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Proposed Alternative for Control of Prostate Cancer Using Food Supplements: A Deterministic Modelling Approach

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Abstract

The recurrence of relapse in the control of Prostate Cancer in males using Intermittent Androgen Suppression (IAS) and Continuous Androgen Suppression(CAS) has been a crucial problem in societies. In a strong immunity situation, every disease can be controlled from the human system. In this study, simple mathematical models were developed taking into consideration the section of immune system micro-environment. Three controls; suppression of androgen (IAS, CAS), immunotherapy (vaccination) and application of food supplement (Lemon Juice) were considered. Lemon is rich in vitamin C, E, B-6, minerals, sugar, lemonoids, fats and dietary fibres which enhances the protective mechanism of the immune system. Lemon as food supplement that regulates normal cell growth (proliferation) and activates Cytotoxic cells (cytotoxic T-lymphocytes and natural killer cells). The activated T-cell plays inhibitory role, hence destroys and clears the prostate cancer tumor cells. The Local and Global stabilities of the model were determined which revealed that the system was asymptotically stable. Numerical simulation of the system to verify the effects of the food supplement (Lemon Juice) on the Prostate Cancer tumor cells was established, and it was

estimated that 0.65 to 0.8 amount of lemon juice of every 15*ml* of lemon juice into 720*mi* of warm water (translating into 5*ml* of warm water three times daily really helps. This clearly shows that lemon juice has medicinal benefits in controlling prostate cancer.

Keyword: Prostate cancer, Lemon juice, cancer cells, cancer model, stability

AMS subject classification: 92D30, 37M05

1. INTRODUCTION

Cancer is the abnormal growth of defective cells anywhere in the body. These cells have the tendency to spread into surrounding tissues. It occurs when genetic changes interfere with order of process. There are several types of cancers, most among them are lung cancer, colon cancer, cancer of the prostate, lymphoma, bladder cancer, endometrial, kidney, leukemia, liver cancer.

2. PROSTATE CANCER

Prostate Cancer is the deviant growth of cells in a man's prostate gland. The prostate is located just below the bladder as shown in Figure 1. The risk of prevalence is directly proportional to the ages of male populace.

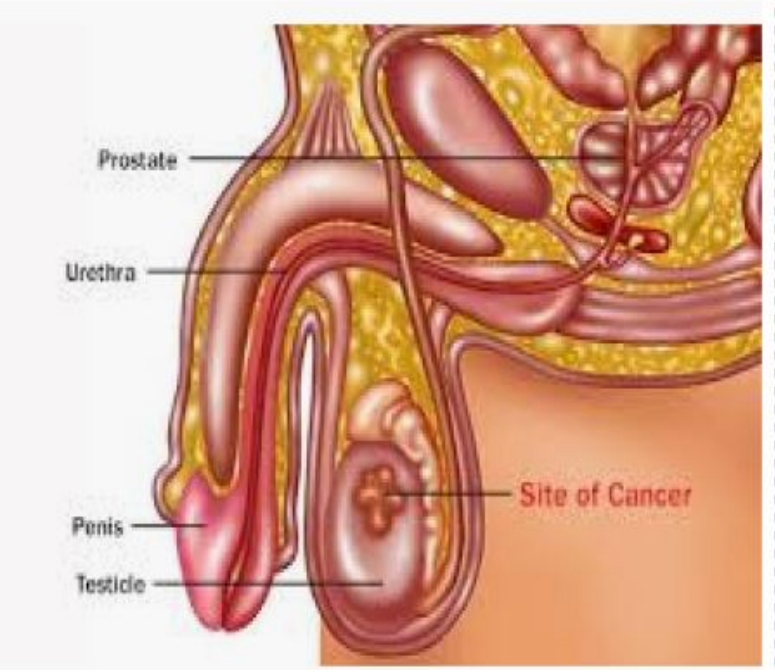

Figure 1: Position of Prostate in male(www.shutterstock.com)

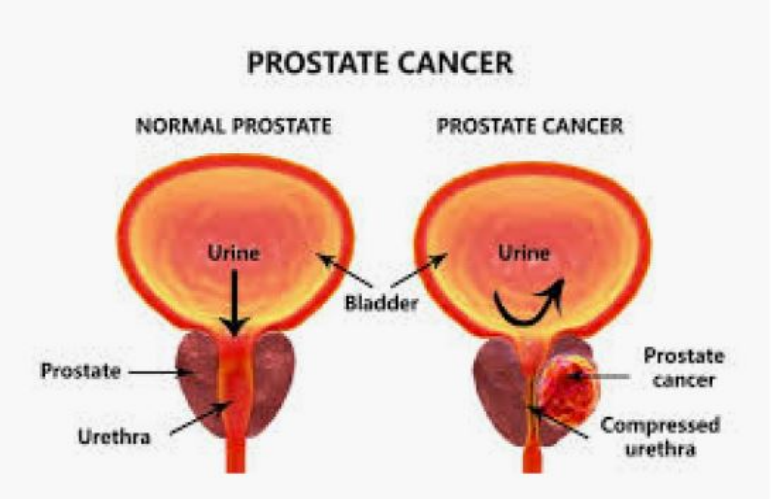

Figure 2: Normal Prostate and Prostate Cancer(www.shutterstock.com)

Prostate cancer is a disease that occurs when defective cells enlarged in the prostate region. The prostate is a walnut-shaped gland in men found in the testes which produces the seminal fluid that feeds and transports sperm (Nave and Elbaz, 2018). It is the second most common (familiar) cancer in aged men after lung cancer [1]. About 65/360 prostate cancer cases are expected which claims about 26,730 men's lives. Figure 2 shows the pictorial cases of a normal prostate and cancer prostrate in men.

Prostate cancer growth is a hormone dependent (testosterone). In view of that, the inhibition of the androgen helps to avoid the growth of the prostate cancer, i.e. intermittent androgen suppression. This strategy impoverish androgen from reaching malignant cells [2].

Prostate cancer incidence has become public health issues especially among the black race in the world [3].

Prostate maturation and function are both harnessed by androgenic hormone, which is the major androgen secreted by the fetal and adult testes. Its responsible as a forerunner for the formation of the efficacious metabolite in target tissues, dihydrotestosterone (DHT) via 5α reductase (5AR) enzymes. DHT is the intercessor of the most androgen effects in male physiology [4].

Androgens play permissive role in the induction of Benign Prostatic Hyperplasia (BPH) as numerous researches have demonstrated that the condition occurs only in the presence of both steroid hormone and androgens [5, 6].

Prostate cancer gland is found between the male sexual organ and the bladder. Prostate organs are cells whose activities are differentiation, proliferation and apoptosis (death of cells) being nourished by a male hormone called androgen [7]. [8] was of the view that

pathological abnormalities occur in the prostate gland than other organs in the human male bodies. Prostate cancer is a carcinoma that may develop tardily and increases as individual (men) ages in bones and lymph nodes [9].
Prostate gland assumes chestnut – shape that produces seminal fluid [10].
Globally, cancer has been proven to be the eleventh leading cause of death among all age groups [11]. Prostate cancer is a disease resulting from abnormal cell development in the region where prostate is situated in male sex reproductive organ [12].
Prostate Specific Antigen (PSA) and digital rectal examinations have adverse effect on many men after screening. This action has been condemned by United State Preventive Services FDA,(2012) [13].
The molecular health problem of prostate cancer is complex; not only are multiple genes involved in its pathogenesis, but additional environmental factors such as diet and inflammation are also involved [14].
In sub-Saharan Africa region, prostate cancer is featured as a major public health issues because of population growth as well as increased preponderance of key endangered factors in men, most frequently in twenty-three (23) countries [15]. According to [16], there has been increasing incidences and rise in mortality rates in sub-Saharan Africa (Kenya).
In West Africa little researches are been conducted on prostate cancer among men and there are no clear policies or measures being put in place to monitor and controlling prostate cancer [16].
A research has shown that only few men whose ages ranging between 50 and 74 years (both asymptomatic and undiagnosed asymptomatic) of prostate cancer has been diagnosed and treated at Korle-Bu Hospital [17]. The leading and most common frequently diagnosed cancer in men is prostate cancer followed by breast and lung cancers. In Ghana, the cancer of the prostate is prevalent among adult men and has led to the death of many [18, 19].
Currently, cancer drugs in use have been reported to be expensive, toxic and have not fulfill their therapeutic expectations [20]. The cost of orthodox medicine is often prohibitive to many individuals. The World Cancer report estimated cancer related expenses at 1.16 billion Dollars per annum in 2010 [21].
Biological models usually explain the transmission dynamics of infectious diseases and can determine the status of the disease in a population with time [22, 23, 24, 25, 26]. The basic reproduction number is the threshold value that determines the persistence or die out of a disease in a population [27, 28, 29, 30].
Optimal control theory are usually employed in biological models to determine the best optimal control strategy in combating infections in a population [31, 32, 33, 34, 35].

