Hamaker Coefficient Concept: The Application to the Mycobacterium Tuberculosis – Macrophage Interactions Mechanism

Chukwuneke J. L.1, Chukwuneke P. C.2, Okolie P. C.1, Sinebe J. E.3

1Department of Mechanical Engineering, Nnamdi Azikiwe University, Awka, Nigeria
2Department of Applied Biochemistry, Nnamdi Azikiwe University, Awka, Nigeria
3Department of Mechanical Engineering, Delta State University, Oleh, Nigeria

Corresponding author: Chukwuneke J. L., Department of Mechanical Engineering, Nnamdi Azikiwe University, P.M.B. 5025 Awka, Nigeria; jl.chukwuneke@unizik.edu.ng

Abstract- M-Tb – macrophage interactions were studied using the Hamaker coefficient concept as a surface energetics tool in determining the interaction processes, with the surface interfacial energies explained using van der Waals concept of particle – particle interactions. Using the previous works that established the role of surface thermodynamics in various processes from the balanced electrostatic repulsion, and the van der waals attraction mechanism, that the concept of attraction or repulsion between the interacting particles were modeled. The Lifshitz derivations for van der Waals forces were applied as an alternative to the contact angle approach which has been widely used in other biological systems. The methodology involved sputum sample collection, mycobacterium and macrophages structural studies, and the study of the mechanism of interaction of the bacterium and macrophage.

Twenty samples each of infected, uninfected and M-Tb/HIV co-infected sputum were collected and screened using GeneXpert and Ziehl-Neelsen staining method. The absorbance, \( \bar{a} \), values of each specimen, for wavelength range of 230-950nm were measured using digital Ultraviolet Visible Spectrophotometer. Matlab software tools were used in the mathematical analysis of the data generated from the absorbance values. The Hamaker constants and the combined Hamaker coefficient \( A_{132} \) were obtained. The values of \( A_{132, \text{abs}} = 0.21631 \times 10^{-21} \) Joule (M-Tb infected sputum) and \( A_{132, \text{abs}} = 0.18825 \times 10^{-21} \) Joule (M-Tb/HIV co-infected sputum) were obtained for M-Tb/HIV – infected macrophage. The implication of this result is the positive value of the absolute combined Hamaker coefficient which entails net positive van der Waals forces demonstrating an attraction between M-Tb and the macrophage. This however, implies that infection is very likely to occur. It was also shown that in the presence of HIV, the interaction energy is reduced by 13% confirming adverse effects observed in HIV patients suffering from tuberculosis. Negative Hamaker coefficient \( (-0.22669 \times 10^{-19} \text{mJ/m}^2) \) indicated that isolation of M-Tb is realistic. The desired outcome is that the bacteria do not adhere to the macrophage to avoid bacteria penetrating it, in which case a condition for rendering combined Hamaker coefficient negative is required. Thus, condition was sought for repulsion to occur and that condition was based on the value of \( A_{33} \) that would render the absolute combined Hamaker coefficient \( A_{132, \text{abs}} \) negative. Mathematically it was derived as \( A_{33} > 0.9527 \times 10^{-21} \) Joule which satisfies this condition for negative \( A_{132, \text{abs}} \). To achieve the condition of \( A_{33} \) above, possible additive(s) in form of drugs to the sputum should be required.

Keywords: Absorbance, Dielectric Constant, Hamaker Coefficient, Lifshitz Formula, Macrophage, Mycobacterium Tuberculosis, van der Waals Forces.
1. Introduction

Tuberculosis (Tb), is the leading infectious killer worldwide; Human Immunodeficiency Virus (HIV) is a strong risk factor for developing active Tb, and Tb is the leading cause of death among HIV-positive individuals. It is of interest to understand how the mycobacterium tuberculosis (M-Tb) interacts with the macrophage. The process involves the bacterium (modeled as a particle) in a liquid medium (sputum) attaching itself on the surface of the macrophage (another particle), penetrating and probably destroying it. The condition under which bacterium attachment on the surface of the macrophage does not take place will be sought, even in the presence of HIV with its destructive effect.

