Research Article

Global Properties of a General Latent Pathogen Dynamics Model with Delayed Pathogenic and Cellular Infections

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This paper studies the global dynamics of a general pathogenic infection model with two ways of infections. The effect of antibody immune response is analyzed. We incorporate three discrete time delays and both latently infected cells and actively infected cells. The infection rate and production and clearance/death rates of the cells and pathogens are given by general functions. We determine two threshold parameters to investigate the global stability of three equilibria. We use Lyapunov method to establish the global stability. We support our theoretical results by numerical simulations.

1. Introduction

The study of mathematical modeling and analysis of pathogen infection is helpful for understanding within-host pathogen dynamics; therefore, it has attracted the attention of many researchers during the last decades [1–19]. In [1], Nowak and Bangham proposed a simple model for the interaction between a replicating virus and host cells. In the same work, they proposed a second model that improves the first model by including the cytotoxic T lymphocytes (CTL) immune response against infected cells. Several extensions of [1] without immunity are given in [2–16] and with CTL immune response in [18, 19]. Antibodies which are produced from the B cells play a prominent role in pathogen dynamics. The function of antibodies is to attack and kill pathogens. Based on the first simple model introduced in [1] and the fact that antibody immune response is more effective than CTL in some infections [20], Murase et al. [21] proposed a mathematical model that describes the interactions between the target cells, the pathogens, and the antibody immune response. This model is given as follows:

$$\dot{S}(t) = \kappa - dS(t) - b_1 S(t) P(t), \quad (1)$$

$$\dot{A}(t) = b_1 S(t) P(t) - \lambda A(t), \quad (2)$$

$$\dot{P}(t) = n\lambda A(t) - cP(t) - qP(t) Z(t), \quad (3)$$

$$\dot{Z}(t) = rP(t) Z(t) - mZ(t), \quad (4)$$

where $S(t)$, $A(t)$, $P(t)$, and $Z(t)$ are the concentrations of susceptible cells, actively infected cells, pathogens and antibodies, respectively. In the literature, several modifications have been done on model (1)–(4) (see, e.g., [22–29]).

In model (1)–(4), the infection rate is given by bilinear incidence which may be not reasonable to describe the dynamics of the pathogen during the several stages of infection [4]. Pathogen dynamics models with antibodies and general incidence rate have been studied in several works (see, e.g., [24–26]), but with only pathogen-to-cell transmission. In [30], the authors considered only cell-to-cell transmission in order to model the interaction of the healthy and infected cells. Both ways of transmissions have been considered in [31–37], but without humoral immunity. In 2017, Lin et al. [38] presented a mathematical model with

humoral immunity and both ways of transmissions that are modeled by two bilinear functions.

Although antiviral drug therapies can significantly limit the level of viruses in the blood, there is still a low viral load due to ongoing latently infected cells reactivation. These cells play the role of viral reservoirs and are considered a major hurdle to virus clearance in patients under treatment. Variant models have been developed to study the dynamics of pathogens in the presence of latent reservoirs (see, e.g., [24, 39–43]). Recently, Elaiw et al. [44] have studied the global stability of a general pathogen dynamics model with delay and with both cellular and pathogenic infections by assuming that all the infected cells are active. In [45], a class of latently infected cells has been added in pathogen dynamics with two routes of infections but with specific forms of the incidence rate and production and clearance/death rates of the pathogens and cells.

The main objective of this study is to develop a general pathogenic infection model with two ways of infections, antibody immune response, three discrete time delays, and both latently infected cells and actively infected cells. This model is described by the following nonlinear system:

$$\dot{S}(t) = \mathcal{F}(S(t)) - [K_1(P(t)) + K_2(A(t))]g(S(t)), \quad (5)$$

$$\begin{aligned} \dot{L}(t) = & \varrho e^{-\varepsilon_1 \omega_1} [K_1(P(t - \omega_1)) + K_2(A(t - \omega_1))] \\ & \cdot g(S(t - \omega_1)) - (\alpha + \lambda_L) \xi(L(t)), \end{aligned} \quad (6)$$

$$\begin{aligned} \dot{A}(t) = & (1 - \varrho) \\ & \cdot e^{-\varepsilon_2 \omega_2} [K_1(P(t - \omega_2)) + K_2(A(t - \omega_2))] \\ & \cdot g(S(t - \omega_2)) - \lambda \psi(A(t)) + \alpha \xi(L(t)), \end{aligned} \quad (7)$$

$$\begin{aligned} \dot{P}(t) = & n \lambda e^{-\varepsilon_3 \omega_3} \psi(A(t - \omega_3)) - c \varphi_1(P(t)) \\ & - q \varphi_1(P(t)) \varphi_2(Z(t)), \end{aligned} \quad (8)$$

$$\dot{Z}(t) = r \varphi_1(P(t)) \varphi_2(Z(t)) - m \varphi_2(Z(t)), \quad (9)$$

where the fractions ϱ and $(1 - \varrho)$ with $0 < \varrho < 1$ are the proportions of infection that lead to latency and actively, respectively. The functions $\mathcal{F}, g, K_1, K_2, \xi, \psi, \varphi_1$, and φ_2 are continuously differentiable and satisfy the following hypotheses:

(H1) (i) there exists $S_0 > 0$ such that $\mathcal{F}(S_0) = 0$, $\mathcal{F}(S) > 0$ for $S \in [0, S_0]$,

(ii) $\mathcal{F}'(S) < 0$ for all $S > 0$,

(iii) there exists $z > 0$ and $\bar{z} > 0$ such that $\mathcal{F}(S) \leq z - \bar{z}S$ for all $S \geq 0$.

(H2) (i) $K_i(\ell), \xi(\ell), \psi(\ell), \varphi_i(\ell), g(\ell) > 0$ for all $\ell > 0$ and $K_i(0) = \xi(0) = \psi(0) = \varphi_i(0) = g(0) = 0, i = 1, 2$,

(ii) $K_i'(\ell) > 0, \xi'(\ell) > 0, \psi'(\ell) > 0$ and $\varphi_i'(\ell) > 0$ for all $\ell \geq 0, i = 1, 2, g'(\ell) > 0$ for all $\ell > 0$,

(iii) there are c_1, c_2, c_3 , and $c_4 > 0$ such that $\xi(\ell) \geq c_1 \ell$, $\psi(\ell) \geq c_2 \ell$, $\varphi_1(\ell) \geq c_3 \ell$, and $\varphi_2(\ell) \geq c_4 \ell$ for all $\ell \geq 0$.

(H3) $(K_1(P)/\varphi_1(P))' \leq 0$ and $(K_2(A)/\psi(A))' \leq 0$ for all $P, A > 0$.

Let the initial conditions for system (5)-(9) be given as

$$\begin{aligned} S(\eta) &= \chi_1(\eta), \\ L(\eta) &= \chi_2(\eta), \\ A(\eta) &= \chi_3(\eta), \\ P(\eta) &= \chi_4(\eta), \\ Z(\eta) &= \chi_5(\eta), \end{aligned} \quad (10)$$

$$\chi_j(\eta) \geq 0, \quad \eta \in [-\kappa, 0], \quad (11)$$

$$\chi_j \in C([-\kappa, 0], \mathbb{R}_{\geq 0}), \quad j = 1, \dots, 5, \quad (12)$$

where $\kappa = \max\{\omega_1, \omega_2, \omega_3\}$ and C is the Banach space of continuous functions mapping the interval $[-\kappa, 0]$ into $\mathbb{R}_{\geq 0}$ with norm $\|\chi_j\| = \sup_{-\kappa \leq \eta \leq 0} |\chi_j(\eta)|$. This shows the uniqueness of the solution for $t > 0$.

1.1. Properties of Solution

Lemma 1. *Let (H1), (H2), and (H3) be valid. Then, the solutions of system (5)-(9) with initial conditions (11) are nonnegative and ultimately bounded.*

Proof. System (5)-(9) can be written as $dX(t)/dt = Y(X(t))$, where

$$\begin{aligned} X(t) &= \begin{pmatrix} S(t) \\ L(t) \\ A(t) \\ P(t) \\ Z(t) \end{pmatrix}, \\ Y &= \begin{pmatrix} Y_1 \\ Y_2 \\ Y_3 \\ Y_4 \\ Y_5 \end{pmatrix}, \end{aligned} \quad (13)$$

and

$$Y(X(t)) = \begin{pmatrix} Y_1(X(t)) \\ Y_2(X(t)) \\ Y_3(X(t)) \\ Y_4(X(t)) \\ Y_5(X(t)) \end{pmatrix} = \begin{pmatrix} \mathcal{F}(S(t)) - \Delta(t) \\ \varrho e^{-\varepsilon_1 \omega_1} \Delta(t - \omega_1) - (\alpha + \lambda_L) \xi(L(t)) \\ (1 - \varrho) e^{-\varepsilon_2 \omega_2} \Delta(t - \omega_2) - \lambda \psi(A(t)) + \alpha \xi(L(t)) \\ n \lambda e^{-\varepsilon_3 \omega_3} \psi(A(t - \omega_3)) - c \varphi_1(P(t)) - q \varphi_1(P(t)) \varphi_2(Z(t)) \\ r \varphi_1(P(t)) \varphi_2(Z(t)) - m \varphi_2(Z(t)) \end{pmatrix}, \quad (14)$$

where

$$\Delta(t) = [K_1(P(t)) + K_2(A(t))]g(S(t)). \quad (15)$$

It follows that

$$Y_i(X(t))|_{X_i(t)=0, X(t) \in \mathbb{R}_{\geq 0}^5} \geq 0, \quad i = 1, \dots, 5. \quad (16)$$

Any solution of system (5)-(9) with the initial conditions (11) satisfies $X(t) \in \mathbb{R}_{\geq 0}^5$ for all $t \geq 0$ [46]. Hence, $\mathbb{R}_{\geq 0}^5$ is positively invariant for system (5)-(9).