3. MODEL

3.1. Compartmental model for Prostate Cancer

Table 1 and 2 shows the prostate cancer model describtion of variable and parameters. The model transfer diagram describes the basic interaction between immune system, prostate cancer, vaccination, androgen suppression and food supplement (Lemon).

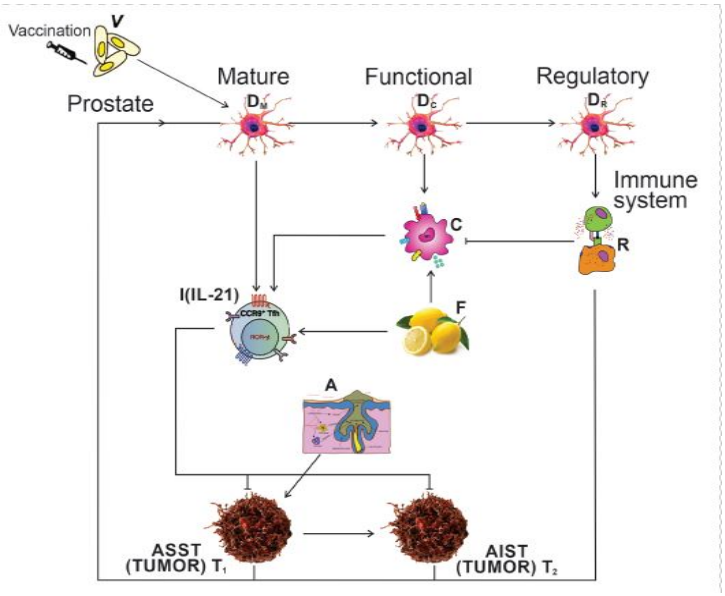

Figure 3: Transfer Diagram of Prostate Cancer

Figure 3 shows prostrate cancer transfer diagram with the various food supplements.

Table 1: Definition of Variables used in the model

Variable	Description
V	Vaccination
Dm	Antigen presenting dendritic cells
Dc	Mature dendritic cells
R	Regulatory T cells
C	Cytotoxic T cells
D_R	Exhausted dendritic cells
I	IL-21 (Interleukin 21)
F	Food Supplement
A	Androgen
T_1	Androgen sensitive suppression tumor
T_2	Androgen insensitive suppression tumor

Table 2: Definition of Parameters used in the model

Parameter	Value	Description	Source
λ_A	0.06	Rate of dendritic cells maturation	(Peng et al., 2016)
α_g	0.55	Fraction of antigen presenting DC entering lymph node	Estimated
k_m	0.017	Rate of Dc migration from skin to lymph node	Estimated
ϕ	0.12	Exhausted Dc rate	Estimated
μ_D	0.014	Death rate of exhausted Dc	(Naue & Elbaz, 2018)
α_R	3×10^{-3}	Inhibitory cell recruitment rate by exhausted Dc	✓
α_c	0.38	Effector cells recruitment rate by mature Dc	✓
n_1	0.42	Rate of food supplement entering the cytotoxic cells per day	Estimated
n_2	0.48	Rate of food supplement entering the Il-21 cell per day	Estimated
γ_3	0.23	Rate of tumor growth	(Peng et al., 2016)
γ_4	0.23	Rate of tumor growth	(Peng et al., 2016)
γ_m	0.25	Tumor growth rates per annum	Estimated
ϖ	0.22	Rate of exhausted IL-21 cell	Estimated
μ_c	0.63	Effector cell death	Estimated
μ_R	0.03	Death rate at a inhibitory cell	(Naue & Elbaz, 2018)
β_c	6×10^{-7}	Rate of effector by inhibitory cells	✓
λ_v	0.08	Rate of Dc maturation following vaccine uptake	(Peng et al., 2016)
γ_1	0.32	Proliferation Rate of ASST	(Peng et al., 2016)
γ_2	0.57	Proliferation Rate of AIST	Estimated
π_D	0.2	Rate of exhausted *Dm* cells	Estimated
α_V	0.52	Rate of Vaccination	Estimated
ψ	0.12	Rate of Tumor spread	Estimated

3.2. Prostrate cancer Model equations

$$
\begin{aligned}
\dot{V} &= -\lambda_v V \\
\dot{A} &= \lambda_A(1-A) - \lambda_A \\
\dot{Dm} &= \alpha_v V - \alpha_D\left[(\gamma_1 - \gamma_1 A + \varpi I)\,T_1 + (\gamma_2 A + \varpi I)\,T_2\right] - (\pi_D + \psi)\,D_m \\
\dot{Dc} &= \alpha_g k_m D_m - \phi D_c \\
\dot{D_R} &= \phi D_c - \mu_D D_R \\
\dot{T_1} &= \gamma_3 A - \left[(\gamma_1 - \gamma_m)\,(1-A) - \varpi I\right] T_1 \\
\dot{T_2} &= (\gamma_4 - \gamma_2 - \varpi I)\,T_2 + \gamma_m(1-A)T_1 \\
\dot{I} &= \psi D_m + \beta_c C + n_1 F - \mu_c I \\
\dot{C} &= \alpha_c Dc + n_2 F - \beta_c C \\
\dot{R} &= \alpha_R D_R - \mu_R R \\
\dot{F} &= -(n_1 + n_2)F
\end{aligned}
\tag{1}
$$

4. POSITIVITY OF THE MODELS

This section considers the non negativity of the solution to the models in equation 1 by demonstrating that $V, D_m, D_c, D_R, R, C, I, F, T_1, T_2, A \geq 0$.

4.1. Preposition

Suppose that $(V, Dm, Dc, D_R, R, C, I, I, F, T_1, T_2, A)$ is a solution to the system of differential equation in (4.1). Then $(V, Dm, Dc, D_R, R, C, I, I, F, T_1, T_2, A) \geqslant 0$, where $[V(0), Dm(0), Dc(0), D_R(0), R(0), C(0), I(0), F(0), T_1(0), T_2(0), A(0)] \geqslant 0$

Proof

From 1 that

$$\dot{V} = -\lambda_v V \tag{2}$$

$\frac{dV}{dt} = -\lambda_v V$
$\ln|v| = -\lambda_v t + y$
$V = ke^{-\lambda_v t}$
At t = 0
$V(0) = Ke^{-\lambda_v * 0}$
Thus
$K = V(0) \geqslant 0$
Hence
$V(t) = V(0)e^{-\lambda_v t} \geqslant 0$

$V(0) = 0$

From 1;

$$\dot{A} = \lambda_A(1-A) - \lambda_A \tag{3}$$

$A(t) \geqslant A(0)e^{-\lambda_A t} \geqslant 0$

From 1;

$$\begin{aligned} \dot{Dm} &= \alpha_v V - \alpha_D\left[\gamma_{\alpha_1} T_1 - \gamma_{\alpha_1} A T_1 + \varpi I T_1 + \gamma_{\alpha_2} T_2 + \varpi I T_2\right] - (\pi_D + \psi) D_m \\ \dot{Dm} &= (\pi_D + \psi) D_m \end{aligned} \tag{4}$$

$Dm(t) \geq Dm(0)e^{(\pi_D+\psi)t}$.
$if\,(\pi_D + \psi) > 0$
$Dm(t) > 0$.

From 1;

$$\dot{Dc} = \alpha_g k_m D_m - \phi D_c \tag{5}$$

$\frac{dDc}{dt} \geq -\phi Dcdt$
$ln|Dc| \geq -\phi dt + y$
$Dc \geq Ye^{-\phi t}$
At t = 0
$Dc(0) \geq Dc(0)e^{-\phi t}$
$Dc(0) \geq 0$

From 1;

$$\dot{D_R} = \phi D_c - \mu_D D_R \tag{6}$$

If $\phi D_c \geq \mu_D D_R$

$\frac{dD_R}{dt} \geq -\mu_D D_R$

$\ln|D_R| \geq -\mu_D dt + Y$

$D_R(t) \geq D_R(0)e^{\mu_D t}$.