The World Health Organization (WHO) declared tuberculosis (Tb) as a global emergency in 1993. Unfortunately, the efforts made by the Stop Tb Strategy were not enough to impede the occurrence of 1.3 million deaths in 2009 (WHO, 2010). However, WHO estimates that the number of cases per capita peaked at 2004 and is slowly falling (WHO, 2009). Nonetheless, the battle against Tb is far from being over, since Mycobacterium tuberculosis (the main causative agent of Tb) proved to be highly adaptive (Kumar and Rao, 2011) and capable of evading the current strategies for treatment of about half million cases of multi-drug-resistant Tb (MDR-Tb) that were reported in 2007, including cases of extensively drug-resistant Tb (XDR-Tb) (WHO, 2009), and the more recently reported totally drug-resistant strains (TDR-TB) (Nunes et al, 2011; Velayati et al, 2009; Velayati et al, 2009).

Mycobacterium Tb is among the world’s most deadly infectious diseases despite the long-standing availability of some effective treatment. The steady emergence of multi-drug resistant (MDR), extremely drug-resistant (XDR) and totally drug-resistant strains (TDR) forms of TB is a cause of concern. Globally MDR-TB accounts for roughly 3.6% of all TB cases, but accounts for up to 28% of TB cases in some regions (De Souza, 2006; Gonzalez-Juarrero et al, 2001). The emergence of MDR, XDR and TDR TB is very
worrying due to the increasing difficulty of treating these forms of TB and rendering even the frontline drugs inactive.

In addition, drugs such as Rifampicin have high levels of adverse effects making them prone to patient incompliance. Another important problem with most of the anti-mycobacterials is their inability to act upon latent forms of the bacillus. To compound the problems further, the complex interactions between the HIV and TB makes the treatment of co-infected patients even more challenging (Nunes et al, 2011; Gonzalez-Juarrero et al, 2001).

Related works are in the phagocytosis of bacteria platelets advanced by (Neumann et al, 1983; van Oss et al, 1975; Absolom et al, 1982), from surface thermodynamics point of view. Their works considered the relationship between free energy of engulfment and number of bacteria ingested. It is against this backdrop that this study explores a novel and rare approach using interfacial free energy approach to seek a way forward in the research on the topic of mycobacterium tuberculosis human sputum interaction. This research work is aimed at employing the concept of surface thermodynamics to evaluate the effects of the bacterium on HIV infected blood with a view to avoiding bacteria penetration. In this work, free energy for the condition where no adhesion should occur is to be predicted from the concept of negative Hamaker coefficient obtained from absorbance methods. It is also desired to determine quantitatively the interaction between the M-Tb and macrophage using the concept of Hamaker coefficient. The sense of this coefficient (i.e. is it positive or negative), will indicate the nature of the interaction. Ultimately, a suggestion will be made as to what should be done to the system to block M-Tb – macrophage interactions.

2. Methodology
The methodology of this research work involved sputum sample collection, mycobacterium and macrophages structural studies, mycobacterium tuberculosis
screening, and the study of the mechanism of interaction of the bacterium and the macrophage. Twenty samples each of infected, uninfected and M-Tb/HIV co-infected sputum were collected from Anambra State University Teaching Hospital (ANSUTH) Awka (formerly General Hospital Awka). Spot Specimens were used to ensure the freshness of the collected Sputum samples and to avoid the samples becoming lysed. Each specimen was screened to determine the infection status using GeneXpert and Ziehl-Neelsen staining method.

![Fig. 1: Sample Preparation: direct sputum](image)

The glass slide of 25.4mm x 76.2 x 1.2mm was used for the preparation of test surfaces and the absorbance, ā, values of each specimen, for wavelength range of 230 – 950nm were measured using digital Ultraviolet Visible Spectrophotometer (UV/VIS MetaSpecAE1405031Pro). The measurements of absorbance were done at the department of Mechanical Engineering Laboratory, Nnamdi Azikiwe University, Awka. The data generated and the various equations governing the relationship among the variables were used in calculating values for the reflectance, R, transmittance, T, refractive index, n, and the dielectric constant, ε. MatLab software tools were employed in the mathematical analysis of the data generated from the absorbance values.
3. Mathematical Formulation

To be able to use the absorbance data to calculate the Hamaker coefficients using the Lifshitz theorem, there is a need to evaluate the dielectric constant $\varepsilon$ of the equation. Some relevant equations are required as presented below.