From (5), we obtain $\dot{S}(t) \leq \mathcal{F}(S(t)) \leq z - \bar{z}S(t)$. It follows that $\lim_{t \rightarrow \infty} \sup S(t) \leq z/\bar{z}$. Let $F_1^G(t) = \varrho e^{-\varepsilon_1 \omega_1} S(t - \omega_1) + (1 - \varrho)e^{-\varepsilon_2 \omega_2} S(t - \omega_2) + L(t) + A(t)$. Then

$$\begin{aligned} \dot{F}_1^G(t) &= \varrho e^{-\varepsilon_1 \omega_1} \{\mathcal{F}(S(t - \omega_1)) - \Delta(t - \omega_1)\} \\ &\quad + (1 - \varrho)e^{-\varepsilon_2 \omega_2} \{\mathcal{F}(S(t - \omega_2)) - \Delta(t - \omega_2)\} \\ &\quad + \varrho e^{-\varepsilon_1 \omega_1} \Delta(t - \omega_1) - (\alpha + \lambda_L)\xi(L(t)) \\ &\quad + (1 - \varrho)e^{-\varepsilon_2 \omega_2} \Delta(t - \omega_2) - \lambda\psi(A(t)) \\ &\quad + \alpha\xi(L(t)) \\ &= \varrho e^{-\varepsilon_1 \omega_1} \mathcal{F}(S(t - \omega_1)) \\ &\quad + (1 - \varrho)e^{-\varepsilon_2 \omega_2} \mathcal{F}(S(t - \omega_2)) - \lambda_L \xi(L(t)) \\ &\quad - \lambda\psi(A(t)) \\ &\leq \varrho e^{-\varepsilon_1 \omega_1} (z - \bar{z}S(t - \omega_1)) \\ &\quad + (1 - \varrho)e^{-\varepsilon_2 \omega_2} (z - \bar{z}S(t - \omega_2)) - \lambda_L c_1 L(t) \\ &\quad - \lambda c_2 A(t) \leq z - \sigma_1^G F_1^G(t), \end{aligned} \quad (17)$$

where $\sigma_1^G = \min\{\bar{z}, \lambda_L c_1, \lambda c_2\}$. It follows that $\lim_{t \rightarrow \infty} \sup F_1^G(t) \leq \varsigma_1^G$, where $\varsigma_1^G = z/\sigma_1^G$, and then $\lim_{t \rightarrow \infty} \sup L(t) \leq \varsigma_1^G$ and $\lim_{t \rightarrow \infty} \sup A(t) \leq \varsigma_1^G$. Moreover, let $F_2^G(t) = P(t) + (q/r)Z(t)$. Then

$$\begin{aligned} \dot{F}_2^G(t) &= n\lambda e^{-\varepsilon_3 \omega_3} \psi(A(t - \omega_3)) - c\varphi_1(P) \\ &\quad - \frac{qm}{r}\varphi_2(Z) \\ &\leq n\lambda e^{-\varepsilon_3 \omega_3} \psi(\varsigma_1^G) - cc_3 P - \frac{qm}{r}c_4 Z \\ &\leq n\lambda\psi(\varsigma_1^G) - \sigma_2^G F_2^G(t), \end{aligned} \quad (18)$$

where $\sigma_2^G = \min\{cc_3, mc_4\}$. Then, $\lim_{t \rightarrow \infty} \sup F_2^G(t) \leq \varsigma_2^G$, where $\varsigma_2^G = n\lambda\psi(\varsigma_1^G)/\sigma_2^G$. This yields $\lim_{t \rightarrow \infty} \sup P(t) \leq \varsigma_2^G$ and $\lim_{t \rightarrow \infty} \sup Z(t) \leq \varsigma_3^G$, where $\varsigma_3^G = (r/q)\varsigma_2^G$. Then, $S(t)$, $L(t)$, $A(t)$, $P(t)$, and $Z(t)$ are ultimately bounded. $\square$

Define the feasible region

$$\Gamma_G = \{(S, L, A, P, Z) \in C : \|S\| \leq \varsigma_1^G, \|L\| \leq \varsigma_1^G, \|A\| \leq \varsigma_1^G, \|P\| \leq \varsigma_2^G, \|Z\| \leq \varsigma_3^G\}. \quad (19)$$

Clearly, Γ_G contains omega limit sets of system (5)-(9) and is also positively invariant for the system.

1.2. Equilibria

Lemma 2. Let (H1)-(H3) be satisfied; then there exist two bifurcation numbers $\mathcal{R}_0^G$ and $\mathcal{R}_1^G > 0$ such that

- (i) there exists only one equilibrium Θ_0 if $\mathcal{R}_0^G \leq 1$ and $\mathcal{R}_1^G \leq 1$,
- (ii) there exist only two equilibria Θ_0 and Θ_1 if $\mathcal{R}_1^G \leq 1 < \mathcal{R}_0^G$, and
- (iii) there exist three equilibria Θ_0 , Θ_1 , and Θ_2 if $\mathcal{R}_0^G > 1$ and $\mathcal{R}_1^G > 1$.

Proof. Let $\Theta(S, L, A, P, Z)$ be any equilibrium satisfying

$$0 = \mathcal{F}(S) - [K_1(P) + K_2(A)]g(S), \quad (20)$$

$$0 = \varrho e^{-\varepsilon_1 \omega_1} [K_1(P) + K_2(A)]g(S) - (\alpha + \lambda_L)\xi(L), \quad (21)$$

$$0 = (1 - \varrho)e^{-\varepsilon_2 \omega_2} [K_1(P) + K_2(A)]g(S) - \lambda\psi(A) + \alpha\xi(L), \quad (22)$$

$$0 = n\lambda e^{-\varepsilon_3 \omega_3} \psi(A) - c\varphi_1(P) - q\varphi_1(P)\varphi_2(Z), \quad (23)$$

$$0 = r\varphi_1(P)\varphi_2(Z) - m\varphi_2(Z). \quad (24)$$

From (24), we have either $\varphi_2(Z) = 0$ or $\varphi_2(Z) \neq 0$. First, we consider $\varphi_2(Z) = 0$; then using (H2), we obtain $Z = 0$. From (20)-(23), we obtain

$$\begin{aligned} \mathcal{F}(S) &= [K_1(P) + K_2(A)]g(S) = \frac{(\alpha + \lambda_L)\xi(L)}{\varrho e^{-\varepsilon_1 \omega_1}} \\ &= \frac{\lambda e^{-\varepsilon_3 \omega_3}}{\gamma} \psi(A) = \frac{c}{\gamma n} \varphi_1(P), \end{aligned} \quad (25)$$

where

$$\gamma = \left(\frac{\alpha\varrho}{\alpha + \lambda_L} e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} + (1 - \varrho)e^{-\varepsilon_2 \omega_2 - \varepsilon_3 \omega_3} \right). \quad (26)$$

Hypothesis (H2) implies that the following functions:

$$\begin{aligned} L &= \xi^{-1} \left(\frac{\varrho e^{-\varepsilon_1 \omega_1}}{\alpha + \lambda_L} \mathcal{F}(S) \right), \\ A &= \psi^{-1} \left(\frac{\gamma}{\lambda e^{-\varepsilon_3 \omega_3}} \mathcal{F}(S) \right), \\ P &= \varphi_1^{-1} \left(\frac{\gamma n}{c} \mathcal{F}(S) \right), \end{aligned} \quad (27)$$

are strictly increasing and continuous.

Substituting (27) into (20), we get

$$\begin{aligned} &\left[K_1 \left(\varphi_1^{-1} \left(\frac{\gamma n}{c} \mathcal{F}(S) \right) \right) \right. \\ &\quad \left. + K_2 \left(\psi^{-1} \left(\frac{\gamma}{\lambda e^{-\varepsilon_3 \omega_3}} \mathcal{F}(S) \right) \right) \right] g(S) - \mathcal{F}(S) = 0. \end{aligned} \quad (28)$$

Let

$$H_1^G(S) = \left[K_1 \left(\varphi_1^{-1} \left(\frac{\gamma n}{c} \mathcal{F}(S) \right) \right) + K_2 \left(\psi^{-1} \left(\frac{\gamma}{\lambda e^{-\varepsilon_3 \omega_3}} \mathcal{F}(S) \right) \right) \right] g(S) - \mathcal{F}(S) = 0. \quad (29)$$

According to (H1) and (H2), we have $H_1^G(0) = -\mathcal{F}(0) < 0$ and $H_1^G(S_0) = 0$.

Substituting $S = S_0$ in (27), we get $L = 0$, $A = 0$, and $P = 0$. This yields pathogen-free equilibrium $\Theta_0 = (S_0, 0, 0, 0, 0)$. Now from (29), we get

$$H_1^{G'}(S) = [K_1(P) + K_2(A)] g'(S) + \left[K_1'(P) \frac{dP}{dS} + K_2'(A) \frac{dA}{dS} \right] g(S) - \mathcal{F}'(S). \quad (30)$$

Moreover, from (25), we have

$$\begin{aligned} \frac{dA}{dS} &= \frac{\gamma}{\lambda e^{-\varepsilon_3 \omega_3}} \left(\frac{\mathcal{F}'(S)}{\psi'(A)} \right), \\ \frac{dP}{dS} &= \frac{\gamma n}{c} \left(\frac{\mathcal{F}'(S)}{\varphi_1'(P)} \right). \end{aligned} \quad (31)$$

Therefore, (30) becomes

$$H_1^{G'}(S_0) = [K_1(0) + K_2(0)] g'(S_0) + \left[K_1'(0) \frac{\gamma n \mathcal{F}'(S_0)}{c \varphi_1'(0)} + K_2'(0) \frac{\gamma \mathcal{F}'(S_0)}{\lambda e^{-\varepsilon_3 \omega_3} \psi'(0)} \right] \cdot g(S_0) - \mathcal{F}'(S_0). \quad (32)$$

Hypothesis (H2) implies that

$$H_1^{G'}(S_0) = \mathcal{F}'(S_0) \left(\frac{\gamma n K_1'(0) g(S_0)}{c \varphi_1'(0)} + \frac{\gamma K_2'(0) g(S_0)}{\lambda e^{-\varepsilon_3 \omega_3} \psi'(0)} - 1 \right). \quad (33)$$

From (H1), we have $\mathcal{F}'(S_0) < 0$. Since $H_1^G(0) < 0$ and $H_1^G(S_0) = 0$, hence, if

$$\frac{\gamma n K_1'(0) g(S_0)}{c \varphi_1'(0)} + \frac{\gamma K_2'(0) g(S_0)}{\lambda e^{-\varepsilon_3 \omega_3} \psi'(0)} > 1, \quad (34)$$

then $H_1^{G'}(S_0) < 0$ and there exists $S_1 \in (0, S_0)$ such that $H_1^G(S_1) = 0$. If inequality (34) is satisfied, then from (27) and (H1)-(H2), we have

$$\begin{aligned} L_1 &= \xi^{-1} \left(\frac{\varrho e^{-\varepsilon_1 \omega_1}}{\alpha + \lambda_L} \mathcal{F}(S_1) \right) > 0, \\ A_1 &= \psi^{-1} \left(\frac{\gamma}{\lambda e^{-\varepsilon_3 \omega_3}} \mathcal{F}(S_1) \right) > 0, \\ P_1 &= \varphi_1^{-1} \left(\frac{\gamma n}{c} \mathcal{F}(S_1) \right) > 0. \end{aligned} \quad (35)$$

It follows that an infected equilibrium without antibodies $\Theta_1 = (S_1, L_1, A_1, P_1, 0)$ exists when condition (34) is satisfied. Therefore, we can define the basic reproduction number for system (5)-(9) as

$$\mathcal{R}_0^G = \gamma g(S_0) \left(\frac{n K_1'(0)}{c \varphi_1'(0)} + \frac{K_2'(0)}{\lambda e^{-\varepsilon_3 \omega_3} \psi'(0)} \right). \quad (36)$$

