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Abstract

Psoriasis is a common chronic inflammatory skin disease that is differentiated by repeated occurrences of raised scaly and red skin plaques. It is generated through several applications of drugs, strains, physical wounds to the skin and also for infectivity. Psoriasis is identified by composite interactions of T-Cells, Dendritic Cells, Cytokines and downstream transcription factors (type 1 Cytokines network). The effects of T-Cells in dermal layer ($CD4^+$ T-Cells) are well-studied in the disease dynamics of Psoriasis from mathematical as well as biological context. But the concept of T-Cells in epidermal layer ($CD8^+$ T-Cells) for disease progression of Psoriasis has not yet been explored till now from mathematical avenue. Here we introduce both $CD4^+$ and $CD8^+$ T-Cell, Dendritic Cell and Keratinocyte population to notice the impact of them on immunopathogenic cell-biological mechanism of Psoriasis. Numerical simulation is also furnished to establish the analytical outcomes.

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Abstract. Psoriasis is a common chronic inflammatory skin disease that is differentiated by repeated occurrences of raised scaly and red skin plaques. It is generated through several applications of drugs, strains, physical wounds to the skin and also for infectivity. Psoriasis is identified by composite interactions of T-Cells, Dendritic Cells, Cytokines and downstream transcription factors (type 1 Cytokines network). The effects of T-Cells in dermal layer ($CD4^+$ T-Cells) are well-studied in the disease dynamics of Psoriasis from mathematical as well as biological context. But the concept of T-Cells in epidermal layer ($CD8^+$ T-Cells) for disease progression of Psoriasis has not yet been explored till now from mathematical avenue. Here we introduce both $CD4^+$ and $CD8^+$ T-Cell, Dendritic Cell and Keratinocyte population to notice the impact of them on immunopathogenic cell-biological mechanism of Psoriasis. Numerical simulation is also furnished to establish the analytical outcomes.

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Keywords. T-Cells, Dendritic Cells, $CD4^+$ T-Cells, $CD8^+$ T-Cells, Keratinocytes, Dermal layer, Epidermal layer, Cytokines.

1. Introduction

A number of histological transformations can be noticed for increasing of lesions for Psoriasis: (1) a condensed epidermis (acanthosis) occurring from immediate proliferation of Keratinocyte, (2) for the unusual separation of Keratinocytes, granular stratum is decreased or not present (hypogranulosis) and preservation of nuclei by corneocytes is occurred (parakeratosis), (3) in the papillary dermis, noticeable dilation of blood vessels reasoning observable erythema and last of all (4) a thick inflammatory penetration, composed of groups for $CD4^+$ T helper Cells and DCs in the dermis and $CD8^+$ T-Cells and neutrophils in the epidermis [1]. In autocrine or paracrine mode, Cytokines usually intervene connections between cells that are in close immediacy by means of involvement for explicit receptors performance. Cytokines are normally capable to manipulate the proliferation, differentiation or discharge of pro-inflammatory or anti-inflammatory aspects by resident and employed cells [2]. IL-22 is almost certainly and extremely over expressed for up regulated IL-23 and IL-6 stages in Psoriasis [3], [4]. The capability of Cytokine IFN- γ is to capture the refined Keratinocytes proliferation intensely and unpredictably. It is done by controlling of recombinant human IFN- γ to the Psoriasis patient systemically [5]. TNF- α fabricating cells are assumed to persuade the adjoining endothelial cells

to manufacture bond molecules such as endothelial cell leukocyte bond molecule 1, vascular cell bond molecule 1 and intercellular bond molecule. It is furnished to speedily endorse the staffing of leukocytes into the skin and also to force epidermal Keratinocytes to produce chemotactic polypeptides such as IL-8. Leukocytes via intercellular adhesion molecule 1 are also kept [6]. Neutrophil attracting CXC chemokines are created by Keratinocytes, which are motivated by means of a potent pro-inflammatory Cytokine IL-17 [7], [8]. IL-17 may stimulate fibroblasts to generate Cytokine IL-6, which assigns naive T-Cells to Th 17. A positive feedback loop is activated potentially that enables Th17 inflammation [9]. Inside the epidermis, CD8⁺ T-Cells constructing IL-17 have been recognized [10].