From the information of light absorbance, reflection and transmittance, it could be seen that;

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

Where; $\bar{a}$ is absorbance, $T$ is transmittance, and $R$ is reflectance. Also, from the information of light absorbance and transmittance;

$$T = \exp^{-\bar{a}} \quad (2)$$

With the values of $\bar{a}$ determined from absorbance experimental results, and substituting the values of $\bar{a}$ into Eq. (2) to obtain $T$; $R$ could easily be derived by substituting the values of $\bar{a}$ and $T$ into Eq.(1).

To find a value for the refractive index, $n$ employing the mathematical relation (Robinson, 1952);

$$n = \left[ \frac{1 - R^{\frac{1}{2}}}{1 + R^{\frac{1}{2}}} \right] \quad (3)$$

A value for the extinction coefficient, $k$ is obtained from the equation;

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

Where; $\alpha$ is the absorption coefficient defined as follows;

$$\alpha = \left[ \frac{\bar{a}}{\lambda \times 10^{-9}} \right] \quad (5)$$

Substituting the value, $\alpha$ of Eq. (5) into Eq. (4);

$$k = \left[ \frac{\bar{a}}{4\pi} \right] \quad (6)$$

The dielectric constant, $\varepsilon$ could thus be given by the formula (Charles, 1996),
For the real part;
\[ \varepsilon_1 = n_1^2 - k^2 \]  
(7)

For the imaginary part;
\[ \varepsilon_2 = 2n_2k \]  
(8)

With these values, it is possible to determine \( A_{ij} \) using the relevant equations to determine \( A_{11} \).

\[ A_{11} = 2.5 \left[ \frac{\varepsilon_{10} - 1}{\varepsilon_{10} + 1} \right]^2 = 2.5 \left[ \frac{n_1^2 - 1}{n_1^2 + 1} \right]^2 \]  
(9)

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

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{interaction_sphere}
\caption{Interaction of a Sphere of Radius, R at a Separation, d from a Solid Surface of the same Material, 1 in Vacuum (Visser, 1981)}
\end{figure}

According to Hamaker, the constant \( A_{11} \) equals;
\[ A_{11} = \pi^2 q_1^2 \beta_{11} \]  
(10)

Where \( q_1 \) is the number of atoms per cm\(^3\) and \( \beta_{11} \) is the London/van der Waals constant for interaction between two molecules. Values for \( \beta \) can be obtained in approximation from the ionization potential of the molecules of interest, and so the Hamaker Constant can be calculated. The corresponding van der Waals force between two condensed bodies of given geometry can be calculated provided their separation distance is known. For combination of two different materials 1 and 2 in approximation;
\[ \beta_{12} \approx \sqrt{\beta_{11} \beta_{22}} \]  
(11)

Thus;
\[ A_{12} = \sqrt{A_{11}A_{22}} \]  
(12)

**Fig. 3: Schematic representation of interaction of two solid bodies, depicted by 1 and 2 which are eventually isolated by d, liquid 3.**

For a combination of two disimilar materials (i.e. macrophage, 1 and the bacteria, 2) with the gap between 1 and 2 is filled with sputum as the medium 3, the combined Hamaker coefficient will be given by;
\[ A_{131} = A_{11} + A_{33} - 2A_{13} \]  
(13)

Also;
\[ A_{132} = A_{12} + A_{33} - A_{13} - A_{23} \]  
(14)

Rewriting these Eqs. (13) and (14);
\[ A_{131} = \left( \sqrt{A_{11}} - \sqrt{A_{33}} \right)^2 \]  
(15)

And;
\[ A_{132} = \left( \sqrt{A_{11}} - \sqrt{A_{33}} \right) \left( \sqrt{A_{12}} - \sqrt{A_{33}} \right) \]  
(16)

Equation (16) shows that, for a three-component system involving three different materials, 1, 2 and 3, \( A_{132} \) can become negative;
\[ A_{132} \leq 0 \]  
(17)

When;
\[ \sqrt{A_{11}} > \sqrt{A_{33}} \text{ and } \sqrt{A_{12}} > \sqrt{A_{33}} \]  
(18)

Or;
\[ \sqrt{A_{11}} < \sqrt{A_{33}} < \sqrt{A_{22}} \]  
(19)

Hamaker’s approach to the interaction between condensed bodies from molecular properties called microscopic approach has limitations. This is true against the
backdrop of its neglect of the screening effect of the molecules which are on the surface of two interacting bodies as regards the underlying molecules. Therefore, Hamaker’s approach is regarded as an over simplification.

