# Surface Free Energies Of Some Antiretroviral Drugs From Spectrophotometric Data And Possible Application To HIV-Infected Lymphocytes

O. I. Ani, S. N. Omenyi, S. C. Nwigbo

**Abstract:** Antiretroviral drugs are usually used for the treatment of Human Immunodeficiency Virus (HIV). This virus specifically attacks the lymphocytes so the antiretroviral drugs are designed specifically to block the virus from penetrating into the interior of the cell. The attachment of the virus on the surface of the lymphocyte will cause a change in the surface area of the cell. Such surface area change is followed by change in surface free energy. This work attempted to estimate the surface free energies of five antiretroviral drugs from absorbance data and their possible effects on the surfaces of the lymphocytes. The absorbance values were measured and using modified form of Lifshitz equation through the concept of Hamaker constants, surface energies were calculated. Coating effectiveness studies showed that the drugs preferentially coated the surfaces of lymphocytes, as expected. The surface free energies for the drugs varied from 48.9 mJ/m$^2$ for drug 1 to 37.7 mJ/m$^2$ for drug 4. This means that drug 4 that has the lowest surface free energy, is more hydrophobic than drug 1. The surface free energies of HIV-infected lymphocytes varied from 9.3 mJ/m$^2$ for drug 3 to 13.9 mJ/m$^2$ for drug 2 being lower than for uninfected lymphocytes by up to a factor of 77% with drug 1 and 62% with drug 4 (in blood of patients without previous drug treatment) confirming the surface energy-reducing capacity of HIV. The low value of the free energy in drug 4 of 39.5mJ/m$^2$ is in line with effectiveness value 0.0245 for drug 4 which is the lowest as shown in table 3. It is interesting to observe that drug 1 which has the highest coating effectiveness (0.5102) also has the highest surface free energy (47.5mJ/m$^2$) confirming the existence of some relationship between drug coating of the surface of the blood cell and the cell surface free energy. It is interesting to note that Ozoihu (2014) reported the surface free energy of infected lymphocyte as 31.81$\pm$2.36 mJ/m$^2$ and that of uninfected cell as 39.94$\pm$2.82 mJ/m$^2$. While the values for uninfected cell are close to within 3.2% of each other, the values for infected are widely different (up to 19.5%). The findings of this research work suggest possible existence of a thermodynamic criterion for HIV-drug interaction prediction that will be a valuable tool in HIV-blood interaction study. This work gives more understanding on the surface properties of antiretroviral drugs and the effects of HIV on the surface energies of blood samples.

**Index Terms:** Absorbance, Dielectric constant, Hamaker constant, HIV, Antiretroviral drug, Lifshitz formula, Lymphocyte, Surface free energy.

## 1 INTRODUCTION

Surface free energy quantifies the disruption of intermolecular bonds that occur when a surface is created - the energy associated with the intermolecular forces at the interface between two media. The term surface energy or surface free energy is used because an increase in the surface area of a solid cannot be accomplished without doing work against the elastic forces and plastic resistance of the solid [1]. The presence of an interface does influence the thermodynamic parameters of a system. There are two models that are commonly used to demonstrate interfacial phenomena, which include the Gibbs ideal interface model and the Guggenheim model. Thermodynamically, the surface energy, $\gamma$ is interpreted as the increase in the Gibbs energy of the system when the area of the interface under consideration is increased reversibly by an infinitesimal amount *dA* at constant temperature (*T*), pressure (P) and composition (*c*) [2]. This can be expressed as $\gamma = \left(\frac{\delta G}{\delta A}\right)_{T,p,c}$. In other words, surface energy can be interpreted as the reversible work required to extend a surface or to bring atoms from the interior to the surface region. There is now wealth of spectroscopic and other analytical techniques for probing the surface properties of solid materials Brady [3] which yield a variety of surface properties of those parts of such materials that are situated anywhere between 1.0 and more than 10 nm below their surfaces [4]. Contact angle technique has been reported as being capable of yielding the actual surface or interfacial properties at the precise surfaces of solids that are relevant to their interaction with other condensed phase materials [5]. The energy of the bulk component of a solid substrate is determined by the types of interactions that hold the substrate together. High energy substrates are held together by bonds, while low energy substrates are held together by forces. High energy substrates are more easily wet than low energy substrates [6]. In addition, more complete wetting will occur if the substrate has a much higher surface energy than the liquid [7]. Many techniques can be used to enhance wetting. Surface treatments (such as Corona treatment and acid etching) can be used to increase the surface energy of the substrate [8]. Additives can also be added to liquid to decrease or increase its surface energy. Additives are employed often in paint formulations to ensure that they will be evenly spread on a surface [9]. The mechanism by which antiretroviral drugs can block the virus from adhering on the surface of the cell needs to be well understood to enable formulation of drugs that can effectively block the virus from penetrating the surface of the lymphocyte. As HIV attaches itself on the surface of a given lymphocyte cell, some area of the surface of the cell is covered, showing that some change in surface energy has occurred. The understanding of the drug coverage of cell surface and the energy exchange


