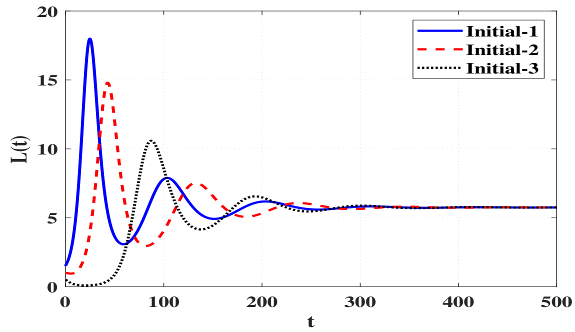


(h) HTLV-specific CTLs

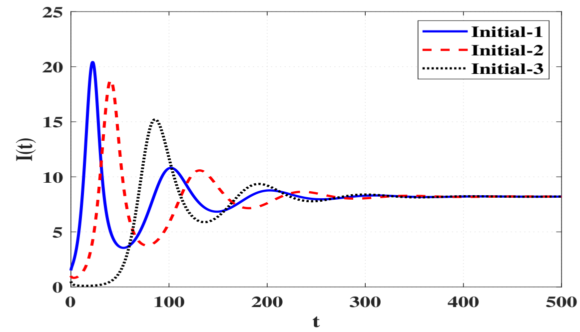
Figure 7. The behavior of solution trajectories of system (2.1) when $\Re_5 > 1$, $\Re_8 \leq 1$ and $\Re_1/\Re_2 > 1$.



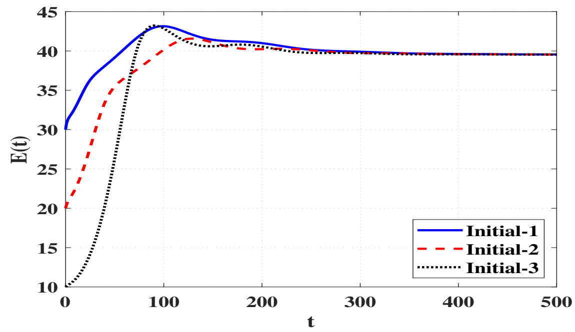
(**a**) Susceptible CD4^{+}T cells



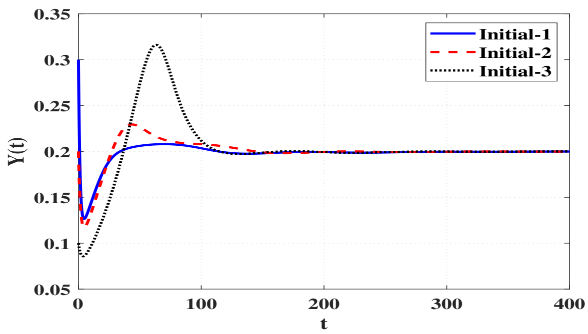
(**b**) Latently HIV-infected cells



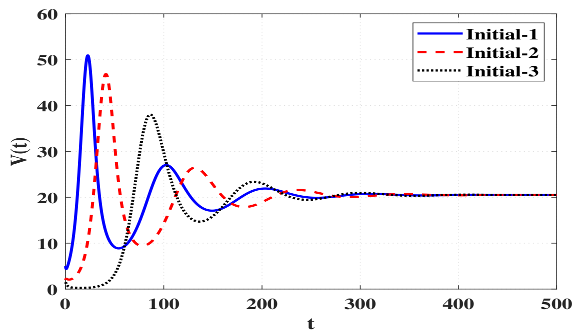
(**c**) Actively HIV-infected cells



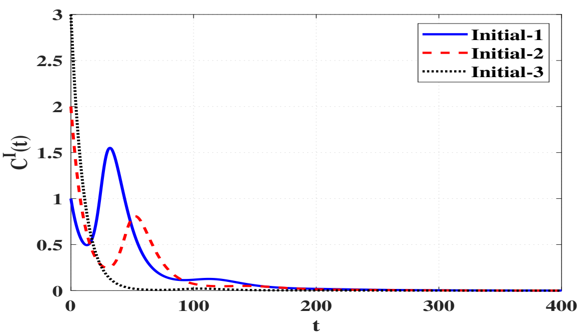
(**d**) Latently HTLV-infected cells



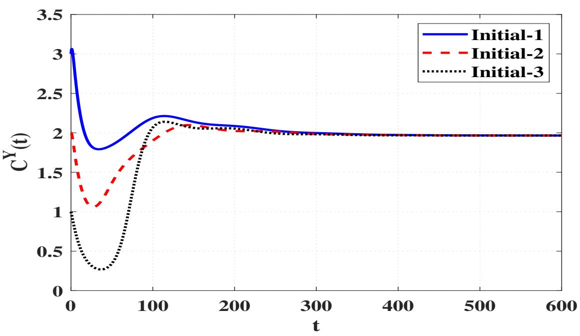
(**e**) Tax-expressing HTLV-infected cells



