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THERAPEUTIC IMPLICATIONS OF THERMODYNAMICS SPECTROPHOTOMETRY IN HIV CONTROL DYNAMICS

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Abstract: **Due to continued HIV prevalence, control infectivity parameter was expressed and quantified through spectrophotometric data using historical absorbance data. The expression was incorporated in an adopted basic viral dynamics model, an Ordinary Differential Equation (ODE) and solved using the numerical integration that utilized explicit Runge-Kutta method in MATLAB™ function ode 23 for the infection time course. The infection dynamics was allowed to progress from day zero to day nineteen without drug intervention while the drug intervention which basically was the introduction of the drug historical thermodynamic spectrophotometric absorbance data in the expressed model was introduced from day nineteen to day three hundred. The solution showed dynamics as expected in drug intervention. A clear change in the dynamics in day nineteen from progressive to regressive dynamics. A comprehensive control infectivity value of less than 1 $\left({}^{mL}/_{copies.d}\right)$ is an indication of curative ability of the expressed model for the two drugs D1 and D3 whose historical data were utilized. This signifies the existence of van der Waals force of repulsion between the two interacting particles. Higher than 1 $\left({}^{mL}/_{copies.d}\right)$ value for control infectivity parameter would have meant attraction. Again the infection time course from simulations validated the quantified result since the two dynamics of the infection time course represented the situation at both normal infection without treatment before day nineteen and at curative afterwards to day three hundred. Pharmaceutical industries should take note of this in drug design.**

Keywords: **Human immunodeficiency virus, Absorbance, Interfacial energetics, Control Infectivity.**

1. INTRODUCTION

WHO, (2024) noted that with an estimated 0.7% (0.6-0.8%) of adults aged 15-49 years, although the burden of the epidemic continues to vary considerably between countries and regions, world HIV population as at the end of 2022 stood at average of 39.0 million people with a range of (33.1-45.7 million people).

Viruses are found in almost every ecosystem on earth and known to infect most types of organisms, including bacteria, fungi, plants, vertebrates, etc. Smith, (1972) observed that the mechanisms by which viruses cause diseases in an organism depend largely on the viral species. Viruses can usually cause damage in the host via cell lysis, production of toxic substances and cell transformation (Doitsh & Greene, 2016). During the course of virus replication, many cytotoxic viral components as well as by-products of viral replication accumulate in the cell (Klatt, 2015). Cell lysis and cytotoxic

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components cause death of the cell (Lai, 2014). When a virus enters a cell and completes its normal replication cycle, the host cell may undergo lysis due to a physical internal pressure exerted by multiplying virus or immune response. Some viruses can cause lifelong or chronic infections where viruses continue to replicate in the body despite the host's defence mechanisms.

A virus is a small agent that is only able to replicate itself inside the living cells of an organism. Viruses multiply by using the host cell's synthesizing machinery to cause the synthesis of viral building blocks, which then self-assemble into new viruses that are released into the environment. Several virual diseases are common in humans, wild and domestic animals or crop plants. Some common human diseases such as cold, influenza, chickenpox and cold sores are caused by viruses. These have continued to plague humans (Lai, 2014). There are currently over twenty one families of viruses known to cause diseases in humans, including human immunodeficiency virus (HIV), Hepatitis, Herpes Simplex, Measles, etc. They are not susceptible to the action of antibodies (Khanal & Shrestha, 2013).

There have been some advances in the analysis of HIV dynamics and immunology. One of which is the use of viral dynamics models to predict the infection dynamics with the subsequent plots. Bonhoeffer *et al*., (1997) gave equation (1) that has served as a good tool in the analysis.

$$\begin{aligned} \dot{x} &= \lambda - dx - \beta xv, \\ \dot{y} &= \beta xv - ay, \\ \dot{v} &= ky - uv. \end{aligned} \tag{1}$$

Where x is susceptible cells, y is infected cells, v is virus particle, λ is rate of production of susceptible cells, d is death rate of susceptible cells, β is infectivity (interaction parameter), a is death rate of infected cells, k is rate of virus production and u is clearance rate of virus particles.

