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The Role of Repulsive Van der Waals Interactions in the Treatment of Human Immunodeficiency Virus (HIV) Infections with Antiretroviral Drugs

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Abstract: Van der Waals interactions mechanism was used to determine and explain the interaction processes in HIV-drug coated blood interactions. The methodology involved the serial dilution of the five different antiretroviral drugs (two HAART/FDC and three single drugs) and the subsequent incubation with the blood samples collected from ten HIV infected persons for the absorbance measurement using a digital Ultraviolet Visible MetaSpecAE1405031Pro Spectrophotometer. The digital CD4 count machine (Cytoflowmeter) was used to obtain the CD4 counts of the blood samples. The variables required for the computations with the Lifshiftz formula were derived from the absorbance data. The MATLAB software tools were employed in the mathematical analysis of the very large body of data generated from the experiments. The Hamaker constants A_{11}, A_{22}, A_{33} and the combined Hamaker coefficients A_{132} of the various drugs interacting with the blood were obtained using the values of the dielectric constant together with the Lifshiftz equation. The absolute combined Hamaker coefficient, A_{132abs} (a mean of all the values of the various Hamaker coefficients) for each antiretroviral drug on both infected blood samples were also calculated. The absolute values for the combined Hamaker coefficient, A_{132abs} obtained for each of the five antiretroviral drugs interacting with infected blood samples are given thus: D1 = -0.03998×10^{-21} Joule, D2 = -0.05305×10^{-21}Joule, D3 = -0.05845×10^{-21}Joule, D4 = -0.02481×10^{-21}Joule, and D5 = -0.05844×10^{-21}Joule. The negative senses of the absolute combined Hamaker coefficient imply net negative van der Waals forces indicating a possible repulsion or blocking of the invading virus by the administered drug which coats the lymphocytes. This, however, confirms a functional cure for HIV infection which had been clinically established by the biological researchers. A thermodynamic criterion for HIV-drug interaction prediction was suggested and found to be a valuable tool in HIV study. The use of the findings of this work by pharmaceutical industries is recommended.

Keywords: Hamaker Constant, Hamaker Coefficient, Human Immunodeficiency Virus, Antiretroviral Drug, Lifshitz Formula, Lymphocyte, Van der Waals Forces, Highly Active Antiretroviral Therapy (HAART)

1. Introduction

The UNAIDS Global report on HIV/AIDS treatment in 2013 (1), declared that an estimated 35.5 (32.2 – 38.8) million people were living with HIV in 2012. About 15 million people with HIV are expected to be reached with the lifesaving antiretroviral treatment by 2015. Hence, the world is within the reach of providing antiretroviral therapy to a good number of HIV infected people across the globe. In 2012, 9.7 million people in low and middle income countries received antiretroviral therapy. Antiretroviral therapy not only prevents AIDS – related illness and death: it also has the potential to significantly reduce the risk of HIV transmission and the spread of tuberculosis. From 1996 to 2012, antiretroviral therapy averted 6.6 million AIDS – related deaths worldwide, including 5.5 million deaths in low and middle income countries. Antiretroviral therapy reduces the risk that a person living with HIV will develop tuberculosis (1).

It could also be noted that the antiretroviral regimens have not yet completely and permanently suppressed the virus in

HIV – infected people. Although, many antiretroviral drugs are being manufactured for the eradication of the HIV infections; but approximately 40,000 new HIV infections occur each year in the United States according to the Joint United Nations Programmes (2). The power of highly active antiretroviral therapy (HAART) to suppress HIV has revolutionized the clinical management of HIV disease in the developed world (3). The capacity for HIV to develop resistance to antiretroviral drugs, however, is a significant cause of the failure of HAART. Genotypic and phenotypic resistance tests have the potential to help identify which drugs in a regimen are failing and to guide the selection of drugs for new regimens (4). The discovery and application of highly active anti-retroviral therapy (HAART) to suppress HIV has revolutionized the clinical management of HIV/AIDS cases. The HIV however, has the capacity to develop resistance to the antiretroviral drugs and this phenomenon has turned out to be a significant cause of failure of HAART (5). HIV, which is a rapidly mutating RNA-based virus, lacks the ability to checkmate the possible genetic mutations that can occur during replication. Hence, this rapid genetic variation has become the major factor for which this menace has consistently defiled clinical solutions. The increasing rate of HIV infection globally is blamed on the ineffectiveness of some available antiretroviral therapy to block or resist perfectly this virus from invading the uninfected white blood cells.