Roy and Bhadra prepared the basic mathematical model of the skin disease Psoriasis [11]. They also analyzed a comparative study for suppression on T-Cells and DCs individually and attained the better outcomes for suppression made on DCs [12]. Next, Roy and Datta expanded the mathematical model of Psoriasis introducing the half-saturation constant [13] and negative feedback control approach in delay induced system [14]. They also examined the effect of Cytokines network in the cell-biological structure of Psoriasis [15] and also the presence of CD8⁺ T-Cells [16] was incorporated by Roy et al. in this disease dynamics of Psoriasis. Interaction between T-Cells and DCs and also interaction between T-Cells and Keratinocytes help to form Keratinocytes, whose excess production generates Psoriasis. From mathematical point of view, the research works regarding the cell-biological system of the disease Psoriasis were done related to the growth of Psoriasis but not on the persistence of Psoriasis. In our present research article, we generate the new concept of survival of the disease. The impact of T-Cells in dermal layer generally Th 1 CD4⁺ T-Cells was considered in all the previous research articles on mathematical approaches for Psoriasis. The notion of epidermal T-Cells essentially CD8⁺ T-Cells in cell-biology of Psoriasis has not yet been properly investigated till now from mathematical aspect. For that reason, we introduce four type of cell populations CD4⁺ T-Cell, DC, CD8⁺ T-Cell and Keratinocyte. Mainly, CD4⁺ T-Cells are one of the factors for the growth of Psoriasis. But CD8⁺ T-Cells in the epidermal layer are responsible for the persistence of the disease. At first, there is a interaction between CD4⁺ T-Cells and DCs in the dermis. Another interaction of CD4⁺ T-Cells with Keratinocytes occurs in the dermal phase. Next with help of various Cytokines network, the effects of the interactions come into the epidermis layer. Finally, Keratinocytes produced in the epidermis stage are one of the major causes to generate and persist the chronic disease Psoriasis. In this research article, we are interested to notice the effect of CD8⁺ T-Cells along with CD4⁺ T-Cells in the growth as well as consistence of the disease Psoriasis.

2. The Basic Assumptions and the Formulation of the Mathematical Model

We consider the mathematical model of chronic skin disease Psoriasis, where there are four different types of cell population, introduced into the model system: $l_D(t)$ is T-Cell density in dermal layer (mainly Th 1 CD4⁺ T-Cells), $m(t)$ is Dendritic Cell density, $l_E(t)$ is epidermal T-Cell (mainly CD8⁺ T-Cells) density and $k(t)$ is Keratinocyte density at time t . Here the constant rates of accumulation of T-Cells and Dendritic Cells are assumed by a and b respectively. Also the accumulation rate of resident T-Cells in secondary lymphatic organs is denoted by c . Again, ξ_1 is the activation rate of CD4⁺ T-Cells by DCs and ξ_2 is the rate of activation of DCs by CD4⁺ T-Cells. Further, the activation rate of Keratinocytes by CD4⁺ T-Cells due to T-Cells mediated Cytokines is considered as η_1 and also β_1 is the rate of activation of CD8⁺ T-Cells by DCs. Here the rate of migration of dermal layer T-Cells to epidermis is regarded as δ under the action of IL-6 and IFN- γ released by T-Cells themselves, which cause further stimulation of DCs and also β_2 is the rate of proliferation of epidermal T-Cells. Moreover, α_1 is

the rate of proliferation of epidermal T-Cells by activated Keratinocytes and the rate of activation of epidermal T-Cells by Keratinocytes under the influence of IL-8 is assumed as α_2 . Here η_2 is the rate of further immigration of dermal T-Cells to epidermis guided by Keratinocytes and mediated by IL-8 and IL-20. Furthermore, λ_1 is the rate of proliferation of Keratinocytes mediated by Cytokines released from epidermal T-Cells like IL-17, IL-20 and also the rate of proliferation for Keratinocytes mediated by Cytokines released from Keratinocytes themselves is considered as λ_2 . Finally, the per capita removal rates of CD4⁺ T-Cells and CD8⁺ T-Cells are denoted by μ_1 and μ_3 respectively and further μ_2 and μ_4 are the per capita removal rates of Dendritic Cell and Keratinocyte population. All the above mentioned parameters are always positive.

Assembling together the above assumptions, we may formulate the mathematical model of the disease Psoriasis given below:

$$\begin{aligned}\frac{dl_D}{dt} &= a - \xi_1 l_D m - \eta_1 l_D k - \mu_1 l_D, \\ \frac{dm}{dt} &= b - \xi_2 l_D m - \beta_1 l_E m - \mu_2 m, \\ \frac{dl_E}{dt} &= c + \delta l_D m + \beta_2 l_E m + \alpha_1 l_E + \eta_2 l_D k - \mu_3 l_E, \\ \frac{dk}{dt} &= \lambda_1 l_D k + \lambda_2 l_E k - \alpha_2 l_E - \mu_4 k,\end{aligned}\tag{1}$$

where $l_D(0) > 0$, $m(0) > 0$, $l_E(0) > 0$ and $k(0) > 0$ at a specific time period t .