Let $\mathcal{R}_0^G = \mathcal{R}_{01}^G + \mathcal{R}_{02}^G$, where

$$\mathcal{R}_{01}^G = \frac{n \gamma g(S_0) K_1'(0)}{c \varphi_1'(0)}, \quad (37)$$

$$\mathcal{R}_{02}^G = \frac{\gamma g(S_0) K_2'(0)}{\lambda e^{-\varepsilon_3 \omega_3} \psi'(0)}$$

The other possibility of (24) is $\varphi_2(Z) \neq 0$ and

$$P_2 = \varphi_1^{-1} \left(\frac{m}{r} \right) > 0. \quad (38)$$

Let $P = P_2$ in (20)-(22) and define function $H_2^G(S)$ as

$$H_2^G(S) = \left[K_1(P_2) + K_2 \left(\psi^{-1} \left(\frac{\gamma}{\lambda e^{-\varepsilon_3 \omega_3}} \mathcal{F}(S) \right) \right) \right] g(S) - \mathcal{F}(S) = 0. \quad (39)$$

Based on (H1) and (H2), we have $H_2^G(0) = -\mathcal{F}(0) < 0$ and $H_2^G(S_0) = K_1(P_2)g(S_0) > 0$. Hence, there exists $S_2 \in (0, S_0)$ such that $H_2^G(S_2) = 0$. Thus, $L_2 = \xi^{-1}((\varrho e^{-\varepsilon_1 \omega_1}/(\alpha + \lambda_L))\mathcal{F}(S_2)) > 0$ and $A_2 = \psi^{-1}((\gamma/\lambda e^{-\varepsilon_3 \omega_3})\mathcal{F}(S_2)) > 0$. Now, from (23), we have

$$Z_2 = \varphi_2^{-1} \left(\frac{c}{q} \left[\frac{r n \lambda e^{-\varepsilon_3 \omega_3}}{c m} \psi(A_2) - 1 \right] \right). \quad (40)$$

From (H2), we have if $(r n \lambda e^{-\varepsilon_3 \omega_3}/c m)\psi(A_2) > 1$, then $Z_2 > 0$. Now we can define

$$\mathcal{R}_1^G = \frac{r n \lambda e^{-\varepsilon_3 \omega_3}}{c m} \psi(A_2) = \frac{r n \gamma}{c m} \mathcal{F}(S_2), \quad (41)$$

which represents the antibody immune response activation number. We have $Z_2 = \varphi_2^{-1}((c/q)(\mathcal{R}_1^G - 1))$; then if $\mathcal{R}_1^G > 1$, there exists an infected equilibrium with antibodies $\Theta_2 = (S_2, L_2, A_2, P_2, Z_2)$. $\square$

1.3. Global Properties. It should be noted that finding an appropriate Lyapunov functional for higher-order nonlinear delay differential equations is a more difficult task. For the construction of Lyapunov functional of fifth-order nonlinear differential equations with multiple deviating arguments, we refer the reader to the work [47]. Here, we study the global stability of equilibria of system (5)-(9) by means of direct Lyapunov method. We first define a function $G(\eta) = \eta - 1 - \ln \eta$ and use the notation $(S, L, A, P, Z) = (S(t), L(t), A(t), P(t), Z(t))$.

Theorem 3. For system (5)-(9), suppose that $\mathcal{R}_0^G \leq 1$ and (H1)-(H3) be held true; then Θ_0 is globally asymptotically stable (GAS).

Proof. Define $U_0^G(S, L, A, P, Z)$ as

$$\begin{aligned} U_0^G = & \gamma \left(S - S_0 - \int_{S_0}^S \frac{g(S_0)}{g(\eta)} d\eta \right) + \frac{\alpha}{\alpha + \lambda_L} e^{-\varepsilon_3 \omega_3} L \\ & + e^{-\varepsilon_3 \omega_3} A + \frac{(1 - \mathcal{R}_{02}^G)}{n} P + \frac{q(1 - \mathcal{R}_{02}^G)}{rn} Z \\ & + e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \frac{\alpha \varrho}{\alpha + \lambda_L} \\ & \cdot \int_0^{\omega_1} [K_1(P(t - \eta)) + K_2(A(t - \eta))] \\ & \cdot g(S(t - \eta)) d\eta + e^{-\varepsilon_2 \omega_2 - \varepsilon_3 \omega_3} (1 - \varrho) \\ & \cdot \int_0^{\omega_2} [K_1(P(t - \eta)) + K_2(A(t - \eta))] \\ & \cdot g(S(t - \eta)) d\eta + e^{-\varepsilon_3 \omega_3} (1 - \mathcal{R}_{02}^G) \\ & \cdot \lambda \int_0^{\omega_3} \psi(A(t - \eta)) d\eta, \end{aligned} \quad (42)$$

where γ is defined by (26). It is seen that $U_0^G(S, L, A, P, Z) > 0$ for all $S, L, A, P, Z > 0$, while at the pathogen-free equilibrium Θ_0 , we get $U_0^G(S_0, 0, 0, 0, 0) = 0$. Calculating dU_0^G/dt along system (5)-(9), we obtain

$$\begin{aligned} \frac{dU_0^G}{dt} = & \gamma \left(1 - \frac{g(S_0)}{g(S)} \right) \{ \mathcal{F}(S) - [K_1(P) + K_2(A)] \\ & \cdot g(S) \} + e^{-\varepsilon_3 \omega_3} \frac{\alpha}{\alpha + \lambda_L} \{ \varrho e^{-\varepsilon_1 \omega_1} [K_1(P(t - \omega_1)) \\ & + K_2(A(t - \omega_1))] g(S(t - \omega_1)) - (\alpha + \lambda_L) \xi(L) \} \\ & + e^{-\varepsilon_3 \omega_3} \{ (1 - \varrho) e^{-\varepsilon_2 \omega_2} [K_1(P(t - \omega_2)) \\ & + K_2(A(t - \omega_2))] g(S(t - \omega_2)) - \lambda \psi(A) \\ & + \alpha \xi(L) \} + \frac{(1 - \mathcal{R}_{02}^G)}{n} \{ n \lambda e^{-\varepsilon_3 \omega_3} \psi(A(t - \omega_3)) \\ & - c \varphi_1(P) - q \varphi_1(P) \varphi_2(Z) \} \\ & + \frac{q(1 - \mathcal{R}_{02}^G)}{rn} \{ r \varphi_1(P) \varphi_2(Z) - m \varphi_2(Z) \} \\ & + e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \frac{\alpha \varrho}{\alpha + \lambda_L} \{ [K_1(P) + K_2(A)] g(S) \\ & - [K_1(P(t - \omega_1)) + K_2(A(t - \omega_1))] \\ & \cdot g(S(t - \omega_1)) \} + e^{-\varepsilon_2 \omega_2 - \varepsilon_3 \omega_3} (1 - \varrho) \{ [K_1(P) \\ & + K_2(A)] g(S) - [K_1(P(t - \omega_2))] \} \end{aligned}$$

$$\begin{aligned} & + K_2(A(t - \omega_2))] g(S(t - \omega_2)) \} + \lambda e^{-\varepsilon_3 \omega_3} (1 \\ & - \mathcal{R}_{02}^G) \{ \psi(A) - \psi(A(t - \omega_3)) \}. \end{aligned} \quad (43)$$

Collecting terms of (43), we get

$$\begin{aligned} \frac{dU_0^G}{dt} = & \gamma \left(1 - \frac{g(S_0)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_0)) \\ & + \gamma [K_1(P) + K_2(A)] g(S_0) \\ & - \frac{c}{n} (1 - \mathcal{R}_{02}^G) \varphi_1(P) \\ & - \frac{qm}{rn} (1 - \mathcal{R}_{02}^G) \varphi_2(Z) - \lambda e^{-\varepsilon_3 \omega_3} \mathcal{R}_{02}^G \psi(A). \end{aligned} \quad (44)$$

From (H3), we have

$$\begin{aligned} \frac{K_1(P)}{\varphi_1(P)} & \leq \lim_{P \rightarrow 0^+} \frac{K_1(P)}{\varphi_1(P)} = \frac{K_1'(0)}{\varphi_1'(0)} \Rightarrow \\ K_1(P) & \leq \frac{K_1'(0) \varphi_1(P)}{\varphi_1'(0)}, \\ \frac{K_2(A)}{\psi(A)} & \leq \lim_{A \rightarrow 0^+} \frac{K_2(A)}{\psi(A)} = \frac{K_2'(0)}{\psi'(0)} \Rightarrow \\ K_2(A) & \leq \frac{K_2'(0) \psi(A)}{\psi'(0)}. \end{aligned} \quad (45)$$

It follows that

$$\begin{aligned} \frac{dU_0^G}{dt} \leq & \gamma \left(1 - \frac{g(S_0)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_0)) \\ & + \gamma \frac{K_1'(0) g(S_0)}{\varphi_1'(0)} \varphi_1(P) \\ & + \gamma \frac{K_2'(0) g(S_0)}{\psi'(0)} \psi(A) - \frac{c}{n} (1 - \mathcal{R}_{02}^G) \varphi_1(P) \\ & - \frac{qm}{rn} (1 - \mathcal{R}_{02}^G) \varphi_2(Z) - \lambda e^{-\varepsilon_3 \omega_3} \mathcal{R}_{02}^G \psi(A). \end{aligned} \quad (46)$$

We have

$$\begin{aligned} \gamma \frac{K_1'(0) g(S_0)}{\varphi_1'(0)} - \frac{c}{n} (1 - \mathcal{R}_{02}^G) & = \frac{c}{n} (\mathcal{R}_0^G - 1), \\ \gamma \frac{K_2'(0) g(S_0)}{\psi'(0)} - \lambda e^{-\varepsilon_3 \omega_3} \mathcal{R}_{02}^G & = 0. \end{aligned} \quad (47)$$

Therefore, we obtain

$$\begin{aligned} \frac{dU_0^G}{dt} \leq & \gamma \left(1 - \frac{g(S_0)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_0)) \\ & + \frac{c}{n} (\mathcal{R}_0^G - 1) \varphi_1(P) \\ & + \frac{qm}{rn} (\mathcal{R}_{02}^G - 1) \varphi_2(Z). \end{aligned} \quad (48)$$

From (H1) and (H2), we have

$$\gamma \left(1 - \frac{g(S_0)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_0)) \leq 0. \quad (49)$$