The mechanism by which drugs can block the virus seems weak and hence it becomes necessary to study the interaction between the HIV and the drug-coated white blood cells. The problem of formulating drugs that can summarily eliminate HIV, remains a challenge. The question arises as to how effective the available antiretroviral drugs are? The answer to such question may be found by studying surface effects in HIV-drug interactions. There are several classes of drugs, which are usually used in combination, to treat HIV infection. The choice for a new approach in proffering a solution to HIV pandemic via the vehicle of surface thermodynamics against the conventional clinical methods is a novel one, and to propose a solution to HIV infection, it was suggested that additive(s) in form of drugs to the serum serving as an intervening medium could possibly be much desired for rendering the absolute combined Hamaker coefficient A_{132abs} negative (5). These antiretroviral drugs or agents are natural blockers - they block the virus at different stages based on its life cycle. The drugs are capable of providing a functional cure by blocking viral replication and transmission in HIV infected patients. Obviously, the optimism stemming from the great successes recorded with this approach in related areas of biology and medicine as the important role of surface properties in various biological processes which is now established cannot be overemphasized.

There are several classes of drugs, which are usually used in combination, to treat HIV infection. Use of these drugs in combination can be termed anti-retroviral therapy (ART), combination anti-retroviral therapy (cART) or highly active anti-retroviral therapy (HAART). Anti-retroviral (ARV) drugs are broadly classified by the phase of the retrovirus life-cycle that the drug inhibits. Typical combinations include 2 NRTIs as a "backbone" along with 1 NNRTI or PI as a "base." (6).

2. Research Methodology

2.1. Major Considerations

The aim of this study is to employ the van der Waals interactions mechanism to study the interaction between HIV and the blood cells coated with the antiretroviral drugs (single drugs or Highly Active Antiretroviral Therapy, HAART/Fixed-Dose Combination, FDC) as a way to understand the use of these drugs in the proffering solution to the HIV/AIDS pandemic.

2.2. Sample Collection

This research work involved the collection of popular and commonly used Antiretroviral drugs (three single tablets and two HAART), from the University of Nigeria Teaching Hospital (UNTH) APIN CENTRE PEPFAR, Ituku – Ozalla, Enugu State, and the collection of blood samples from ten HIV infected persons. The collected blood samples were screened to determine the infection status thus giving a total of ten blood samples from different individuals. The blood samples were collected from Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi and Anambra State Teaching Hospital, Amaku. Anticoagulant test tubes and ice packs were used to ensure the freshness of the collected samples and to avoid the samples becoming lysed (spoilt). Storage facilities like refrigerators regulated at temperature range of -4 to 2^{o}C, were also used to ensure that the samples were healthy enough so as to obtain good results.

Figure 1 below gives a display of the antiretroviral drug samples used in the research; table 1 gives informed details of the drug samples.

Figure 1. *The Tablets of the five different antiretroviral drugs used.*

Drugs 1 and 2 are both Highly Active Antiretroviral Therapy (HAART) as well as Fixed Dose Combination (FDC), while drugs 3, 4 and 5 are single antiretroviral drugs. Drugs 1,

3 and 5 are administered to HIV patients twice daily while drugs 2 and 4 are taken once a day. It is worthy to note that all the antiretroviral drugs used were not yet expired during the period of the experiments.

Table 1. *The details of the five different Antiretroviral Drugs used in the Study.*

Drug Number	TABLETS	Abbreviation	Size	Type of Drug	Manufacturing Date	Expiration Date	Frequency of use (Dosage)	Batch Number	Pharmaceutical Company
1	Lamivudine, Nevirapine & Zidovudine	3TC + NVP + ZDV	150mg/200 mg/300mg	HAART and FDC	02/2014	01/2016	Twice Daily	7220929	Strides Arcolab Limited
2	Tenofovir, Lamivudine & Efavirenz	TDF + 3TC + EFV	300mg/300 mg/600mg	HAART and FDC	10/ 2013	09/ 2015	Once Daily (at night)	3018522	Mylan Laboratories Limited
3	Nevirapine	NVP	200mg	Single Drug	05/2012	04/2015	Twice Daily	7216348	Strides Arcolab Limited
4	Efavirenz	EFV	600mg	Single Drug	08/2012	07/2015	Once Daily	E121035A	HETERO LABS LIMITED
5	Lamivudine	3TC	150mg	Single Drug	05/2014	04/ 2016	Twice Daily	LEX – 023	MCNEIL & DRUGS Pharmaceuticals Ltd.