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therefore, may be understood if surface free energies of both the drugs and the surfaces of the cells are determined. To prevent the HIV from effectively attaching itself on the surface of the lymphocyte, one may expect each drug in solution in the plasma to selectively and effectively coat the surface of the lymphocyte blocking every possible target site. The question arises as to whether the drug film coating the surface of lymphocyte increases or reduces the surface free energy of the cell surface? Is an increase or decrease in surface free energy required for effective blocking of the virus? To answer these questions, a study of surface effects in HIV-drug interactions becomes necessary. We intend to determine the surface free energies using the concept of absorbance. The work of Achebe and Omenyi [10] and [11] showed absorbance to be a surface phenomenon. The peak absorbance of the surface of each blood component was shown to be reduced by the presence of the virus. These authors however did not determine the extent of the reduction of the peak absorbance of the surface of HIV-infected lymphocyte due to the administration of anti retroviral drugs? T-here are several classes of drugs, which are usually used in combination, to treat HIV infection. Use of these drugs in combination is 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 (Nucleoside Reverse Transcriptase Inhibitors) as a "backbone" along with 1 PI (Protease Inhibitor) or 1 NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitor) as a "base" [12]-[13].

## 2 METHODOLOGY

### 2.1 Major Considerations

The approach in this study was to collect some commonly used antiretroviral drugs, dissolve each in water and produce a film of the drug on a glass slide. In addition, the drugs were added to some quantities of blood components and thin films formed on glass slides. Spectrophometric techniques were them used to determine the absorbance characteristics and then the surface free energies. We will consider patients that were on antiretroviral drug administration (with ARV) before this study together with other HIV patients that had not started taking the drugs (no ARV). As a control, blood from HIV-negative persons will also be used.

### 2.2 Sample Collection

The popular and commonly used unexpired antiretroviral drugs (three single tablets and two HAART), were sourced Ani [14] from the University of Nigeria Teaching Hospital (UNTH) APIN CENTRE PEPFAR, Ituku – Ozalla, Enugu State. Table 1 shows the five different antiretroviral drugs used in the study. 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. Blood samples (from ten HIV-infected, ten uninfected patients and ten HIV-negative patients) were sourced from Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi and Anambra State Teaching Hospital, Amaku (this was made possible by the Ethical Clearance, ANSUTH/AA/VOL.XI/008 of August 13, 2015, issued by Anambra State University Teaching Hospital, Amaku, Awka). Altogether, a total of thirty samples were collected, screened to determine the infection status, stored in anticoagulant test tubes placed in ice packs to avoid the samples becoming lysed. The samples were thereafter stored in a refrigerator for proper preservation [15].