It follows from 1 that;

$$\dot{T}_1 = \gamma_3 A T_1 - \gamma_1(1-A)T_1 - \gamma_m(1-A)T_1 - \varpi I T_1 \tag{7}$$

$\frac{dT_1}{T_1} = [\gamma_3 A - \gamma_1(1-A) - \gamma_m(1-A) - \varpi I]\,dt$
$T_1(t) = e^{[\gamma_3 A - \gamma_1(1-A) - \gamma_m(1-A) - \varpi I] + y}$
$T_1(t) = T_1(0)e^{[\gamma_3 A - \gamma_1(1-A) - \gamma_m(1-A) - \varpi I]} \geqslant 0$

From 1;

$$\dot{T}_2 = \gamma_4 T_2 - \gamma_2 T_2 + \gamma_m(1-A)T_2 - \varpi I T_2 \tag{8}$$

$\frac{dT_2}{T_2} = [\gamma_4 - \gamma_2 + \gamma_m(1-A) - \varpi I]\,dt$
$\ln|T_2| = [\gamma_4 - \gamma_2 + \gamma_m(1-A(t)) - \varpi I]\,t + y$

$T_2 = ye^{[\gamma_4 - \gamma_2 + \gamma_m(1-A(t)) - \varpi I]t}$
At $t = 0$
$T_2(t) = T_2(0)e^{[\gamma_4 - \gamma_2 + \gamma_m(1-A(0)) - \varpi I]t} > 0$

From 1;

$$\dot{I} = \psi D_m + \beta_c C + n_1 F - \mu_c I \tag{9}$$

$\frac{dI}{dt} \geq -\mu_c I$
$\ln|I| \geq -\mu_c t + y$
$I(t) \geq I(0)e^{-\mu_c t} > 0$ for all t

From 1;

$$\dot{C} = \alpha_c Dc + n_2 F - \beta_c C \tag{10}$$

$\frac{dC}{dt} \geq -\beta_c C$
$\ln|C| \geq -\beta_c C + y$
$C(t) \geq C(0)ye^{\beta_c C} > 0$

Recall from 1 that

$$\dot{R} = \alpha_R D_R - \mu_R R \tag{11}$$

$\dot{R} \geq -\mu_R R$
$\frac{dR}{dt} \geq -\mu_R R$
$\ln|R| \geq -\mu_R t + y$
$R(t) \geq R(0)e^{-\mu_R t} > 0$

From 1:

$$\dot{F} = -(n_1 + n_2)F \tag{12}$$

$\dot{F} = -(n_1 + n_2)F$
$\frac{dF}{dt} = -(n_1 + n_2)t$
$\ln|F| = -(n_1 + n_2)t + y$
$F(t) = F(0)e^{-(n_1+n_2)t}$
$F(t) \geq 0$

From above, the positivity testing indicates that the variables $(V, Dm, Dc, DR, C, I, T_1, T_2,$
$A, F)$ are all non negative [36, 37].

4.2. Tumor Free Equilibrium Point

For a tumor free equilibrium state, $V = A = T_1 = T_2 = F = 0$
At the critical point at $t = 0$, $\dot{V} = 0$, $\dot{A} = 0$, $\dot{D}m = 0$, $\dot{D}c = 0$, $\dot{D}_R = 0$, $\dot{T}_1 = 0$, $\dot{T}_2 = 0$, $\dot{I} = 0$, $\dot{C} = 0$, $\dot{R} = 0$ and $\dot{F} = 0$.

$$\begin{aligned} &\text{From} - (\pi_D + \psi)\, Dm = 0 \\ &Dm = 0 \end{aligned} \tag{13}$$

$$\begin{aligned} &From \quad \alpha_g k_m Dm - \phi Dc \\ &\phi Dc = \alpha_g k_m Dm \\ &Dc = \frac{\alpha_g k_m Dm}{\phi} \\ &but \quad Dm = 0 \\ &\therefore Dc = 0 \end{aligned} \tag{14}$$

$$\begin{aligned} &From \quad \phi Dc - \mu_D D_R = 0 \\ &D_R = \frac{\phi Dc}{\mu_D} \\ &D_R = 0 \end{aligned} \tag{15}$$

$$\begin{aligned} &From \quad \psi Dm + \beta_c + n_1 F - \mu_c I = 0 \\ &I = \frac{\psi Dm + \beta_c + n_1 F}{\mu_c} \\ &But \quad Dm = F = 0 \\ &I = \frac{\beta_c}{\mu_c} \end{aligned} \tag{16}$$

$$
\begin{aligned}
&From \;\; \alpha_c Dc + n_2 F - \beta_c C = 0 \\
&C = \frac{\alpha_c Dc + n_1 F}{\beta_c} \\
&C = 0
\end{aligned} \tag{17}
$$

$$
\begin{aligned}
&From \;\; \alpha_R D_R - \mu_R R = 0 \\
&R = \frac{\alpha_R D_R}{\mu_R} \\
&But \quad D_R = 0 \\
&R = 0
\end{aligned} \tag{18}
$$

Therefore, $E_0 = (V_0, A_0, Dm_0, Dc_0, DR_0, T_1(0), T_2(0), I_0, C_0, R_0, F_0)$

$$(0,0,0,0,0,0,0,\frac{\beta_c}{\mu_c},0,0,0)$$

5. LOCAL STABILITY OF TUMOR FREE EQUILIBRIUM

Theorem 1. *The tumor free equilibrium point of the system of ordinary differential equation 1 is locally asymptotically stable if* $R_0 < 1$.

5.1. Jacobian Matrix

5.1.1 The Jacobian matrix for our system of equations in 1 is

$$
J = \begin{bmatrix}
-\lambda_v & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & -\lambda_A & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\alpha_v & h & -\pi_D - \psi & 0 & 0 & a & b & c & 0 & 0 & 0 \\
0 & 0 & \alpha_g k_m & -\phi & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & \phi & -\mu_D & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & d & 0 & 0 & 0 & e & 0 & -\varpi T_1 & 0 & 0 & 0 \\
0 & -\gamma_m T_1 & 0 & 0 & 0 & \gamma_m(1-A) & f & -\varpi T_2 & 0 & 0 & 0 \\
0 & 0 & \psi & 0 & 0 & 0 & 0 & -\mu_c & \beta_c & 0 & n_1 \\
0 & 0 & 0 & \alpha_c & 0 & 0 & 0 & 0 & -\beta_c & 0 & n_2 \\
0 & 0 & 0 & 0 & \alpha_R & 0 & 0 & 0 & 0 & -\mu_R & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -(n_1+n_2)
\end{bmatrix} \tag{19}
$$

where,

$a = -\alpha_D(\gamma_1 - \gamma_1 A + \varpi I)$, $b = -\alpha_D(\gamma_2 A + \varpi I)$, $c = -\alpha_D \varpi (T_1 + T_2)$

$d = \gamma_3 + (\gamma_1 - \gamma_m)T_1$, $e = -[(\gamma_1 - \gamma_m)1 - A) - \varpi I]$,

$f = \gamma_4 - \gamma_2 - \varpi I$, $h = \alpha_D \gamma_1 T_1 + \gamma_2 T_2$

$$J(E_0) = \begin{bmatrix} -\lambda_v & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\lambda_A & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \alpha_v & 0 & -\pi_D - \psi & 0 & 0 & G & M & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha_g k_m & -\phi & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \phi & -\mu_D & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_3 & 0 & 0 & 0 & X & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma_m & Y & 0 & 0 & 0 & 0 \\ 0 & 0 & \psi & 0 & 0 & 0 & 0 & -\mu_c & \beta_c & 0 & n_1 \\ 0 & 0 & 0 & \alpha_c & 0 & 0 & 0 & 0 & -\beta_c & 0 & n_2 \\ 0 & 0 & 0 & 0 & \alpha_R & 0 & 0 & 0 & 0 & -\mu_R & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -(n_1+n_2) \end{bmatrix} \tag{20}$$

where,

$$G = -\alpha_D \left(\gamma_1 + \frac{\beta_c \varpi}{\mu_c} \right), M = -\alpha_D \left(\frac{\varpi \beta_c}{\mu_c} \right)$$
$$X = -(\gamma_1 - \gamma_m - \frac{\varpi \beta_c}{\mu_c}), Y = \gamma_4 - \gamma_2 - \frac{\varpi \beta_c}{\mu_c}$$

The characteristic equation,$P(\xi) = \mid \xi I - J(E_0) \mid = 0$ where I is the identity matrix given by:

$$\begin{bmatrix} \xi+\lambda_v & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \xi+\lambda_A & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \alpha_v & 0 & \xi+\pi_c-\psi & 0 & 0 & G & M & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha_g k_m & \xi+\phi & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \phi & \xi+\mu_D & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \xi-X & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma_m & \xi-Y & 0 & 0 & 0 & 0 \\ 0 & 0 & \psi & 0 & 0 & 0 & 0 & \xi+\mu_c & \beta_c & 0 & n_1 \\ 0 & 0 & 0 & \alpha_c & 0 & 0 & 0 & 0 & \xi+\beta_c & 0 & n_2 \\ 0 & 0 & 0 & 0 & \alpha_R & 0 & 0 & 0 & 0 & \xi+\mu_R & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \delta \end{bmatrix} \tag{21}$$

where $\delta = \xi + (n_1 + n_2)$.

