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On the interaction of the human immune system with foreign body: mathematical modeling approach

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Abstract

In this study, we present a simple but novel mathematical model to show the interaction of the five immunological cells in the lymphocyte family – the cytotoxic-Lymphocytes (T), B-cell antibody, killer T – cell (K), the helper T – cell (H) and the Regulatory T – cell (R) –with foreign bodies with or without treatment. The feasibility of the model and important parameters of invasion in mathematical epidemiology: the reproductive number, free and infection persistence equilibrium, local and global stability among others were established. Results confirm the effectiveness of booster (vaccination or drugs) of these cells (of the immune system as recovery of infected cells is quicker and sustainable with vaccinations that boost these body cells. By this study drug producers are better informed about the effectiveness of the boosting components of vaccination and drugs they produce and health workers have good insight and handful understanding of the efficacy of drugs and vaccines administered in the treatment of virus infection.

Keywords: Immunological cells; Vaccination; Drug usage; Ebola virus; Global stability; T – cell; B – cell; H – cell; R – cell; K – cell

1. Introduction

The human body's physical health is not a given; rather, it is the outcome of a complex interplay of several mechanisms that work continually to guard against illnesses of all kinds [1, 2, 3]. The immune system is the collective name for all of these parts and functional units working in concert in a highly clever, methodical way [3, 4, 5, 6, 7]. Immune response refers to the coordinated, collective action of all the chemicals and cells that make up the immune system [4, 6, 9, 10]. Many studies have been conducted to better understand this complex defensive mechanism, and one of these studies has focused on the activation of T cells that results from the formation of a transient synapse between a T cell and an antigen-presenting cell [7, 11, 12]. The T cell gathers information about the pathogen during this intercellular interaction in order to start certain disease-prevention procedures [13, 14, 15, 16].Specificity, diversity, flexibility, adaptability, complexity, and memory are some characteristics of the immune system [17, 18, 19, 20]. It is capable to identifying a wide variety of agents, including viruses, parasites, bacteria, infected, and transformed host cells [5, 21, 22]. In order to prevent infection, it separates them from the organism's healthy cells before attacking healthy tissue [19, 23, 24]. Additionally, it has the capacity to form memories that will enable it to respond much more quickly upon subsequent interaction with pathogens [23, 25, 26]. The majority of the parts are cellular in nature and aren't connected to any one organ specifically; instead, they're implanted or moving about in different tissues all throughout the body [27, 28, 29]. Because of its omnipresence, the system is able to respond in any situation and is not constrained to one location [8, 18, 30].

Two distinct immune system subtypes can respond against perturbations [19, 31]. The immune systems include innate immunity and adaptive immunity [26, 27]. All of the first, non-specific, generic immunological tactics are part of the innate immune system [29, 30]. Examples of these include putting up physical and chemical barriers to infections or utilizing specialized chemical cues to draw certain immune cells to infection locations [31, 32, 33]. The pathogens are identified in a matter of minutes and are entirely removed in a matter of hours. Pathogen-specific receptors, which are present in all types of plant and animal life and are already encoded in the genetic material, serve as the foundation for innate immunity [34, 35]. The capacity to respond quickly is caused by the genetic specification of the protein structure, which limits flexibility [33, 34, 35, 36].

In order to avoid infection by the same virus or bacteria, vaccinations, also known as immunizations, utilize a small quantity of weakened or destroyed bacteria, viruses, or fragments of lab-made proteins that mimic the viruses [37, 38, 39]. You are injected with a disease that has been weakened (or a portion of it) when you receive a vaccination [29, 30]. This sets off your body's immunological response, which either causes it to develop antibodies to that specific disease or to instigate other processes that boost immunity[33]. Your immune system will then be ready to combat the illness if you are ever exposed to the real disease-causing bacteria again [35, 36].

A vaccination will often stop a disease from spreading or lessen its effects. Immunity lasts for differing amounts of time with various diseases and vaccinations. Lifetime immunity may not always be achieved with either vaccination or spontaneous infection [37, 38]. The purpose of the suggested timing of vaccination doses is to provide the best immune protection to cover the stage of life with the greatest susceptibility to the disease. Since many of the vaccines used today are still relatively new, data on how long

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they last before losing their effectiveness is constantly being updated. Natural infections cause a decline in immunity to numerous diseases. The duration of protection provided by vaccinations depends on a number of factors, chief among them the vaccination itself. Live vaccinations typically result in longer-lasting protection than subunit vaccines. Memory cells with a long lifespan are not produced by polysaccharide vaccines. If there is not enough time between dosages, immunity may not last as long. As a result, few gaps are required. Very small children and very old persons may have brief immunity periods [40, 41].

Measurements of specific antibodies in the blood are typically used to determine vaccine immunogenicity, which evaluates the immunological response to a vaccine. A set threshold of particular antibody levels has been associated with protection for some vaccines, but not all. This, however, does not unambiguously indicate whether a person is completely immune to disease. Following a booster dose of the vaccination, antibody levels significantly increase if good immunological memory has been formed [42].

Measures of vaccine efficacy and effectiveness contrast illness incidence rates in the vaccinated and unvaccinated populations. Efficacy is assessed before the vaccine is authorized for use in the general public, whereas effectiveness is assessed during controlled clinical trials. These allow us to determine the percentage of immunized individuals who should be protected by the vaccination [41, 42].

A crucial defense mechanism for the greater population is herd immunity, also known as community immunity. For some diseases, transmission is slowed or stopped if a sufficient number of people are immune. This is especially true for illnesses like pneumococcal disease and rubella. The disease must be kept from re-entering the community by maintaining high vaccination rates. No vaccine is 100% effective; a tiny proportion of recipients do not experience protection, and for some, the impact of the vaccine may wear off over time. Additionally, some people cannot receive vaccinations because of medical disorders including immune suppression. Those close to these people are kept healthy, which shields them from illness [23, 42].

Since studies suggest that the immune system has the ability to suppress the increase in infected cells as well as virus load with the aid of drug use, mathematical modeling of the dynamics of virus cell and host cell (and/or the immune system) can be helpful to interpret infection kinetics on quantitative grounds. Therefore, the development of new avenues of thinking to advance quantitative understanding of infection virus and its interaction with the host cells is constantly needed to tackle many of the existing diseases that threaten global health [14, 43]

In earlier research on vaccination treatment of say, Ebola virus, only Cytotoxic-Lymphocyte (T) and B-cell (Antibody) (B) were considered as the only host cells that combat the Ebola virus in human body system and usage of drugs to enhance this host cells (i.e., cytotoxic-Lymphocyte and B-cell Antibody) in the body system was also clearly explained[34, 37, 38]. However there are still some other vital cells in the human immune(the H- cells that energize both the B and T cells to effectively and efficiently combat the virus, the R – cells that regulate the T, H and B cells to prevent negative effect after the virus is cleared and the K – cells, natural killer cells that react instantly when there is infection in the body system) that combat with virus cells and their interaction with this foreign cell during treatment need be comprehensively explained and understood to optimize treatment, control of the virus and drug content that boost these cells in the body system. Hence we present a feasible and novel mathematical model to include the killer T – cell (K), the helper T – cell (H) and the Regulatory T – cell (R) and comprehensively unravel the interaction of these cells with virus cell, virus-free body cells, infected body cells and uninfected body cells during treatment [44].

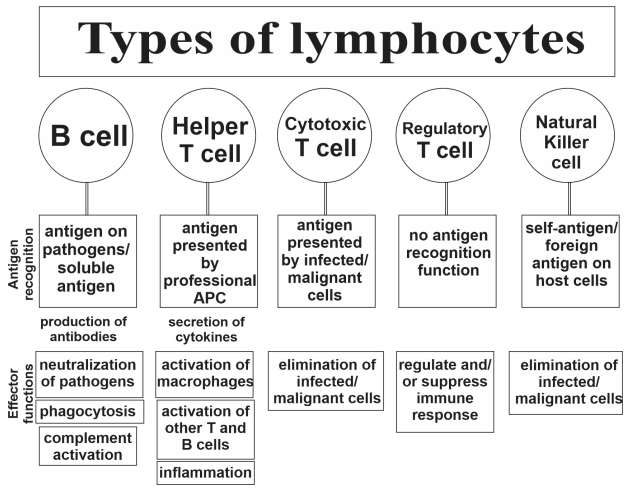

Figure 1: Types of lymphocytes.

1.1. Components of the immune system

There are five immunological cells in the lymphocyte family: B cells transform into cells that produce antibodies once they identify soluble antigen and pathogens (Fig. 1); Helper T cells become activated when they detect a specific antigen on the surface of antigen presenting cells (APCs) and begin to trigger other immune response mechanisms; Cytotoxic T cells and NK cells both recognize infected or malignant cells and destroy them immediately, but regulatory T cells stop an excessive immune response, including actions against healthy tissue. NK cells only exhibit a very limited receptor diversity and are supposed to use a strategy known as missing self.

We'll skim over a lot of the biological details of each key immune system component in the sections that follow. Immune disorders can have an impact on one or more bodily parts. Immune deficiencies might show up as a specific infection or as a more widespread susceptibility to sickness. Certain immunological deficiencies can only be connected to a very small subset of infections because of the intricate relationships between immune system cells and proteins. For specific immunological deficiencies, there are extra elements that "take up the slack" and can at least partially compensate. In other cases, the person could struggle mightily with infections and have a very weak overall immune system [45, 46]. The many immune system cells include neutrophils, monocytes/macrophages, and lymphocytes (T-cells, B-cells, and NK cells). The several types of white blood cells are as follows. Antibodies complement proteins, and signaling proteins (commonly known as cytokines) make up the majority of immune system proteins [47].