The limitations of Hamaker’s approach led (Lifshitz et al, 1961) to develop an alternative derivation of van der Waals forces between solid bodies. The interaction between solids on the basis of their macroscopic properties considers the screening and other effects in their calculations. Thus the Hamaker Coefficient $A_{132}$ becomes:

$$A_{132} = \frac{3}{4} \frac{\pi h}{\zeta} \left[ \frac{\varepsilon_1(i\zeta) - \varepsilon_3(i\zeta)}{\varepsilon_1(i\zeta) + \varepsilon_3(i\zeta)} \right] \left[ \frac{\varepsilon_1(i\zeta) - \varepsilon_3(i\zeta)}{\varepsilon_1(i\zeta) + \varepsilon_3(i\zeta)} \right] d\zeta$$  \hspace{1cm} (20)

Where, $\varepsilon_j(i\zeta)$ is the dielectric constant of material $j$, along the imaginary $i$, frequency axis ($i\zeta$) which can be obtained from the imaginary part $\varepsilon_1''(\omega)$ of the dielectric constant $\varepsilon_1(\omega)$.

A system containing two planes could be considered for computing the free energy of interaction. This can be done for semi-infinite, parallel bodies belonging to material 1 and 2 isolated by material 3, bearing thickness $d$ (refer fig. 3) (Hamaker, 1937). This is calculated by the following equation:

$$\Delta F_{132}(d) = \left[ -\frac{A_{132}}{12\pi d^2} \right]$$  \hspace{1cm} (21)

In this, $A_{132}$ refers to the Hamaker coefficient for a respective system.

Considering nominal isolation distance $d_0$, and Eq.(21) as valid for such a small distance, the Hamaker coefficient should be expressed as (Chukwunke et al, 2015; Hamaker, 1937):

$$A_{132} = -12\pi d_0^2 \Delta F^{adh}(d_0)$$  \hspace{1cm} (22)

The Hamaker coefficient $A_{132}$ for the interactions between two different bodies in a liquid can be calculated from Eq.(22) once the free energy of adhesion between the two bodies is known or through the pair-wise additivity approach as originally proposed by (Hamaker, 1937) or by the macroscopic approach of (Lifshitz et al, 1961). Influence of neighbouring atoms remains major hurdle during the pair-wise summation computing
between various molecular interactions. In case of highly disperse media such influence is insignificant, for instance, gases whereas for condensed media it is important (Hough and White, 1987).

As the actual material atomic structures are overlooked, the Lifshitz method is suitable in certain cases. In this method, bulk material properties are considered for calculation of interactions between the macroscopic bodies. Properties like refractive indices and dielectric permittivity \( \epsilon(i\zeta) \) are considered for such calculations. Dielectric permittivity represents the microscopic polarizability as a manifested macroscopic property for the constant atoms belonging to certain materials. The Hamaker coefficient represents the macroscopic resultant for the interactions happened due to the atom polarizations in a material (Hough and White, 1987).

Following Lifshitz theory, the Hamaker coefficient is represented as follows:

\[
A_{ikj} = \frac{3}{4} \frac{\mathcal{A}}{\hbar} \int_0^\infty \left[ \frac{\epsilon_i(i\zeta) - \epsilon_k(i\zeta)}{\epsilon_i(i\zeta) + \epsilon_k(i\zeta)} \right] \left[ \frac{\epsilon_j(i\zeta) - \epsilon_k(i\zeta)}{\epsilon_j(i\zeta) + \epsilon_k(i\zeta)} \right] d\zeta
\]  

(23)

Where, \( \epsilon(i\zeta) \) refers to the dielectric constant of a specific material \( j \), this is considered through the imaginary \( i \), frequency axis (\( i\zeta \)), \( \hbar \) is planck’s constant. The molecular contact was maintained at (\( d=0 \)). Interestingly, constituent molecule numbers are of finite size and for that it is not possible to attain \( d=0 \) for two macroscopic surface. Therefore, whenever the surfaces attain a distance \( d_0 \), molecular contacts are considered. The divergences according to Lifshitz theory are eliminated by the parameter \( d_0 \).