Using Row/Column reduction and co-factor expansion approach, the characteristics polynomial of equation (4.23)is as follows: $(\xi+\lambda_v)(\xi+\lambda_A)(\xi-X)(\xi+n_1+n_2)(\xi-Y)(\xi+\pi_c+\psi)(\xi+\phi)(\xi+\mu_D)(\xi+\mu_R)(\xi+\beta_c)(\xi+\mu_c)[\xi+(n_1+n_2)] = 0$

From the above characteristics polynomial, these are the eigenvalues, ξ

$(\xi_1, \xi_2, \xi_3, \xi_4, \xi_5, \xi_6, \xi_7, \xi_8, \xi_9, \xi_{10}, \xi_{11})$ determined as;

$$\xi_1 = -\lambda_v,\ \xi_2 = -\lambda_A,\ \xi_3 = -\left(\gamma_1 - \gamma_m - \frac{\varpi\beta_c}{\mu_c}\right)$$

$$\xi_4 = -(n_1 + n_2),\ \xi_5 = \gamma_4 - \gamma_2 - \frac{\varpi\beta_c}{\mu_c},\ \xi_6 = -(\pi_c + \psi)$$

$$\xi_7 = -\phi,\ \xi_8 = -\mu_D,\ \xi_9 = -\mu_c,\ \xi_{10} = -\beta_c,\ \xi_{11} = -\mu_R.$$

Clearly, its observed from above that all the eigenvalues have negative real part if $\gamma_2 + \dfrac{\varpi\beta_c}{\mu_c} > \gamma_4$, therefore the tumor free equilibrium point is asymptotically stable.

6. BASIC REPRODUCTIVE NUMBER

Proof. By application of a matrix - theoretic Vector approach. The tumor compartment, $U = (T_1, T_2)$.

Let $P_{(}i) = \begin{bmatrix} \gamma_3 A T_1 \\ 0 \end{bmatrix}$

$$P = \begin{bmatrix} \gamma_3 A & 0 \\ 0 & 0 \end{bmatrix}$$

$$Q_{(}i) = \begin{bmatrix} \gamma_3 A - [(\gamma_1 - \gamma_m)(1-A) - \varpi I]\, T_1 \\ (\gamma_4 - \gamma_2 - \varpi I)\, T_2 + \gamma_m (1-A) T_1 \end{bmatrix}$$

$$Q = \begin{bmatrix} \gamma_1(1-A) + \gamma_m(1-A) + \varpi I & 0 \\ \gamma_m(1-A) & \gamma_4 + \gamma_2 + \varpi I \end{bmatrix}$$

$$|Q| = [\gamma_1(1-A) + \gamma_m(1-A) + \varpi I][\gamma_4 + \gamma_2 + \varpi I]$$

$$Q^{-1} = \frac{1}{|Q|} \begin{bmatrix} \gamma_4 + \gamma_2 + \varpi I & 0 \\ \gamma_m(1-A) & \gamma_1(1-A) + \gamma_m(1-A) + \varpi I \end{bmatrix}$$

$$Q^{-1} = \begin{bmatrix} \dfrac{\gamma_4 + \gamma_2 + \varpi I}{\eta} & 0 \\ 0 & \dfrac{\gamma_1(1-A) + \gamma_m(1-A) + \varpi I}{\eta} \end{bmatrix}$$

where $\eta = \gamma_1(1-A) + \gamma_m(1-A) + \varpi I]\,[\gamma_4 + \gamma_2 + \varpi I]$

$$Q^{-1} = \begin{bmatrix} \dfrac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} & 0 \\ 0 & \dfrac{1}{\gamma_4+\gamma_2+\varpi I} \end{bmatrix}$$

$$PQ^{-1} = \begin{bmatrix} \gamma_3 A & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \dfrac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} & 0 \\ 0 & \dfrac{1}{\gamma_4+\gamma_2+\varpi I} \end{bmatrix}$$

$$PQ^{-1} = \begin{bmatrix} \dfrac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} & 0 \\ 0 & 0 \end{bmatrix}$$

$$\rho(PQ^{-1}) = \left(\frac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}, 0 \right)$$

$$R_0 = \frac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I},$$

7. GLOBAL STABILITY OF TUMOR - FREE EQUILIBRIUM POINT

Theorem 2. *The tumor free equilibrium point E_0 of the dynamical system is globally asymptotically stable if $R_0 < 1$.*

Theorem 3. *Let P, Q and f(x, y) be defined. If $f(x,y) \geqslant 0, P \geqslant 0, Q^{-1} \geqslant 0$, and $R_0 \leqslant 1$, then the function $L' = TQ^{-1}x$ is a Lyapunov function for model 1.*

Proof.

The left eigenvector of the non negative matrix PQ^{-1} corresponding to the eigenvalue $\rho(PQ^{-1}) = R_0$ and $x = (T_1, T_2)^T$ can be determined as shown below.

Let $W^T = (w_1, w_2)$.

$W^T PQ^{-1} = R_0(w_1, w_2)$

$(w_1, w_2)(PQ^{-1}) = R_0(w_1, w_2)$

$$(w_1, w_2) \begin{bmatrix} \dfrac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} & 0 \\ 0 & 0 \end{bmatrix} = R_0(w_1, w_2)$$

$$\left(\frac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} w_1, 0\ w_2 \right) = R_0(w_1\ , w_2)$$

$$R_0 w_1 = \frac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}$$

$$w_1 = \frac{\dfrac{\gamma_3 A}{\gamma_{\alpha 1}(1-A)+\gamma_m(1-A)+\varpi I}}{R_0}$$

$$= \frac{\dfrac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}}{\dfrac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}}$$

$$w_1 = \left(\frac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}\right)\left(\frac{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}{\gamma_3 A}\right)$$

$w_1 = 1 \therefore W^T = (1,0)$. The left eigenvector of the matrix $Q^{-1}P$ corresponding to the eigenvalue R_0 is $W^T = (w_1, w_2) = (1,0)$.

From the above eigenvector, the Lyapunov function to determine the tumor free equilibrium of the model 1 is given by

$$L = W^T Q^{-1} x$$

$$= (1,0)Q^{-1}\begin{bmatrix} T_1 \\ T_2 \end{bmatrix}.$$

$$= (1,0)\begin{bmatrix} \dfrac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} & 0 \\ 0 & \dfrac{1}{\gamma_4+\gamma_2-\gamma_m(1-A)+\varpi I} \end{bmatrix}\begin{bmatrix} T_1 \\ T_2 \end{bmatrix}$$

$$= \left[\frac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}, 0\right]\begin{bmatrix} T_1 \\ T_2 \end{bmatrix}$$

$$= \left[\frac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}T_1 + 0\right]$$

$$\therefore L = \frac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}.$$

Clearly,

1. $L(x) > 0$ for all $x \in P$
2. $||L(x)|| \longrightarrow \infty \Longrightarrow ||x|| \longrightarrow \infty$ (which means it is unbounded radially).

. Let $f(x,y) = (P-Q)x - P_i(x,y) + Q_i(x,y)$ where $x = (T_1, T_2)$ as defined in section 3.8,

$$f(x,y) = \begin{bmatrix} \gamma_3 A - \gamma_1(1-A) - \gamma_m(1-A) + \varpi I & 0 \\ 0 & -\gamma_4 - \gamma_2 + \gamma_m(1-A) - \varpi I \end{bmatrix}\begin{bmatrix} T_1 \\ T_2 \end{bmatrix} -$$

$$\begin{bmatrix} \gamma_1 A & 0 \\ 0 & 0 \end{bmatrix} + \begin{bmatrix} \gamma_3 A - [(\gamma_1 - \gamma_m)(1-A) - \varpi I]T_1 \\ (\gamma_4 - \gamma_2 - \varpi I)T_2 + \gamma_m(1-A)T_1 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$

and let $x' = (P-Q)x - f(x,y)$ but $f(x,y) = 0$
$\therefore x' = (P-Q)x$
$L' = W^T Q^{-1} x'$
$= W^T Q^{-1}[(P-Q)x - f(x,y)]$
$= W^T Q^{-1}[(P-Q)x - W^T Q^{-1} f(x,y)]$
$= W^T Q^{-1} Px - W^T Q Q^{-1} x - 0$
$= W^T Q^{-1} Px - W^T x$

$$= (1,0)\begin{bmatrix} \dfrac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I} & 0 \\ 0 & \dfrac{1}{\gamma_4+\gamma_2+\varpi I} \end{bmatrix} x - (1,0)x$$

$$L' = \frac{1}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}(1,0)\begin{bmatrix} T_1 \\ T_2 \end{bmatrix} - (1,0)\begin{bmatrix} T_1 \\ T_2 \end{bmatrix}$$

$$= R_0(1,0)\begin{bmatrix} T_1 \\ T_2 \end{bmatrix} - (1,0)\begin{bmatrix} T_1 \\ T_2 \end{bmatrix}$$