Therefore, if $\mathcal{R}_0^G \leq 1$, then $dU_0^G/dt \leq 0$ for all $S, P, Z > 0$. Moreover, $dU_0^G/dt = 0$ when $Z(t) = 0$, $P(t) = 0$, and $S(t) = S_0$. The solutions of system (5)-(9) tend to $\mathcal{D}_0^G$ the largest invariant subset of $\mathcal{D}_0^G = \{(S, L, A, P, Z) : dU_0^G/dt = 0\}$ [48]. For each solution in $\mathcal{D}_0^G$ satisfies $P(t) = 0$ and from (8), we get

$$\dot{P}(t) = 0 = n\lambda e^{-\varepsilon_3\omega_3} \psi(A(t - \omega_3)). \quad (50)$$

Then, $A(t) = 0$. Similarly, from (7), we get $L(t) = 0$. It follows that $\mathcal{D}_0^G = \{\Theta_0\}$. From LaSalle's invariance principle, Θ_0 is GAS when $\mathcal{R}_0^G \leq 1$. $\square$

Remark 4. From (H1)-(H3), we have

$$\begin{aligned} \left(\frac{K_1(P)}{\varphi_1(P)} - \frac{K_1(P_1)}{\varphi_1(P_1)} \right) (K_1(P) - K_1(P_1)) &\leq 0, \\ \left(\frac{K_2(A)}{\psi(A)} - \frac{K_2(A_1)}{\psi(A_1)} \right) (K_2(A) - K_2(A_1)) &\leq 0. \end{aligned} \quad (51)$$

Thus,

$$\begin{aligned} \left(\frac{K_1(P)}{K_1(P_1)} - \frac{\varphi_1(P)}{\varphi_1(P_1)} \right) \left(1 - \frac{K_1(P_1)}{K_1(P)} \right) &\leq 0, \\ \left(\frac{K_2(A)}{K_2(A_1)} - \frac{\psi(A)}{\psi(A_1)} \right) \left(1 - \frac{K_2(A_1)}{K_2(A)} \right) &\leq 0. \end{aligned} \quad (52)$$

Obviously, the equilibrium Θ_1 does not exist if $\mathcal{R}_0^G < 1$, and $\Theta_1 = \Theta_0$ if $\mathcal{R}_0^G = 1$. When $\mathcal{R}_0^G > 1$, we have the following theorem.

Theorem 5. For system (5)-(9), assume that $\mathcal{R}_1^G \leq 1 < \mathcal{R}_0^G$ and let (H1)-(H3) be held true; then, Θ_1 is GAS.

Proof. Let $U_1^G(S, L, A, P, Z)$ be given as follows:

$$\begin{aligned} U_1^G = & \gamma \left(S - S_1 - \int_{S_1}^S \frac{g(S_1)}{g(\eta)} d\eta \right) \\ & + \frac{\alpha e^{-\varepsilon_3\omega_3}}{\alpha + \lambda_L} \left(L - L_1 - \int_{L_1}^L \frac{\xi(L_1)}{\xi(\eta)} d\eta \right) \\ & + e^{-\varepsilon_3\omega_3} \left(A - A_1 - \int_{A_1}^A \frac{\psi(A_1)}{\psi(\eta)} d\eta \right) \\ & + \frac{\gamma K_1(P_1) g(S_1)}{n\lambda e^{-\varepsilon_3\omega_3} \psi(A_1)} \left(P - P_1 - \int_{P_1}^P \frac{\varphi_1(P_1)}{\varphi_1(\eta)} d\eta \right) \\ & + \frac{\gamma q K_1(P_1) g(S_1)}{rn\lambda e^{-\varepsilon_3\omega_3} \psi(A_1)} Z + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_1(P_1) g(S_1) \\ & \cdot \int_0^{\omega_1} G \left(\frac{K_1(P(t - \eta)) g(S(t - \eta))}{K_1(P_1) g(S_1)} \right) d\eta \end{aligned}$$

$$\begin{aligned} & + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1 - \varrho) K_1(P_1) g(S_1) \\ & \cdot \int_0^{\omega_2} G \left(\frac{K_1(P(t - \eta)) g(S(t - \eta))}{K_1(P_1) g(S_1)} \right) d\eta \\ & + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_2(A_1) g(S_1) \\ & \cdot \int_0^{\omega_1} G \left(\frac{K_2(A(t - \eta)) g(S(t - \eta))}{K_2(A_1) g(S_1)} \right) d\eta \\ & + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1 - \varrho) K_2(A_1) g(S_1) \\ & \cdot \int_0^{\omega_2} G \left(\frac{K_2(A(t - \eta)) g(S(t - \eta))}{K_2(A_1) g(S_1)} \right) d\eta \\ & + \gamma K_1(P_1) g(S_1) \int_0^{\omega_3} G \left(\frac{\psi(A(t - \eta))}{\psi(A_1)} \right) d\eta. \end{aligned} \quad (53)$$

We have $U_1^G(S, L, A, P, Z) > 0$ for all $S, L, A, P, Z > 0$ and $U_1^G(S_1, L_1, A_1, P_1, 0) = 0$. Calculating dU_1^G/dt , we obtain

$$\begin{aligned} \frac{dU_1^G}{dt} = & \gamma \left(1 - \frac{g(S_1)}{g(S)} \right) \{ \mathcal{F}(S) - [K_1(P) + K_2(A)] \\ & \cdot g(S) \} + \frac{e^{-\varepsilon_3\omega_3} \alpha}{\alpha + \lambda_L} \left(1 - \frac{\xi(L_1)}{\xi(L)} \right) \\ & \cdot \{ \varrho e^{-\varepsilon_1\omega_1} [K_1(P(t - \omega_1)) + K_2(A(t - \omega_1))] \\ & \cdot g(S(t - \omega_1)) - (\alpha + \lambda_L) \xi(L) \} + e^{-\varepsilon_3\omega_3} \left(1 \right. \\ & \left. - \frac{\psi(A_1)}{\psi(A)} \right) \{ (1 - \varrho) \\ & \cdot e^{-\varepsilon_2\omega_2} [K_1(P(t - \omega_2)) + K_2(A(t - \omega_2))] \\ & \cdot g(t - \omega_2) - \lambda \psi(A) + \alpha \xi(L) \} \\ & + \frac{\gamma K_1(P_1) g(S_1)}{n\lambda e^{-\varepsilon_3\omega_3} \psi(A_1)} \left(1 - \frac{\varphi_1(P_1)}{\varphi_1(P)} \right) \\ & \cdot (n\lambda e^{-\varepsilon_3\omega_3} \psi(A(t - \omega_3)) - c\varphi_1(P) - a\varphi_1(P) \\ & \cdot \varphi_2(Z)) + \frac{\gamma q K_1(P_1) g(S_1)}{rn\lambda e^{-\varepsilon_3\omega_3} \psi(A_1)} (r\varphi_1(P) \varphi_2(Z) \\ & - m\varphi_2(Z)) + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_1(P_1) g(S_1) \\ & \cdot \left[\frac{K_1(P) g(S)}{K_1(P_1) g(S_1)} - \frac{K_1(P(t - \omega_1)) g(S(t - \omega_1))}{K_1(P_1) g(S_1)} \right. \\ & \left. + \ln \left(\frac{K_1(P(t - \omega_1)) g(S(t - \omega_1))}{K_1(P) g(S)} \right) \right] \\ & + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1 - \varrho) K_1(P_1) g(S_1) \left[\frac{K_1(P) g(S)}{K_1(P_1) g(S_1)} \right. \end{aligned}$$

$$\begin{aligned}
& - \frac{K_1(P(t-\omega_2))g(S(t-\omega_2))}{K_1(P_1)g(S_1)} \\
& + \ln \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))}{K_1(P)g(S)} \right) \Bigg] \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_1)g(S_1) \left[\frac{K_2(A)g(S)}{K_2(A_1)g(S_1)} \right. \\
& - \frac{K_2(A(t-\omega_1))g(S(t-\omega_1))}{K_2(A_1)g(S_1)} \\
& + \ln \left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))}{K_2(A)g(S)} \right) \Bigg] \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_2(A_1)g(S_1) \\
& \cdot \left[\frac{K_2(A)g(S)}{K_2(A_1)g(S_1)} - \frac{K_2(A(t-\omega_2))g(S(t-\omega_2))}{K_2(A_1)g(S_1)} \right. \\
& + \ln \left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))}{K_2(A)g(S)} \right) \Bigg] \\
& + \gamma K_1(P_1)g(S_1) \left[\frac{\psi(A)}{\psi(A_1)} - \frac{\psi(A(t-\omega_3))}{\psi(A_1)} \right. \\
& + \ln \left(\frac{\psi(A(t-\omega_3))}{\psi(A)} \right) \Bigg].
\end{aligned} \tag{54}$$

Simplifying (54), we get

$$\begin{aligned}
\frac{dU_1^G}{dt} &= \gamma \left(1 - \frac{g(S_1)}{g(S)} \right) \mathcal{F}(S) \\
&+ \gamma [K_1(P) + K_2(A)] g(S_1) \\
&- \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} \left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_1)}{\xi(L)} \right. \\
&+ \frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_1)}{\xi(L)} \Bigg) \\
&+ \alpha e^{-\varepsilon_3\omega_3}\xi(L_1) - \lambda e^{-\varepsilon_3\omega_3}\psi(A) \\
&- e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) \\
&\cdot \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{\psi(A)} \right. \\
&+ \frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{\psi(A)} \Bigg) \\
&+ \lambda e^{-\varepsilon_3\omega_3}\psi(A_1) - \alpha e^{-\varepsilon_3\omega_3}\xi(L) \\
&\cdot \frac{\psi(A_1)}{\psi(A)} \\
&- \gamma K_1(P_1)g(S_1) \\
&\cdot \left(\frac{c\varphi_1(P)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_1)} + \frac{\psi(A(t-\omega_3))\varphi_1(P_1)}{\psi(A_1)\varphi_1(P)} \right. \\
&- \frac{c\varphi_1(P_1)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_1)} - \frac{q\varphi_1(P_1)\varphi_2(Z)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_1)}
\end{aligned}$$

$$\begin{aligned}
& + \frac{qm\varphi_2(Z)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_1)} \Bigg) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_1(P_1)g(S_1) \ln \left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))}{K_1(P)g(S)} \right) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_1(P_1)g(S_1) \ln \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))}{K_1(P)g(S)} \right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_1)g(S_1) \ln \left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))}{K_2(A)g(S)} \right) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_2(A_1)g(S_1) \ln \left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))}{K_2(A)g(S)} \right) \\
& + \gamma K_1(P_1)g(S_1) \ln \left(\frac{\psi(A(t-\omega_3))}{\psi(A)} \right) \\
& + \gamma K_1(P_1)g(S_1) \left(\frac{\psi(A)}{\psi(A_1)} \right).
\end{aligned} \tag{55}$$