1.2. B-Cells

B-cells, also known as B-lymphocytes or CD19 or CD20 cells on lab reports, are specialized immune system cells whose main job is to create antibodies (also called immunoglobulins or gammaglobulins). In the bone marrow, hematopoietic stem cells give rise to B-cells. B-cells are taught or trained throughout their maturation in the bone marrow not to make antibodies against healthy tissues. When fully developed, B-cells are present in the bloodstream, lymph nodes, spleen, some regions of the gut, and bone marrow. B-cells respond to foreign substances (antigens) by developing into plasma cells, a different cell type. B-cells can develop into memory cells, enabling a quick response in the event that the same illness recurs. The mature cells that actually manufacture the antibodies are known as plasma cells.

Plasma cells' primary output, antibodies, can enter the tissues, bloodstream, digestive secretions, tears, and respiratory secretions. The highly specialized serum protein molecules that make up antibodies. There are antibody molecules created especially to fit each foreign antigen like a lock and key [22, 48, 49]. For instance, there are antibody molecules that physically suit the diphtheria virus, the measles virus, and the poliovirus. Since there are many distinct antibody molecules, B-cells can make them against almost all of the bacteria in our surroundings. However, only one type of antibody is produced by each plasma cell.When antibody molecules identify a bacterium as foreign, they physically bind to it, starting a complicated series of processes that eventually result in the eradication of the germ. The particular roles that each type of antibody plays in the body differ. The chemical structure of the antibody determines these variances, which in turn determine the class of the antibody (or immunoglobulin) [50, 51, 52].

Additionally, antibodies-coated bacteria are considerably simpler for neutrophils to swallow and kill than non-antibody-coated bacteria. Antibodies work in a variety of ways to stop microorganisms from successfully colonizing bodily tissues and causing harmful infections. We can maintain immunity to viruses and bacteria that attacked us years ago thanks to the long lifespan of plasma cells [53, 54, 55]. People who have received a full course of live vaccine strains of the measles virus, for instance, almost never contract the disease because the vaccine leaves them with long-lasting plasma cells and antibodies that guard against infection [56, 57, 58].

1.3. T-Cells

T-cells, also known as T-lymphocytes or CD3 cells in lab studies, are an additional category of immune cell. T-cells function as immune system regulators and assault virus-infected cells directly. Though they begin their development from hematopoietic stem cells in the bone marrow, T-cells complete it in the thymus. The immune system's specialized organ in the chest is called the thymus. Immature lymphocytes become mature T-cells in the thymus, whereas T-cells that have the potential to harm healthy tissues are removed [16]. T-cell development depends on the thymus, which the fetus lacks, T-cells cannot form.Mature T-cells move from the thymus and are found in the blood, spleen, lymph nodes, bone marrow, and other immune system organs [17, 18]. Similar to how each antibody molecule reacts with a particular antigen, each T-cell also responds to a particular antigen.

In fact, T-cells have molecules that resemble antibodies on their surfaces. Since there are so many different T-cell types, the body possesses T-cells that can respond to almost any antigen [59, 60, 61].

T-cells serve a variety of purposes and exhibit various antigen-recognition capacities. There are three types of T cells: regulatory T cells, helper T cells, and "killer" or cytotoxic T cells (commonly referred to as CD8 T cells in lab studies). Each has a unique role in the immune system [3, 62, 63].

1.4. Killer T-cells

Killer T-cells, also known as cytotoxic T-cells, are what actually kill infected cells. When certain bacteria and viruses can live and even reproduce inside of the body's own cells, the body is protected by killer T-cells. Killer T-cells can react to organ transplants or other foreign tissues when they are present in the body. To assure its annihilation, the killer cell must get to the infection site and connect to its target directly[40].

1.5. Helper T-cells

B-cells use helper T-cells to make antibodies, and killer T-cells use helper T-cells to target foreign molecules[4, 5].

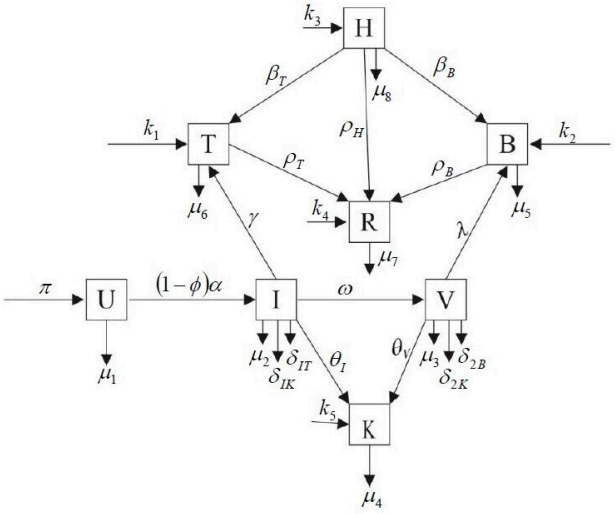

Figure 2: Flow diagram for dynamism of immune body system with virus cells.

1.6. Regulatory T-cells

Other T-lymphocytes are suppressed or turned off by regulatory T cells. Without regulatory cells, the immune system would continue to fight infections even after they were treated. The body could "overreact" to the infection if regulatory T-cells are absent. Regulatory T-cells regulate the lymphocyte system's level of activation, keeping it just right—neither too high nor too low [22].

2. Model formulation and description

To better comprehend the dynamic transmission of viral infections in the human cell population, the study employs an eight-compartment, deterministic mathematical model of the U, I, V, K, T, B, H, and R (Fig. 2). Uninfected cells (U), infected cells (I), free virus (V), cytotoxic T-cells (T), natural killer cells (K), B-cell (antibody) (B), helper T-cells (H), and regulatory T-cells(R) are the different subgroups of the human cell population N(t), where

$$N = U + I + V + K + T + B + H + R.$$

Uninfected cell U are recruited at the rate $\pi$with mortality rate $\mu_1$and get infected at rate $\alpha$and progress to class$I$. These infected cell (I) has mortality rate $\mu_2$and some of them becomes virus free at the rate ωwithout antibodies' help and move to class$V$. To eliminate the infected cells, the cytotoxic T-class (T) and natural killer (K) begin to interact with them at the respective clearance rateδ_{IT}andδ_{IK} During this interaction process, the Helper T-cells, (H) also interact with antibody B-cells (B) to create antibodies for virus- free cells (V) to ward off further attack from the foreign body, and Helper T-cells (H) furthermore interact with cytotoxic T-cells (T) during their attack on infected cells (I).

To suppress or deactivate them, Regulatory T-cells (R) work with Helper T-cells (H), Cytotoxic T-cells (T), and B-cells (Antibody) class. Without Regulatory T-cells, the immune system would continue to function even after a disease has been treated. Without Regulatory T-cells (R), the body may respond to the infection "overreacting." To keep the lymphocyte system just the right amount of activated—neither too much nor too little—Regulatory T-cells (R) serve as the thermostat.

The production rate of Uninfected cells (U) is and have mortality rate. When a free virus infect the uninfected cells, U, and produced infected cells, I, at rate and with death rate. Infected cells, I, move to Free virus class, V, at rate and die at rate.

Table 1: Description of state variables and parameters of the model.

States variables or Parameters	Description
$U(t)$	Uninfected Cells
$I(t)$	Infected cells
$V(t)$	Free virus cells
$T(t)$	Cytotoxic T-cells
$B(t)$	Antibody B-cells
$K(t)$	Natural killer cells
$H(t)$	Helper T-cells
$R(t)$	Regulatory T-cells
π	rate at which uninfected cell are recruited
α	rate at which uninfectedcell are infected
ω	recovery rate of infected cell into free virus cells, V
γ	rate at which Cytotoxic T-cells are produced
λ	rate at which antibodies are produced
θ_I	rate at which natural killer cells are produced
θ_v	rate at which natural killer cells are produced
β_T	Help rate of cytotoxic, T-cells
β_B	Help rate of antibody, B-cells
ρ_H	Regulatory rate of Helper, T-cells
ρ_B	Regulatory rate of antibody, B-cells
δ_{IK}	Clearance rate of infected cells by natural killer cells
δ_{IT}	Clearance rate of the viruses by antibodies
δ_{2K}	Clearance rate of the viruses by Natural Killer cells
δ_{2B}	Clearance rate of the viruses by antibodies, B-cells
μ_1	Natural death rate of uninfected cell U
μ_2	Death rate of infected cell I
μ_3	Decay rate of the virus
μ_4	Death rate of Natural killer cells
μ_5	Death rate of antibody B-cells
μ_6	Death rate of Cytotoxic T-cells
μ_7	Death rate of Regulatory T-cells
μ_8	Death rate of Helper T-cells
k_1	Booster rate of Cytotoxic T-cells
k_2	Booster rate of antibody B-cells
k_3	Booster rate of Helper T-cells
k_4	Booster rate of Regulatory T-cells
k_5	Booster rate of Natural killer cells
$ø$	Effectiveness of drug usage

As Infected cells, I, activate Cytotoxic T-class, T, the population grows at a rapid rate , helped by Helper T-cells to attack the infected cells at a rapid rate and would be regulated at a rapid rate , boosted at a rapid rate , killing infected cells, I, at a rapid rate , and dying at a rapid rate .
Antibody B-cells are triggered by free virus cells, V, and produced at rate, boosted at rate, neutralized the free virus, V, at rate with death rate of B-cells as. Antibody B-cells are assisted by Helper T-cells, H, to attack the free virus cells at rate and are regulated at rate.
Helper T-cells, H, are boosted at rate, and die at rate, Helper T-cells, H, assist antibody B-cells (B) to produce antibodies and assist cytotoxic T-cells (T) in their attack on the infected virus classes (I).
Regulatory T-cells (R) are produced by regulating Cytotoxic T-cells (T), H-cells, and B-cells at rates respectively. Regulatory T-cells (R) are boosted at rate and die at rate.
Natural killer cell (K), are triggered by Infected cells (I) at rate, and free virus cells (V) at rate . Natural killer cell (K) are boosted at rate, they kill infected cells (I) at rate and also kill free virus cells (V) at rate and die at rate .
The effect of the drug () is to reduce the proliferation of infected cells (I), the range of effectiveness of drug usage as thus measuring the efficacy of drug.means the drug is wholly effective thereby completely stopping the resurgence of infected cells while implies there is no drug and control intervention against the virus infection.