$= R_0 T_1 - T_1$
$= (R_0 - 1)T_1.$

It has been clearly shown that $R_0 \leq 1$ then $L' \leq 0$. Thus L is a Lyapunov function of the system.
Also if $T_1 = 0$, $L' = 0$.
By La Salle's invariance principle, tumor free equilibrium is asymptotically stable if $R_0 \leq 1$ [38, 39, 40, 41]. □

7.1. Endemic Equilibrium Values

By algebraic manipulations;

$V^* = 0, A^* = 1$
$Dm^* = \dfrac{\mu_c(\gamma_3+\gamma_1+\gamma_m)}{\varpi(\phi\psi+\alpha_c\alpha_g k_m)}, Dc^* = \dfrac{\alpha_g k_m \mu_c(\gamma_3+\gamma_1+\gamma_m)}{\varpi\phi(\phi\psi+\alpha_c\alpha_g k_m)}$
$D_R^* = \dfrac{\phi\alpha_g k_m \mu_c(\gamma_3+\gamma_1+\gamma_m)}{\mu_D\phi(\phi\psi+\alpha_c\alpha_g k_m)\varpi}, C^* = \dfrac{\alpha_c\alpha_g k_m \mu_c(\gamma_{p1}+\gamma_1+\gamma_m)}{\varpi\phi(\phi\psi+\alpha_c\alpha_g k_m(\beta_c)}$
$R^* = \dfrac{\alpha_R(\phi\alpha_g k_m \mu_c(\gamma_{p1}+\gamma_1+\gamma_m))}{\mu_R(\mu_R\phi(\phi\psi+\alpha_c\alpha_g k_m)\varpi}, I^* = \dfrac{\mu_c(\gamma_{p1}+\gamma_1+\gamma_m)}{\varpi}$
$T_1^* = \dfrac{\pi\mu_c(\gamma_3+\gamma_1+\gamma_m)+\psi\mu_c(\gamma_3+\gamma_1+\gamma_m)+\alpha_D\gamma_1-\varpi I\alpha_D Z_1}{(\alpha_D\gamma_1-\alpha_D\varpi I)(\varpi(\phi\psi+\alpha_c\alpha_g k_m)^2)}$
$T_2^* = Z_1 \geqslant 0$
$F^* = 0$

8. LOCAL STABILITY OF THE ENDEMIC EQUILIBRIUM POINT

Theorem 4. *The endemic equilibrium point of the system of ordinary differential equation is locally asymptotically stable if* $R_0 < 1$.

Proof. The Jacobian matrix (E^*) of the system of the endemic point for local stability was determined as

$$J(E^*) = \begin{bmatrix} -\lambda_v & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\lambda_A & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \alpha_v & h & \pi_D - \psi & 0 & 0 & a & b & c & 0 & 0 & 0 \\ 0 & 0 & \alpha_g k_m & -\phi & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \phi & -\mu_D & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & d & 0 & 0 & 0 & e & 0 & -\varpi T_1^* & 0 & 0 & 0 \\ 0 & -\gamma_m T_2^* & 0 & 0 & 0 & 0 & f & -\varpi T_2^* & 0 & 0 & 0 \\ 0 & 0 & \psi & 0 & 0 & 0 & 0 & -\mu_c & \beta_c & 0 & n_1 \\ 0 & 0 & 0 & \alpha_c & 0 & 0 & 0 & 0 & -\beta_c & 0 & n_2 \\ 0 & 0 & 0 & 0 & \alpha_R & 0 & 0 & 0 & 0 & -\mu_R & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -(n_1+n_2) \end{bmatrix} \tag{22}$$

where,
$a = -\alpha_D(\gamma_1 - \gamma_1 A^* + \varpi I^*)$, $b = -\alpha_D(\gamma_2 A^* + \varpi I^*)$
$c = -\alpha_D \varpi (T_1^* + T_2^*)$, $d = (\gamma_3 + \gamma_1 + \gamma_m) T_1^*$
$e = -\gamma_4 - \gamma_m(1 - A^*) - \varpi I^*$, $f = \gamma_4 - \gamma_2 - \varpi I^*$
$h = \alpha_D \gamma_1 T_1^* + \gamma_2 T_2^*$

From (26) the matrix $J(E^*)$ is strictly column diagonally dominant matrix if; $|\pi_D - \psi| > |\alpha_v + h + a + b + c|$, $|\phi| > |\alpha_g k_m|$, $|\mu_D| > |\phi|$, $|e| > |\varpi T_1^* + d|$, $|f| > |\gamma_m T_2^* + \varpi T_2^*|$, $|\mu_c| > |\beta_c + n_1 + \psi|$, $|\beta_c| > |n_2 + \alpha_c|$, $|\mu_R| > |\alpha_R|$.

Also all the diagonal elements are negative provided $\pi_D - \psi < 0$ and $f = \gamma_4 - \gamma_2 - \varpi I^* < 0$.
From the Gershgorin circle theorem,
$|\xi - a_{ii}| \leqslant \sum_{i \neq j} |a_{ij}| = R_i$
where ξ_i is the eigenvalue, a_{ii} and R_i are the centres and the radii respectively of the Gershgorin disc.
Considering the fact that $a_{ii} < 0$, $|a_{ii}| > R_i$ and $|\xi - a_{ii}| < R_i$, then the eigenvalue (ξ) of the matrix $J(E^*)$ are all negatives.
Therefore the endemic equilibrium is locally asymptotically stable. □

9. GLOBAL STABILTY OF ENDEMIC EQUILIBRIUM POINT

Theorem 5. *The endemic equilibrium of 1 is globally asymptotically stable if* $R_0 < 1$

Theorem 6. *Lyapunov Functions were developed from the first integral of the Lokta - Volterra system of the form*
$L = \sum_{i=1}^{n} C_i \left(x_i - x_i^* - x_i^* ln \frac{x_i}{x_i^*} \right)$

Proof. To prove the global asymptotic stability of the endemic equilibrium, the method of Lyapunov function is defined as follows:
$N(V^*, A^*, Dm^*, Dc^*, DR^*, T_1^*, T_2^*, I^*, C^*, R^*, F^*) = N_1 + N_2 + N_3 + N_4 + N_5 + N_6 + N_7 + N_8 + N_8 + N_9 + N_{10} + N_{11}$

$$N_1 = V - V^* - V^* ln \frac{V}{V^*}, N_2 = A - A^* - A^* ln \frac{A}{A^*},$$
$$N_3 = Dm - Dm^* - Dm^* ln \frac{Dm}{Dm^*}, N_4 = DC - DC^* - DC^* ln \frac{DC}{DC^*},$$
$$N_5 = DR - DR^* - DRl^* n \frac{DR}{DR^*}, N_6 = T_1 - T_1^* - T_1^* ln \frac{T_1}{T_1^*},$$
$$N_7 = T_2 - T_2^* - T_2^* ln \frac{T_2}{T_2^*}, N_8 = I - I^* - I^* ln \frac{I}{I^*},$$
$$N_9 = C - C^* - C^* ln \frac{C}{C^*}, N_{10} = R - R^* - R^* ln \frac{R}{R^*},$$
$$N_{11} = F - F^* - F^* ln \frac{F}{F^*},$$

Substituting the endemic equilibrium values into equation 1, we obtain the endemic equilibrium relations below,

$$\begin{aligned}
0 &= \lambda_v V^* \\
0 &= -\lambda_A (1 - A^*) + \lambda_A \\
0 &= \alpha_v V^* - \alpha_D \left[(\gamma_1 - \gamma_1 A^* + \varpi I^*) T_1^* + (\gamma_2 A^* + \varpi I^*) T_2^* \right] - (\pi_D - \psi) D_m^* \\
0 &= -\alpha_g k_m Dm^* + \phi Dc^* \\
0 &= -\phi Dc^* + \mu_R D_R^* \\
0 &= -\gamma_3 A^* - \left[(\gamma_1 - \gamma_m)(1 - A^*) - \varpi I^* \right] T_1^* \\
0 &= (\gamma_4 - \gamma_2 - \varpi I^*) T_2^* + \gamma_m (1 - A^*) T_1^* \\
0 &= -\psi D_{m^*} - \beta_c C^* - n_1 F^* - \mu_c I^* \\
0 &= -\alpha_c Dc^* - n_2 F^* + \beta_c C^* \\
0 &= -\alpha_R D_R^* + \mu_R R^* \\
0 &= (n_1 - n_2) F^*
\end{aligned} \tag{23}$$