The components of Θ_1 satisfy

$$\begin{aligned}
\mathcal{F}(S_1) &= [K_1(P_1) + K_2(A_1)] g(S_1), \\
\frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_1) + K_2(A_1)] g(S_1) \\
&= \alpha e^{-\varepsilon_3\omega_3}\xi(L_1), \\
\gamma [K_1(P_1) + K_2(A_1)] g(S_1) &= \lambda e^{-\varepsilon_3\omega_3}\psi(A_1), \\
\varphi_1(P_1) &= \frac{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_1)}{c}.
\end{aligned} \tag{56}$$

We get

$$\begin{aligned}
\frac{dU_1^G}{dt} &= \gamma \left(1 - \frac{g(S_1)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_1)) \\
&+ \gamma [K_1(P_1) + K_2(A_1)] g(S_1) - \gamma [K_1(P_1) + K_2(A_1)] g(S_1) \\
&\cdot \frac{g(S_1)}{g(S)} + \gamma [K_1(P) + K_2(A)] g(S_1) \\
&- \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} \left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_1)}{\xi(L)} \right. \\
&+ \frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_1)}{\xi(L)} \Bigg) \\
&+ \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_1) + K_2(A_1)] g(S_1) - \gamma K_2(A_1)g(S_1) \frac{\psi(A)}{\psi(A_1)} \\
&- e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) \\
&\cdot \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{\psi(A)} \right. \\
&+ \frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{\psi(A)} \Bigg)
\end{aligned}$$

$$\begin{aligned}
& + \gamma [K_1(P_1) + K_2(A_1)] g(S_1) \\
& - \frac{e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \alpha \varrho}{\alpha + \lambda_L} [K_1(P_1) + K_2(A_1)] g(S_1) \frac{\xi(L) \psi(A_1)}{\xi(L_1) \psi(A)} \\
& - \gamma K_1(P_1) g(S_1) \\
& \cdot \left(\frac{\varphi_1(P)}{\varphi_1(P_1)} + \frac{\psi(A(t-\omega_3)) \varphi_1(P_1)}{\psi(A_1) \varphi_1(P)} - 1 \right) \\
& + \frac{\gamma q K_1(P_1) g(S_1)}{c \varphi_1(P_1)} (\varphi_1(P_1) - \varphi_1(P_2)) \varphi_2(Z) \\
& + \frac{e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \alpha \varrho}{\alpha + \lambda_L} K_1(P_1) g(S_1) \ln \left(\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1))}{K_1(P) g(S)} \right) \\
& + e^{-\varepsilon_2 \omega_2 - \varepsilon_3 \omega_3} (1 - \varrho) K_1(P_1) g(S_1) \ln \left(\frac{K_1(P(t-\omega_2)) g(S(t-\omega_2))}{K_1(P) g(S)} \right) \\
& + \frac{e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \alpha \varrho}{\alpha + \lambda_L} K_2(A_1) g(S_1) \ln \left(\frac{K_2(A(t-\omega_1)) g(S(t-\omega_1))}{K_2(A) g(S)} \right) \\
& + e^{-\varepsilon_2 \omega_2 - \varepsilon_3 \omega_3} (1 - \varrho) K_2(A_1) g(S_1) \ln \left(\frac{K_2(A(t-\omega_2)) g(S(t-\omega_2))}{K_2(A) g(S)} \right) \\
& + \gamma K_1(P_1) g(S_1) \ln \left(\frac{\psi(A(t-\omega_3))}{\psi(A)} \right).
\end{aligned} \tag{57}$$

Using the equalities in case of $i = 1$,

$$\begin{aligned}
& \ln \left(\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1))}{K_1(P) g(S)} \right) \\
& = \ln \left(\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1)) \xi(L_i)}{K_1(P_i) g(S_i) \xi(L)} \right) \\
& + \ln \left(\frac{\xi(L) \psi(A_i)}{\xi(L_i) \psi(A)} \right) + \ln \left(\frac{\psi(A) K_1(P_i)}{\psi(A_i) K_1(P)} \right) \\
& + \ln \left(\frac{g(S_i)}{g(S)} \right), \\
& \ln \left(\frac{K_1(P(t-\omega_2)) g(S(t-\omega_2))}{K_1(P) g(S)} \right) \\
& = \ln \left(\frac{K_1(P(t-\omega_2)) g(S(t-\omega_2)) \psi(A_i)}{K_1(P_i) g(S_i) \psi(A)} \right) \\
& + \ln \left(\frac{\psi(A) K_1(P_i)}{\psi(A_i) K_1(P)} \right) + \ln \left(\frac{g(S_i)}{g(S)} \right), \\
& \ln \left(\frac{K_2(A(t-\omega_1)) g(S(t-\omega_1))}{K_2(A) g(S)} \right) \\
& = \ln \left(\frac{K_2(A(t-\omega_1)) g(S(t-\omega_1)) \xi(L_i)}{K_2(A_i) g(S_i) \xi(L)} \right)
\end{aligned}$$

$$\begin{aligned}
& + \ln \left(\frac{\xi(L) \psi(A_i)}{\xi(L_i) \psi(A)} \right) + \ln \left(\frac{\psi(A) K_2(A_i)}{\psi(A_i) K_2(A)} \right) \\
& + \ln \left(\frac{g(S_i)}{g(S)} \right), \\
& \ln \left(\frac{K_2(A(t-\omega_2)) g(S(t-\omega_2))}{K_2(A) g(S)} \right) \\
& = \ln \left(\frac{K_2(A(t-\omega_2)) g(S(t-\omega_2)) \psi(A_i)}{K_2(A_i) g(S_i) \psi(A)} \right) \\
& + \ln \left(\frac{\psi(A) K_2(A_i)}{\psi(A_i) K_2(A)} \right) + \ln \left(\frac{g(S_i)}{g(S)} \right), \\
& \ln \left(\frac{\psi(A(t-\omega_3))}{\psi(A)} \right) \\
& = \ln \left(\frac{\psi(A(t-\omega_3)) \varphi_1(P_i)}{\psi(A_i) \varphi_1(P)} \right) \\
& + \ln \left(\frac{\psi(A_i) \varphi_1(P)}{\psi(A) \varphi_1(P_i)} \right),
\end{aligned} \tag{58}$$

Therefore, we obtain

$$\begin{aligned}
\frac{dU_1^G}{dt} & = \gamma \left(1 - \frac{g(S_1)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_1)) + \gamma K_1(P_1) \\
& \cdot g(S_1) \left[\frac{K_1(P_1) \varphi_1(P)}{K_1(P) \varphi_1(P_1)} + \frac{K_1(P)}{K_1(P_1)} - 1 - \frac{\varphi_1(P)}{\varphi_1(P_1)} \right] \\
& + \gamma K_2(A_1) g(S_1) \left[\frac{\psi(A) K_2(A_1)}{\psi(A_1) K_2(A)} + \frac{K_2(A)}{K_2(A_1)} - 1 \right. \\
& \left. - \frac{\psi(A)}{\psi(A_1)} \right] - \gamma [K_1(P_1) + K_2(A_1)] g(S_1) \left[\frac{g(S_1)}{g(S)} \right. \\
& \left. - 1 - \ln \left(\frac{g(S_1)}{g(S)} \right) \right] - \frac{e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \alpha \varrho}{\alpha + \lambda_L} K_1(P_1) g(S_1) \\
& \cdot \left[\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1)) \xi(L_1)}{K_1(P_1) g(S_1) \xi(L)} - 1 \right. \\
& \left. - \ln \left(\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1)) \xi(L_1)}{K_1(P_1) g(S_1) \xi(L)} \right) \right] \\
& - \frac{e^{-\varepsilon_1 \omega_1 - \varepsilon_3 \omega_3} \alpha \varrho}{\alpha + \lambda_L} K_2(A_1) g(S_1) \\
& \cdot \left[\frac{K_2(A(t-\omega_1)) g(S(t-\omega_1)) \xi(L_1)}{K_2(A_1) g(S_1) \xi(L)} - 1 \right. \\
& \left. - \ln \left(\frac{K_2(A(t-\omega_1)) g(S(t-\omega_1)) \xi(L_1)}{K_2(A_1) g(S_1) \xi(L)} \right) \right] \\
& - e^{-\varepsilon_2 \omega_2 - \varepsilon_3 \omega_3} (1 - \varrho) K_1(P_1) g(S_1)
\end{aligned}$$

$$\begin{aligned}
& \cdot \left[\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{K_1(P_1)g(S_1)\psi(A)} - 1 \right. \\
& - \ln \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{K_1(P_1)g(S_1)\psi(A)} \right) \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_2(A_1)g(S_1) \\
& \cdot \left[\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{K_2(A_1)g(S_1)\psi(A)} - 1 \right. \\
& - \ln \left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{K_2(A_1)g(S_1)\psi(A)} \right) \Big] \\
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_1)+K_2(A_1)]g(S_1) \\
& \cdot \left[\frac{\xi(L)\psi(A_1)}{\xi(L_1)\psi(A)} - 1 - \ln \left(\frac{\xi(L)\psi(A_1)}{\xi(L_1)\psi(A)} \right) \right] \\
& - \gamma K_1(P_1)g(S_1) \left[\frac{\psi(A(t-\omega_3))\varphi_1(P_1)}{\psi(A_1)\varphi_1(P)} - 1 \right. \\
& - \ln \left(\frac{\psi(A(t-\omega_3))\varphi_1(P_1)}{\psi(A_1)\varphi_1(P)} \right) \Big] - \gamma K_1(P_1)g(S_1) \\
& \cdot \left[\frac{K_1(P_1)\varphi_1(P)}{K_1(P)\varphi_1(P_1)} - 1 - \ln \left(\frac{K_1(P_1)\varphi_1(P)}{K_1(P)\varphi_1(P_1)} \right) \right] \\
& - \gamma K_2(A_1)g(S_1) \left[\frac{\psi(A)K_2(A_1)}{\psi(A_1)K_2(A)} - 1 \right. \\
& - \ln \left(\frac{\psi(A)K_2(A_1)}{\psi(A_1)K_2(A)} \right) \Big] \\
& + \frac{\gamma q K_1(P_1)g(S_1)}{c\varphi_1(P_1)} (\varphi_1(P_1) - \varphi_1(P_2))\varphi_2(Z). \\
\frac{dU_1^G}{dt} &= \gamma \left(1 - \frac{g(S_1)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_1)) + \gamma K_1(P_1) \\
& \cdot g(S_1) \left(\frac{K_1(P)}{K_1(P_1)} - \frac{\varphi_1(P)}{\varphi_1(P_1)} \right) \left(1 - \frac{K_1(P_1)}{K_1(P)} \right) \\
& + \gamma K_2(A_1)g(S_1) \left(\frac{K_2(A)}{K_2(A_1)} - \frac{\psi(A)}{\psi(A_1)} \right) \left(1 - \frac{K_2(A_1)}{K_2(A)} \right) \\
& - \gamma [K_1(P_1) + K_2(A_1)]g(S_1) \\
& \cdot G \left(\frac{g(S_1)}{g(S)} \right) - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_1(P_1)g(S_1) \\
& \cdot G \left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_1)}{K_1(P_1)g(S_1)\xi(L)} \right) \\
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_1)g(S_1)
\end{aligned}$$

$$\begin{aligned}
& \cdot G \left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_1)}{K_2(A_1)g(S_1)\xi(L)} \right) \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_1(P_1)g(S_1) \\
& \cdot G \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{K_1(P_1)g(S_1)\psi(A)} \right) \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_2(A_1)g(S_1) \\
& \cdot G \left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_1)}{K_2(A_1)g(S_1)\psi(A)} \right) \\
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_1)+K_2(A_1)]g(S_1) \\
& \cdot G \left(\frac{\xi(L)\psi(A_1)}{\xi(L_1)\psi(A)} \right) - \gamma K_1(P_1)g(S_1) \\
& \cdot G \left(\frac{\psi(A(t-\omega_3))\varphi_1(P_1)}{\psi(A_1)\varphi_1(P)} \right) - \gamma K_1(P_1)g(S_1) \\
& \cdot G \left(\frac{K_1(P_1)\varphi_1(P)}{K_1(P)\varphi_1(P_1)} \right) - \gamma K_2(A_1)g(S_1) \\
& \cdot G \left(\frac{\psi(A)K_2(A_1)}{\psi(A_1)K_2(A)} \right) + \frac{\gamma q K_1(P_1)g(S_1)}{c\varphi_1(P_1)} (\varphi_1(P_1) \\
& - \varphi_1(P_2))\varphi_2(Z).
\end{aligned}$$