For the issue of self-interaction of a particle Eqn. (23) should be considered;

\[
A_j = \frac{3}{4} \frac{\mathcal{A}}{\hbar} \int_0^\infty \left[ \frac{\epsilon_i(i\zeta) - \epsilon_j(i\zeta)}{\epsilon_i(i\zeta) + \epsilon_j(i\zeta)} \right]^2 d\zeta
\]  

(24)

Thus, the Hamaker coefficient, \( A_{132} \) could readily be gotten from the relations as in Eq. (16);
Where; \( A_{33} \) = Hamaker constant for sputum, \( A_{13} \) = Hamaker constant between both materials (i.e. macrophage and sputum), and \( A_{23} \) = Hamaker constant between two materials (i.e. the bacteria and sputum).

Integrating all the values of the combined Hamaker coefficient, \( A_{132} \) gives an absolute value for the coefficient denoted by \( A_{132\text{abs}} \) (refer to Eq. 20) and applying Lifshitz derivation for van der Waals forces as in Eq.(20).

The absolute value for the Hamaker coefficient could be derived by obtaining the mean of all the \( A_{132} \) values got from the Lifshitz relation;

\[
A_{132\text{abs}} = \frac{\sum_{0}^{N} (A_{132})}{N} \quad (25)
\]

Also

\[
A_{131\text{abs}} = \frac{\sum_{0}^{N} (A_{131})}{N} \quad (26)
\]

And

\[
A_{232\text{abs}} = \frac{\sum_{0}^{N} (A_{232})}{N} \quad (27)
\]

4. Results and Discussions

The raw data obtained for both M-Tb and M-Tb/HIV positive and negative sputum samples were collated. This paved the way for the data analysis. However, since extinction coefficient “\( k \)”, absorption coefficient “\( \alpha \)” and dielectric constant “\( \varepsilon \)” are obtained as functions of wavelength \( \lambda \text{ (nm)} \), an integration of Eq. (23) will give a more accurate value. The data on absorbance obtained as a function of wavelength are plotted on fig. 4. Eq.(24) was used to obtain for each interacting system, \( A_{ij} \) (\( A_{11}, A_{22}, A_{33}, A_{12}, A_{13}, A_{23} \)) by approximate change of variables. MatLab computation tools were used in the analysis. This involved the numerical integration of Eq.(24) for each wavelength from 230 to 950 for all the twenty samples in each category.
Analysis based on the mathematical formulations outlined yielded values for the needed variables and are presented in appendix. Such variables as the transmittance $T$, reflectance $R$, refractive index (real and imaginary) $n$, extinction coefficient $k$, absorption coefficient $\alpha$, dielectric constants (real and imaginary) $\varepsilon_{ij}$, Hamaker Constants $A_{ij}$ and Hamaker Coefficients $A_{132}$ were calculated. Fig. 4 depict the results obtained for infected and uninfected sputum samples respectively. The determination of a value for the absolute combined Hamaker coefficient set the pace for modeling for the zero/negative Hamaker coefficient.

![Graph showing absorbance vs wavelength](image)

**Fig. 5: Variation of Average Absorbance, $\bar{\alpha}$ with Wavelength, $\lambda$ for M-Tb, M-Tb/HIV Sputum and M-Tb, M-Tb/HIV Macrophages**

Fig. 5 shows a peak absorbance value of greater than 0.60 and 0.45 for M-Tb negative and positive sputum respectively and a peak absorbance value of greater than 0.07 and 0.04 for M-Tb positive and negative macrophages respectively were recorded at wavelength of 320nm. This peak values falls within the visible range of ultraviolet radiation which is between 300 – 600nm. This is important as a reference point in the study of the infection mechanism and may be of importance in determining the critical
Hamaker coefficient that favours repulsion between the bacterium and the macrophage. It could be well-known that the infected M-Tb sputum has lower absorbance values than the uninfected ones. This also point toward that the sputum holds the means to energy change of the interacting system as it shows quite the reverse of the trend obtained in the other cases.

The absorbance values of both the M-Tb positive and negative Macrophages were increasing with increase in wavelength. This is the opposite of the result obtained with the M-Tb sputum samples. This may be explained away by the fact of a higher energy level of these cells. The M-Tb infected macrophages gave higher absorbance values than the M-Tb uninfected macrophages. This is a clear indication that infection had occurred and shows the alteration in absorbance values due to M-Tb infection.