3. Theoretical Analysis of the Dynamical System

3.1. Existence, Uniqueness and Boundedness of the System

The right hand sides of system of equations (1) are smooth functions of the variables l_D , m , l_E and k and also the parameters, given that these quantities are always non-negative. Henceforth, the local existence, uniqueness and boundedness of the system dynamics are guaranteed in the positive octant. In the following theorem, we will exemplify that the linear combination of CD4⁺ T-Cells, Dendritic Cells, CD8⁺ T-Cells and Keratinocytes concentrations is less than a pre-assumed quantity. Alternatively, we can conclude that the solution of the dynamical system is bounded.

THEOREM 3.1. *The solution $x(t)$ of the system (1), where $x = (l_D, m, l_E, k)$, is uniformly bounded for $x_0 \in R_{0,+}^4$.*

Proof. We consider a function $U(t) : R_{0,+} \rightarrow R_{0,+}$ by $U(t) = l_D + m + l_E + k$. We study that U is precise and differentiable function on some maximal interval $(0, t_f)$. The time derivative of system of equations (1) is

$$\begin{aligned}\frac{dU}{dt} &= (a + b + c) + l_D m (\delta - \xi_1 - \xi_2) + l_D k (\eta_2 + \lambda_1 - \eta_1) + l_E m (\beta_2 - \beta_1) \\ &\quad + \lambda_2 l_E k + l_E (\alpha_1 - \alpha_2) - \mu_1 l_D - \mu_2 m - \mu_3 l_E - \mu_4 k.\end{aligned}$$

For the simplicity of computation, we here consider the sum of the rate of immigration of dermal T-Cells to epidermis guided by Keratinocytes and the rate of proliferation of Keratinocytes mediated by Cytokines released from epidermal T-Cells is almost same with the activation rate of Keratinocytes by CD4⁺ T-Cells due to T-Cells mediated Cytokines, i.e., $\eta_2 + \lambda_1 = \eta_1$. Again we assume the rate of activation of CD8⁺ T-Cells by DCs and the rate of proliferation of epidermal T-Cells is almost identical, i.e., $\beta_1 = \beta_2$. The rate of proliferation of epidermal

T-Cells by activated Keratinocytes and the rate of activation of epidermal T-Cells by Keratinocytes under the influence of IL-8 is assumed to be same for the sake of simplicity in the calculation ($\alpha_1 = \alpha_2$). Finally, we neglect the rate of proliferation for Keratinocytes mediated by Cytokines released from Keratinocytes themselves (λ_2) as we consider the rate of proliferation of Keratinocytes mediated by Cytokines released from epidermal T-Cells like IL-17, IL-20.

Therefore the above equation becomes,

$$\frac{dU}{dt} = (a + b + c) - l_D m (\xi_1 + \xi_2 - \delta) - \mu_1 l_D - \mu_2 m - \mu_3 l_E - \mu_4 k.$$

Now for all $\omega > 0$, the following inequality holds [12],

$$\begin{aligned} \frac{dU}{dt} + \omega U(t) &\leq (a + b + c) - (\xi_1 + \xi_2 - \delta) \left(\frac{l_D^2 + m^2}{2} \right) - (\mu_1 - \omega) l_D - (\mu_2 - \omega) m - (\mu_3 - \omega) l_E \\ - (\mu_4 - \omega) k &\leq (a + b + c) + \frac{(\mu_1 - \omega)^2 + (\mu_2 - \omega)^2 + (\mu_3 - \omega)^2}{2(\xi_1 + \xi_2 - \delta)} - (\mu_4 - \omega) k. \end{aligned}$$

If we assume that $0 < \omega < \mu_4$, then there exists $\epsilon > 0$ such that

$$\frac{dU(t)}{dt} + \omega U(t) \leq \epsilon \text{ for each } t \in (0, t_f).$$

Let $G(t, x) = \epsilon - \omega x$, which ensures the Lipschitz condition everywhere. Certainly,

$$\frac{dU(t)}{dt} \leq \epsilon - \omega U(t) = G(t, U(t)) \forall t \in (0, t_f).$$

Let $\frac{dy}{dt} = G(t, y) = \epsilon - \omega y$ and $y(0) = U(0) = U_0$. Now this ODE has the solution

$$y(t) = \frac{\epsilon}{\omega} (1 - e^{-\omega t}) + U_0 e^{-\omega t}.$$

It is obvious that $y(t)$ is bounded on $(0, t_f)$. By Comparison Theorem of Birkhoff and Rota (1982) [17],

$$U(t) \leq y(t) = \frac{\epsilon}{\omega} (1 - e^{-\omega t}) + U_0 e^{-\omega t} \forall t \in (0, t_f).$$

Now assume $t_f < \infty$, then $U(t_f) \leq y(t_f) < \infty$. Now the solution is established to be unique in some interval $(0, t_f)$ by the Picard-Lindelof Theorem. This contradicts our earlier assumption that $t_f < \infty$. Hence $U(t)$ must be bounded for all non-negative t and as a result $x(t)$ is uniformly bounded on $R_{0,+}$ [12]. ■

3.2. Permanence of the System

The system of equations (1) is considered to be permanent [18], if there exists a compact set D in the interior of $R_+^4 = \{(l_D(t), m(t), l_E(t), k(t)) \in R_+^4 \mid l_D(t) > 0, m(t) > 0, l_E(t) > 0, k(t) > 0\}$ such that, all solutions inside the interior of R_+^4 finally come into D and stay in D .