Now finding the derivative of N along the equation solutions,

$$\frac{dN}{dt} = \frac{dN_1}{dt} + \frac{dN_2}{dt} + \frac{dN_3}{dt} + \frac{dN_4}{dt} + \frac{dN_5}{dt} + \frac{dN_6}{dt} + \frac{dN_7}{dt} + \frac{dN_8}{dt} + \frac{dN_9}{dt} + \frac{dN_{10}}{dt} + \frac{dN_{11}}{dt}$$

From,

$$N_1 = V - V^* - V^* ln \frac{V}{V^*}$$
$$= V - V^* - V^* (lnV - lnV^*)$$
$$= V - (V^* lnV - V^* lnV^*)$$
$$\frac{dN_1}{dt} = V' - \frac{V^* V'}{V}$$
$$= \left(1 - \frac{V^*}{V}\right) V'$$
$$= \left(\frac{V - V^*}{V}\right) V'$$
$$\frac{dN_1}{dt} = \left(\frac{V - V^*}{V}\right) [-\lambda_v V - \lambda_v V^*]$$
$$= -\left(\frac{V - V^*}{V}\right) [\lambda_v V + \lambda_v V^*]$$
$$= -\left[\left(\frac{V - V^*}{V}\right) (\lambda_v V) + \left(\frac{V - V^*}{V}\right) (\lambda_v V^*)\right]$$
$$= -\lambda_v V^* \left(1 - \frac{V^*}{V}\right) \left(\frac{V}{V^*} + 1\right)$$
$$= -\lambda_v V^* \left(\frac{V}{V^*} + 1 - 1 - \frac{V^*}{V}\right)$$
$$= -\lambda_v V^* \left(\frac{V}{V^*} - \frac{V^*}{V}\right)$$
$$\frac{dN_1}{dt} < 0, \text{ where } V > V^*$$

Also,

$$N_2 = A - A^* - A^* ln \frac{A}{A^*}$$
$$= A - A^* - A^* (lnA - lnA^*)$$
$$= A - A^* - (A^* lnA - A^* lnA^*)$$
$$\frac{dN_2}{dt} = A' - 0 - \frac{A^* A'}{A}$$
$$= A' \left(1 - \frac{A^*}{A}\right)$$
$$= \left(\frac{A - A^*}{A}\right) .A'$$

$$\frac{dN_2}{dt} = \left(\frac{A-A^*}{A}\right)[\lambda_A(1-A) - \lambda_A(1-A^*) + \lambda_A - \lambda_A]$$
$$= \left(\frac{A-A^*}{A}\right)(-\lambda_A A + \lambda_A A^*)$$
$$= \left(\frac{A-A^*}{A}\right)(\lambda_A A^* - \lambda_A A)$$
$$= \left(1-\frac{A^*}{A}\right)\lambda_A A^* \left(1-\frac{A}{A^*}\right)$$
$$= \lambda_A A^* \left(1-\frac{A^*}{A}\right)\left(1-\frac{A}{A^*}\right)$$
$$= \lambda_A A^* \left(1-\frac{A}{A^*}-\frac{A^*}{A}+1\right).$$
$$= \lambda_A A^* \left(-\frac{A}{A^*}-\frac{A^*}{A}+2\right).$$
$$\frac{dN_2}{dt} < 0, \text{ where } A > A^*$$

Similarly,
$$N_{11} = F - F^* - F^* ln\frac{F}{F^*}$$
$$= F - F^* - F^*(lnF - lnF^*)$$
$$= F - F^* - (F^* lnF - F^* lnF^*)$$
$$\frac{dN_{11}}{dt} = F' - \frac{F^* F'}{F}$$
$$= F'\left(1-\frac{F^*}{F}\right)$$
$$= \left(\frac{F-F^*}{F}\right)F'$$
$$\frac{dN_{11}}{dt} = \left(\frac{F-F^*}{F}\right)[(-n_1 F - n_2 F) - (-n_1 F^* + n_2 F^*)]$$
$$= \left(1-\frac{F^*}{F}\right)\left[-n_1 F^*\left(-\left(1-\frac{F}{F^*}\right)\right) - n_2 F^*\left(1-\frac{F}{F^*}\right)\right]$$
$$= \left[-n_1 F^*\left(-\left(1-\frac{F}{F^*}\right)\right) - n_2 F^*\left(1-\frac{F}{F^*}\right)\right]$$
$$-\frac{F^*}{F}\left[-n_1 F^*\left(-\left(1-\frac{F}{F^*}\right)\right) - n_2 F^*\left(\left(1-\frac{F}{F^*}\right)\right)\right]$$
$$= -(n_1+n_2)F^*\left(1-\frac{F}{F^*}-\frac{F^*}{F}+1\right)$$

Therefore from the proves above,
$\frac{dN}{dt} < 0.$

By La Salle's invariance principle the endemic equilibrium, E^* is globally asymptotically stable [42, 43, 44, 45]. □

10. NUMERICAL SIMULATIONS

The possible intake of Food Supplement (Lemon Juice) in reducing Prostate Cancer disease in men has been investigated by the perturbation of the amount of food supplement (n_1) and the effects or its relation with the Tumor Cells within a year has been summarised in the graphs below.

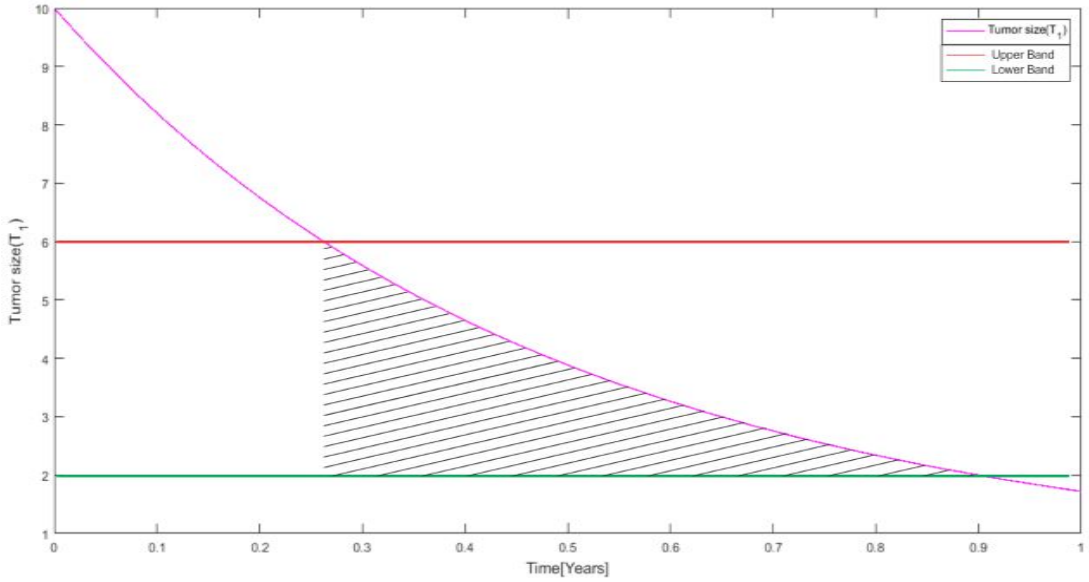

Figure 4: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.1$

From Figure 4, the amount of lemon juice $n_1 = 0.1$ corresponds to $1.5ml$ of Lemon Juice per day. There is a possible that this dose can take approximately 3.0 months and 10.68 months to reach the highest and the lowest normal sizes of the prostate respectively.