(**f**) Free HIV particles

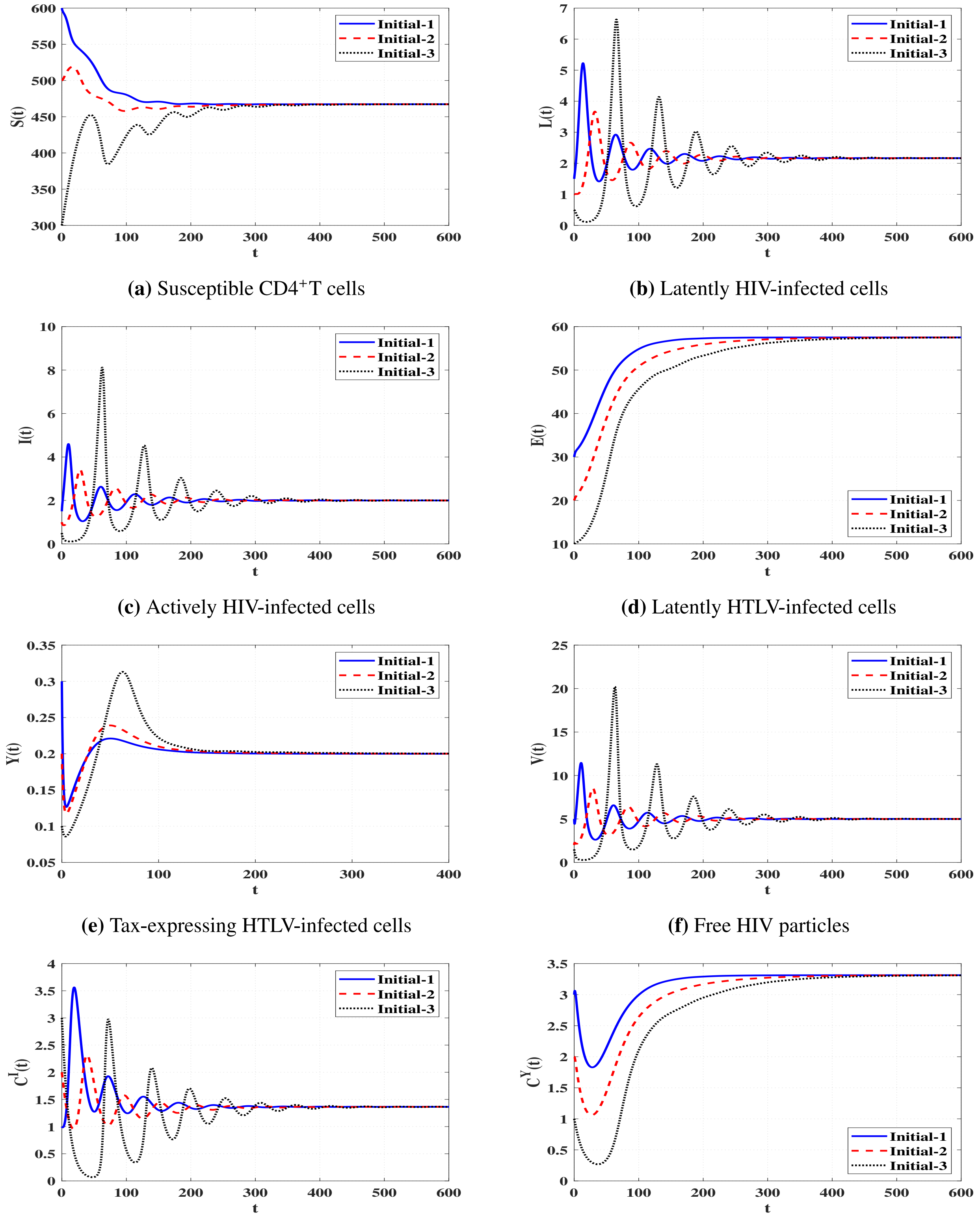


(**g**) HIV-specific CTLs



(**h**) HTLV-specific CTLs

Figure 8. The behavior of solution trajectories of system (2.1) when $\Re_6 > 1$, $\Re_7 \leq 1$ and $\Re_2/\Re_1 > 1$.