***TABLE 1***

*THE DETAILS OF THE FIVE DIFFERENT ANTIRETROVIRAL DRUGS USED IN THE STUDY [14]*

| Drug Number | Tablets | Abbreviation |
|---|---|---|
| **1** | Lamivudine, Nevirapine & Zidovudine | 3TC + NVP + ZDV |
| **2** | Tenofovir, Lamivudine & Efavirenz | TDF + 3TC + EFV |
| **3** | Nevirapine | NVP |
| **4** | Efavirenz | EFV |
| **5** | Lamivudine | 3TC |

### 2.3 Sample Preparation

The solutions of antiretroviral drugs were prepared Ani [14] at the Tahilah Diagnostic Laboratories, Awka, to conform with the right concentration of drug in the blood. After the serial dilutions to $10^{-2}$, the drug solutions were mixed with the blood and incubated at normal body temperature of $37^{o}$C. 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 [14]. These sample solutions were loaded into a centrifugal separator at Tahilah Diagnostic Laboratories, Awka. The blood samples were spun at the speed of 3000 rpm for 5 minutes in the centrifuge [16]. It works by the principle of centrifugal force which is the outward pull due to rotation exerted by the centrifuge which is greater than the force of gravity thereby causing the particles in the fluid to sediment. 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. Glass slides were prepared and smeared with the samples for absorbance measurements [17]. The slide preparations and sample smearing were done at the same laboratory [18]. About 600 slides were successfully prepared at 20 slides per sample.

### 2.4 Measurements

To determine the requisite thermodynamic parameters, the absorbance data required for quantification of the relevant information on the interacting systems were obtained for all the infected and uninfected blood samples using a digital Ultraviolet Visible MetaSpecAE1405031Pro Spectrophotometer at the laboratory of the Department of Mechanical Engineering, Nnamdi Azikiwe University, Awka. Absorbance measurements were made over a range of wavelength between 230 and 970 Å alongside with their corresponding transmittance values [14].

# 3 RESULTS AND DISCUSSION

## 3.1 Absorbance data

The absorbance values of each blood component measured for each of the samples incubated in each antiretroviral drug were obtained from the work of Ani [14]. The following features were observed:

- Each blood sample, whether infected with HIV or not, exhibits a maximum in its absorbance.
- The graph for each blood sample has a different peak absorbance value.
- The whole blood and red blood cells samples exhibit maximum absorbance at a wavelength of 410 Å while the white blood cells and plasma samples exhibit maxima in absorbance at a wavelength of 320Å.
- The wavelengths at which the maxima occurred are not affected by previous drug treatment of the blood component.
- Table 2 gives the average absorbance data for the blood of the patients that were on antiretroviral drug medication (with ARV), those that were not (No ARV) and those that were HIV negative.
- On the whole, the peak absorbance values for the five antiretroviral drugs on lymphocytes range from 0.08 to 0.18, on Plasma they range from 0.08 to 0.20, on Red blood cells they range from 0.80 to 1.58, for those that had commenced treatment with antiretroviral drugs.
- The peak absorbance values for the five antiretroviral drugs on Lymphocytes range from 0.18 to 0.30, on the Plasma they range from 0.08 to 0.28, on Red blood cells they range from 0.60 to 2.10, for those that had not commenced treatment with antiretroviral drugs. All these fall within the visible range of the ultraviolet radiation which is 300 – 600Å.

***TABLE 2***

*DATA FOR PEAK ABSORBANCE FOR BLOOD COMPONENTS OF PATIENTS: $\alpha_{+m}$ = HIV +VE WITH MEDICATION (WITH ARV), $\alpha_{+n}$ = HIV+VE WITHOUT MEDICATION (NO ARV), $\alpha_{-O}$ = HIV NEGATIVE*

| Drug No. | RBC | | | WBC | | | Plasma | | |
|---|---|---|---|---|---|---|---|---|---|
| | $\alpha_{+m}$ | $\alpha_{+n}$ | $\alpha_{-o}$ | $\alpha_{+m}$ | $\alpha_{+n}$ | $\alpha_{-o}$ | $\alpha_{+m}$ | $\alpha_{+n}$ | $\alpha_{-o}$ |
| **1** | 1.50 | 1.60 | 1.50 | 0.14 | 0.18 | 0.48 | 0.20 | 0.16 | 0.22 |
| **2** | 1.20 | 1.76 | 1.88 | 0.10 | 0.26 | 0.52 | 0.08 | 0.08 | 0.18 |
| **3** | 1.58 | 2.10 | 1.90 | 0.08 | 0.20 | 0.30 | 0.12 | 0.19 | 0.26 |
| **4** | 1.20 | 2.08 | 2.28 | 0.17 | 0.30 | 0.28 | 0.18 | 0.28 | 0.30 |
| **5** | 0.80 | 1.70 | 2.18 | 0.18 | 0.19 | 0.27 | 0.16 | 0.20 | 0.20 |