2.3. Sample Preparation

The drugs passed through serial dilution at Tahilah Diagnostic Laboratories, Awka, in order to get the right concentration of drug in the blood. After the serial dilutions to 10^{-2}, the drug solution mixed with the blood was incubated at normal body temperature (37^{o}C) to facilitate drug – blood interactions (This is an in vitro experiment). The knowledge of the onset and duration of action of each drug was used in administering the start dose and the maintenance dose in the blood samples. These collected samples with drug concentrations were loaded into a centrifugal separator and the blood components were separated at Tahilah Diagnostic Laboratories, Awka. This helped to obtain such components as White Blood Cells (WBC) also called the Lymphocytes, Red Blood Cells (RBC), and the Plasma or Serum each sample at a time. The glass slides were prepared and smeared with the samples for absorbance measurements. The slide preparations and sample smearing were done at the same laboratory. About 200 slides were successfully prepared in the laboratory.

2.4. Measurements

The CD4 cells count of the blood samples collected were obtained using a digital CD4 count machine which is known as Cytoflowmeter or Flow cytometry instrument. This in a sense is an indicator of the level and progression of the HIV infection process in the subjects. Absorbance measurements were done on all the different components of all ten samples (HIV infected blood samples). A digital Ultraviolet Visible MetaSpecAE1405031Pro Spectrophotometer was used at the laboratory of the Department of Mechanical Engineering, Nnamdi Azikiwe University, Awka in the measurements. The absorbance values of the samples were measured over a range of wavelength spanning between 230 and 970 Hertz alongside with their corresponding transmittance values.

2.5. Summary

These processes were repeatedly done to ensure reliability of the collected data. The collected samples of popular and unexpired antiretroviral drugs were preserved at ambient temperature. To prevent the collected blood samples getting lysed (spoilt) especially whole blood samples and the isolated red blood cells which are readily susceptible to bacterial and thermal attacks adequate refrigeration was employed. Diligence, persistence and determination on the part of the researcher eventually paid off giving rise to the emergence of this work.

3. Theoretical Considerations

3.1. The Concept of Interfacial Free Energy

Considering the work done by a force F to move a flat plate along another surface by a distance dx is given, for a reversible process by;

$$\delta w = Fdx \tag{1}$$

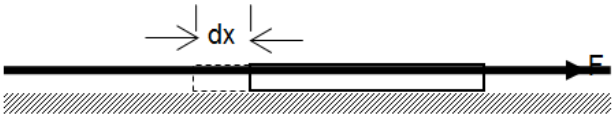

Figure 2. *Schematic Diagram Showing Application of a Force F, on a Surface (Source: 6).*

However, the force F is given by;

$$F = L\gamma \tag{2}$$

Where L is the width of the plate and γ is the surface free energy per unit surface area (interfacial free energy)

Hence;

$$\delta w = L\gamma dx \tag{3}$$

But;

$$\delta A = Ldx \tag{4}$$

Therefore;

$$\delta w = \gamma dA \tag{5}$$

This is the work required to form a new surface of area dA. For pure materials, γ is a function of T only, and the surface is considered a thermodynamic system for which the coordinates are γ, A and T. The unit of γ is J/m^2. In many processes that involve surface area changes, the concept of interfacial free energy is applicable.

3.2. The Thermodynamic Approach to Particle-Particle Interaction

The thermodynamic free energy of adhesion of a particle P on a solid S in a liquid L at a separation d_O (7), is given by;

$$\Delta F_{PLS}^{adh}\left(d_O\right) = \gamma_{PS} - \gamma_{PL} - \gamma_{SL} \tag{6}$$

Where ΔF^{adh} is the free energy of adhesion, integrated from infinity to the equilibrium separation distance d_O; γ_{PS} is the interfacial free energy between P and S; γ_{PL} is that between P and L and γ_{SL} that between S and L.