3. Model formulation and analysis

3.1. Model equation

$$\begin{aligned}
\frac{dU}{dt} &= \pi - (1-\phi)\alpha UV - \mu_1 U \\
\frac{dI}{dt} &= (1-\phi)\alpha UV - \omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT \\
&\quad - \delta_{IK} IK \\
\frac{dV}{dt} &= \omega I - \lambda VB - \theta_v VK - \mu_3 V - \delta_{2K} KV - \delta_{2B} BV \\
\frac{dK}{dt} &= k_5 K + \theta_I IK + \theta_V VK - \mu_4 K \frac{dT}{dt} = k_1 T + \gamma IT \\
&\quad + \beta_T T\mathrm{H} - \mu_6 T - \rho_T TR \\
\frac{dB}{dt} &= k_2 B + \lambda VB + \beta_B B\mathrm{H} - \mu_5 B - \rho_B BR \\
\frac{dH}{dt} &= k_3 H - \beta_B B\mathrm{H} - \rho_{\mathrm{H}} HR - \beta_T TH - \mu_8 H \\
\frac{dR}{dt} &= k_4 R + \rho_T TR + \rho_H HR + \rho_B BR - \mu_7 R
\end{aligned} \tag{1}$$

3.2. Basic Properties of the model

3.2.1. Positivity of solutions

Since the human-cell population is being tracked by models Eq.1, all of the parameters are positive. As a result, it is necessary to demonstrate that all state variables are positive at all times t > 0.

Theorem 1. *Consider the initial condition,*

$$\begin{aligned}
&\{U(0) \geq 0,\ I(0) \geq 0,\ V(0) \geq 0,\ K(0) \geq 0,\ T(0) \geq 0, \\
&B(0) \geq 0,\ H(0) \geq 0,\ R(0) \geq 0\} \in D
\end{aligned}$$

the solution set $\{U,\ I,\ V,\ K,\ T,\ B,\ H,\ R\}$ of the system Eq. 1 is positive for all$t \geq 0$.
Proof

Recall from the system of Eq. 1

$$\frac{dU}{dt} = \pi - (1-\phi)\alpha UV - \mu_1 U \tag{2}$$

Removing the positivity term π on RHS

$$\frac{dU}{dt} \geq -U[(1-\phi)\alpha V + \mu_1 \tag{3}$$

Writing Eq. 3 in the form of linear differential equation

$$\frac{dU}{dt} = -[(1-\phi)\alpha V + \mu_1]U \tag{4}$$

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$$\frac{dU}{dt} + [(1-\phi)\alpha V + \mu_1]U = 0 \tag{5}$$

This is solvable by integrating factor (IF) method as;

$$I.F = \ell^{\int[(1-\phi)\alpha V+\mu_1]dt}$$

$$U(t) \times \ell^{\int[(1-\phi)\alpha V+\mu_1]dt} = \int 0 \times \ell^{\int[(1-\phi)\alpha V+\mu_1]dt}dt + C$$

$$U(t) \times \ell^{\int[(1-\phi)\alpha V+\mu_1]dt} = C$$

$$U(t) = C\ell^{-\int[(1-\phi)\alpha V+\mu_1]dt}$$

Since U(0) = U_0

$$U(t) = U_0\ell^{-\int[(1-\phi)\alpha V+\mu_1]dt}$$

Then the general solution of Eq.5 is

$$U(t) = U_0\ell^{-\int[(1-\phi)\alpha V+\mu_1]dt} \tag{6}$$

$$U(t) > 0, \forall t \geq 0$$

From the system of Eq.1

$$\frac{dI}{dt} = (1-\phi)\alpha UV - \omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK$$

Removing the positivity term $(1-\phi)\alpha UV$ on RHS

$$\frac{dI}{dt} \geq -[\omega + \gamma T + \theta_1 K + \mu_2 + \delta_{1T} T + \delta_{IK} K]I \tag{7}$$

Writing Eq. 7 in the form of linear differential equation

$$\frac{dI}{dt} = -[\omega + \gamma T + \theta_1 K + \mu_2 + \delta_{1T} T + \delta_{IK} K + \mu_2 + \delta_{1T} T + \delta_{IK} K]I$$

$$\frac{dI}{dt} + [\omega + \gamma T + \theta_1 K + \mu_2 + \delta_{1T} T + \delta_{IK} K + \mu_2 + \delta_{1T} T + \delta_{IK} K]I = 0 \tag{8}$$

This is also solvable by IF method to give a general solution;

$$I(t) = (I_0)\ell^{-\int[\omega+\gamma T+\theta_1 K+\mu_2+\delta_{1T}T+\delta_{IK}K+\mu_2+\delta_{1T}T+\delta_{IK}K]dt} = I(t) > 0, \forall t \geq 0 \tag{9}$$

Following the same process for the system of Eq. 1, we obtain;

$$\begin{aligned} V(t) &= V_0\ell^{-\int[\lambda B-\theta_v K+\mu_3+\delta_{2K}K+\delta_{2B}B]dt}, V(t) > 0, \forall t \geq 0 \\ K(t) &= K_0\ell^{-\int \mu_4 dt}, K(t) > 0, \forall t \geq 0 \\ T(t) &= T_0\ell^{-\int[\mu_6+\rho_T R]dt}, T(t) > 0, \forall t \geq 0 \\ B(t) &= B_0\ell^{-\int[\mu_5+\rho_B R]dt}, B(t) > 0, \forall t \geq 0 \\ H(t) &= H_0\ell^{-\int[\beta_B \mathrm{B}+\rho_\mathrm{H} R+\beta_T T+\mu_8]dt}, H(t) > 0, \forall t \geq 0 \\ R(t) &= R_0\ell^{-\int \mu_7 dt}, R(t) > 0, \forall t \geq 0 \end{aligned} \tag{10}$$

3.2.2. Boundedness of solutions

The addition of cell compartments of the system of Eq. 1.
The total population size is $N = U+I+V+K+T+B+H+R$

$$\begin{aligned} &\tfrac{dN}{dt} = \pi - (1-\phi)\alpha UV - \mu_1 U + (1-\phi)\alpha UV - \omega I - \gamma IT \\ &-\theta_1 IK - \mu_2 I - \delta_{1T} IT \\ &-\delta_{IK} IK + \omega I - \mu_3 V - \delta_{2K} KV - \delta_{2B} BV + k_5 k + \theta_I IK \\ &+\theta_V VK - \mu_4 K + k_1 T + \gamma IT \\ &+\beta_T T\mathrm{H} - \mu_6 T - \rho_T TR + k_2 B + \lambda VB + \beta_B B\mathrm{H} - \mu_5 B \\ &-\rho_B BR + k_3 H - \beta_B B\mathrm{H} - \rho_\mathrm{H} HR \\ &-\beta_T TH - \mu_8 H + k_4 R + \rho_T TR + \rho_H HR + \rho_B BR - \mu_7 R \end{aligned}$$

$$\begin{aligned} &\tfrac{dN}{dt} = \pi - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK - \mu_3 V - \delta_{2K} KV \\ &-\delta_{2B} BV + k_5 k + \theta_I IK + \theta_V VK - \mu_4 K + k_1 T + \gamma IT \\ &-\mu_6 T + k_2 B + \lambda VB - \mu_5 B + k_3 H - \mu_8 H + k_4 R - \mu_7 7 \end{aligned} \tag{11}$$

Theorem 2:
The solution of the system Eq. 1 is feasible at $t > 0$ if they enter the region $D = \{U, I, V, K, T, B, H, R\} \in R^8$.
Proof:
Let $D = \{U, I, V, K, T, B, H, R\} \in R^8$ be any solution of the system Eq. 1 with non-zero conditions.
Assuming that there is no infection i.e.