## 3.2 Effects of the drugs on the absorbance

### 3.2.1 Effects of antiretroviral drug films on blood components

From the effects of antiretroviral drug treatment and the HIV on the absorbance values of blood components, the combined effect ($\eta_{dh}$) of the drug and HIV on the surface of the blood component will be determined from eq.(1) [16].

$$\eta_{dh} = \left(\frac{\tilde{\alpha}_d - \tilde{\alpha}_o}{\tilde{\alpha}_d}\right)\left(\frac{\tilde{\alpha}_d - \tilde{\alpha}_h}{\tilde{\alpha}_d}\right) \quad (1)$$

Where $\tilde{\alpha}_d$ is peak absorbance for drug film on blood component, and $\tilde{\alpha}_o$is peak absorbance for blood component alone. The first term on the right hand side of the equation, which is the drug effect, is actually saying that, from absorbance concept, the difference the drug film makes in the absorbance of a blood component when compared with that of the absorbance of the blood component alone is some measure of drug effect. The antiretroviral drug has the capacity to increase the absorbance of a given blood component surface. HIV has the effect of reducing the absorbance of the surface of a given blood component. The amount by which the surface of a blood component surface is decreased by HIV will be given by the second term on the right hand side. If HIV fails to reduce the absorbance of a drug film coated blood surface, it means that the HIV has not attached itself to the surface, then $\tilde{\alpha}_h = \tilde{\alpha}_d$ and the effect of HIV will be zero. The above analysis will give us the idea of the effect of both the HIV and the antiretroviral drugs acting together on the blood and its components. Using the relevant data of table 2 together with eq. (1), the combined effect was calculated and listed in table 3.

***TABLE 3***

*COMBINED EFFECT OF COATING, $\eta_{dh}$*

| Drug | HIV infected without previous drug treatment | | | HIV infected with previous drug treatment | | |
|---|---|---|---|---|---|---|
| | WBC | RBC | Plasma | WBC | RBC | Plasma |
| **1** | 0.5102 | 0.0108 | 0.1809 | 0.5782 | 0.0000 | 0.0535 |
| **2** | 0.4152 | 0.0005 | 0.3269 | 0.6707 | 0.0262 | 0.3269 |
| **3** | 0.2353 | -0.0009 | 0.1925 | 0.5177 | 0.0138 | 0.3850 |
| **4** | 0.0245 | 0.0206 | 0.0502 | 0.2691 | 0.1114 | 0.3012 |
| **5** | 0.1995 | 0.0440 | 0.1632 | 0.2244 | 0.1266 | 0.2565 |

Table 3 shows the combined effect of coating of the HIV infected blood components with the antiretroviral drugs [14]. The effectiveness of coating of the antiretroviral drugs on Red blood cells gave varied, low and inconsistent results. Here, they are so small that it is clear that the antiretroviral drugs do not have any discernible and reproducible effect on the red blood cells. The covariance, which is the average of the products of deviations between the data of WBC and RBC is -0.0012 and for WBC and plasma, it is 0.011 for blood that had not received prior treatment before this test. However, for the blood that had received previous drug treatment, the variance between WBC and RBC is -0.008 and between WBC and plasma, it is -0.002. Pearson rho also gave a negative correlation (-0.42) coefficient. These low and/or negative variations and correlations show that the absorbance data for WBC do not correlate with those of RBC and plasma, confirming the fact that the antiretroviral drugs are specifically designed to target white blood cells. Further considerations of HIV-blood interactions in antiretroviral environment will therefore dwell on HIV-WBC interactions. It is found from table 3 that previous treatment improves the coating effectiveness for all the drugs on WBC: for drugs 1 to 5, the increases being 11.7%, 38.1%, 54.5%, 90.9% and 11.1% respectively. The change is very remarkable with drug 4 and least remarkable with drug 5, the two drugs with lowest effectiveness.