For the interaction between the individual components, similar equations can be written also;

$$\Delta F_{ps}^{adh} = \gamma_{ps} - \gamma_{pv} - \gamma_{sv} \tag{7}$$

$$\Delta F_{sl}^{adh}\left(d_1\right) = \gamma_{sl} - \gamma_{sv} - \gamma_{lv} \tag{8}$$

$$\Delta F_{pl}^{adh}\left(d_1\right) = \gamma_{pl} - \gamma_{pv} - \gamma_{lv} \tag{9}$$

For a liquid, the force of cohesion, which is the interaction with itself, is described by;

$$\Delta F_{11}^{coh}\left(d_1\right) = -2\gamma_{lv} \tag{10}$$

ΔF^{adh} can be determined by several approaches, apart from the above surface free energy approach. The classical work of Hamaker (8) is very appropriate.

To explain the concept of Hamaker Constants, van der Waals explanation of the derivations of the ideal gas law is used thus;

$$PV = RT \tag{11}$$

It was discovered that the kinetic energy of the molecules which strike the container wall is less than that of the bulk molecules. This effect was explained by the fact that the surface molecules are attracted by the bulk molecules (as shown in figure 3 below) even when the molecules have no permanent dipoles. It then follows that molecules can attract each other by some kind of cohesive force (9). These forces have come to be known as van der Waals forces. Van der Waals introduced the following corrections to (11);

$$\left[P + \frac{a}{V^2}\right]\left(V - b\right) = RT \tag{12}$$

The correction term to the pressure, $\left(\frac{a}{V^2}\right)$ indicates that the kinetic energy of the molecules which strike the container wall is less than that of the bulk molecules. This signifies the earlier mentioned attraction between the surface molecules and the bulk molecules.

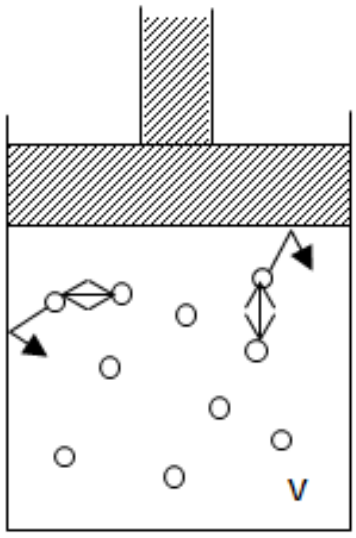

Figure 3. *Attraction of Surface Molecules by Bulk Molecules in a Container of Volume V (Source: 10).*

After the development of the theory of quantum mechanics, London quantified the van der Waals statement for molecules without a dipole and so molecular attraction forces began to be known as London/van der Waals forces (11). London stated that the mutual attraction energy, V_A of two molecules in a vacuum can be given by the equation;

$$V_A = -\frac{3}{4}h\upsilon_0\left[\frac{\alpha^2}{H^6}\right] = -\left[\frac{\beta_{11}}{H^6}\right] \tag{13}$$

Where; h = Planck's constant
υ_o = the characteristic frequency of the molecule
α = the polarizability of the molecule
H = their separation

3.3. Mathematical Model for the Interactions Mechanism

The mutual attraction energy, V_A of two molecules in a vacuum is given by;

$$V_A = -\frac{3}{4}h\upsilon_0\left[\frac{\alpha^2}{H^6}\right] = -\left[\frac{\beta_{11}}{H^6}\right] \tag{14}$$

Where; h = Planck's constant
v_0 = characteristic frequency of the molecule
α = polarizability of the molecule
H = their separation distance

The assemblies of molecules as in a solid body have interaction energy as the summation of all the interaction energies of all the molecules present and the van der Waals pressure, P_{vdw} as follows;

$$P_{vdw} = \left[\frac{A_{11}}{6\pi d^3}\right] \quad (15)$$

For a sphere of radius, R and a semi-infinite body at a maximum separation distance, d the van der Waals force of attraction, F_{vdw} is given as;

$$F_{vdw} = \left[\frac{A_{11}R}{6d^2}\right] \quad (16)$$

Where A_{11} = Hamaker constant

$$A_{11} = \pi^2 q_1^2 \beta_{11} \quad (17)$$

Where q_1 = number of atoms per cm^3
β_{11} = London-van der Waals constant

Figure 4 below depicts that given two dissimilar condensed bodies of given geometry with a separation distance, d, the corresponding van der Waals force between them can be determined. For the system under study, the interacting bodies are the lymphocytes, 1 and the virus, 2.