$$\delta_{1T} = \delta_{IK} = \omega = \delta_{2K} = \delta_{2B} = k_5 = \theta_I = \theta_V = k_1 = \gamma = k_2 = \lambda = k_3 = k_4 = 0,$$

then Eq. 11 becomes

$$\frac{dN}{dt} = \pi - \mu_1 N \tag{12}$$

Where $\mu_1 = \mu_2 = \mu_3 = \mu_4 = \mu_6 = \mu_5 = \mu_8 = \mu_7$
Eq.12 becomes;

$$\frac{dN}{dt} + \mu_1 N = \pi$$

Which is solvable by IF to get

$$N(t) = \frac{\pi}{\mu_1}[1 - \ell^{-\mu_1 t}] + N_0\ell^{-\mu_1 t} \tag{13}$$

And as $t \to \infty$, $N(t) = \frac{\pi}{\mu_1}$
N approaches $\frac{\pi}{\mu_1}$ as $t \to \infty$ in Eq. 13,
Hence all feasible solution of Eq. 1 enter in the region

$$\begin{aligned} &D = \{U(t),\ I(t),\ V(t),\ K(t),\ T(t),\ B(t),\ H(t),\ R(t) \in R^8 : \\ &U(t),\ I(t),\ V(t),\ K(t),\ T(t),\ B(t),\ H(t),\ R(t) \geq 0 \\ &U(t) + I(t) + V(t) + K(t) + T(t) + B(t) + H(t) + R(t) \leq N; \\ &N \leq \tfrac{\pi}{\mu_1}\} \end{aligned}$$

Therefore, the region of the model is positively invariant and equation Eq. 1 are epidemiologically meaningful and mathematically well posed in the domain D.

$$\Rightarrow N_0 \leq N(t) \leq \frac{\pi}{\mu_1} \tag{14}$$

Hence, the total cell population is bounded.

3.2.3. Equilibrium states of the model

At equilibrium states,

$$\frac{dU}{dt} = \frac{dI}{dt} = \frac{dV}{dt} = \frac{dK}{dt} = \frac{dT}{dt} = \frac{dB}{dt} = \frac{dH}{dt} = \frac{dR}{dt} = 0 \tag{15}$$

Therefore, Infection Free Equilibrium (IFE) denoted as

$$\begin{aligned} E_0 &= (U^0, I^0, V^0, K^0, T^0, B^0, H^0, R^O) \\ &= [\frac{\pi}{\mu_1},\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0] \end{aligned} \tag{16}$$

3.3. Control reproductive number

We introduce the method of next generation to derive the control reproductive number of model Eq. 1, [9]. We therefore have the following;

$$\frac{dI}{dt} = (1-\phi)\alpha UV - \omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK$$

$$\frac{dV}{dt} = \omega I$$

$$F = \begin{pmatrix} (1-\phi)\alpha U^0 V^0 \\ \omega I^0 \end{pmatrix}$$

$$V = \begin{pmatrix} \omega I^0 + \gamma I^0 T^0 + \theta_1 I^0 K^0 + \mu_2 I^0 + \delta_{1T} I^0 T^0 + \delta_{IK} I^0 K^0 \\ \lambda V^0 B^0 + \theta_v V^0 K^0 + \mu_3 V^0 + \delta_{2K} K^0 V^0 + \delta_{2B} B^0 V^0 \end{pmatrix}$$

Let I = f_1, V=f_2

$$F = \begin{bmatrix} \frac{df_1}{dI} & \frac{df_1}{dV} \\ \frac{df_2}{dI} & \frac{df_2}{dV} \end{bmatrix} = \begin{bmatrix} 0 & (1-\phi)\alpha U^0 \\ \omega & 0 \end{bmatrix} \tag{17}$$

Let I = v_1, V=v_2

$$F = \begin{bmatrix} \frac{df_1}{dI} & \frac{df_1}{dV} \\ \frac{df_2}{dI} & \frac{df_2}{dV} \end{bmatrix} = \begin{bmatrix} 0 & (1-\phi)\alpha U^0 \\ \omega & 0 \end{bmatrix} \tag{18}$$

Let I = v_1, V=v_2

$$V = \begin{bmatrix} \frac{dv_1}{dI} & \frac{dv_1}{dV} \\ \frac{dv_2}{dI} & \frac{dv_2}{dV} \end{bmatrix} = \begin{bmatrix} \omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0 & 0 \\ 0 & \lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0 \end{bmatrix} \tag{19}$$

$$V^{-1} = \frac{1}{|V|} adjV$$

$$FV^{-1} = \begin{bmatrix} 0 & \frac{(1-\phi)\alpha\pi}{\mu_1(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0)} \\ \frac{\omega}{(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0)} & 0 \end{bmatrix} \tag{20}$$

The characteristic equation of Eq. 20 is

$$\left|FV^{-1} - \lambda\right| = \begin{vmatrix} -\lambda & \frac{(1-\phi)\alpha\pi}{\mu_1(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0)} \\ \frac{\omega}{(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0)} & -\lambda \end{vmatrix} \tag{21}$$

And the Determinant of Eq. 21 is

$$\lambda^2 = -\frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0)(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0)} = 0$$

$$\lambda = \sqrt{\frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0)(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0)}} \tag{22}$$

where λ is the largest eigenvalue which is spectral of $\ell(FV^{-1})$. Therefore, the control reproductive number is

$$R_c = \sqrt{\frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0)(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0)}} \tag{23}$$

3.4. Stability analysis of the DFE

Existence of the DFE points are the stable-state solutions where the virus infection dies out from all the cells, which connotes the total is uninfected cells.
Then

$$U^0 \neq 0, \tag{24}$$

We obtain the DFE point at E^0 by putting

$$U = I = V = K = T = B = H = R = 0 \tag{25}$$

Where their respect First Differential Equation is zero

$$\begin{aligned}
&\pi - (1-\phi)\alpha UV - \mu_1 U = 0\\
&(1-\phi)\alpha UV - \omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT\\
&- \delta_{IK} IK = 0\\
&\omega I - \lambda VB - \theta_v VK - \mu_3 V - \delta_{2K} KV - \delta_{2B} BV = 0\\
&k_5 k + \theta_I IK + \theta_V VK - \mu_4 K = 0\\
&k_1 T + \gamma IT + \beta_T T\mathrm{H} - \mu_6 T - \rho_T TR = 0\\
&k_2 B + \lambda VB + \beta_B B\mathrm{H} - \mu_5 B - \rho_B BR = 0\\
&k_3 H - \beta_B B\mathrm{H} - \rho_{\mathrm{H}} HR - \beta_T TH - \mu_8 H = 0\\
&k_4 R + \rho_T TR + \rho_H HR + \rho_B BR - \mu_7 R = 0
\end{aligned} \tag{26}$$

Since $U^0 \neq 0$, at DFE,

$$U^0 = I^0 = V^0 = K^0 = T^0 = B^0 = H^0 = R^0 = 0$$

Thus the system Eq. 26 now becomes

$$\pi - \mu_1 U^0 = 0$$

$$\Rightarrow U^0 = \frac{\pi}{\mu_1} \tag{27}$$

This gives the equilibrium states of the model, therefore, Infected Free Equilibrium (IFE), denoted

$$\begin{aligned}
E_0 &= (U^0, I^0, V^0, K^0, T^0, B^0, H^0, R^O)\\
&= \left[\frac{\pi}{\mu_1},\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0\right]
\end{aligned} \tag{28}$$

3.5. Local stability of infected free equilibrium (E^0)

Theorem 3:
The Infection Free Equilibrium of the model equations Eq. 1 is local asymptotically stable if all eigenvalues of the system's Jacobian are non-positive real values.
Proof:
Owing to the above theorem, Jacobian Matrix of the systems of equation Eq. 1 at IFE

$$E_0 = (\frac{\pi}{\mu_1},\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0)$$

We have Jacobian Matrix, $J(U,\ I,\ V,\ K,\ T,\ B,\ H,\ R)$

$$J = \begin{bmatrix}
-\mu_1 & 0 & -(1-\phi)\alpha\frac{\pi}{\mu_1} & 0 & 0 & 0 & 0 & 0\\
0 & -\omega-\mu_2 & (1-\phi)\alpha\frac{\pi}{\mu_1} & 0 & 0 & 0 & 0 & 0\\
0 & \omega & -\mu_3 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & (k_5-\mu_4) & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & (k_1-\mu_6) & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & (k_2-\mu_5) & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & (k_3-\mu_8) & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & (k_4-\mu_7)
\end{bmatrix} \tag{29}$$

$$|J-\lambda I| = \begin{vmatrix}
-\mu_1-\lambda & 0 & -(1-\phi)\alpha\frac{\pi}{\mu_1} & 0 & 0 & 0 & 0 & 0\\
0 & -(\omega+\mu_2)-\lambda & (1-\phi)\alpha\frac{\pi}{\mu_1} & 0 & 0 & 0 & 0 & 0\\
0 & \omega & -\mu_3-\lambda & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & (k_5-\mu_4)-\lambda & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & (k_1-\mu_6)-\lambda & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & (k_2-\mu_5)-\lambda & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & (k_3-\mu_8)-\lambda & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & (k_4-\mu_7)-\lambda
\end{vmatrix} \tag{30}$$