(59)

If $\mathcal{R}_1^G \leq 1$, then Θ_2 does not exist since $Z_2 = \varphi_2^{-1}((c/q)(\mathcal{R}_1^G - 1)) \leq 0$. This means $Z(t) = (r\varphi_1(P) - m)\varphi_2(Z) = r(\varphi_1(P) - \varphi_1(P_2))\varphi_2(Z) \leq 0$, for all $Z > 0$. Thus, $\varphi_1(P) \leq \varphi_1(P_2)$ for all $P \geq 0$. It follows that $\varphi_1(P_1) \leq \varphi_1(P_2)$. Then according to (H1)-(H3), we have $dU_1^G/dt \leq 0$. The solutions of system (5)-(9) tend to $\mathcal{D}_1^G$ the largest invariant subset of $\mathcal{D}_1^G = \{(S, L, A, P, Z) : dU_1^G/dt = 0\}$. It is easy to show that $\mathcal{D}_1^G = \{\Theta_1\}$. Applying LaSalle's invariance principle, we get that if $\mathcal{R}_1^G \leq 1$ and $\mathcal{R}_0^G > 1$, then Θ_1 is GAS. $\square$

On the other hand, it is not hard to verify that the equilibrium Θ_2 does not exist if $\mathcal{R}_1^G < 1$, and $\Theta_2 = \Theta_1$ if $\mathcal{R}_1^G = 1$. When $\mathcal{R}_1^G > 1$, we have the following result.

Theorem 6. For system (5)-(9), suppose that $\mathcal{R}_1^G > 1$ and let (H1)-(H3) be held true; then, Θ_2 is GAS.

Proof. Consider $U_2^G(S, L, A, P, Z)$

$$\begin{aligned}
U_2^G &= \gamma \left(S - S_2 - \int_{S_2}^S \frac{g(S_2)}{g(\eta)} d\eta \right) \\
&+ \frac{\alpha e^{-\varepsilon_3\omega_3}}{\alpha+\lambda_L} \left(L - L_2 - \int_{L_2}^L \frac{\xi(L_2)}{\xi(\eta)} d\eta \right) \\
&+ e^{-\varepsilon_3\omega_3} \left(A - A_2 - \int_{A_2}^A \frac{\psi(A_2)}{\psi(\eta)} d\eta \right)
\end{aligned}$$

$$\begin{aligned}
& + \frac{\gamma K_1(P_2) g(S_2)}{n\lambda e^{-\varepsilon_3\omega_3} \psi(A_2)} \left(P - P_2 - \int_{P_2}^P \frac{\varphi_1(P_2)}{\varphi_1(\eta)} d\eta \right) \\
& + \frac{\gamma q K_1(P_2) g(S_2)}{rn\lambda e^{-\varepsilon_3\omega_3} \psi(A_2)} \left(Z - Z_2 - \int_{Z_2}^Z \frac{\varphi_2(Z_2)}{\varphi_2(\eta)} d\eta \right) \\
& + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_1(P_2) g(S_2) \\
& \cdot \int_0^{\omega_1} G \left(\frac{K_1(P(t-\eta)) g(S(t-\eta))}{K_1(P_2) g(S_2)} \right) d\eta \\
& + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1-\varrho) K_1(P_2) g(S_2) \\
& \cdot \int_0^{\omega_2} G \left(\frac{K_1(P(t-\eta)) g(S(t-\eta))}{K_1(P_2) g(S_2)} \right) d\eta \\
& + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_2(A_2) g(S_2) \\
& \cdot \int_0^{\omega_1} G \left(\frac{K_2(A(t-\eta)) g(S(t-\eta))}{K_2(A_2) g(S_2)} \right) d\eta \\
& + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1-\varrho) K_2(A_2) g(S_2) \\
& \cdot \int_0^{\omega_2} G \left(\frac{K_2(A(t-\eta)) g(S(t-\eta))}{K_2(A_2) g(S_2)} \right) d\eta \\
& + \gamma K_1(P_2) g(S_2) \int_0^{\omega_3} G \left(\frac{\psi(A(t-\eta))}{\psi(A_2)} \right) d\eta.
\end{aligned} \tag{60}$$

We have $U_2^G(S, L, A, P, Z) > 0$ for all $S, L, A, P, Z > 0$, while U_2^G reaches its global minimum at Θ_2 . Calculate dU_2^G/dt as

$$\begin{aligned}
\frac{dU_2^G}{dt} & = \gamma \left(1 - \frac{g(S_2)}{g(S)} \right) \{ \mathcal{F}(S) - [K_1(P) + K_2(A)] \\
& \cdot g(S) \} + \frac{e^{-\varepsilon_3\omega_3} \alpha}{\alpha + \lambda_L} \left(1 - \frac{\xi(L_2)}{\xi(L)} \right) \\
& \cdot \{ \varrho e^{-\varepsilon_1\omega_1} [K_1(P(t-\omega_1)) + K_2(A(t-\omega_1))] \\
& \cdot g(S(t-\omega_1)) - (\alpha + \lambda_L) \xi(L) \} + e^{-\varepsilon_3\omega_3} \left(1 \right. \\
& \left. - \frac{\psi(A_2)}{\psi(A)} \right) \{ (1-\varrho) \\
& \cdot e^{-\varepsilon_2\omega_2} [K_1(P(t-\omega_2)) + K_2(A(t-\omega_2))] \\
& \cdot g(S(t-\omega_2)) - \lambda \psi(A) + \alpha \xi(L) \} \\
& + \frac{\gamma K_1(P_2) g(S_2)}{n\lambda e^{-\varepsilon_3\omega_3} \psi(A_2)} \left(1 - \frac{\varphi_1(P_2)}{\varphi_1(P)} \right) \\
& \cdot (n\lambda e^{-\varepsilon_3\omega_3} \psi(A(t-\omega_3)) - c\varphi_1(P) - q\varphi_1(P) \varphi_2(Z)) \\
& + \frac{\gamma q K_1(P_2) g(S_2)}{rn\lambda e^{-\varepsilon_3\omega_3} \psi(A_2)} \left(1 - \frac{\varphi_2(Z_2)}{\varphi_2(Z)} \right) (r\varphi_1(P) \varphi_2(Z)
\end{aligned}$$

$$\begin{aligned}
& - m\varphi_2(Z)) + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_1(P_2) g(S_2) \\
& \cdot \left[\frac{K_1(P) g(S)}{K_1(P_2) g(S_2)} - \frac{K_1(P(t-\omega_1)) g(S(t-\omega_1))}{K_1(P_2) g(S_2)} \right. \\
& \left. + \ln \left(\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1))}{K_1(P) g(S)} \right) \right] \\
& + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1-\varrho) K_1(P_2) g(S_2) \left[\frac{K_1(P) g(S)}{K_1(P_2) g(S_2)} \right. \\
& \left. - \frac{K_1(P(t-\omega_2)) g(S(t-\omega_2))}{K_1(P_2) g(S_2)} \right. \\
& \left. + \ln \left(\frac{K_1(P(t-\omega_2)) g(S(t-\omega_2))}{K_1(P) g(S)} \right) \right] \\
& + \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} K_2(A_2) g(S_2) \left[\frac{K_2(A) g(S)}{K_2(A_2) g(S_2)} \right. \\
& \left. - \frac{K_2(A(t-\omega_1)) g(S(t-\omega_1))}{K_2(A_2) g(S_2)} \right. \\
& \left. + \ln \left(\frac{K_2(A(t-\omega_1)) g(S(t-\omega_1))}{K_2(A) g(S)} \right) \right] \\
& + e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1-\varrho) K_2(A_2) g(S_2) \left[\frac{K_2(A) g(S)}{K_2(A_2) g(S_2)} \right. \\
& \left. - \frac{K_2(A(t-\omega_2)) g(S(t-\omega_2))}{K_2(A_2) g(S_2)} \right. \\
& \left. + \ln \left(\frac{K_2(A(t-\omega_2)) g(S(t-\omega_2))}{K_2(A) g(S)} \right) \right] \\
& + \gamma K_1(P_2) g(S_2) \left[\frac{\psi(A)}{\psi(A_2)} - \frac{\psi(A(t-\omega_3))}{\psi(A_2)} \right. \\
& \left. + \ln \left(\frac{\psi(A(t-\omega_3))}{\psi(A)} \right) \right].
\end{aligned}$$

(61)