The absorbance of the M-Tb/HIV co-infectious sputum samples systematically increased as the wavelength increased until a critical wavelength of 290nm, where peak absorbance values of greater than 0.60 and 0.06 for M-Tb/HIV negative and positive sputum respectively were accomplished. The trend here shows that the uninfected sputum reveals a higher absorbance values at all wavelengths. This indicates that a shift in the energy equation of the system is tenable by some alteration to the sputum as an intervening medium in the M-Tb/HIV – Macrophage interaction. It then suggests a possibility of attaining repulsion between the M-Tb/HIV and the Macrophage cells by some additives to the sputum.

The absorbance values of the M-Tb/HIV positive Macrophages were increasing with increase in wavelength. This is the opposite of the result obtained with the sputum. The M-Tb/HIV co-infected macrophages also gave higher absorbance values than the uninfected ones at wavelengths greater than 400nm. This may explained away by the fact of a higher energy level of these cells. This is a clear indicator that bacteria ingestion had occurred and shows the alteration in absorbance values due to M-Tb/HIV infection.
Fig. 5 reveals the disparity between the peak absorbance values of M-Tb/HIV positive and negative sputum samples respectively, and this shows an indication of how the bacteria affects the properties of sputum.

**Table 1: Comparison between Peak Absorbance values of M-TB Positive, M-TB/HIV Positive and Negative Sputum Components respectively**

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Wavelength, λ(Å) Peak Values</th>
<th>Mean Absorbance, ā Peak Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M-TB Positive</td>
<td>M-TB Negative</td>
</tr>
<tr>
<td>Sputum</td>
<td>320</td>
<td>0.4588±0.1468</td>
</tr>
<tr>
<td></td>
<td></td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>290</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
<td>---</td>
</tr>
<tr>
<td>Macrophage</td>
<td>320</td>
<td>0.0496±0.0116</td>
</tr>
<tr>
<td></td>
<td></td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>290</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
<td>---</td>
</tr>
</tbody>
</table>

From results presented in Figs. 4 and summarized in table 1, it could be seen that the peak absorbance values of the various sputum samples and components vary in magnitude revealing the notable effect of the bacteria on them. The comparison between the positive and negative samples of the macrophages is imperative to this research. This is because Mycobacterium Tuberculosis actually attacks the macrophages by attaching itself to the macrophage cells.

The difference between the peak absorbance values of M-Tb positive, M-Tb/HIV co-infected and negative sputum components respectively is an indication of how the bacteria affects the properties of the macrophage cells. The trend is such that the mean absorbance peak values of M-Tb negative sputum samples are reduced by infection.
from $0.6244\pm0.3545$ to $0.4588\pm0.1468$ by a factor of about 26.5%. In M-Tb macrophage samples, the reduction is from $0.0784\pm0.0206$ to $0.0496\pm0.0116$, a factor of about 36.7%. While in M-Tb/HIV co-infected macrophage samples, the reduction is from $0.0784\pm0.0206$ to $0.0456\pm0.0106$ by a factor of about 41.8%. Comparing the mean absorbance peak values of M-Tb positive sputum samples and the mean absorbance peak values of M-Tb/HIV co-infected sputum samples; the results of the mean absorbance peak values reveal that the mean absorbance peak value of the M-Tb/HIV co-infected samples is generally reduced as compared to that of the mean absorbance peak values of the M-Tb positive sputum samples (see table 1). The macrophages are of particular interest to this research since the bacteria attacks this T-cells component which serves as receptor cells. Comparing the mean absorbance peak values of M-Tb positive macrophage samples and the mean absorbance peak values of M-Tb/HIV co-infected macrophage samples; the results of the mean absorbance peak values reveal that the mean absorbance peak values of the M-Tb/HIV co-infected samples is generally reduced by infection from $0.0784\pm0.0206$ to $0.0456\pm0.0106$ by a factor of about 41.8% as compared to that of the mean absorbance peak values of the M-Tb positive macrophage sample with a factor of about 36.7%. It could be seen that the reduction between the peak values absorbance (mean) of the sputum component is such that the macrophages reduced from M-Tb to M-Tb/HIV by a factor of about 8.1%. The reduction in the absorbance of the M-Tb/HIV infected sputum samples reveals the role of the bacteria in drastically affecting the surface properties of the infected macrophage cells and specimens.
Table 2: Values of the Hamaker Constants and Hamaker Coefficients for the Infected and Uninfected Samples