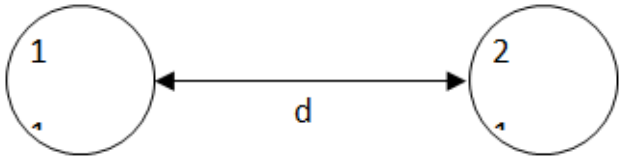

Figure 4. *Interaction of Two Un - Identical Molecules of drug – coated lymphocyte, 1 and (HIV) Virus, 2 at a Separation, d.*

The van der Waals force between the drug – coated lymphocyte, 1 and the virus, 2 is given by the relations;

$$F_{vdw} = -\left[\frac{A_{12}R_{12}}{6d^2}\right] \quad (18)$$

Where; $A_{11} = \pi^2 q_1^2 \beta_{11}$ = Hamaker constant for drug – coated lymphocyte

$A_{22} = \pi^2 q_2^2 \beta_{22}$ = Hamaker constant for the virus (HIV)

$A_{12} = \pi^2 q_{12}^2 \beta_{12}$ = Hamaker constant for both materials

Where; $\beta_{12} = \sqrt{\beta_{11}\beta_{22}}$

Thus the Hamaker constant becomes;

$$A_{12} = \sqrt{\left(\pi^2 q_1^2 \beta_{11}\right)\left(\pi^2 q_2^2 \beta_{22}\right)} \quad (19)$$

$$A_{12} = \sqrt{A_{11}A_{22}} \quad (20)$$

For a combination of our two dissimilar materials (i.e. lymphocyte, 1 and the virus, 2) with the gap between them filled with plasma or serum as the medium, 3 the combined Hamaker coefficient will be given by;

$$A_{132} = \left(\sqrt{A_{11}} - \sqrt{A_{33}}\right)\left(\sqrt{A_{22}} - \sqrt{A_{33}}\right) \quad (21)$$

$$A_{132} = A_{12} + A_{33} - A_{13} - A_{23} \quad (22)$$

Applying the equation above gives values of the combined Hamaker coefficients, A_{132} which agrees with the Lifshitz formula below;

$$A_{132} = \frac{3}{4}\pi\hbar\int_0^\infty \left[\frac{\varepsilon_1(i\zeta) - \varepsilon_3(i\zeta)}{\varepsilon_1(i\zeta) + \varepsilon_3(i\zeta)}\right]\left[\frac{\varepsilon_2(i\zeta) - \varepsilon_3(i\zeta)}{\varepsilon_2(i\zeta) + \varepsilon_3(i\zeta)}\right] d\zeta \quad (23)$$

A_{33} = Hamaker constant for plasma (serum)

A_{13} = Hamaker constant for both materials (i.e drug-coated lymphocyte and plasma)

A_{23} = Hamaker constant for both materials (i.e the virus and plasma)

Obtaining the mean of the Hamaker coefficients derived from the equations above gives the absolute value of Hamaker coefficient A_{132abs};

$$A_{132abs} = \frac{\sum_0^N (A_{132})}{N} \quad (24)$$

Alternatively,

This gives a value to the Hamaker constant $A_{11,}$ and by extension to other Hamaker constants A_{22} and $A_{33.}$

Thus, the Hamaker coefficient, A_{132} could readily be gotten from the relations as in (21) and (22) above.

Where

A_{33} = Hamaker constant for plasma (serum)

A_{13} = Hamaker constant for both materials (i.e drug-coated lymphocyte and plasma)

A_{23} = Hamaker constant for both materials (i.e the virus and plasma)

Obtaining the mean of the Hamaker coefficients derived from the equations above gives the absolute value of Hamaker coefficient A_{132abs};

3.4. Relevant Mathematical Applications

Applying the following relations to the obtained raw data the Hamaker coefficient could be derived;

$$\bar{a} + T + R = 1 \quad (25)$$

Where; ā is absorbance, T is transmittance, and R is

reflectance

Also;

$$T = 10^{-\bar{a}} \tag{26}$$

With the values of ā and T ascertained, R could easily be derived by substituting into (25).