$-\mu_1 - \lambda$ is the only non-zero entry in the first column;
Hence

$$\lambda_1 = -\mu_1 < 0 \tag{31}$$

Delete the perpendicular rows and columns

$$J_0 = \begin{vmatrix} -(\omega+\mu_2)-\lambda & (1-\phi)\alpha\frac{\pi}{\mu_1} & 0 & 0 & 0 & 0 & 0 \\ \omega & -\mu_3-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & (k_5-\mu_4)-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & (k_1-\mu_6)-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (k_2-\mu_5)-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & (k_3-\mu_8)-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & (k_4-\mu_7)-\lambda \end{vmatrix} \tag{32}$$

Similarly in row 3 $(k_5-\mu_4)-\lambda$ is the only non-zero entry,
Hence

$$\lambda_2 = -(\mu_4-k_5) < 0, if, \mu_4 > k_5 \tag{33}$$

$$J_1 = \begin{vmatrix} -(\omega+\mu_2)-\lambda & \frac{(1-\phi)\alpha\pi}{\mu_1} & 0 & 0 & 0 & 0 \\ \omega & -\mu_3-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & (k_1-\mu_6)-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & (k_2-\mu_5)-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & (k_3-\mu_8)-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & (k_4-\mu_7)-\lambda \end{vmatrix} \tag{34}$$

Similarly in row 3, $(k_1-\mu_6)-\lambda$as the only entry
Hence

$$\lambda_3 = -(\mu_6-k_1) < 0, if, \mu_6 > k_1 \tag{35}$$

$$J_2 = \begin{vmatrix} -(\omega+\mu_2)-\lambda & \frac{(1-\phi)\alpha\pi}{\mu_1} & 0 & 0 & 0 \\ \omega & -\mu_3-\lambda & 0 & 0 & 0 \\ 0 & 0 & (k_2-\mu_5)-\lambda & 0 & 0 \\ 0 & 0 & 0 & (k_3-\mu_8)-\lambda & 0 \\ 0 & 0 & 0 & 0 & (k_4-\mu_7)-\lambda \end{vmatrix} \tag{36}$$

Similarly in row 3, $(k_2-\mu_5)-\lambda$as the only entry
Hence

$$\lambda_4 = -(\mu_5-k_2) < 0, if, \mu_5 > k_2 \tag{37}$$

$$J_3 = \begin{vmatrix} -(\omega+\mu_2)-\lambda & \frac{(1-\phi)\alpha\pi}{\mu_1} & 0 & 0 \\ \omega & -\mu_3-\lambda & 0 & 0 \\ 0 & 0 & (k_3-\mu_8)-\lambda & 0 \\ 0 & 0 & 0 & (k_4-\mu_7)-\lambda \end{vmatrix} \tag{38}$$

Following above process of deleting required column and row to reduce matrix to echelon form, we have,

$$\lambda_5 = -(\mu_8-k_3) < 0, if\ with\ \mu_8 > k_3,$$

$$\lambda_6 = -(\mu_7-k_4) < 0, if\ with\ \mu_7 > k_4, \lambda_7 = -\mu_2 < 0,$$

$$R_c = \sqrt{\frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0+\theta_v K^0+\mu_3+\delta_{2K}K^0+\delta_{2B}B^0)(\omega+\gamma T^0+\theta_1 K^0+\mu_2+\delta_{1T}T^0+\delta_{IK}K^0)}}$$

$$\lambda_8 = \frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0+\theta_v K^0+\mu_3+\delta_{2K}K^0+\delta_{2B}B^0)} - (\omega+\gamma T^0+\theta_1 K^0+\mu_2+\delta_{1T}T^0+\delta_{IK}K^0),$$

$$\lambda_8 = \frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0+\theta_v K^0+\mu_3+\delta_{2K}K^0+\delta_{2B}B^0)(\omega+\gamma T^0+\theta_1 K^0+\mu_2+\delta_{1T}T^0+\delta_{IK}K^0)} - 1 < 0 \tag{39}$$

Eq. 31- 42 gives the eigenvalues of the Infection Free Equilibrium of model Eq. 1.

Theorem 4:

The Infection Free Equilibrium (IFE) of the model Eq.1 is local asymptotically stable if$R_c < 1$

Proof

From $\lambda_8$of the obtain eigenvalues, then we have

$$R_c = \sqrt{\frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0+\theta_v K^0+\mu_3+\delta_{2K}K^0+\delta_{2B}B^0)(\omega+\gamma T^0+\theta_1 K^0+\mu_2+\delta_{1T}T^0+\delta_{IK}K^0)}}$$

$${R_c}^2 = \frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0+\theta_v K^0+\mu_3+\delta_{2K}K^0+\delta_{2B}B^0)(\omega+\gamma T^0+\theta_1 K^0+\mu_2+\delta_{1T}T^0+\delta_{IK}K^0)}$$

At

$$\lambda_8 = \frac{\omega(1-\phi)\alpha\pi}{\mu_1(\lambda B^0+\theta_v K^0+\mu_3+\delta_{2K}K^0+\delta_{2B}B^0)(\omega+\gamma T^0+\theta_1 K^0+\mu_2+\delta_{1T}T^0+\delta_{IK}K^0)} - 1 < 0$$

We can then write

$$\lambda_8 = R_c^2 - 1 < 0 \tag{40}$$

$$R_c^2 - 1 < 0$$
$$R_c^2 < 1$$

Therefore,

$$R_c < 1 \tag{41}$$

Eq. 41 holds and justifying theorem 2.
Thus, the Infection Free Equilibrium, E^0 of Eq. 1 is locally asymptotically stable if $R_c<1$. Hence the epidemiological implications of the theorem is that Ebola virus may be control or eradicated from cell population when$R_c < 1$.

3.6. Global stability of infected free equilibrium (E^0)

Theorem 5:
The Infection Free Equilibrium is globally asymptotically stable (GAS) if.
Proof
Lyapunov function is used to investigate the stability of the (IFE). To establish the global stability of the IFE, we selected infected classes for construction of Lyapunov function, we have

$$R_c < 1$$

$$\frac{dI}{dt} = (1-\phi)\alpha UV - \omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK$$
$$\frac{dV}{dt} = \omega I - \lambda VB - \theta_v VK - \mu_3 V - \delta_{2K} KV - \delta_{2B} BV$$
$$\omega I - \lambda VB - \theta_v VK - \mu_3 V - \delta_{2K} KV - \delta_{2B} BV$$

$$L(I,V) = (\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)I + (1-\phi)\alpha UV \tag{42}$$

And as good candidate for a lyapunov function and must satisfied

$$\dot{L}(I,V) \leq 0, for, R_c \leq 1 \tag{43}$$

Derivative of Eq. 42

$$\dot{L}(I,V) = (\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)\dot{I} + (1-\phi)\alpha U\dot{V} \tag{44}$$

Substitute for $\dot{I}$and $\dot{V}$from Eq. 1 into Eq. 44

$$\dot{L}(I,V) = (\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)$$
$$((1-\phi)\alpha UV - \omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK)$$
$$+(1-\phi)\alpha U\,(\omega I - \lambda VB - \theta_v VK - \mu_3 V - \delta_{2K} KV - \delta_{2B} BV)$$

$$L(I,V) = (1-\phi)\alpha UV\,(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)$$
$$+(-\omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK)$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)$$
$$+(1-\phi)\alpha U(\omega I) - (\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)$$
$$(1-\phi)\alpha U \tag{45}$$

$$\dot{L}(I,V) = (1-\phi)\alpha UV\,(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$+(-\omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK)$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$+(1-\phi)\alpha U(\omega I) -$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} BV)\,(1-\phi)\alpha U$$

$$\dot{L}(I,V) = (1-\phi)\alpha UV\,(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$-(1-\phi)\alpha U\,(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$+(-\omega I - \gamma IT - \theta_1 IK - \mu_2 I - \delta_{1T} IT - \delta_{IK} IK)$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$+(1-\phi)\alpha U(\omega I)$$

$$L(I,V) = (1-\phi)\alpha UV\,(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$-(1-\phi)\alpha U\,(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)$$
$$+(-\omega - \gamma T - \theta_1 K - \mu_2 - \delta_{1T} T - \delta_{IK} K)$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B) + (1-\phi)\alpha U\omega I \tag{46}$$

Eq. 46 reduced to

$$\dot{L}(I,V) = (-\omega - \gamma T - \theta_1 K - \mu_2 - \delta_{1T} T - \delta_{IK} K) \tag{47}$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B) + (1-\phi)\alpha U\omega I$$

Implies

$$\dot{L}(I,V) = (1-\phi)\alpha U\omega -$$
$$(\omega + \gamma T + \theta_1 K + \mu_2 + \delta_{1T} T + \delta_{IK} K) \tag{48}$$
$$(\lambda B + \theta_v K + \mu_3 + \delta_{2K} K + \delta_{2B} B)\,I$$

At the infraction -free equilibrium state, Eq. 48 gives,

$$L(I,V) = \frac{(1-\phi)\alpha\pi\omega}{\mu_1} -$$
$$\left(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0\right) \tag{49}$$
$$\left(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0\right) I$$

From Eq. 49 we have

$$\dot{L}(I,V) = \left(\omega + \gamma T^0 + \theta_1 K^0 + \mu_2 + \delta_{1T} T^0 + \delta_{IK} K^0\right) \tag{50}$$
$$\left(\lambda B^0 + \theta_v K^0 + \mu_3 + \delta_{2K} K^0 + \delta_{2B} B^0\right)\left(R_c^2 - 1\right) I$$

Hence we have, $\dot{L}(I,V) \leq 0$; If $R_c^2 - 1 \leq 0, then, R_c^2 \leq 1$
Therefore

$$R_c \leq 1 \tag{51}$$

This completes the proof.
The infection free equilibrium is globally asymptotically stable (GAS) if$R_c \leq 1$.