To study the permanence of the system of equations (1), let us consider $R_+^4 = \{(l_D(t), m(t), l_E(t), k(t)) \in R_+^4 \mid l_D(t) > 0, m(t) > 0, l_E(t) > 0, k(t) > 0\}$ is the positively invariant set of the system of equations (1) and $(l_D(t), m(t), l_E(t), k(t))$ is the arbitrary positive solution of the system of equations (1) with the help of positive initial value.

THEOREM 3.2. *For the system of equations (1) satisfying the initial condition $(l_D(0), m(0), l_E(0), k(0)) \in R_+^4$, there exists positive $l_{D \max}^*$, m_{\max}^* , $l_{E \max}^*$ and k_{\max}^* , such that for any $(l_D(t), m(t), l_E(t), k(t)) \in R_+^4$, $l_D(t) \leq l_{D \max}^*$, $m(t) \leq m_{\max}^*$, $l_E(t) \leq l_{E \max}^*$ and $k(t) \leq k_{\max}^*$ for large t .*

Proof. We have $U(t) = l_D + m + l_E + k$ is bounded, which is ensured for every non-negative t and consequently $x(t) = (l_D(t), m(t), l_E(t), k(t))$ is uniformly bounded on R_+ . Hence the theorem. ■

THEOREM 3.3. For the system of equations (1) satisfying the initial condition $(l_D(0), m(0), l_E(0), k(0)) \in R_+^4$, there exists positive $l_D^*_{min}$, m^*_{min} , $l_E^*_{min}$ and k^*_{min} , such that for any $(l_D(t), m(t), l_E(t), k(t)) \in R_+^4$, $l_D(t) \geq l_D^*_{min}$, $m(t) \geq m^*_{min}$, $l_E(t) \geq l_E^*_{min}$ and $k(t) \geq k^*_{min}$ for large t .

Obviously the system is bounded below. So we achieve a compact set $D = \{l_D(t), m(t), l_E(t), k(t) \mid l_D^*_{min} \leq l_D(t) \leq l_D^*_{max}, m^*_{min} \leq m(t) \leq m^*_{max}, l_E^*_{min} \leq l_E(t) \leq l_E^*_{max} \text{ and } k^*_{min} \leq k(t) \leq k^*_{max}\}$ corresponding to the system of equations (1), where each and every solution of the system with positive initial value will enter in to the compact set D and stay in D . Hence the positive invariant solution of the system of equations (1) is permanent [12].

3.3. Total Cell Count

Now, if assume the relation $\mu_1 < \mu_2 < \mu_3 < \mu_4$ then,

$$\frac{dT_{tot}}{dt} \equiv \frac{d(l_D + m + l_E + k)}{dt} \leq (a + b + c) - \mu_1(l_D + m + l_E + k),$$

providing the sum of the activation rate of CD4⁺ T-Cells by DCs and the rate of activation of DCs by CD4⁺ T-Cells is the same with the rate of migration of dermal layer T-Cells to epidermis. Furthermore, we here consider the sum of the rate of immigration of dermal T-Cells to epidermis guided by Keratinocytes and the rate of proliferation of Keratinocytes mediated by Cytokines released from epidermal T-Cells is almost same with the activation rate of Keratinocytes by CD4⁺ T-Cells due to T-Cells mediated Cytokines. Again we assume the rate of activation of CD8⁺ T-Cells by DCs and the rate of proliferation of epidermal T-Cells is almost identical. The rate of proliferation of epidermal T-Cells by activated Keratinocytes and the rate of activation of epidermal T-Cells by Keratinocytes under the influence of IL-8 is assumed to be same for the sake of simplicity in the calculation. Finally, the rate of proliferation for Keratinocytes mediated by Cytokines released from Keratinocytes themselves is neglected because we consider the rate of proliferation of Keratinocytes mediated by Cytokines released from epidermal T-Cells like IL-17, IL-20.

Lemma 3.4. Consider v is a variable satisfying $v'(t) < d - f(\phi)v(t)$, where d is a constant and $f(\phi)$ is independent of v and t . Then If $v(0) < \frac{d}{f(\phi)}$, it pursues that $v(t) < \frac{d}{f(\phi)}$ for every t .

Proof. See Smith and Wahl (2004, Lemma 4.1) [19]. ■

Remark 3.5. If the inequalities are reversed, Lemma 3.4 also holds.