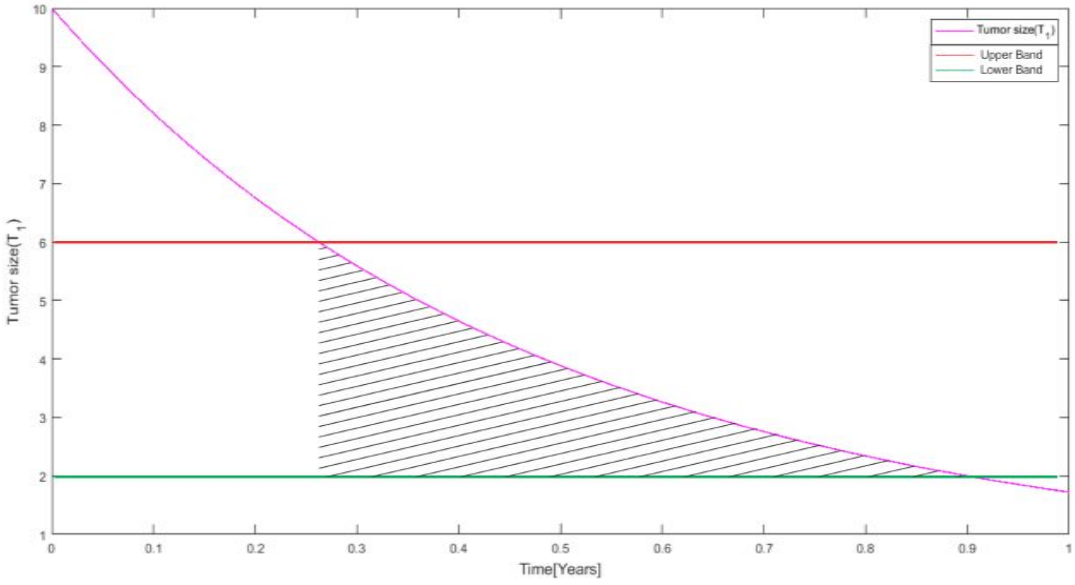

Figure 5: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.15$

From Figure 5, the amount of lemon juice $n_1 = 0.15$ corresponds to $2.25ml$ of Lemon Juice per day. This is an indication of a possibility of this dose taking approximately 3.0 months and 10.68 months to reach the highest and the lowest normal sizes of prostate respectively.

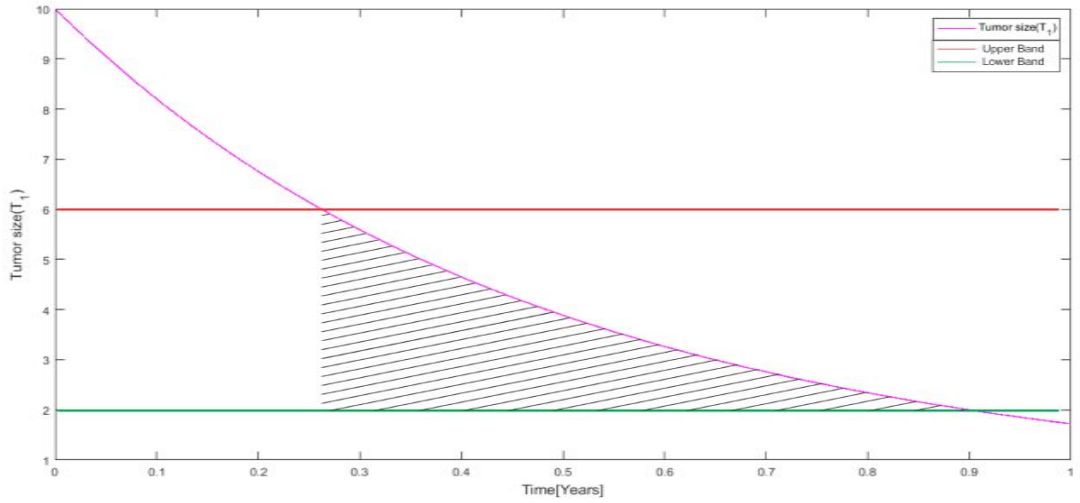

Figure 6: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.2$

From figure 6, the amount of lemon juice $n_1 = 0.2$ corresponds to$3ml$ of Lemon Juice per day.This is an indication that it is possible for this dose to take approximately 2.4

months and 7.8 months to reach the highest and the lowest normal sizes of prostate respectively.

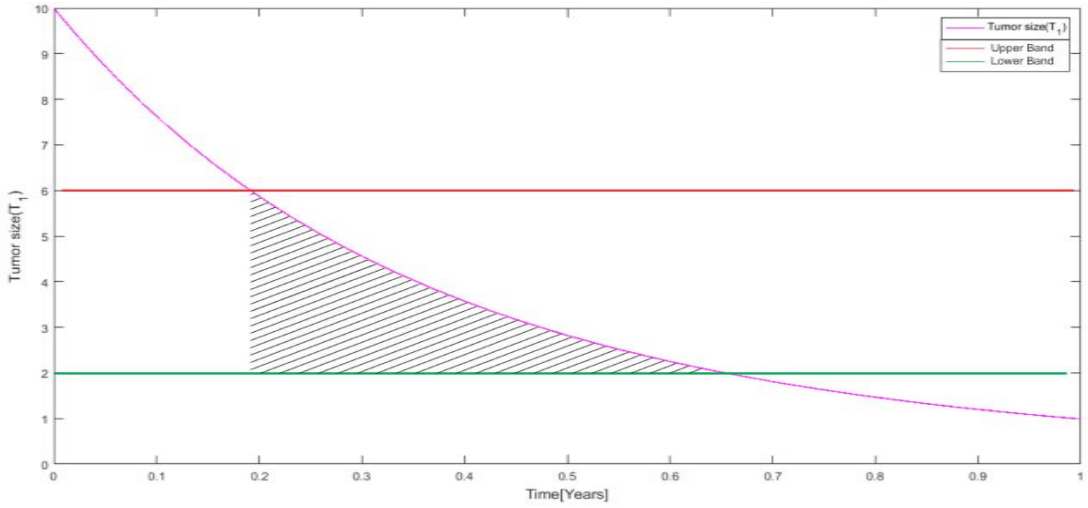

Figure 7: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.25$

From Figure 7, the amount of lemon juice $n_1 = 0.25$ corresponds to3.75ml of Lemon Juice per day. This clearly indicates that this dose might take approximately 2.4 months and 7.68 months to reach the highest and the lowest normal sizes of prostate respectively.

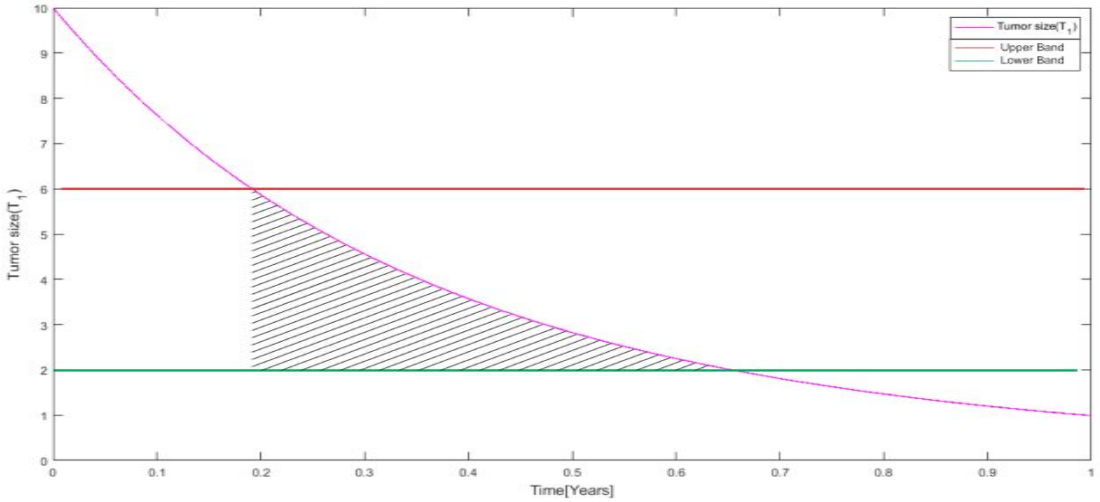

Figure 8: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.3$

From figure 8, the amount of lemon juice $n_1 = 0.3$ corresponds to4.5ml of Lemon Juice per day. This is a possibility that this dose might take approximately 2.16 months and 7.2 months to reach the highest and the lowest normal sizes of prostate respectively.