(a) Susceptible CD4$^+$T cells

(b) Latently HIV-infected cells

(c) Actively HIV-infected cells

(d) Latently HTLV-infected cells

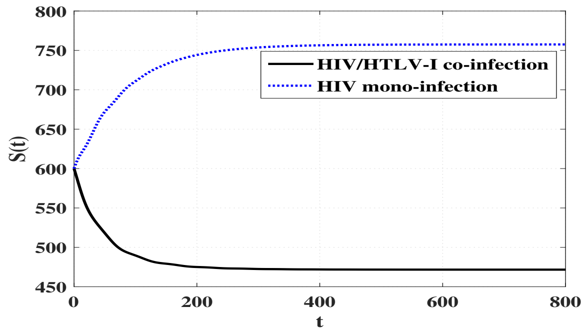
(e) Tax-expressing HTLV-infected cells

(f) Free HIV particles

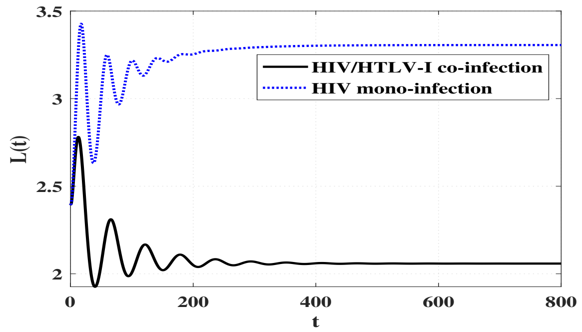
(g) HIV-specific CTLs

(h) HTLV-specific CTLs

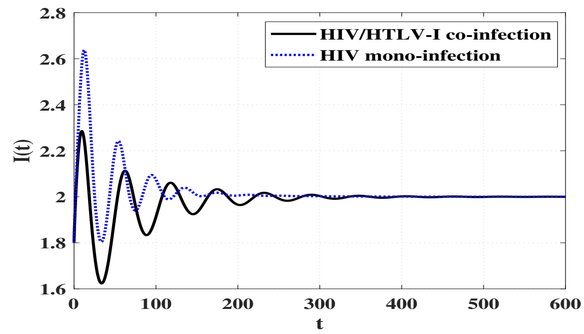
Figure 9. The behavior of solution trajectories of system (2.1) when $\Re_7 > 1$ and $\Re_8 > 1$.