<table>
<thead>
<tr>
<th>Variable (x10^{-21} Joule)</th>
<th>M-Tb</th>
<th>M-Tb/HIV</th>
<th>M-Tb</th>
<th>M-Tb/HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Value</td>
<td>Infected Sputum</td>
<td>Uninfected Sputum</td>
<td>Absolute Value</td>
<td>Infected Sputum</td>
</tr>
<tr>
<td>A_{11}</td>
<td>---</td>
<td>0.94188</td>
<td>A_{11}</td>
<td>---</td>
</tr>
<tr>
<td>A_{22}</td>
<td>0.96068</td>
<td>---</td>
<td>A_{22}</td>
<td>0.97862</td>
</tr>
<tr>
<td>A_{33}</td>
<td>0.23067</td>
<td>0.42470</td>
<td>A_{33}</td>
<td>0.28812</td>
</tr>
<tr>
<td>A_{132}</td>
<td>0.21631</td>
<td>---</td>
<td>A_{132}</td>
<td>0.18825</td>
</tr>
<tr>
<td>A_{131}</td>
<td>---</td>
<td>0.10165</td>
<td>A_{131}</td>
<td>---</td>
</tr>
<tr>
<td>A_{232}</td>
<td>0.24986</td>
<td>---</td>
<td>A_{232}</td>
<td>0.20474</td>
</tr>
</tbody>
</table>

The Hamaker constants A_{33} for the sputum show greater values for the uninfected samples which regularly indicate a higher surface energy than the infected samples. The higher absolute values of A_{132} and A_{232} as against that of A_{131}, as well as the lower value of the absolute combined Hamaker coefficient A_{131,abs} for the uninfected samples is a clear suggestion of the relevance of the concept of Hamaker coefficient in the M-Tb infection process. The surface energy A_{131} of the macrophages is less than the surface energy A_{232} of the disease (M-Tb).

A_{33}, which serves as the energy of sputum as an intervening medium, is seen in M-Tb data to be reduced by infection from 0.4247 x10^{-21}J to 0.23067 x10^{-21}J by a factor of about 45.7% (see table 2). In M-Tb/HIV co-infection, the reduction is from 0.4247 x10^{-21}J to 0.28812 x10^{-21}J, a factor of about 32.2% (see table 2). The reduction is lower in M-Tb/HIV co-infection probably because of the interaction between HIV and Tb. For the combined Hamaker coefficient, the value is 0.21631 x10^{-21}J for M-Tb and 0.18825 x10^{-21}J for M-Tb/HIV. This result is as expected. HIV has the tendency to reduce the energy on
the surface of a given material, in this case by about 13%, conforming adverse effects observed in HIV patients with tuberculosis. Note that the values of $A_{132}$ are all positive showing that attraction exists between the macrophage and the M-Tb particles. The effect of the infection can only be abated if a drug, in the form of additive is added that can change the value of $A_{132}$ to negative under that condition, mutual repulsion will occur and it will be expected that, in principle, the Tb bacteria will not attack the macrophage.

I. Deductions for the Absolute Combined Negative Hamaker Coefficient

To define the condition where the absolute Hamaker coefficient becomes negative will require employing the relations that express that condition. Hence, recalling Eqs. (17) – (19), a state where the Hamaker Coefficient, $A_{132}$ is less than zero can be derived. This situation could be possible with the following already stated conditions (refer to Eqs. (17) – (19);

The mean of all values of $A_{11}$ and $A_{22}$ could be obtained and substituted into the relation in Eq. (16) in order to derive a value for $A_{33}$ at which $A_{132}$ is equal to zero in agreement with the earlier stated reasons.