Three (3) main stages, namely the acute HIV infection (primary infection), asymptomatic and the advanced – aids as clearly shown in a typical HIV infection course Fig. 1 have been identified in HIV infection dynamics. Antibodies to the virus may develop in about a week to several months or more after infection with HIV and one could test positive on antibody test after antibodies to HIV appear in the blood as depicted in Fig. 1.

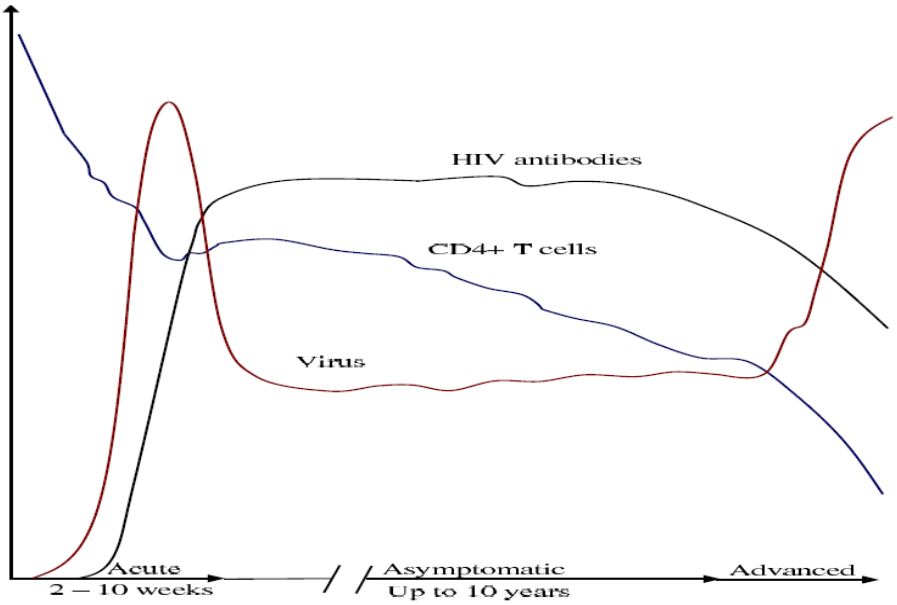

Fig. 1: Approximate Time-Course of HIV Infection, (Jeffrey, 2006; Hunt, 2005).

When infection is not yet established, normal $CD4^+$ T cell counts range from five hundred (500) to one thousand six hundred (1600) cells per cubic micro litre, on the average (1000) cells per cubic micro litre and drops to less than hundred (500) cells per µL (cells mm^{-3}) if infection is fully established.

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Variability in infection as well as in response to highly antiretroviral therapy (HAART) relating to infectivity has been a problem. The problem therefore is the difficulty in the determination of a new knowledge in HIV/drug interactions required by drug manufacturers that would translate to production of more effective drugs. The identification of the actual mechanisms of virus/blood interactions parameters within the existing mathematical models has not been easy. A very serious problem in the mathematical modelling is the unavailability of experimental data on HIV/blood interactions. Lack of HIV experimental data for some comparison with research results has remained a challenge.

Ilo, (2022) through thermodynamics spectrophotometry gave an insight control infectivity in HIV dynamics. Ilo, (2024a) had developed a validated model through concepts of thermodynamics implementation to unravel the mystery of transcriptional bifurcation in HIV dynamics. Ilo, (2024b) had also established HIV adhesion driven infectivity through electrostatics interaction mechanism. Ilo, Omenyi, and Dim, (2021a) had applied thermodynamics in the dynamics of HIV. Ilo, Omenyi and Ani, (2021b) had quantified drug primary mechanism of action through thermodynamics Hamaker concept. All these successes gave the impetus to unravel the thermodynamics spectrophotometry of control in HIV dynamics.