Simplify (61) as

$$\begin{aligned}
\frac{dU_2^G}{dt} & = \gamma \left(1 - \frac{g(S_2)}{g(S)} \right) \mathcal{F}(S) \\
& + \gamma [K_1(P) + K_2(A)] g(S_2) \\
& - \frac{e^{-\varepsilon_1\omega_1 - \varepsilon_3\omega_3} \alpha \varrho}{\alpha + \lambda_L} \left(\frac{K_1(P(t-\omega_1)) g(S(t-\omega_1)) \xi(L_2)}{\xi(L)} \right. \\
& \left. + \frac{K_2(A(t-\omega_1)) g(S(t-\omega_1)) \xi(L_2)}{\xi(L)} \right) \\
& + \alpha e^{-\varepsilon_3\omega_3} \xi(L_2) - \lambda e^{-\varepsilon_3\omega_3} \psi(A) \\
& - e^{-\varepsilon_2\omega_2 - \varepsilon_3\omega_3} (1-\varrho) \\
& \cdot \left(\frac{K_1(P(t-\omega_2)) g(S(t-\omega_2)) \psi(A_2)}{\psi(A)} \right.
\end{aligned}$$

$$\begin{aligned}
& + \frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{\psi(A)} \\
& + \lambda e^{-\varepsilon_3\omega_3}\psi(A_2) - \alpha e^{-\varepsilon_3\omega_3}\xi(L) \\
& \cdot \frac{\psi(A_2)}{\psi(A)} \\
& - \gamma K_1(P_2)g(S_2) \\
& \cdot \left(\frac{c\varphi_1(P)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_2)} + \frac{\psi(A(t-\omega_3))\varphi_1(P_2)}{\psi(A_2)\varphi_1(P)} \right. \\
& - \frac{c\varphi_1(P_2)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_2)} - \frac{q\varphi_1(P_2)\varphi_2(Z)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_2)} \\
& + \frac{qm\varphi_2(Z)}{rn\lambda e^{-\varepsilon_3\omega_3}\psi(A_2)} + \frac{q\varphi_1(P)\varphi_2(Z_2)}{n\lambda e^{-\varepsilon_3\omega_3}\psi(A_2)} \\
& \left. - \frac{qm\varphi_2(Z_2)}{rn\lambda e^{-\varepsilon_3\omega_3}\psi(A_2)} \right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_1(P_2)g(S_2)\ln\left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))}{K_1(P)g(S)}\right) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3}(1-\varrho)K_1(P_2)g(S_2)\ln\left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))}{K_1(P)g(S)}\right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_2)g(S_2)\ln\left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))}{K_2(A)g(S)}\right) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3}(1-\varrho)K_2(A_2)g(S_2)\ln\left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))}{K_2(A)g(S)}\right) \\
& + \gamma K_1(P_2)g(S_2)\ln\left(\frac{\psi(A(t-\omega_3))}{\psi(A)}\right) \\
& + \gamma K_1(P_2)g(S_2)\frac{\psi(A)}{\psi(A_2)}.
\end{aligned} \tag{62}$$

The components of Θ_2 satisfy

$$\begin{aligned}
\mathcal{F}(S_2) &= [K_1(P_2) + K_2(A_2)]g(S_2), \\
\frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_2) + K_2(A_2)]g(S_2) \\
&= \alpha e^{-\varepsilon_3\omega_3}\xi(L_2), \\
\gamma [K_1(P_2) + K_2(A_2)]g(S_2) &= \lambda e^{-\varepsilon_3\omega_3}\psi(A_2), \\
n\lambda e^{-\varepsilon_3\omega_3}\psi(A_2) &= c\varphi_1(P_2) + q\varphi_1(P_2)\varphi_2(Z_2), \\
\varphi_1(P_2) &= \frac{m}{r},
\end{aligned} \tag{63}$$

we get

$$\begin{aligned}
\frac{dU_2^G}{dt} &= \gamma \left(1 - \frac{g(S_2)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_2)) \\
&+ \gamma [K_1(P_2) + K_2(A_2)]g(S_2) - \gamma [K_1(P_2) + K_2(A_2)]g(S_2) \\
&\cdot \frac{g(S_2)}{g(S)} + \gamma [K_1(P) + K_2(A)]g(S_2)
\end{aligned}$$

$$\begin{aligned}
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} \left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{\xi(L)} \right. \\
& + \frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{\xi(L)} \left. \right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_2) + K_2(A_2)]g(S_2) - \gamma K_2(A_2)g(S_2)\frac{\psi(A)}{\psi(A_2)} \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3}(1-\varrho) \\
& \cdot \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{\psi(A)} \right. \\
& + \frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{\psi(A)} \left. \right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_2) + K_2(A_2)]g(S_2) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3}(1-\varrho)[K_1(P_2) + K_2(A_2)]g(S_2) \\
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_2) + K_2(A_2)]g(S_2)\frac{\xi(L)\psi(A_2)}{\xi(L_2)\psi(A)} \\
& - \gamma K_1(P_2)g(S_2) \\
& \cdot \left(\frac{\varphi_1(P)}{\varphi_1(P_2)} + \frac{\psi(A(t-\omega_3))\varphi_1(P_2)}{\psi(A_2)\varphi_1(P)} - 1 \right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_1(P_2)g(S_2)\ln\left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))}{K_1(P)g(S)}\right) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3}(1-\varrho)K_1(P_2)g(S_2)\ln\left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))}{K_1(P)g(S)}\right) \\
& + \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_2)g(S_2)\ln\left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))}{K_2(A)g(S)}\right) \\
& + e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3}(1-\varrho)K_2(A_2)g(S_2)\ln\left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))}{K_2(A)g(S)}\right) \\
& + \gamma K_1(P_2)g(S_2)\ln\left(\frac{\psi(A(t-\omega_3))}{\psi(A)}\right).
\end{aligned} \tag{64}$$

Using equalities (58) when $(i = 2)$, we obtain

$$\begin{aligned}
\frac{dU_2^G}{dt} &= \gamma \left(1 - \frac{g(S_2)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_2)) + \gamma K_1(P_2) \\
&\cdot g(S_2) \left[\frac{K_1(P_2)\varphi_1(P)}{K_1(P)\varphi_1(P_2)} + \frac{K_1(P)}{K_1(P_2)} - 1 - \frac{\varphi_1(P)}{\varphi_1(P_2)} \right] \\
&+ \gamma K_2(A_2)g(S_2) \left[\frac{K_2(A_2)\psi(A)}{K_2(A)\psi(A_2)} + \frac{K_2(A)}{K_2(A_2)} - 1 \right. \\
&- \left. \frac{\psi(A)}{\psi(A_2)} \right] - \gamma [K_1(P_2) + K_2(A_2)]g(S_2) \left[\frac{g(S_2)}{g(S)} \right. \\
&- \left. 1 - \ln\left(\frac{g(S_2)}{g(S)}\right) \right] - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_1(P_2)g(S_2) \\
&\cdot \left[\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{K_1(P_2)g(S_2)\xi(L)} - 1 \right. \\
&- \left. \ln\left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{K_1(P_2)g(S_2)\xi(L)}\right) \right] \\
&- \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_2)g(S_2)
\end{aligned}$$

$$\begin{aligned}
& \cdot \left[\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{K_2(A_2)g(S_2)\xi(L)} - 1 \right. \\
& \left. - \ln \left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{K_2(A_2)g(S_2)\xi(L)} \right) \right] \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_1(P_2)g(S_2) \\
& \cdot \left[\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{K_1(P_2)g(S_2)\psi(A)} - 1 \right. \\
& \left. - \ln \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{K_1(P_2)g(S_2)\psi(A)} \right) \right] \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_2(A_2)g(S_2) \\
& \cdot \left[\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{K_2(A_2)g(S_2)\psi(A)} - 1 \right. \\
& \left. - \ln \left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{K_2(A_2)g(S_2)\psi(A)} \right) \right] \\
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_2)+K_2(A_2)]g(S_2) \\
& \cdot \left[\frac{\xi(L)\psi(A_2)}{\xi(L_2)\psi(A)} - 1 - \ln \left(\frac{\xi(L)\psi(A_2)}{\xi(L_2)\psi(A)} \right) \right] \\
& - \gamma K_1(P_2)g(S_2) \left[\frac{\psi(A(t-\omega_3))\varphi_1(P_2)}{\psi(A_2)\varphi_1(P)} - 1 \right. \\
& \left. - \ln \left(\frac{\psi(A(t-\omega_3))\varphi_1(P_2)}{\psi(A_2)\varphi_1(P)} \right) \right] - \gamma K_1(P_2)g(S_2) \\
& \cdot \left[\frac{K_1(P_2)\varphi_1(P)}{K_1(P)\varphi_1(P_2)} - 1 - \ln \left(\frac{K_1(P_2)\varphi_1(P)}{K_1(P)\varphi_1(P_2)} \right) \right] \\
& - \gamma K_2(A_2)g(S_2) \left[\frac{K_2(A_2)\psi(A)}{K_2(A)\psi(A_2)} - 1 \right. \\
& \left. - \ln \left(\frac{K_2(A_2)\psi(A)}{K_2(A)\psi(A_2)} \right) \right]. \\
\frac{dU_2^G}{dt} &= \gamma \left(1 - \frac{g(S_2)}{g(S)} \right) (\mathcal{F}(S) - \mathcal{F}(S_2)) + \gamma K_1(P_2) \\
& \cdot g(S_2) \left(\frac{K_1(P)}{K_1(P_2)} - \frac{\varphi_1(P)}{\varphi_1(P_2)} \right) \left(1 - \frac{K_1(P_2)}{K_1(P)} \right) \\
& + \gamma K_2(A_2)g(S_2) \left(\frac{K_2(A)}{K_2(A_2)} - \frac{\psi(A)}{\psi(A_2)} \right) \left(1 - \frac{K_2(A_2)}{K_2(A)} \right) \\
& - \gamma [K_1(P_2) + K_2(A_2)]g(S_2) \\
& \cdot G \left(\frac{g(S_2)}{g(S)} \right) - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_1(P_2)g(S_2) \\
& \cdot G \left(\frac{K_1(P(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{K_1(P_2)g(S_2)\xi(L)} \right)
\end{aligned}$$

$$\begin{aligned}
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} K_2(A_2)g(S_2) \\
& \cdot G \left(\frac{K_2(A(t-\omega_1))g(S(t-\omega_1))\xi(L_2)}{K_2(A_2)g(S_2)\xi(L)} \right) \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_1(P_2)g(S_2) \\
& \cdot G \left(\frac{K_1(P(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{K_1(P_2)g(S_2)\psi(A)} \right) \\
& - e^{-\varepsilon_2\omega_2-\varepsilon_3\omega_3} (1-\varrho) K_2(A_2)g(S_2) \\
& \cdot G \left(\frac{K_2(A(t-\omega_2))g(S(t-\omega_2))\psi(A_2)}{K_2(A_2)g(S_2)\psi(A)} \right) \\
& - \frac{e^{-\varepsilon_1\omega_1-\varepsilon_3\omega_3}\alpha\varrho}{\alpha+\lambda_L} [K_1(P_2)+K_2(A_2)]g(S_2) \\
& \cdot G \left(\frac{\xi(L)\psi(A_2)}{\xi(L_2)\psi(A)} \right) - \gamma K_1(P_2)g(S_2) \\
& \cdot G \left(\frac{\psi(A(t-\omega_3))\varphi_1(P_2)}{\psi(A_2)\varphi_1(P)} \right) - \gamma K_1(P_2)g(S_2) \\
& \cdot G \left(\frac{K_1(P_2)\varphi_1(P)}{K_1(P)\varphi_1(P_2)} \right) - \gamma K_2(A_2)g(S_2) \\
& \cdot G \left(\frac{K_2(A_2)\psi(A)}{K_2(A)\psi(A_2)} \right).
\end{aligned}$$