The next step is to find a value for the refractive index, *n* employing the mathematical relation

$$n = \left[\frac{1 - R^{1/2}}{1 + R^{1/2}}\right] \tag{27}$$

A value for the extinction coefficient, *k* is obtained from the equation:

$$k = \left[\frac{\alpha\lambda \times 10^{-9}}{4\pi}\right] \tag{28}$$

Where; α is the absorption coefficient defined as follows:

$$\alpha = \left[\frac{\bar{a}}{\lambda \times 10^{-9}}\right] \tag{29}$$

The dielectric constant, *ε* could thus be given by the formula For the real part;

$$\varepsilon_1 = n^2 - k^2 \tag{30}$$

For the imaginary part;

$$\varepsilon_2 = 2nk \tag{31}$$

Also A_{11} is given as

$$A_{11} = 2.5\left[\frac{\varepsilon_{10} - 1}{\varepsilon_{10} + 1}\right]^2 = 2.5\left[\frac{n_1^{\,2} - 1}{n_1^{\,2} + 1}\right]^2 \tag{32}$$

This gives a value to the Hamaker constant $A_{11,}$ and by extension to other Hamaker constants A_{22} and $A_{33.}$

Thus, the Hamaker coefficient, A_{132} could readily be gotten from the relations as in (21);

According to Hamaker, the constant A_{11} equals;

Where q_1 is the number of atoms per cm^3 and β_{11} is the London/van der Waals constant for interaction between two molecules.

For combination of two different materials 1 and 2 in approximation:

$$B_{12} \approx \sqrt{\beta_{11}\beta_{22}} \tag{33}$$

For a combination of three materials when the gap between 1 and 2 is filled with a medium 3, from Hamaker's calculations;

$$A_{131} = A_{11} + A_{33} - 2A_{13} \tag{34}$$

And

$$A_{232} = A_{22} + A_{33} - 2A_{23} \tag{35}$$

Also;

Rewriting these equations will give;

$$A_{131} = \left(\sqrt{A_{11}} - \sqrt{A_{33}}\right)^2 \tag{36}$$

$$A_{232} = \left(\sqrt{A_{22}} - \sqrt{A_{33}}\right)^2 \tag{37}$$

Equation (21) shows that, for a three-component system involving three different materials, 1, 2 and 3, A_{132} can become negative;

$$A_{132} \prec 0 \tag{38}$$

When;

$$\sqrt{A_{11}} \succ \sqrt{A_{33}} and \sqrt{A_{22}} \prec \sqrt{A_{33}} \tag{39}$$

Or;

$$\sqrt{A_{11}} \prec \sqrt{A_{33}} \prec \sqrt{A_{22}} \tag{40}$$

The limitations of Hamaker's approach led Lifshitz *et al* to develop an alternative derivation of van der Waals forces between solid bodies.

4. Data Analysis

4.1. Computation for the Absolute Value of the Hamaker Constants of Different Interacting Systems

The computation for the absolute value of the Hamaker constants of different interacting systems derived from;

Hence,

$$A_{ijabs} = \frac{\sum_{0}^{N}(A_{ij})}{N} \tag{41}$$

Or

$$A_{11} < A_{33} < A_{22} \quad A_{11} > A_{33} > A_{22} \tag{42}$$

Hamaker constant A_{ij} peak value for each antiretroviral drug in water was computed using (32) while (41) and (32) were used to compute for absolute value. The computation was done for each drug and for each blood component and the results are listed in table 2 below.

Table 2. *Comparison of the values of A11 for each antiretroviral drug on uninfected blood, and values of A22, A33 and A132 for each antiretroviral drug on infected blood.*

Variable ($\times 10^{-21}$ Joule)	D1	D2	D3	D4	D5
A_{11}	1.186941	1.052179	1.083603	0.986577	1.119971
A_{33}	0.458831	0.571147	0.40075	0.491265	0.481885
A_{22}	0.276751	0.347462	0.232341	0.378151	0.292538
A_{132}	-0.03998	-0.05305	-0.05845	-0.02481	-0.05844

Table 2 above reveals that A_{11} is greater than A_{33} which is also greater than A_{22} for each antiretroviral drug in HIV positive blood which is a condition for rendering the combined Hamaker coefficient, A_{132} negative. This indicates that the five different antiretroviral drugs used in the study are effective for HIV treatment since the negative sense of the Hamaker coefficient entails repulsive van der Waals forces indicating that the drug – coated lymphocytes would repeal or block the HIV from attacking the lymphocytes. This will eventually boost the surface energy of the HIV infected blood and a resultant increase of the CD4 cells count as a result of reduced viral loads (13).