### 3.3 Determination of surface free energy

To estimate the surface free energy of the surface of the lymphocyte coated or not by a given drug, use will be made of an expression by Lifshitz [19] which involves the use of absorbance data. Lifshitz's equation which is rather difficult to use, gives the energy of interaction between surfaces, the Hamaker constants [20]. This equation was further approximated by several authors Nir [21], Viser [22], Israelachivili [23]. The "physical" meaning of the approximate equation has been demonstrated [24]. It was shown that for a group of materials like polymers, the curves are identical while starting at a different position at zero frequency. Applying the absorption data of polystyrene, the expression of $A_{ii}$ in terms of the refractive index (which can be calculated from the absorbance data) becomes;

$$A_{ii} = 2.5\left[\frac{n_i^2 - 1}{n_i^2 + 1}\right]^2 \qquad (2)$$

This equation has been successfully applied in biological systems interactions [21],[24]. For this study, the symbols for the various Hamaker constants will be as follows:

$A_{33}$ = Hamaker constant for plasma, drug - treated HIV positive or negative serum

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

$A_{22}$ = Hamaker constant for HIV, 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 and thereby changing the nature of the cells. This thus makes the use of the infected lymphocytes a close approximation for the virus in calculating the Hamaker constants. For each sample, there are twenty slides, thus the absolute value of the Hamaker constant is the average over all the data for the twenty slides as given below

$$A_{ijabs} = \frac{\sum_{0}^{N}(A_{ij})}{N} \qquad (3)$$

The surface free energy is a derivative of van der Waals force of cohesion which is the force of attraction between similar particles in a liquid, just as the surface energy or energy of interaction is a function of van der Waals force of adhesion which is the force of attraction between different particles suspended in a liquid medium.

Given that; see Achebe [25]

$$A_{ij} = -12\pi d_0^{\,2}\Delta F_{ij}(d_0) \qquad (4)$$

$$\Delta F_{ij}^{coh} = -2\gamma_{iv} \qquad (5)$$

Then, it can be shown that the surface free energy is given by;

$$\gamma_{iv} = \frac{A_{ij}}{24\pi d_0^2} \qquad (6)$$

Where the minimum distance $d_o$ between the same particles in a liquid is given as Omenyi [26]-[27];

$$d_o = 1.82 Angstrom$$

The Hamaker constants calculated using the absorbance data are listed in table 4 together with the corresponding surface free energies for drug films and for WBC.

***TABLE 4***

*THE HAMAKER CONSTANTS, $A_{11}$, AND THE SURFACE FREE ENERGIES $\gamma_{sv}$ FOR EACH ANTIRETROVIRAL DRUG AND FOR THE DRUG COATED UNINFECTED LYMPHOCYTES*

| Drug number | Drug alone $A_{11}(\times 10^{-14}mJ)$ | $\gamma_{sv}$ (mJ/m$^2$) | Drug coated $A_{11}(\times 10^{-14}mJ)$ | WBC alone $\gamma_{sv}$ (mJ/m$^2$) |
|---|---|---|---|---|
| **D1** | 1.221281 | 48.9 | 1.186941 | 47.5 |
| **D2** | 0.952115 | 38.1 | 1.052179 | 42.1 |
| **D3** | 0.974949 | 39.0 | 1.083603 | 43.4 |
| **D4** | 0.941676 | 37.7 | 0.986577 | 39.5 |
| **D5** | 1.182887 | 47.4 | 1.119971 | 44.8 |