Applying the above Lemma 3.4, we can state that $T_{tot} < \frac{a+b+c}{\mu_1}$, if $T_{tot}(0) < \frac{a+b+c}{\mu_1}$. Therefore, if the above mentioned assumptions are hold, then the limiting value of the total cell population should not exceed the quantity $\frac{a+b+c}{\mu_1}$ [20].

3.4. Equilibria of the System

The system of equations (1) has only the interior equilibrium point $E^*(l_D^*, m^*, l_E^*, k^*)$. From the first equation of the system (1), we have $l_D^* = \frac{a}{\xi_1 m^* + \eta_1 k^* + \mu_1}$, which is always positive. From the second equation we find that $m^* = \frac{b}{\xi_2 l_D^* + \beta_1 l_E^* + \mu_2}$, which is again positive by our assumptions.

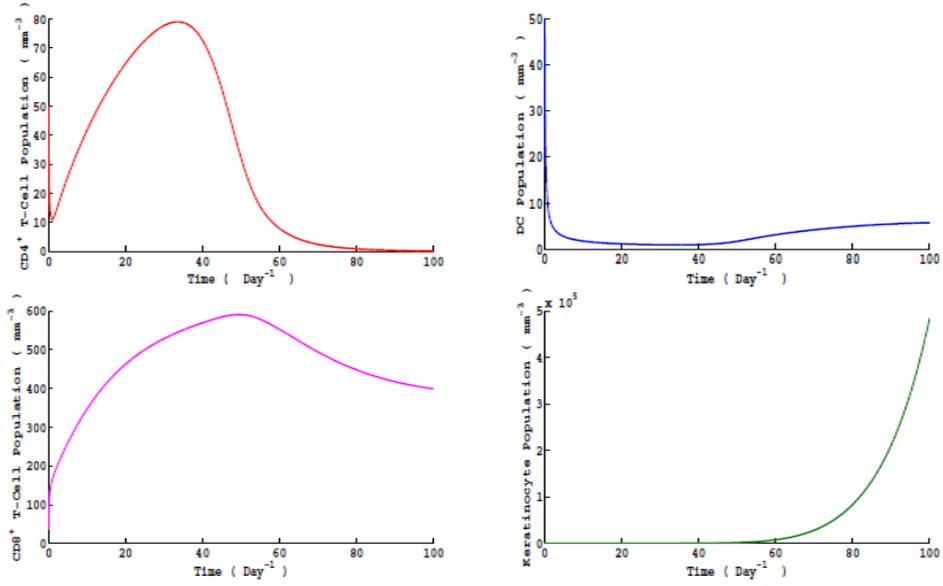


FIGURE 1. Population densities of CD4⁺ T-Cell, Dendritic Cell, CD8⁺ T-Cell and Keratinocyte, which are plotted as a function of time and the value of the parameters are given in Table.

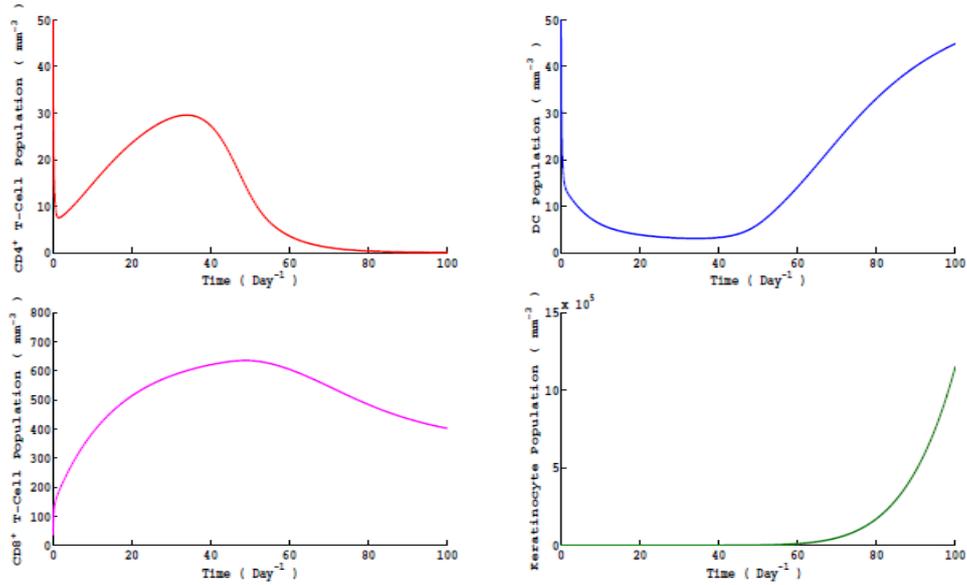


FIGURE 2. Population densities of CD4⁺ T-Cell, Dendritic Cell, CD8⁺ T-Cell and Keratinocyte, which are plotted as a function of time, $\beta_1=0.0005$ and $\beta_2=0.0003$ and the value of the other parameters are given in Table.

we get $I_E^* = \frac{c+l_D^*(\delta m^*+\eta_2 k^*)}{\mu_3 - (\beta_2 m^* + \alpha_1)}$, which is positive if $\mu_3 > \beta_2 m^* + \alpha_1$ from the third equation of the system (1). Finally from the fourth as well as last equation of the model system we obtain,

$k^* = \frac{\alpha_2 l_E^*}{\lambda_1 l_D^* + \lambda_2 l_E^* - \mu_4}$, which is positive when $\lambda_1 l_D^* + \lambda_2 l_E^* > \mu_4$.