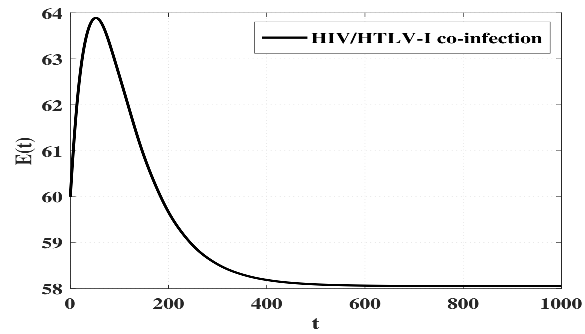
(**a**) Susceptible CD4$^+$T cells



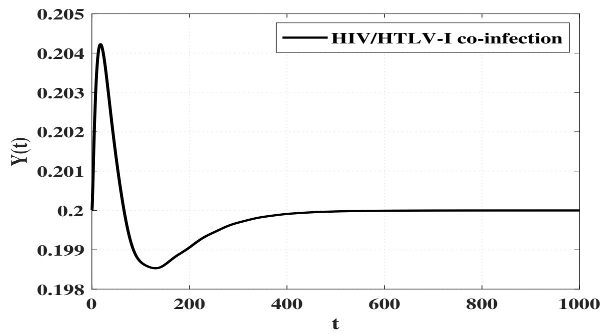
(**b**) Latently HIV-infected cells



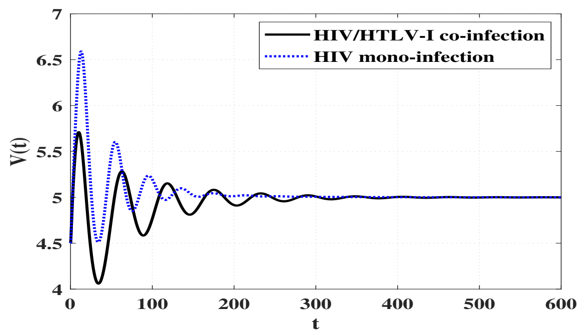
(**c**) Actively HIV-infected cells



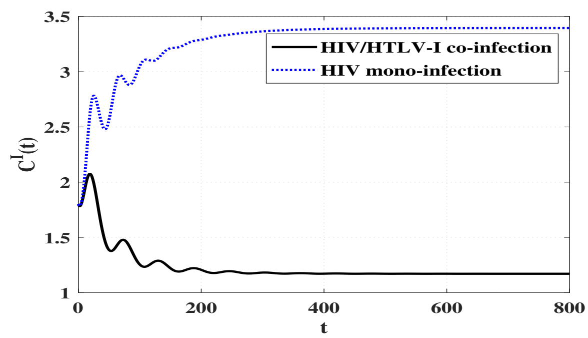
(**d**) Latently HTLV-infected cells



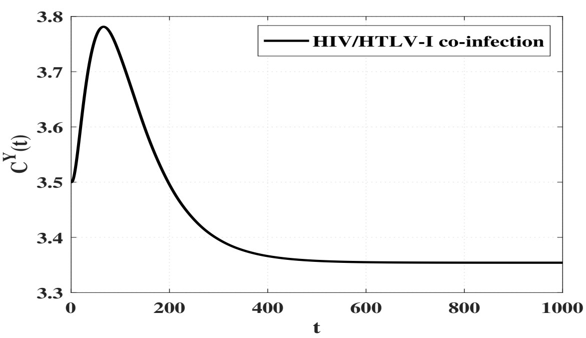
(**e**) Tax-expressing HTLV-infected cells