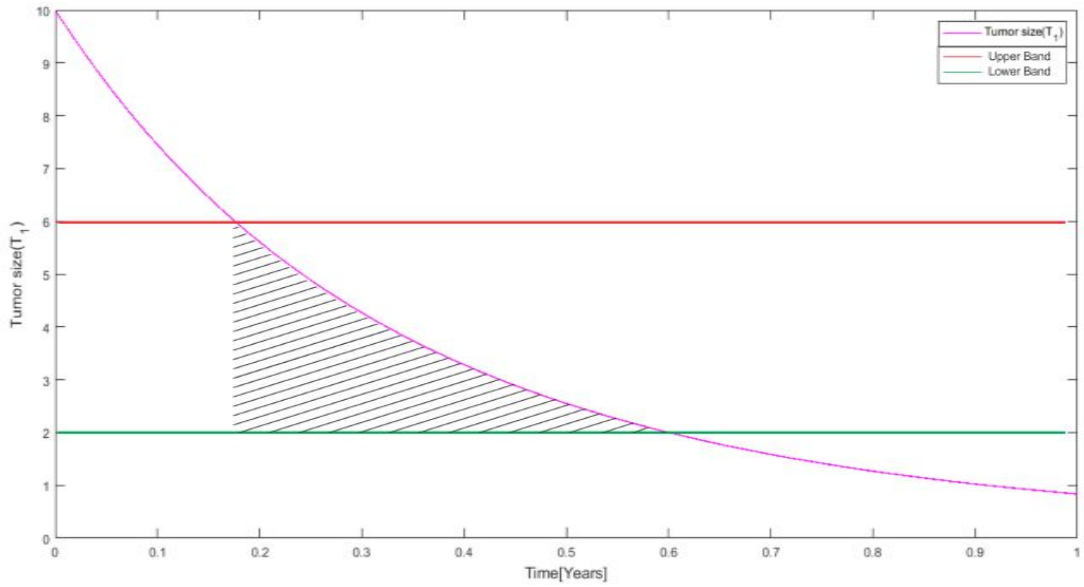

Figure 9: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.35$

From Figure 9, the amount of lemon juice $n_1 = 0.35$ corresponds to$5.25ml$ of Lemon Juice per day. This dose can possibly take approximately 2.04 months and 6.6 months to reach the highest and the lowest normal sizes of prostate respectively.

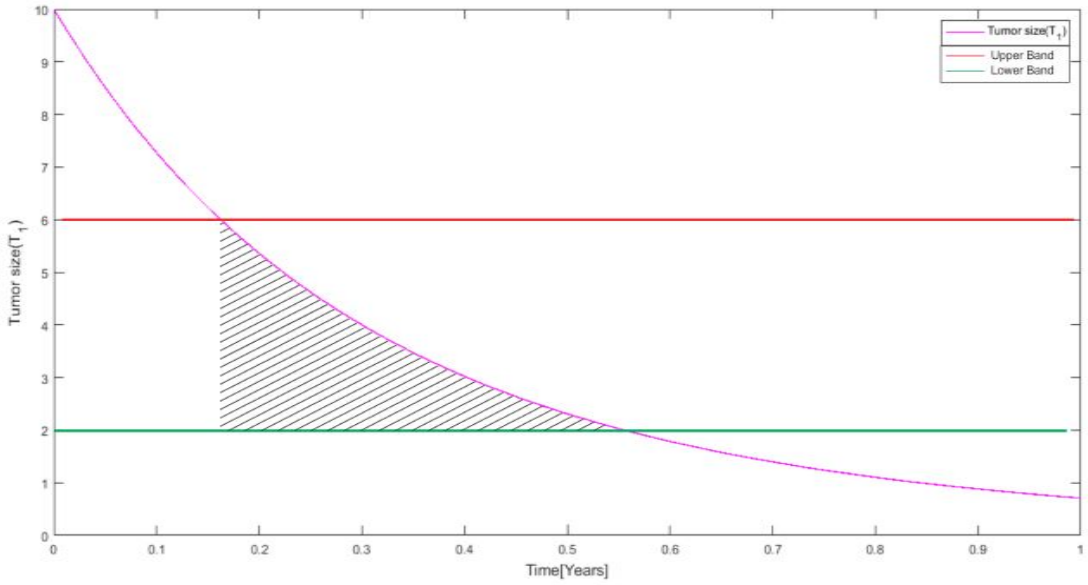

Figure 10: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.4$

From Figure 10, the amount of lemon juice $n_1 = 0.4$ corresponds to$6ml$ of Lemon Juice per day. This is an indication of a possibility of a dose taking approximately 1.92

months and 6.48 months to reach the highest and the lowest normal sizes of prostate respectively.

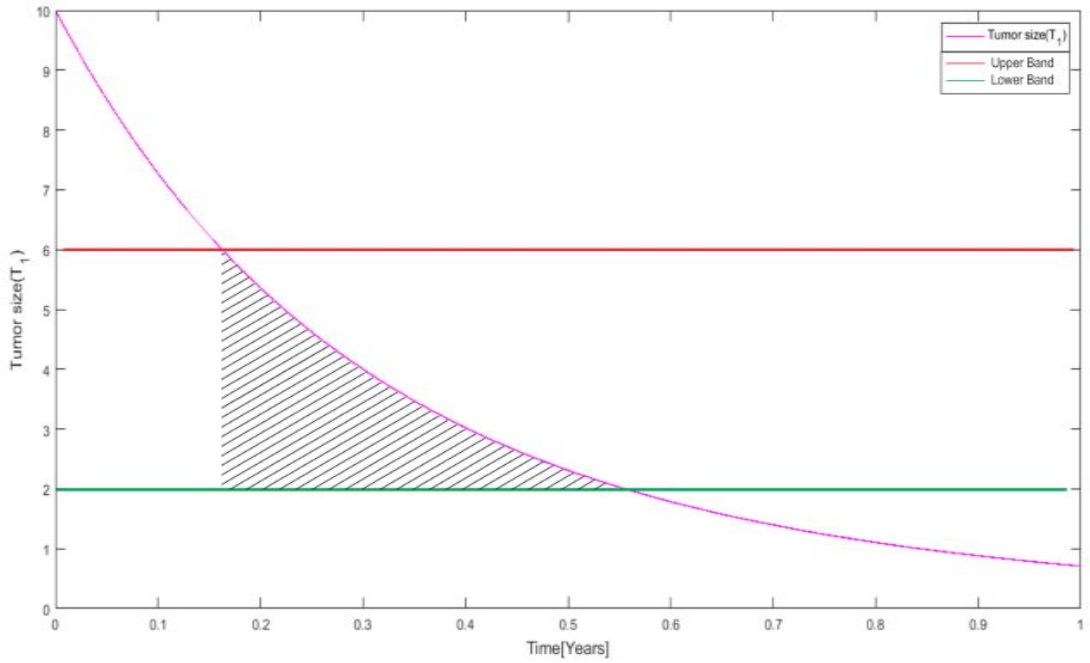

Figure 11: Tumor size (T_1) in Gleason Score(GS) over time at $n_1 = 0.45$

From Figure 11, the amount of lemon juice $n_1 = 0.45$ corresponds to $6.75ml$of Lemon Juice per day. This suggest that it is possible foor this dose to take approximately 1.8 months and 6.24 months to reach the highest and the lowest normal sizes of prostate respectively.

11. CONCLUSION

A schematic diagram was developed consisting of Prostate Cancer and Immune System components. The model was categorised into eleven compartments. Based on the compartments, a system of non-linear ordinary differential equations was established.
The following controls were considered in the prostrate cancer model; suppression of Androgen from reaching the prostate tumor for its growth, application of vaccine to reduce the proliferation of tumor cells causing possible cell apoptosis, introduction of food supplement (Lemon) to strengthen the immune system to fighting the cancerous cells.
The prostate cancer equilibrium points and their stability were established. It indicated that the local tumor free and tumor endemic as well as global tumor free and tumor endemic equilibrium states were locally and globally asymptotically stable. The

prostate cancer reproductive number was found to be;
$R_0 = \dfrac{\gamma_3 A}{\gamma_1(1-A)+\gamma_m(1-A)+\varpi I}$.

Numerical simulations of the prostate cancer system of equations indicates that despite the vaccination and suppression of androgen, there will still be a relapse. But the introduction of food supplement $(Lemon)$ might empower the immune system to fight the cancer tumor.
Analysis of the graphs showed there exist a possible positive effects of food supplement $(Lemon\,juice)$ on the prostate cancer tumor cells. Clearly, it indicates that Lemon Juice might have a tendency of reducing prostate cancer with time. The amount of Lemon Juice (n_1) is estimated from 0.65 to 0.80 of every $15ml$ of Lemon juice into $720ml$ of water. That is $5ml$ into $240ml$ of water three times daily. This dosage has the likelihood to reduce any form of chemical reaction such as the decay of tooth enamel, sunburns, heartburns, migraine, frequent urination, dehydration, stomach ulcer.
Hence, there is need to intensify prostate cancer screening and awareness nationwide free of charge to enable early detection. Lemon juice is rich in vitamin C, B-6, mineral,sugar, fat $(polysaturated)$ and dietary fibres. This can possibly help in reducing cancerous cells in any form, however every individual should inculcate the habit of taking $5ml$ of lemon juice into $240ml$ of water thrice daily.

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Data Availability Statement
Some of the parameter values were assumed and others taken from published articles and are cited in this paper. These published articles were also cited at relevant places within the text as references.

Conflict of interest
Authors declare that there are no conflict of interest regarding the publication of this paper.

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