Now the variational matrix at the interior equilibrium point $E^*(l_D^*, m^*, l_E^*, k^*)$ is given by $V(l_D^*, m^*, l_E^*, k^*) =$

$$\begin{pmatrix} -\xi_1 m^* - \eta_1 k^* - \mu_1 & -\xi_1 l_D^* & 0 & -\eta_1 l_D^* \\ -\xi_2 m^* & -\xi_2 l_D^* - \beta_1 l_E^* - \mu_2 & -\beta_1 m^* & 0 \\ \delta m^* + \eta_2 k^* & \delta l_D^* + \beta_2 l_E^* & \beta_2 m^* + \alpha_1 - \mu_3 & \eta_2 l_D^* \\ \lambda_1 k^* & 0 & \lambda_2 k^* - \alpha_2 & \lambda_1 l_D^* + \lambda_2 l_E^* - \mu_4 \end{pmatrix},$$

i.e.,

$$V(l_D^*, m^*, l_E^*, k^*) = \begin{pmatrix} -\frac{a}{l_D^*} & -\xi_1 l_D^* & 0 & -\eta_1 l_D^* \\ -\xi_2 m^* & -\frac{b}{m^*} & -\beta_1 m^* & 0 \\ \delta m^* + \eta_2 k^* & \delta l_D^* + \beta_2 l_E^* & \beta_2 m^* + \alpha_1 - \mu_3 & \eta_2 l_D^* \\ \lambda_1 k^* & 0 & \lambda_2 k^* - \alpha_2 & \frac{\alpha_2 l_E^*}{k^*} \end{pmatrix},$$

i.e.,

$$V(l_D^*, m^*, l_E^*, k^*) = \begin{pmatrix} -\frac{a}{l_D^*} & -\xi_1 l_D^* & 0 & -\eta_1 l_D^* \\ -\xi_2 m^* & -\frac{b}{m^*} & -\beta_1 m^* & 0 \\ d_{31} & d_{32} & d_{33} & \eta_2 l_D^* \\ \lambda_1 k^* & 0 & d_{43} & \frac{\alpha_2 l_E^*}{k^*} \end{pmatrix},$$

where $d_{31} = \delta m^* + \eta_2 k^*$, $d_{32} = \delta l_D^* + \beta_2 l_E^*$, $d_{33} = \beta_2 m^* + \alpha_1 - \mu_3$ and $d_{43} = \lambda_2 k^* - \alpha_2$.

The characteristic equation is given by,

$$\phi^4 + A_1 \phi^3 + A_2 \phi^2 + A_3 \phi + A_4 = 0, \tag{2}$$

where

$$A_1 = -d_{33} + \frac{a}{l_D^*} + \frac{b}{m^*} - \frac{\alpha_2 l_E^*}{k^*},$$

$$A_2 = -\frac{a(d_{33})}{l_D^*} - \frac{b(d_{33})}{m^*} + \frac{ab}{l_D^* m^*} + \frac{\alpha_2(d_{33})l_E^*}{k^*} - \frac{a\alpha_2 l_E^*}{l_D^* k^*} - \frac{b\alpha_2 l_E^*}{m^* k^*} + \beta_1(d_{32})m^* + \eta_1 \lambda_1 l_D^* k^* - \eta_2(d_{43})l_D^* - \xi_1 \xi_2 l_D^* m^*,$$