Table 4 shows the values of the surface free energies $\gamma_{sv}$ for the five different antiretroviral drugs in air together with the values estimated for drug coated HIV negative lymphocytes. The values of the surface free energies of the drugs range from 37.7 – 48.9 mJ/m$^2$. Drug 4 has the lowest surface free energy while Drug 1 has the highest surface free energy. This shows that drug 4 is most hydrophobic while drug 1 is the least, i.e., it is most hydrophilic. However, the drug coated erythrocytes present data that are not exactly the same as for the drugs alone. They are not in reality expected to be the same because it depends on the coating effectiveness of the drugs on the lymphocytes' surfaces. These results appear consistent as the free energy for WBC in drug 4 is the lowest (39.5mJ/m$^2$) in line with effectiveness value of drug 4 (0.0245) which is the lowest as shown in table 3. It is interesting to observe that drug 1 with WBC which has the highest coating effectiveness (0.5102) also has the highest surface free energy (47.5mJ/m$^2$) confirming the existence of some relationship between drug coating of the surface of the blood cell and the cell surface free energy. It may be instructive to study the relationship between the surface free energy of WBC with coating effectiveness.

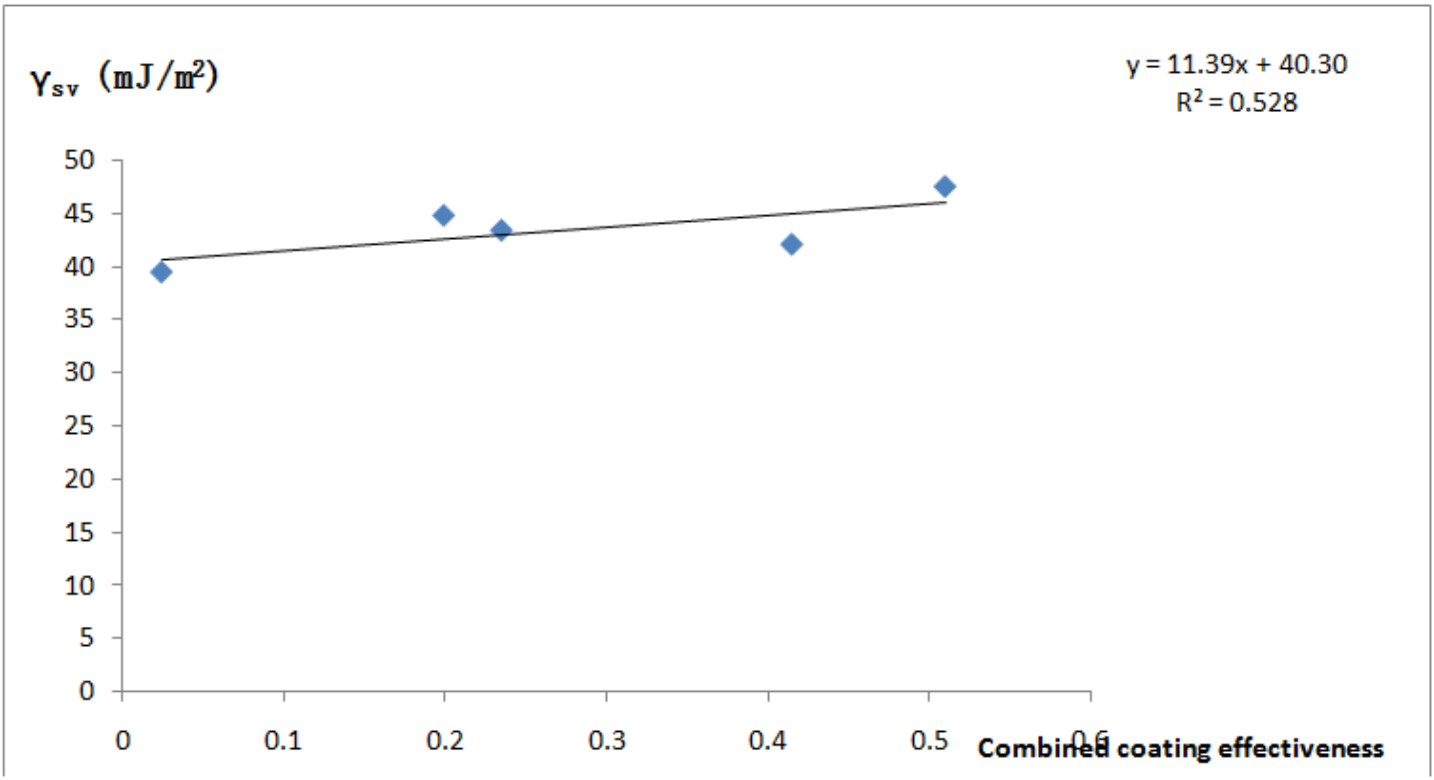


***Fig. 1*** *Relationship between the surface free energy and coating effectiveness for WBC, without previous ARV treatment*

Fig. 1 shows that coating effectiveness is improved by the surface free energy. Therefore, it may suggest that antiretroviral drugs with high surface free energy will coat the surface of WBC better and thus more effective in blocking the surfaces of the lymphocytes against HIV. Higher surface energy implies low contact angle, i.e., better wetting, and hence more hydrophilic.

***TABLE 5***

*COMPARISON OF THE VALUES OF SURFACE FREE ENERGY $\gamma_{sv}$ OF EACH ANTIRETROVIRAL DRUG IN DIFFERENT INTERACTING SYSTEMS (INFECTED WBC WITH ANTIRETROVIRAL TREATMENT, INFECTED WBC WITHOUT ANTIRETROVIRAL TREATMENT AND UNINFECTED WBC)*

| Variable ($\times 10^{-14}$mJ) | HIV+ve WBC with ARV Treatment | | | | | HIV+ve WBC without ARV Treatment | | | | | HIV-ve WBC | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $\gamma_{sv}$ (mJ/m$^2$) | | | | | $\gamma_{sv}$ (mJ/m$^2$) | | | | | $\gamma_{sv}$ (mJ/m$^2$) | | | | |
| | D1 | D2 | D3 | D4 | D5 | D1 | D2 | D3 | D4 | D5 | D1 | D2 | D3 | D4 | D5 |