3.6.1. Infection persistence equilibrium

Theorem 5:
Let

$$E_1 \quad = \quad (U, I, V, K, T, B, H, R) = (U^{\#}, I^{\#}, V^{\#}, K^{\#}, T^{\#}, B^{\#}, H^{\#}, R^{\#})$$

be an infection persistence equilibrium point, Eq. 50 becomes

$$\pi - (1-\phi)\alpha U^{\#} V^{\#} - \mu_1 U^{\#} = 0$$
$$(1-\phi)\alpha U^{\#} V^{\#} - \left(\omega + \gamma T^{\#} + \theta_1 K^{\#} + \mu_2 + \delta_{1T} T^{\#} + \delta_{IK} K^{\#}\right) I^{\#} = 0$$
$$\omega I^{\#} - \left(\lambda B^{\#} + \theta_v K^{\#} + \mu_3 + \delta_{2K} K^{\#} + \delta_{2B} B^{\#}\right) V^{\#} = 0$$
$$\left(k_5 + \theta_I I^{\#} + \theta_V V^{\#} - \mu_4\right) K^{\#} = 0$$
$$\left(k_1 + \gamma I^{\#} + \beta_T \mathrm{H}^{\#} - \mu_6 - \rho_T R^{\#}\right) T^{\#} = 0$$
$$\left(k_2 + \lambda V^{\#} + \beta_B \mathrm{H}^{\#} - \mu_5 - \rho_B R^{\#}\right) B^{\#} = 0$$
$$\left(k_3 - \beta_B B^{\#} - \rho_{\mathrm{H}} R^{\#} - \beta_T T^{\#} - \mu_8\right) H^{\#} = 0$$
$$\left(k_4 + \rho_T T^{\#} + \rho_H H^{\#} + \rho_B B^{\#} - \mu_7\right) R^{\#} = 0 \tag{52}$$

Table 2: Values and source of state variables.

State Variables	Value	Source
U	50	Assumed
I	17	Assumed
V	100	Assumed
K	5	Assumed
T	3	Assumed
B	5	Assumed
H	5	Assumed
R	5	
Total	190	

And we have the simplified equations to be

$$\begin{aligned}
&\pi-(1-\phi)\alpha U^{\#}V^{\#}-\mu_1U^{\#}=0\\
&\pi-\mu_1U^{\#}-\\
&\left(\omega+\gamma T^{\#}+\theta_1K^{\#}+\mu_2+\delta_{1T}T^{\#}+\delta_{IK}K^{\#}\right)I^{\#}=0\\
&\omega I^{\#}-\left(\lambda B^{\#}+\theta_vK^{\#}+\mu_3+\delta_{2K}K^{\#}+\delta_{2B}B^{\#}\right)V^{\#}=0\\
&k_5+\theta_II^{\#}+\theta_VV^{\#}-\mu_4=0\\
&k_1+\gamma I^{\#}+\beta_T\mathrm{H}^{\#}-\mu_6-\rho_TR^{\#}=0\\
&k_2+\lambda V^{\#}+\beta_B\mathrm{H}^{\#}-\mu_5-\rho_BR^{\#}=0\\
&k_3-\beta_BB^{\#}-\rho_{\mathrm{H}}R^{\#}-\beta_TT^{\#}-\mu_8=0\\
&k_4+\rho_TT^{\#}+\rho_HH^{\#}+\rho_BB^{\#}-\mu_7=0
\end{aligned}\tag{53}$$

By further simplification we have,

$$\begin{aligned}
U^{\#}&=\frac{\pi}{((1-\phi)\alpha V^{\#}-\mu_1)}\\
I^{\#}&=\frac{\mu_4-k_5-\theta_VV^{\#}}{\theta_I}\\
\mathrm{H}^{\#}&=\frac{\mu_6+\rho_TR^{\#}k_1-\gamma\left(\frac{\mu_4-k_5-\theta_VV^{\#}}{\theta_I}\right)}{\beta_T}\\
R^{\#}&=\frac{\mu_5-k_2-\lambda V^{\#}-\beta_B\left(\frac{\mu_6+\rho_TR^{\#}k_1-\gamma\left(\frac{\mu_4-k_5-\theta_VV^{\#}}{\theta_I}\right)}{\beta_T}\right)}{\rho_B}\\
B^{\#}&=-\frac{\beta_BB^{\#}+\rho_{\mathrm{H}}R^{\#}+\beta_TT^{\#}+\mu_8-k_3}{\beta_B}\\
T^{\#}&=\frac{k_4+\rho_HH^{\#}+\rho_BB^{\#}-\mu_7}{\rho_T}
\end{aligned}\tag{54}$$

(55)

4. Numerical simulations

The numerical simulations were carried out and the results are shown in Table 2-3, and Fig. 3-10.

Table 3: Values and Source of Parameters.

Parameter	Value	Source
π	5.05cells/ml/day	Wester, 2015
α	0.1-0.8cell/ml/day	CDC, 2014
ω	0.9	Assumed
γ	0.1ml/cell/day	Banton et al., 2010
λ	0.1nl/cell/day	Lasisi et al., 2018
θ_I	0.1cell/day	Assumed
θ_v	0.1cell/day	Assumed
β_T	0.1cell/day	Assumed
β_B	0.25cell/day	Assumed
ρ_H	0.25cell/day	Assumed
ρ_B	0.1cell/day	Assumed
δ_{IK}	0.1cell/day	Assumed
δ_{IT}	0.1ml/cell/day	Wester, 2015
δ_{2K}	0.1cell/day	Assumed
δ_{2B}	0.1ml/cell/day	Lasisi et al., 2018
μ_1	0.1cell/day	Assumed
μ_2	0.5cell/day	Lasisi et al., 2018
μ_3	0.015cell/day	Assumed
μ_4	0.1cell/day	Assumed
μ_5	0.02cell/day	Lasisi et al, 2018
μ_6	0.5cell/day	Wester 2015
μ_7	0.1cell/day	Assumed
μ_8	0.5cell/day	Assumed
k_1	0.25	Lasisi et al, 2018
k_2	0.25	Lasisi et al, 2018
k_3	0.02	Assumed
k_4	0.02	Assumed
k_5	0.25	Assumed
ø	$0< ø <1$	Lasisi et al, 2018

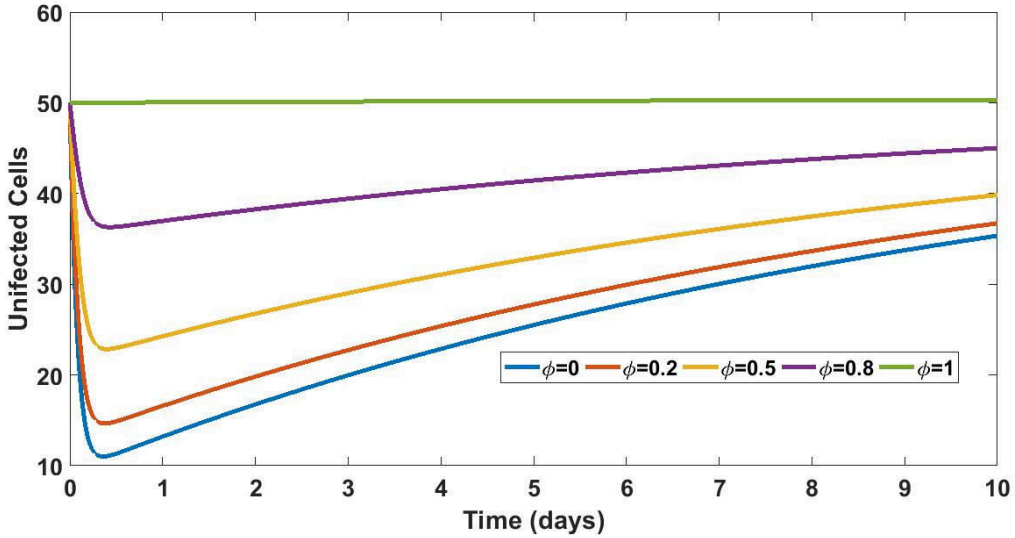

Figure 3: Efficacy of Drugs on the uninfected cell population within the first ten days.