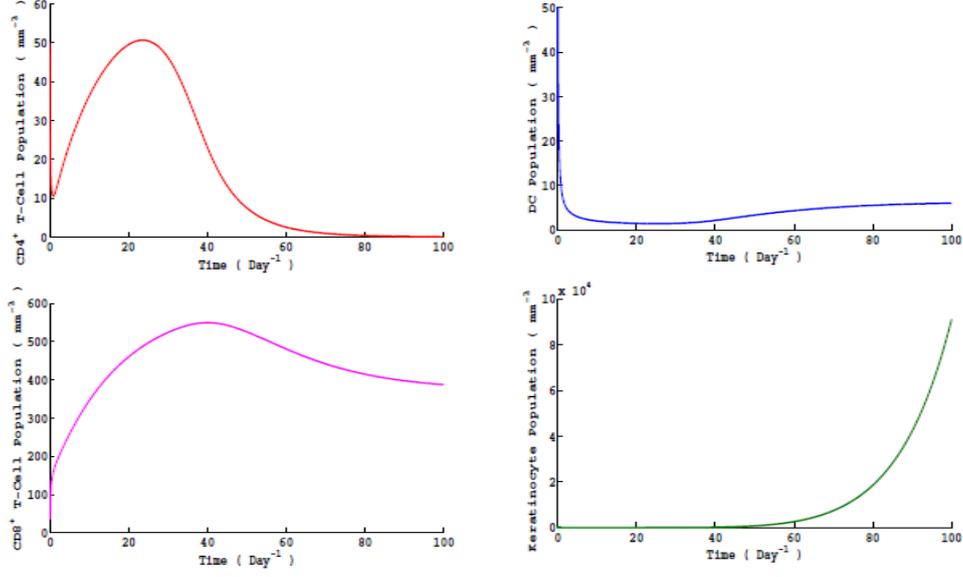


FIGURE 3. Population densities of $CD4^+$ T-Cell, Dendritic Cell, $CD8^+$ T-Cell and Keratinocyte, which are plotted as a function of time $\eta_1=0.002$ and $\eta_2=0.001$ and the value of the other parameters are given in Table.

$$\begin{aligned}
 A_3 = & -\frac{ab(d_{33})}{l_D^* m^*} + \frac{a(d_{33})\alpha_2 l_E^*}{l_D^* k^*} + \frac{b(d_{33})\alpha_2 l_E^*}{m^* k^*} - \frac{ab\alpha_2 l_E^*}{l_D^* m^* k^*} + \frac{a(d_{32})\beta_1 m^*}{l_D^*} - \frac{\alpha_2 \beta_1 (d_{32}) l_E^* m^*}{k^*} \\
 & + \eta_1 (d_{31})(d_{43}) l_D^* - \eta_1 \lambda_1 (d_{33}) l_D^* k^* + \frac{b\eta_1 \lambda_1 l_D^* k^*}{m^*} - a\eta_2 (d_{43}) - \frac{b\eta_2 (d_{43}) l_D^*}{m^*} \\
 & - \beta_1 \xi_1 (d_{31}) l_D^* m^* + \xi_1 \xi_2 (d_{33}) l_D^* m^* + \frac{\alpha_2 \xi_1 \xi_2 l_D^* l_E^* m^*}{k^*},
 \end{aligned}$$

and

$$\begin{aligned}
 A_4 = & \frac{ab(d_{33})\alpha_2 l_E^*}{l_D^* m^* k^*} - \frac{a(d_{32})\alpha_2 \beta_1 l_E^* m^*}{l_D^* k^*} + \frac{b\eta_1 (d_{31})(d_{43}) l_D^*}{m^*} - \xi_2 \eta_1 (d_{32})(d_{43}) l_D^* m^* \\
 & - \frac{b(d_{33})\eta_1 \lambda_1 l_D^* k^*}{m^*} + \beta_1 \eta_1 \lambda_1 (d_{32}) l_D^* m^* k^* - \frac{ab\eta_2 (d_{43})}{m^*} + \frac{\alpha_2 \beta_1 \xi_1 (d_{31}) l_D^* l_E^* m^*}{k^*} \\
 & - \frac{\alpha_2 \xi_1 \xi_2 (d_{33}) l_D^* l_E^* m^*}{k^*} + \eta_2 \xi_1 \xi_2 (d_{43}) (l_D^*)^2 m^* - \beta_1 \lambda_1 \eta_2 \xi_1 (l_D^*)^2 m^* k^*.
 \end{aligned}$$

From Routh-Hurwitz criterion, the interior equilibrium point $E^*(l_D^*, m^*, l_E^*, k^*)$ is said to be stable if the following conditions are hold: (a) $A_1 > 0$, (b) $A_4 > 0$, (c) $A_1 A_2 - A_3 > 0$ and (d) $[(A_1 A_2 - A_3) A_3] - A_1^2 A_4 > 0$.

Now, according to the Routh-Hurwitz criterion, the interior equilibrium point E^* is stable if

- (1) $\frac{a}{l_D^*} > d_{33}$, (2) $\frac{b}{m^*} > \frac{\alpha_2 l_E^*}{k^*}$, (3) $d_{31} d_{43} > \lambda_1 d_{33} k^*$, (4) $\beta_1 \lambda_1 k^* > \xi_2 d_{43}$, (5) $ak^* > \frac{d_{31} d_{43} l_D^*}{\lambda_1} + \alpha_2 l_D^* l_E^*$ and (6) $[(A_1 A_2 - A_3) A_3] - A_1^2 A_4 > 0$.