In this paper, the virus/blood repulsive interaction parameters required for regressive dynamics of HIV (control), is expressed in terms of the spectrophotometric absorbance parameters for a thermodynamic model of HIV dynamics.

2. PREVIOUS WORK/LITERATURE SURVEY

Absorbance values of drugs and blood samples in HIV dynamics

Ani, (2015) established that for drugs to be effective HIV blockers, they should be able to coat the surfaces of the lymphocyte and that to establish the extent of coating or coating effectiveness, he analyzed absorbance parameters of the interaction between HIV particles, susceptible cell and the drugs as $\tilde{a}_d$ peak absorbance for drug film only, $\tilde{a}_b$ peak absorbance for blood component only and $\tilde{a}_{bd}$ peak absorbance for drug film coated given blood component. From his absorbance concept, it actually says that the difference the drug film makes in the absorbance of a blood component when compared with the difference in the absence of the drug can give idea of the drug effectiveness. When coating is not complete, $(\tilde{a}_d - \tilde{a}_b)$ will be greater than $(\tilde{a}_{bd} - \tilde{a}_b)$. Finally, if the blood component surface is completely covered or coated/blocked by the drug film which is desirable, $\tilde{a}_{bd} = \tilde{a}_d$ and one would in principle expect 100% effective drug.

Basic HIV control model

Following basic infection dynamics model, equation 2 serves as a model for control infectivity which is usually incorporated in the basic viral dynamics to have control dynamics model as equation 3.

$$\beta_c = \beta_0(1-\eta) \tag{2}$$

$$\begin{aligned} \dot{x} &= \lambda - dx - (1-\eta)\beta_0 xv \\ \dot{y} &= (1-\eta)\beta_0 xv - ay, \\ \dot{v} &= ky - uv. \end{aligned} \tag{3}$$

3. METHODOLOGY

This study involved expressing and quantification of control infectivity parameter through spectrophotometric data using historical absorbance data from Ani 2015 and incorporating it in an adopted basic viral dynamics model, an Ordinary Differential Equation (ODE) and the solution of the ensued model from numerical integration that utilized explicit Runge-Kutta method simulated for the infection time course using MATLAB™ function ode 23. D1 represents data for Lamivudine, Nevirapine & Zidovudine while D3 represents data for Nevirapine. The infection dynamics was allowed to progress from day zero to day nineteen without drug intervention while the drug intervention was introduced with the drugs historical spectrophotometric data from day nineteen to day three hundred. The solution showed dynamics as expected in drug intervention. A clear change in the dynamics in day nineteen from progressive to regressive dynamics.

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Expressing HIV control model with thermodynamic absorbance parameter

As articulated by (Ani, 2015) that, if coating is not complete, $(\tilde{a}_d - \tilde{a}_b)$ will be greater than $(\tilde{a}_{bd} - \tilde{a}_b)$, analytically and in principle for efficiency, it would be in right perspective if the drug mechanism of action parameter is incorporated in the basic viral dynamics to have equation 4.

$$\dot{x} = \lambda - dx - \left(1 - \left(\frac{\tilde{a}_{bd} - \tilde{a}_b}{\tilde{a}_d - \tilde{a}_b}\right)\right)\beta_0 xv$$

$$\dot{y} = \left(1 - \left(\frac{\tilde{a}_{bd} - \tilde{a}_b}{\tilde{a}_d - \tilde{a}_b}\right)\right)\beta_0 xv - ay,$$