4.2. Computation of the Hamaker Coefficients

This involves the computation of the Hamaker coefficients of the antiretroviral drugs interacting with the HIV positive blood and HIV negative blood.

4.2.1. Computation of the Hamaker Coefficients of Drugs in Infected Blood

The values of the Hamaker constants, A_{11}, A_{22} and A_{33} obtained for the various drugs interacting with the whole blood and the three blood components were employed in the derivation of the Hamaker coefficients, A_{132}. The variables required for the computations with the Lifshiftz formula (23) were derived from the absorbance data. The MATLAB software tools were employed in the mathematical analysis of the very large body of data generated from the experiments. The Hamaker constants A_{11}, A_{22}, A_{33} and the combined Hamaker coefficients $A_{132,}$ A_{232} and A_{131} of the various drugs interacting with the blood were obtained using the values of the dielectric constant together with the Lifshiftz equation (23). The absolute combined Hamaker coefficient, A_{132abs} and A_{131abs} (an integral of all the values of the various Hamaker coefficients) for each drug as well as for all drugs on both infected and uninfected blood samples were also calculated. The underlying equation here is (12) together with (25 – 31), (40), (22), (21) and (36).

The modifications to these equations involve the definitions of terms given below:

A_{11} = Hamaker constant, A_{11} values for drug – coated HIV negative lymphocytes;

A_{22} = Hamaker constant, A_{11} values for drug – coated HIV positive lymphocytes.

The infected lymphocytes are used in lieu of the virus because there is currently no known means of isolating the virus. The assumption here is that the infected lymphocyte is an approximation of the actual virus owing to the manner of the infection. The mechanism of the viral infection is such that it actually attaches its CD8+ cells on the wild CCR5 dendrites of the blood CD4+ T4 cells while changing the nature of the cells. The important issue is that the virus does not encyst the blood cells as it were but actually infuses the cells thereby altering the nature and characteristics of the cells. This thus makes the use of the infected lymphocytes a close replacement for the virus in calculating the Hamaker coefficients.

A_{33} = Hamaker constant, A_{11} values for drug – coated HIV positive plasma (serum) as the intervening medium.

4.2.2. Computation of the Hamaker Coefficients of Drugs on Uninfected Blood

To obtain a value for the combined Hamaker coefficient A_{131} for the drugs interacting with the HIV negative blood the relations in (34) and (36) are employed, with

A_{33} = Hamaker constant, A_{11} values for drug – coated HIV negative plasma (serum) as the intervening medium.

4.2.3. Deductions for the Absolute Combined Negative Hamaker Coefficients of the Interacting Systems

Integrating using (23) all the values of the combined Hamaker coefficient, A_{132} gives an absolute value for the coefficient denoted by A_{132abs}. Applying the limits of integration (for the minimum and maximum values of A_{132} respectively), the absolute value for the combined Hamaker coefficient for each antiretroviral drug interacting with infected blood could thus be derived from (5);

$$A_{132abs} = \frac{\sum_{0}^{N}(A_{132})}{N} \tag{43}$$

Similarly, the absolute combined Hamaker coefficient A_{232abs} and A_{131abs} for each antiretroviral drug interacting with infected blood and uninfected blood respectively are given thus:

$$A_{131abs} = \frac{\sum_{0}^{N}(A_{131})}{N} \tag{44}$$

And,

$$A_{232abs} = \frac{\sum_{0}^{N}(A_{232})}{N} \tag{45}$$

Table 3 below reveals that the interaction energy of the lymphocytes, A_{131} is greater than the interaction energy of the virus (HIV), A_{232}. This results in decreased viral loads and increased CD4 counts which in effect, indicates the much desired possible solution to HIV jinx by the administration of the antiretroviral drugs to HIV positive systems. Hence for $A_{132} < 0$, $A_{131(\text{Lymphocyte})} > A_{232(\text{Virus})}$.