4. Numerical Simulation

In the preceding section, we have introduced analytical method for qualitative study of the system. In this division, we execute numerical simulation of the model system. We have taken approximate values of the parameters during our analytical outcomes. Numerical values of the model parameters, mainly taken from [12], have been specified in the **Table** given below.

Table. Values of parameters used for model system

Parameter	Default Values (Day ⁻¹)	Parameter	Default Values (Day ⁻¹)
a	15 mm^{-3}	δ	0.35 mm^3
b	12 mm^{-3}	α_1	0.007
c	9 mm^{-3}	α_2	0.004
ξ_1	0.15 mm^3	λ_1	0.0003 mm^3
ξ_2	0.12 mm^3	λ_2	0.0004 mm^3
η_1	0.0002 mm^3	μ_1	0.02
η_2	0.0001 mm^3	μ_2	0.05
β_1	0.005 mm^3	μ_3	0.07
β_2	0.003 mm^3	μ_4	0.08

We are trying to observe the cell behavioral outline of different types of cells, involved in our model system for deviation in the values of the model parameters. In **Figure 1**, CD4⁺ T-Cell population increases from initial position to higher level and then decreases to ground level gradually in first **100** days. From very beginning DC population decreases and afterward slightly increases. CD8⁺ T-Cell population also increases from initial situation up to the highest point and next tendency of decreasing nature is observed. Finally Keratinocyte population remains constant at first near about **60** days. Then it increases sharply to the pick within **100** days. In **Figure 2**, we decrease the values of the rate of activation of CD8⁺ T-Cells by DCs (β_1) and the rate of proliferation of epidermal T-Cells (β_2). We consider here $\beta_1=0.0005$ and $\beta_2=0.0003$ for **Figure 2**. Now, CD4⁺ T-Cell population increases but not as much as **Figure 1**. DC population after **40** days increases gradually. Same behaviors are observed for the case of CD8⁺ T-Cell and Keratinocyte population as like **Figure 1**. In **Figure 3**, we increase the values of the activation rate of Keratinocytes by CD4⁺ T-Cells due to T-Cells mediated Cytokines (η_1) and the rate of further immigration of dermal T-Cells to epidermis guided by Keratinocytes and mediated by IL-8 and IL-20 (η_2). We assume $\eta_1=0.002$ and $\eta_2=0.001$. Here CD4⁺ T-Cell population increases but range lies between **Figure 1** and **Figure 2**. The nature of DC population behaves as like as **Figure 1**. The behaviors of the other two populations CD8⁺ T-Cell and Keratinocyte population perform as like as the previous figures.

5. Discussion

In our article, we introduce CD4⁺ T-Cell and CD8⁺ T-Cell populations. Next, we obtain unique equilibrium point $E^*(l_D^*, m^*, l_E^*, k^*)$ (interior equilibrium point) and then attain its stability analysis. From Routh-Hurwitz condition, the interior equilibrium point $E^*(l_D^*, m^*, l_E^*, k^*)$ is said to be stable if the following conditions are hold: (1) $\frac{a}{l_D^*} > d_{33}$, (2) $\frac{b}{m^*} > \frac{\alpha_2 l_E^*}{k^*}$, (3) $d_{31} d_{43} > \lambda_1 d_{33} k^*$, (4) $\beta_1 \lambda_1 k^* > \xi_2 d_{43}$, (5) $a k^* > \frac{d_{31} d_{43} l_D^*}{\lambda_1} + \alpha_2 l_D^* l_E^*$ and (6) $\Delta A_3 - A_1^2 A_4 > 0$, where $\Delta = A_1 A_2 - A_3 > 0$.

6. Conclusion

In the cell-biological scenario, we can conclude that if the values of the rate of activation of CD8⁺ T-Cells by DCs (β_1) and the rate of proliferation of epidermal T-Cells (β_2) are decreased, then DC population is increased. As a result, CD4⁺ T-Cell population is decreased and also CD8⁺ T-Cell population is increased. Further the values of the activation rate of Keratinocytes

by CD4⁺ T-Cells due to T-Cells mediated Cytokines (η_1) and the rate of further immigration of dermal T-Cells to epidermis guided by Keratinocytes and mediated by IL-8 and IL-20 (η_2) are increased. As an effect, CD4⁺ T-Cell and CD8⁺ T-Cell populations both are decreased. DC population is unchanged for the variation of η_1 and η_2 . The deviations in the values of β_1 , β_2 , η_1 and η_2 have not any significant impact on Keratinocyte population. The increasing nature of Keratinocytes remains unchanged. Therefore, we may bring to an end that CD8⁺ T-Cell along with CD4⁺ T-Cell population has an effect not only growing criteria of the disease but also the survival of Psoriasis. Thus if we can communicate our research findings into the treatment policy of Psoriasis, we are able to expect a better outcome for welfare of our society.

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