(65)

From (H1)-(H3), we have that $dU_2^G/dt \leq 0$ for all S, L, A, P and $Z > 0$. One can show that $dU_2^G/dt = 0$ at Θ_2 ; then apply LaSalle's invariance principle to show the global asymptotic stability of Θ_2 . $\square$

2. Numerical Simulations

For numerical simulation purpose, we consider model (5)-(9) with the following specific functions:

$$\begin{aligned}
\mathcal{F}(S) &= \kappa - dS, \\
g(S) &= \frac{S}{1 + \gamma^H S}, \\
K_1(P) &= b_1 P, \\
K_2(A) &= b_2 A, \\
\xi(L) &= L, \\
\psi(A) &= A, \\
\varphi_1(P) &= P, \\
\varphi_2(Z) &= Z.
\end{aligned} \tag{66}$$

First, we show that (H1)-(H3) are satisfied. We have $S_0 = \kappa/d$, $\mathcal{F}(S_0) = 0$, $\mathcal{F}(0) = \kappa > 0$, and $\mathcal{F}'(S) = -d < 0$. It

follows that $\mathcal{F}(S) > 0$ for all $S \in [0, S_0)$. Moreover, (H1)(iii) is satisfied with $z = \kappa$ and $\bar{z} = d$. Thus, (H1) is satisfied. We have $g(S), K_1(P), K_2(A), \xi(L), \psi(A), \varphi_1(P), \varphi_2(Z) > 0$ for all $S, P, A, L, Z > 0$ and $g(0) = K_1(0) = K_2(0) = \xi(0) = \psi(0) = \varphi_1(0) = \varphi_2(0) = 0$. We also have

$$\begin{aligned} g'(S) &= \frac{1}{(1 + \gamma^H S)^2} > 0 \quad \forall S > 0, \\ K_1'(P) &= b_1 > 0 \quad \forall P \geq 0, \\ K_2'(A) &= b_2 > 0 \quad \forall A \geq 0, \\ \xi'(L) &= 1 > 0 \quad \forall L \geq 0, \\ \psi'(A) &= 1 > 0 \quad \forall A \geq 0, \\ \varphi_1'(P) &= 1 > 0 \quad \forall P \geq 0, \\ \varphi_2'(Z) &= 1 > 0 \quad \forall Z \geq 0. \end{aligned} \quad (67)$$

Hence, (H2) (i)-(ii) are satisfied. Moreover, (H2) (iii) is satisfied, where $c_1 = c_2 = c_3 = c_4 = 1$. Finally, we have

$$\begin{aligned} \left(\frac{K_1(P)}{\varphi_1(P)} \right)' &= 0 \quad \forall P > 0, \\ \left(\frac{K_2(A)}{\psi(A)} \right)' &= 0 \quad \forall A > 0. \end{aligned} \quad (68)$$

Thus, (H3) is also valid.

With the above choice, system (5)-(9) will be

$$\dot{S}(t) = \kappa - dS(t) - \frac{b_1 S(t) P(t)}{1 + \gamma^H S(t)} - \frac{b_2 S(t) A(t)}{1 + \gamma^H S(t)}, \quad (69)$$

$$\begin{aligned} \dot{L}(t) &= \varrho e^{-\varepsilon_1 \omega_1} \left[\frac{b_1 S(t - \omega_1) P(t - \omega_1)}{1 + \gamma^H S(t - \omega_1)} \right. \\ &\quad \left. + \frac{b_2 S(t - \omega_1) A(t - \omega_1)}{1 + \gamma^H S(t - \omega_1)} \right] - (\alpha + \lambda_L) L(t), \end{aligned} \quad (70)$$

$$\begin{aligned} \dot{A}(t) &= (1 - \varrho) e^{-\varepsilon_2 \omega_2} \left[\frac{b_1 S(t - \omega_2) P(t - \omega_2)}{1 + \gamma^H S(t - \omega_2)} \right. \\ &\quad \left. + \frac{b_2 S(t - \omega_2) A(t - \omega_2)}{1 + \gamma^H S(t - \omega_2)} \right] - \lambda A(t) + \alpha L(t), \end{aligned} \quad (71)$$

$$\dot{P}(t) = n\lambda e^{-\varepsilon_3 \omega_3} A(t - \omega_3) - cP(t) - qP(t) Z(t), \quad (72)$$

$$\dot{Z}(t) = rP(t) Z(t) - mZ(t), \quad (73)$$

where γ^H is the Holling-type II constant. The numbers $\mathcal{R}_0^G$ and $\mathcal{R}_1^G$ are given as

$$\mathcal{R}_0^G = \frac{\gamma S_0 (n\lambda e^{-\varepsilon_3 \omega_3} b_1 + cb_2)}{c\lambda e^{-\varepsilon_3 \omega_3} (1 + \gamma^H S_0)}, \quad (74)$$

$$\mathcal{R}_1^G = \frac{rn\lambda e^{-\varepsilon_3 \omega_3}}{cm} A_2. \quad (75)$$

TABLE 1: The values of $\mathcal{R}_0^G$ and $\mathcal{R}_1^G$ for system (69)-(73) with different values of γ^H .

γ^H	Equilibrium	$\mathcal{R}_0^G$	$\mathcal{R}_1^G$
0.0	Θ_2	2.29091	2.52851
0.0007	Θ_2	1.34759	1.37541
0.0009	Θ_2	1.20574	1.19569
0.00118999	Θ_1	1.04608	1
0.00125	Θ_1	1.01818	0.966725
0.00129091	Θ_0	1	0.945205
0.05	Θ_0	0.0449198	0.0325008
1.0	Θ_0	0.00228862	0.0016358

Therefore, Theorems 3–6 are valid for such choice.

Let us consider $\omega = \omega_1 = \omega_2 = \omega_3$ and the following initial values:

IV₁: $\chi_1(\eta) = 800, \chi_2(\eta) = 2, \chi_3(\eta) = 2, \chi_4(\eta) = 6, \chi_5(\eta) = 2$,

IV₂: $\chi_1(\eta) = 600, \chi_2(\eta) = 4, \chi_3(\eta) = 6, \chi_4(\eta) = 9, \chi_5(\eta) = 4$,

IV₃: $\chi_1(\eta) = 400, \chi_2(\eta) = 6, \chi_3(\eta) = 9, \chi_4(\eta) = 15, \chi_5(\eta) = 6$,

IV₄: $\chi_1(\eta) = 700, \chi_2(\eta) = 1, \chi_3(\eta) = 1, \chi_4(\eta) = 9, \chi_5(\eta) = 4, \eta \in [-\omega, 0]$.

The stability of the equilibria will be investigated by varying some parameters r, γ^H, b_1, b_2 , and ω and fixing the other parameters as $\kappa = 10, d = 0.01, \lambda = \lambda_u = 0.5, c = 2, \varrho = 0.5, \alpha = 0.05, n = 10, q = 0.1, m = 0.1$, and $\varepsilon_1 = \varepsilon_2 = \varepsilon_3 = 1$.

Case (I) (effect of the parameters b_1, b_2 , and r). We take $\gamma^H = 0, \omega = 0$. We choose three sets of the parameters b_1, b_2 , and r to confirm Theorems 3–6 (see Figure 1).

Set (1) (stability of Θ_0). $b_1 = 0.0001, b_2 = 0.0001$, and $r = 0.001$. This yields $\mathcal{R}_0^G = 0.3818 < 1$ and $\mathcal{R}_1^G = 0.1401 < 1$.

Set (2) (stability of Θ_1). $b_1 = 0.0006, b_2 = 0.0006$, and $r = 0.001$. With these values, we obtain $\mathcal{R}_0^G = 2.2909 > 1$ and $\mathcal{R}_1^G = 0.2367 < 1$.

Set (3) (stability of Θ_2). $b_1 = 0.0006, b_2 = 0.0006$, and $r = 0.04$ and then $\mathcal{R}_0^G = 2.2909 > 1$ and $\mathcal{R}_1^G = 2.5285 > 1$.

Case (II) (effect of the Holling-type II parameter). Let us take IV₁ and choose the values $b_1 = 0.0006, b_2 = 0.0006, \omega = 0$, and $r = 0.04$. Figure 2 and Table 1 show the effect of Holling-type II parameter γ^H on the stability of the system. We observe that as γ^H is increased, the pathogen-to-susceptible and infected-to-susceptible transmission rates are decreased. Then, the concentrations of the susceptible cells are increased, while the concentrations of the infected cells and free pathogens are decreased. In addition,

(i) Θ_2 is GAS when $0 \leq \gamma^H < 0.00099$,

(ii) Θ_1 is GAS when $0.00099 \leq \gamma^H < 0.00129$,

(iii) Θ_0 is GAS when $\gamma^H \geq 0.00129$.

FIGURE 1: The evolution of system (69)-(73) for Case (I).

Case (III) (effect of time delay parameters). For this case, we take IV_4 and choose the values $b_1 = 0.0006$, $b_2 = 0.0006$, $\gamma^H = 0.00035$, and $r = 0.04$. Figure 3 and Table 2 show the effect of the time delay on the dynamical behavior of the pathogen. We have the following cases:

- (i) Θ_2 is GAS when $0 \leq \omega < 0.2412$,
- (ii) Θ_1 is GAS when $0.2412 \leq \omega < 0.314637$,
- (iii) Θ_0 is GAS when $\omega \geq 0.314637$.

Therefore, if the time delay is long enough, then the system can be stabilized around Θ_0 , where the pathogens are cleared

Data Availability

There is no data available supporting this paper.

FIGURE 2: The evolution of system (69)-(73) with different values of γ^H for Case (II).

FIGURE 3: The evolution of system (69)-(73) with different values of ω for Case (III).

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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TABLE 2: The values of $\mathcal{R}_0^G$ and $\mathcal{R}_1^G$ for system (69)–(73) with different values of ω .

ω	Equilibrium	$\mathcal{R}_0^G$	$\mathcal{R}_1^G$
0.0	$\Theta_2 = (832.667, 1.52121, 1.82545, 2.5, 16.5091)$	1.69697	1.82545
0.1	$\Theta_2 = (841.463, 1.3041, 1.56491, 2.5, 8.31986)$	1.43111	1.41599
0.2412	$\Theta_1 = (851.503, 1.06065, 1.27278, 2.50001, 0)$	1.12918	1
0.29	$\Theta_1 = (946.997, 0.360549, 0.432659, 0.809357, 0)$	1.04146	0.889019
0.314637	$\Theta_0 = (1000, 0, 0, 0, 0)$	1	0.838138
0.5	$\Theta_0 = (1000, 0, 0, 0, 0)$	0.73999	0.542645
1	$\Theta_0 = (1000, 0, 0, 0, 0)$	0.342409	0.177726

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