$$\dot{v} = ky - uv. \qquad (4)$$

4. RESULTS AND DISCUSSIONS

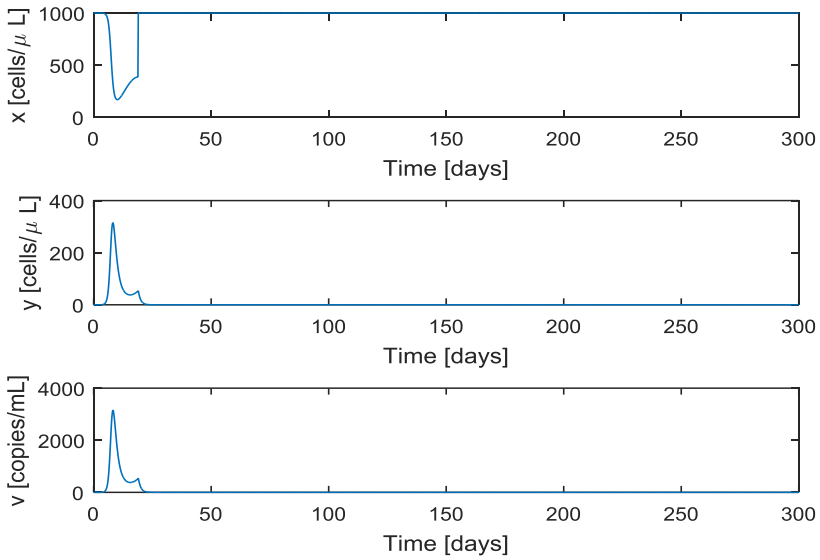

Fig 2: Simulation for drug intervention with D1 absorbance parameters

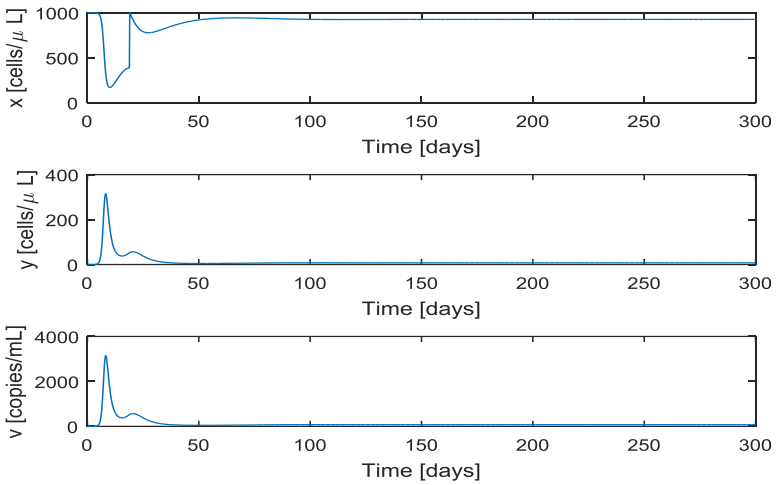

Fig 3: Simulation for drug intervention with D3 absorbance parameters

Expression and quantification of thermodynamic spectrophotometric HIV control parameters of some drugs were done. The results of the simulations show actually that the expressed model incorporated into the adopted basic viral dynamics model was able to change the dynamics of the disease course from progressive to regressive hence validating the model of being able to represent drug control mechanism of action. A less than one value of the model showed actually a repulsive tendency of the model. A comprehensive infectivity value of less than 1 $\left({}^{mL}/_{copies.d}\right)$ is an indication of curative ability of the expressed model.

This has been given a physical meaning by thermodynamically expressing, quantifying and validating it with simulations that showed change in dynamics as expected. The result of this novel research is another mile stone in the sands of time for solution to myriads of problems facing humanity using surface thermodynamics and in particular in the area of biological processes in the quest to unravel HIV-blood control interaction. Note that a less than one 1 $\left({}^{mL}/_{copies.d}\right)$ in the value of control infectivity parameter means ability to repel attraction between virus and lymphocyte, a condition generally encountered in HIV-blood interaction in the presence of antiretroviral drugs intervention. This approach should be explored towards finding a lasting solution or vaccine to other viral diseases like ebola, lassa fever, e.t.c.

The expression and subsequent quantification of control infectivity parameter in HIV dynamics is a novel one. Drug designers should try this approach to certify its validity. An option of preventing or counteracting HIV-blood interaction could be achieved by application of this result. The application of this study in pharmaceutical industries, in the area of drug design and in clinical studies cannot be overemphasized.

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