(**f**) Free HIV particles

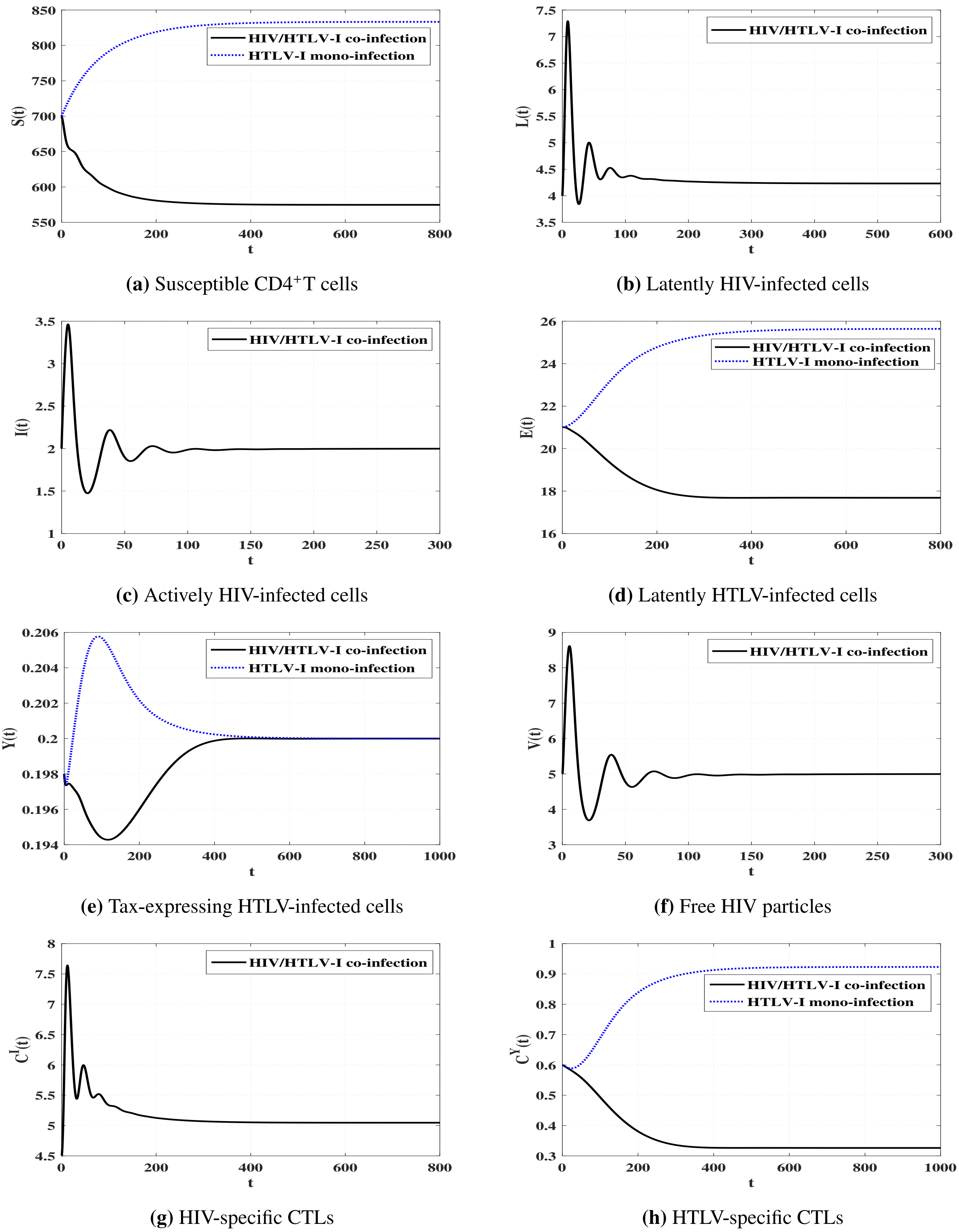


(**g**) HIV-specific CTLs



(**h**) HTLV-specific CTLs

Figure 10. The influence of HTLV-I infection rate ($\eta_3 \neq 0$) on HIV mono-infection dynamics (6.1) will cause a chronic HIV/HTLV-I co-infection.



(**a**) Susceptible CD4$^+$T cells

(**b**) Latently HIV-infected cells

(**c**) Actively HIV-infected cells

(**d**) Latently HTLV-infected cells

(**e**) Tax-expressing HTLV-infected cells

(**f**) Free HIV particles

(**g**) HIV-specific CTLs

(**h**) HTLV-specific CTLs

Figure 11. The influence of HIV infection rates ($\eta_1, \eta_2 \neq 0$) on HTLV mono-infection dynamics (6.2) will cause a chronic HIV/HTLV-I co-infection.

7. Conclusion

This research work formulates a mathematical model which describes the within host dynamics of HIV/HTLV-I co-infection. The model incorporated the effect of HIV-specific CTLs and HTLV-specific CTLs. HIV has two predominant infection modes: the classical VTC infection and CTC spread. The HTLV-I has two ways of transmission, (i) horizontal transmission via direct CTC contact, and (ii) vertical transmission through mitotic division of Tax-expressing 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 equilibria of the model. We constructed appropriate Lyapunov functions and applied Lyapunov-LaSalle asymptotic stability theorem to prove the global asymptotic stability of all equilibria. We conducted numerical simulations to support and clarify our theoretical results. We studied the effect of HIV infection on HTLV-I mono-infection dynamics and vice versa. The model analysis suggested that co-infected individuals with both viruses will have smaller number of healthy $CD4^{+}T$ cells in comparison with HIV or HTLV-I mono-infected individuals. We discussed the influence of CTL immune response on the co-infection dynamics.

Our model can be extended in many directions:

- In our model (2.1), we assumed that susceptible $CD4^{+}T$ cells are produced at a constant rate ρ and have a linear death rate αS. It would be more reasonable to consider the density dependent production rate. One possibility is to assume a logistic growth for the susceptible $CD4^{+}T$ cells in the absence of infection. Moreover, the model assumed bilinear incidence rate of infections, $\eta_1 S V$, $\eta_2 S I$ and $\eta_3 S Y$. 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 [56–58].
- Model (2.1) assumed that once susceptible $CD4^{+}T$ cell is contacted by an HIV or HIV-infected or HTLV-infected cell it becomes latently or actively infected instantaneously. However, such process needs time. Intracellular time delay has a significant effect on the virus dynamics. Delayed viral infection models have been constructed and analyzed in several works (see, e.g., [59–64]).
- Model (2.1) assumes that cells and viruses are equally distributed in the domain with no spatial variations. Taking into account spatial variations in the case of HIV/HTLV-I co-infection will be significant [65, 66].

We leave these extensions as a future project.

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Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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