| $A_{11}$ (WBC) | | | | | | | | | | | 47.5 | 42.1 | 43.4 | 39.5 | 44.8 |
| $A_{22}$ (HIV) | 11.7 | 10.2 | 13.4 | 13.3 | 11.3 | 11.1 | 13.9 | 9.3 | 15.1 | 11.7 | | | | | |
| $A_{33}$ (Plasma) | 72.8 | 43.3 | 38.4 | 43.7 | 44.1 | 18.4 | 22.9 | 16.0 | 19.7 | 19.3 | 20.4 | 15.7 | 19.0 | 11.6 | 13.8 |

Table 5 shows that HIV generally has the capacity to lower the surface free energy Ozoihu [28] of the WBC by up to a factor of 77% with drug 1 and 62% with drug 4 in blood of patients without previous drug treatment; the decrease in surface free energy makes the surface of the WBC more hydrophobic. In the case where the patients had started ARV treatment before this study, the changes in free energy were 75% and 66% respectively. Previous treatment appears not to exhibit discernible difference in surface free energy. It should be noted that the drugs used for initial treatment were not known. Effects of opportunistic diseases can also affect the results in a way that has not yet been determined. For the plasma, previous drug treatment has tremendous effects on the surface free energy. The antiretroviral drugs have the tendency to increase the surface free energy of the lymphocytes therefore making them more hydrophilic. In the presence of the antiretroviral drugs in an infected blood, the surface free energy of the virus is lower than the surface free energy of the plasma as revealed in table 5. Hence, the antiretroviral drug lowers the surface free energy of the virus while increasing the surface free energy of the plasma in HIV positive system as noted when tables 5 and 6 are compared. The antiretroviral drug increases the surface free energy of the lymphocytes while reducing or lowering the surface free energy of the virus to the point or extent that HIV is repelled or separated from the lymphocytes in HIV positive plasma serving as the intervening medium. However, in the absence of the antiretroviral drugs, the surface free energy of the virus is greater than the surface free energy of plasma but lower surface free energy of the lymphocytes. Also, the surface free energy of the uninfected plasma 17.6mJ/m$^2$ was seemingly reduced to 10.0mJ/m$^2$ when HIV invaded the system. Hence, the viral presence lowers the surface free energy of the infected plasma as shown in table 6. This in effect indicates that HIV has a surface energy reducing capacity as reported by Ozoihu [28], while the antiretroviral drugs have surface energy increasing capacity.