Rearranging Eq. (16) and making $A_{33}$ subject of the formula we obtain;

$$A_{33} = \left[ \frac{2\sqrt{A_{11}} \sqrt{A_{22}} - A_{132}}{\sqrt{A_{11}} + \sqrt{A_{22}}} \right]^2$$

(28)

The mean of all the values of $A_{11}$ and $A_{22}$ respectively gave the absolute values of the Hamaker constants as shown below;

For Mycobacterium Tuberculosis: $A_{11} = 0.94188 \times 10^{-21}$ Joule and $A_{22} = 0.96068 \times 10^{-21}$ Joule

For M-Tb/HIV Coinfection: $\tilde{A}_{11} = 0.94188 \times 10^{-21}$ Joule and $\tilde{A}_{22} = 0.97862 \times 10^{-21}$ Joule

Thus, inserting these values into Eq. (25) and rendering $A_{132} \leq 0$ will give the critical value of $A_{33C}$ that satisfies the condition for the combined Hamaker coefficient to be
equal to or less than zero. Hence any value of $A_{33}$ greater than the critical would be the desired value necessary to attain a negative combined Hamaker coefficient. Hence, the critical absolute Hamaker constant $A_{33C}$ for the sputum which renders the $A_{132}$ negative is given as;

For mycobacterium Tuberculosis: $A_{33C} = 0.9527 \times 10^{-21}$ Joule

For M-Tb/HIV Coinfection: $\tilde{A}_{33C} = 0.9598 \times 10^{-21}$ Joule

Thus for negative combined Hamaker coefficient $A_{132}$, $\tilde{A}_{132}$ of the infected M-Tb, M-Tb/HIV sputum to be attained respectively, the combined Hamaker constant of the sputum as the intervening medium $A_{33}$, $\tilde{A}_{33}$ respectively should be of the magnitude;

$A_{33C} \geq 0.9527 \times 10^{-21}$ Joule and $\tilde{A}_{33C} \geq 0.9598 \times 10^{-21}$ Joule respectively

Inserting the above values of $A_{33}$, $\tilde{A}_{33}$ into Eq. (16) would yield negative values for $A_{132}$, $\tilde{A}_{132}$ respectively as follows; $A_{132} = -0.22669 \times 10^{-25}$ Joule (when $A_{33} = 0.9527 \times 10^{-21}$ Joule) and $\tilde{A}_{132} = -0.08786 \times 10^{-25}$ Joule (when $A_{33} = 0.9598 \times 10^{-21}$ Joule)

To obtain a value for the combined Hamaker coefficient $A_{131}$ for the uninfected sputum using the relations in Eqs. (13) and (15).

Upon integration of all values of $A_{131}$ for the twenty uninfected sputum samples, an absolute value for both $A_{131abs}$ and $\tilde{A}_{131abs}$ was derived as given below; $A_{131abs} = \tilde{A}_{131abs} = 0.10165 \times 10^{-21}$ Joule

This value is very nearly equal to zero which is a clear indication of the validity of the concept of Hamaker coefficient to the process and progress of human infection with the M-Tb as an opportunistic disease. The near zero value of the $A_{131abs}$ and $\tilde{A}_{131abs}$ shows the absence of infection in the sputum samples thus suggesting the usefulness of the concept of negative Hamaker coefficient in finding a solution to M-Tb and M-Tb/HIV co-infection.
5. Conclusion

This work reveals that the interactions of M-Tb and the Macrophages could be mathematically modeled. The values of the Hamaker coefficients and constants derived as a proof of the relevance of the concept of Hamaker coefficient to the M-Tb – macrophage interactions and by extension to other biological and particulate systems. The significance of negative Hamaker coefficient ($-0.2267 \times 10^{-19} \text{mJ/m}^2$) indicated that segregation of bacteria is realistic. This study equally reveals the possibility of solving for the value of $A_{33C}$ which would favour the prevalence of a negative combined absolute Hamaker coefficient $A_{132abs}$. The desired outcome is that the bacteria do not adhere to the macrophage to avoid penetration, in which case a condition for rendering combined Hamaker coefficient negative is required. Thus, a condition was sought for repulsion to occur and that condition was based on the value of $A_{33}$ that would render the absolute combined Hamaker coefficient $A_{132abs}$ negative. A mathematical model for the infection process/mecchanism was developed employing the principle of particle – particle interaction. Mathematically, it was derived as $A_{33} \geq 0.9527 \times 10^{-21} \text{Joule}$ which satisfies this condition for negative $A_{132abs}$. To achieve the condition of $A_{33}$ above, possible additive(s) to the system (in form of drugs) to the sputum as intervening medium should be required. A synergy of Engineers, Pharmacists, Doctors, Medical Laboratory Scientists, Pharmacologists etc. may well be needed in interpreting the meaning of the $A_{33C}$ values and the Medical, Biological and Toxicity implications of additive(s) in form of drugs that could yield the required characteristics.
References