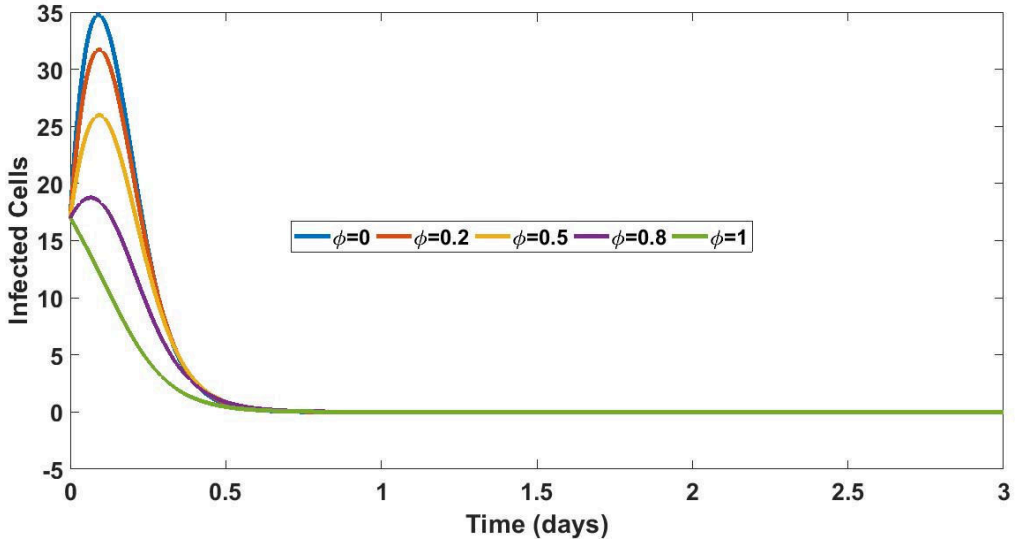

Figure 4: Efficacy of Drugs on the infected cell population within the first ten days

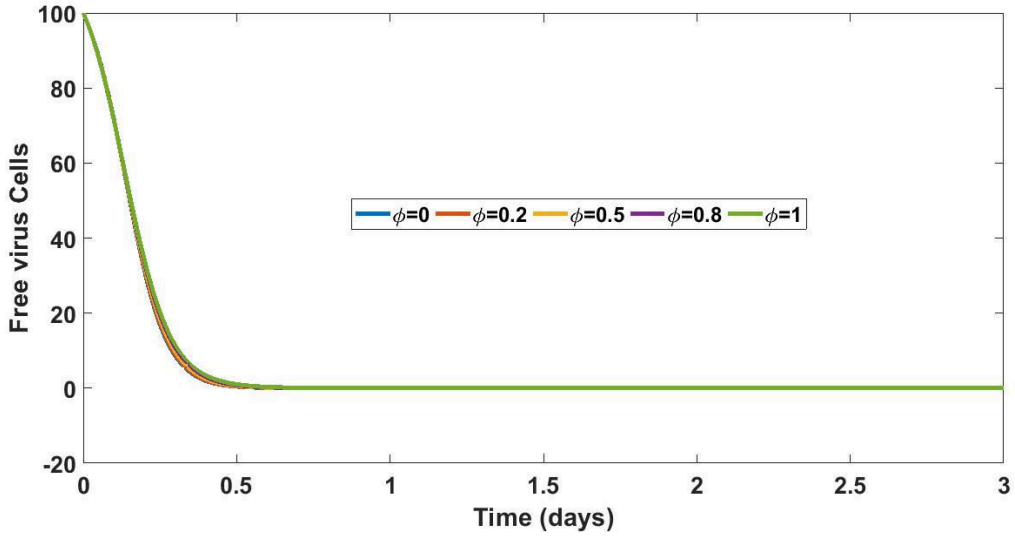

Figure 5: Efficacy of Drugs on the free virus cell population within the first ten days

5. Discussion and interpretation of results

5.1. Efficacy of Drugs on the uninfected cell population within the first ten days

We conducted simulations by manipulating drug usage with the parameter values outlined in Table 3. Fig. 3 illustrates an increase in the count of uninfected cells (U), indicating that the utilization of drugs as an intervention strategy can effectively manage the infection rate within the population. Additionally, the findings demonstrate that maintaining optimal drug usage leads to a consistent level of uninfected cells.

5.2. Efficacy of Drugs on the Infected Cell Population within the First Ten Days

By manipulating the drug usage in accordance with the parameter values provided in Table 3, we observed a significant reduction in infected cells within the first two days, as depicted in Fig. 4. This observation underscores the role of drug usage in effectively curbing the infection rate in the population. Furthermore, it is noteworthy that a stable condition is achieved one day after the initiation of drug intervention.

5.3. Efficacy of Drugs on the Free Virus Cell Population within the First Ten Days

In Fig. 5, it is evident that as the efficiency of drug administration improves, there is no notable alteration in the population of free virus cells. This observation aligns with the findings reported by [31], which suggest that antiviral medications primarily operate by interrupting the infectious process rather than directly eliminating viruses.

5.4. Efficacy of Drugs on the Cytotoxic T-cell Population Within the First Ten Days

The simulation conducted using the parameter values specified in Table 3 demonstrates a significant decline in cytotoxic T-cells with an increase in drug usage (Fig. 6). This underscores the importance of a delicate balance in the administration of drugs for virus treatment. It serves as a clear reminder to healthcare professionals that when administering drugs to combat viruses, it's essential to strike a careful equilibrium between alleviating the patient's symptoms by reducing the virus's inflammatory effects and minimizing potential harm from the drug's toxic side effects. This approach often involves the use of drugs like corticosteroids, which are employed in transplant recipients and for the treatment of inflammatory, autoimmune, and allergic conditions. In these cases, combining such drugs with others is a common strategy aimed at minimizing both the dosage and the associated toxic effects, as discussed by [15].

5.5. Efficacy of Drugs on the Antibody B-cell Population within the First Ten Days

Fig. 7 illustrates that when we conduct simulations using the parameter values outlined in Table 3, there is typically little to no significant impact of drugs on antibody B-cells. This outcome can be attributed to the fact that antibody B-cells remain free from viruses. B cells are responsible for producing antibodies, which are specialized proteins that have the ability to bind to pathogens or foreign substances, such as toxins, in order to neutralize them. For instance, antibodies can attach themselves to viruses, preventing them from entering healthy cells and causing infections. Additionally, B cells can also recruit other immune cells to assist in the elimination of infected cells. Consequently, healthcare practitioners may not need to assess the effectiveness of drugs on antibody B-cells when administering them for viral treatments.

5.6. Efficacy of Drugs on the Natural Killer Cell Population within the First Ten Days

The numerical outcomes from the simulation, as depicted in Fig. 8, reveal that there is a reduction in the population of natural killer cells as the drug dosage increases. In simpler terms, a reduction in the drug dosage would lead to an increase in the natural killer cell population. Typically, immune cells recognize the presence of the major histocompatibility complex (MHC) on cell surfaces, which triggers the release of cytokines and leads to the lysis or apoptosis of cells that either lack MHC I or express significantly lower levels of it compared to normal cells [28]. Unlike phagocytes, natural killer (NK) cells do not require the target cells to be opsonized (marked) by antibodies before they can take action, resulting in a quicker immune response. However, opsonins can expedite this process.

5.7. Efficacy of Drugs on the Helper T-cell Population within the First Ten Days

Fig. 9 provides a detailed illustration of the interaction between drugs and Helper T-cells in the presence of a foreign agent. Helper T-cells are arguably the most crucial cells in the context of adaptive immunity, as they play an essential role in nearly all adaptive immune responses. Their functions extend to not only activating B cells for antibody secretion and enabling macrophages to eliminate ingested microbes but also aiding in the activation of cytotoxic T cells for the destruction of infected target cells. As vividly demonstrated in AIDS patients, the absence of helper T cells leaves us vulnerable even to many microbes that are typically harmless [12]. Therefore, healthcare professionals must ensure the maintenance of Helper T-cell functionality regardless of the drug dosage administered in the treatment of viral infections.

5.8. Efficacy of Drugs on the Regulatory T-cell Population within the First Ten Days

In conclusion, we conducted a simulation to examine the impact of drugs on regulatory T-cells, as depicted in Fig. 9 and Fig. 10. The results reveal a modest increase in the population of regulatory T-cells as the drug dosage escalates. This occurrence is due to the fact that as the drug dosage increases, the response of cytotoxic T-cells intensifies. Consequently, there's a need for an increase in the population of regulatory T-cells to effectively modulate the response of cytotoxic T-cells within the body. This adjustment serves to mitigate the consequences of the drug administration by healthcare professionals in the context of viral infection treatment. Regulatory T cells (Tregs) represent a specialized subset of T cells with the unique function of suppressing immune responses, thereby preserving homeostasis and self-tolerance. Studies have demonstrated that Tregs possess the ability to inhibit T cell proliferation and cytokine production, playing a critical role in preventing autoimmune reactions [24].