Table 4 below is the summary of the results of HIV - drug coated blood interactions. The various antiretroviral drugs are shown alongside with their respective abbreviations and sizes. The absolute combined Hamaker coefficients A_{132abs} of each of the drugs in HIV positive blood gave a negative value. This indicates that the van der Waals forces are repulsive; hence there is repulsion between HIV particles and T cells. This is a possible therapy for HIV infection.

Table 3. *Comparison between the absolute values of A_{131} for Uninfected blood and A_{132}, A_{232} for Infected blood for the five different antiretroviral drugs.*

Variable ($\times 10^{-21}$ Joule)	D1	D2	D3	D4	D5
A_{131}	0.367603	0.463371	0.530208	0.509707	0.495986
A_{232}	0.213619	0.276577	0.141540	0.186744	0.144346
A_{132}	-0.03998	-0.05305	-0.05845	-0.02481	-0.05844

Table 4. *Summary of the results of HIV - Drug Coated Blood Interactions.*

Drug Number	Type of Drug	ARV	Abbr.	Size	Absolute Combined Hamaker coefficient A_{132abs} ($\times 10^{-21}$ Joule) of HIV Positive Blood	Sign of A_{132abs} obtained	Van der Waals Forces	Nature of Interaction
Drug 1	HAART and FDC	Lamivudine, Nevirapine & Zidovudine	3TC + NVP+ ZDV or AZT	150mg/200 mg/300mg	-0.03998	-ve	Repulsive	Repulsion (HIV therapy)
Drug 2	HARRT and FDC	Tenofovir, Lamivudine & Efavirenz	TDF + 3TC + EFV	300mg/300 mg/600mg	-0.05305	- ve	Repulsive	Repulsion (HIV therapy)
Drug 3	Single Drug	Nevirapine	NVP	200mg	-0.05845	- ve	Repulsive	Repulsion (HIV therapy)
Drug 4	Single Drug	Efavirenz	EFV	600mg	-0.02481	-ve	Repulsive	Repulsion (HIV therapy)
Drug 5	Single Drug	Lamivudine	3TC	150mg	-0.05844	- ve	Repulsive	Repulsion (HIV therapy)

5. Conclusion

The significance of engineering thermodynamics in proffering solutions to various biological processes is an interesting phenomenon. In the twenty first century research works, there is a growing need to achieve a more reliable research result through a synergy between engineers and biological researchers. The concept of negative Hamaker coefficient formerly declared in principle has been validated in practice. The absolute values for the combined Hamaker coefficient, A_{132abs} obtained for each of the five antiretroviral drugs interacting with infected blood without antiretroviral treatment are given thus: D1 = -0.03998×10^{-21}Joule, D2 = -0.05305×10^{-21}Joule, D3 = -0.05845×10^{-21}Joule, D4 = -0.02481×10^{-21} Joule, and D5 = -0.05844×10^{-21}Joule. The negative values of the absolute combined Hamaker coefficients obtained for the five antiretroviral drugs on HIV positive blood samples, indicate that there are repulsive van der Waals forces which means that the interacting bodies (that is HIV and drug-coated lymphocytes) repel each other. This is to say that the antiretroviral drugs on the surface of the lymphocytes successfully blocked the HIV at different stages of its replication. Hence, this is a possible route to detecting a solution or therapy for HIV infection. Another significance of this negative value of the absolute combined Hamaker coefficient is that the combination of the five antiretroviral drugs used in the study is very effective in reducing the viral loads, improving the CD4 cells count as well as increasing the surface energy of the HIV positive blood. It is interesting to note that the interacting system of most of the antiretroviral drugs with the HIV positive blood samples gave a negative value for the absolute combined Hamaker coefficient, A_{132abs}. The findings of this research work suggest a thermodynamic criterion for HIV-drug interaction prediction that will be a valuable tool in HIV study. This research work affirms the predictions, speculations and assertions for the solution to HIV infection given by the previous researchers that studied HIV–blood interactions by using surface thermodynamics approaches. The antiretroviral drugs used as additive(s) to the serum serving as the intervening medium rendered the absolute combined Hamaker coefficient negative as speculated. This concludes that the available and popular antiretroviral drugs used in the study are effective from thermodynamic point of view. These drugs will provide possible avenue to search for cure for HIV pandemic when administered to HIV patients in a properly controlled manner. The use of the findings of this work by pharmaceutical industries will help in the search for more effective antiretroviral drugs for the treatment of HIV patients.

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