***TABLE 6***

*COMPUTED VALUES OF SURFACE FREE ENERGIES $\gamma_{sv}$ OF THE HIV-WBC INTERACTING SYSTEMS (IN THE ABSENCE OF ANTIRETROVIRAL DRUGS)*

| Interacting System | $A_{11}$ ($\times 10^{-14}$mJ) (Lymphocyte) | $\gamma_{sv}$ (mJ/m$^2$) (Lymphocyte) | $A_{22}$ ($\times 10^{-14}$mJ) (HIV) | $\gamma_{sv}$ (mJ/m$^2$) (HIV) | $A_{33}$ ($\times 10^{-14}$mJ) (Plasma) | $\gamma_{sv}$ (mJ/m$^2$) (Plasma) |
|---|---|---|---|---|---|---|
| **Infected blood** | --- | --- | 0.9868 | 39.5 | 0.2486 | 10.0 |
| **Uninfected blood** | 0.9659 | 38.7 | --- | --- | 0.4388 | 17.6 |

It is interesting to note that Ozoihu [28] reported the surface free energy of infected WBC as 31.81$\pm$2.36 mJ/m$^2$ and that of uninfected WBC as 39.94$\pm$2.82 mJ/m$^2$. While the values for uninfected WBC are close to within 3.2% of each other, the values for infected WBC are widely different (up to 19.5%). This large difference is borne out by the fact of the uncertainty of the stage of infection and the probable presence of opportunistic diseases in the HIV infected blood.

## 4 Conclusion

It is known that HIV in its attempt to attack the lymphocyte, first attaches itself on the surface of the cell. It was reasoned that such attachment of HIV on the surface of a given cell will cause displacement of a portion of the surface area of the cell. Such surface area change is followed by change in surface free energy. This research work attempted to estimate the surface free energies of five

antiretroviral drugs and their effects on the surfaces of the lymphocytes. It was found that the effectiveness of coating of the lymphocyte surface was highest compared with other blood components. This confirms the fact that these drugs were specifically formulated as blockers on the surfaces of the lymphocytes. The results also show that HIV generally has the capacity to lower the surface free energy Ozoihu [28] of the WBC by up to a factor of 77% with drug 1 and 62% with drug 4 in systems without previous drug treatment; the decrease in surface free energy makes the surface of the WBC more hydrophobic. Comparison of surface free energy data for the drugs and the lymphocyte surfaces shows the drug coated erythrocytes to present data that are not exactly the same as for the drugs alone. They are not in reality expected to be the same because it depends on the coating effectiveness of the drugs on the lymphocytes surfaces. These results appear consistent as the free energy for WBC in drug 4 is the lowest (39.5mJ/$m^2$) in line with effectiveness value of drug 4 (0.0245) which is the lowest as shown in table 3. It is interesting to observe that drug 1 which has the highest coating effectiveness (0.5102) also has the highest surface free energy (47.5mJ/$m^2$) confirming the existence of some relationship between drug coating of the surface of the blood cell and the cell surface free energy. It is interesting to note that Ozoihu [28] reported the surface free energy of infected WBC as 31.81$\pm$2.36 mJ/$m^2$ and that of uninfected WBC as 39.94$\pm$2.82 mJ/$m^2$. While the values for uninfected WBC are close to within 3.2% of each other, the values for infected WBC are widely different (up to 19.5%). The findings of this research work suggest a thermodynamic criterion for HIV-drug interaction prediction that will be a valuable tool in HIV-blood-drug interaction study. The use of the findings of this work by pharmaceutical industries may be valuable in the search for more effective antiretroviral drugs for the treatment of HIV patients.

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