6. Conclusion

In this research paper, we introduced a unique mathematical model aimed at elucidating the dynamics of virus cell interactions with the human immune system. To validate the viability of this innovative model, we derived equilibrium points for infection-free states, persistent infection states, and calculated the control reproduction number. These parameters were essential for analyzing both the local and global stability of the infection-free equilibrium. Our simulations yielded noteworthy results, indicating that the population of natural killer cells increases its effectiveness in eliminating foreign viruses from infected cells and free

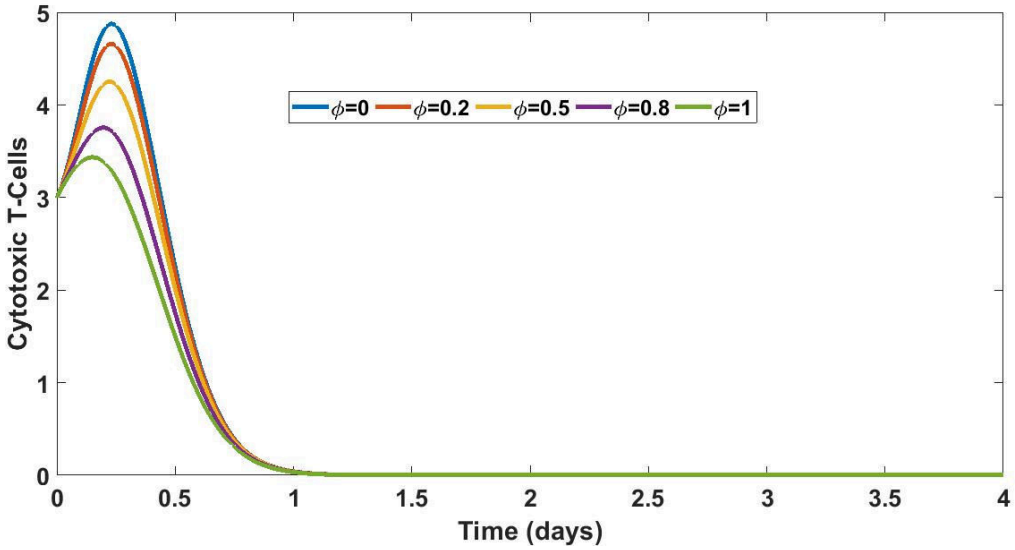

Figure 6: Efficacy of Drugs on the cytotoxic T-cell population within the first ten days

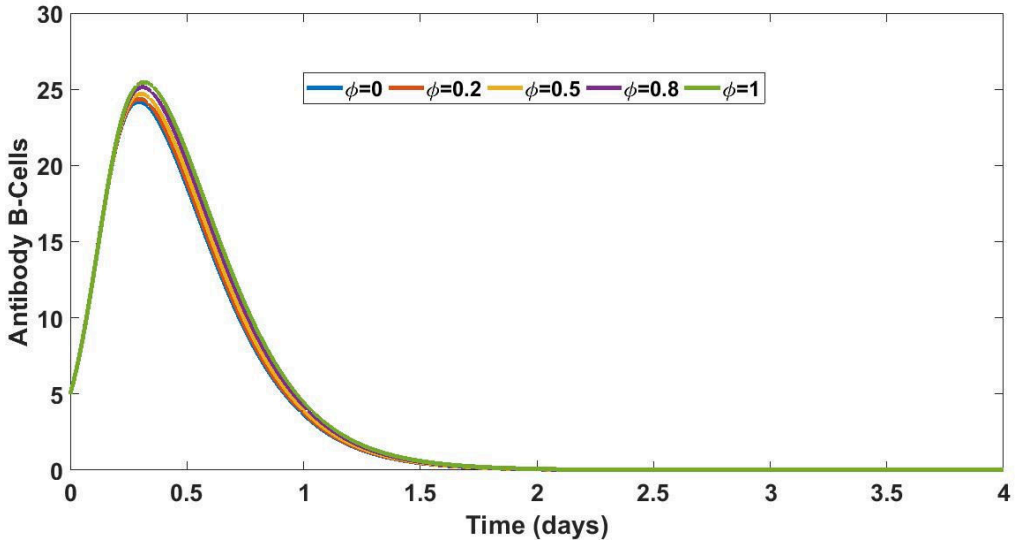

Figure 7: Efficacy of Drugs on the Antibody B-cell population within the first ten days

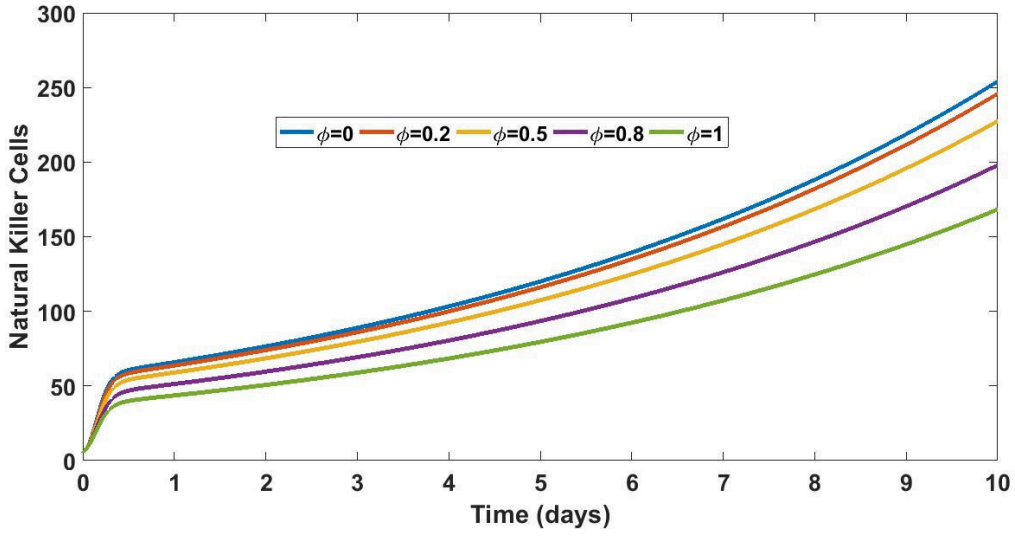

Figure 8: Efficacy of Drugs on the Natural killer cells population within the first ten days

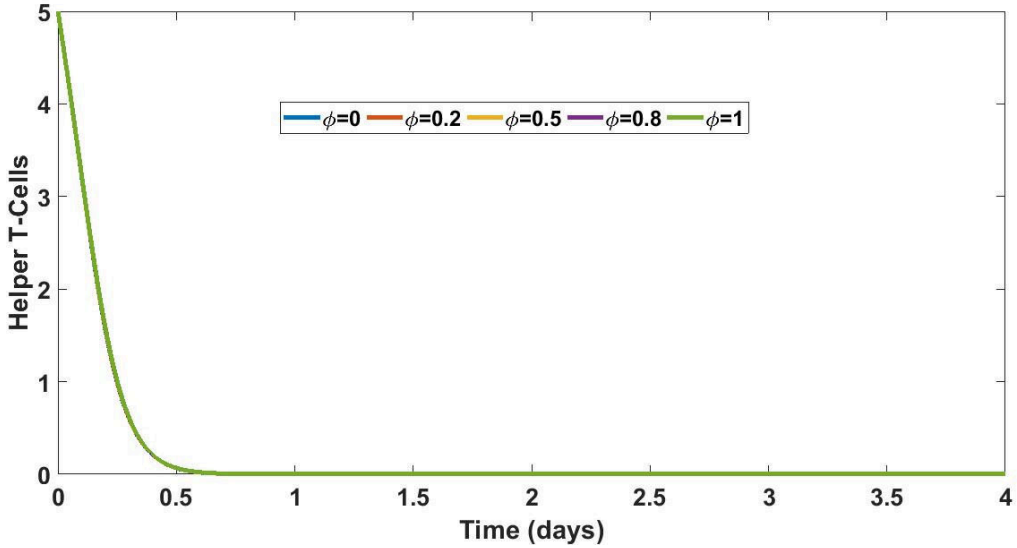

Figure 9: Efficacy of Drugs on the Helper T-cells population within the first ten days

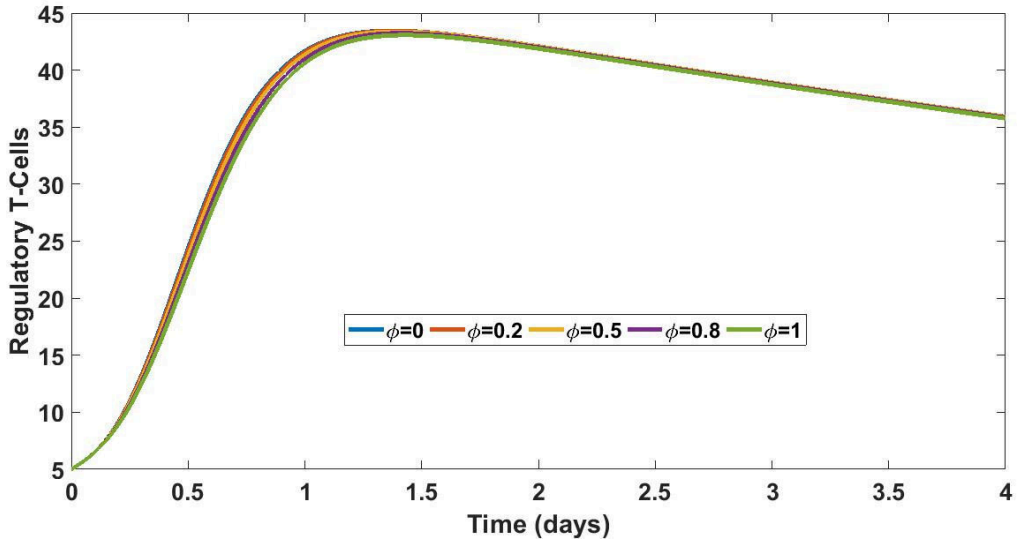

Figure 10: Efficacy of Drugs on the Regulatory T-cells population within the first ten days

virus cells. This outcome supports our decision to incorporate natural killer cells into the model, affirming their crucial role. Similarly, regulatory T-cells demonstrated an increase in their population, contributing to the regulation of immune responses within the body. The collective impact of boosters, including vaccinations and drugs, on various immune cell populations in combating foreign agents proved to be highly significant. This study provides valuable insights into the intricate interplay between immune system cells and virus cells, shedding light on the dynamics of these interactions.

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The authors declare that they have no competing interests.
The datasets generated during and/or analyzed during the current study are available from the corresponding author on plausible request.

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