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MOLECULAR SIMULATION AND STOCHASTIC DOMINANCE ANALYSIS OF LIGANDS IN DRUGS FOR TREATMENT OF TB/HIV USING THE WEIGHTED GAMMA-RAYLEIGH DISTRIBUTION

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ABSTRACT. The recent treatment for Tuberculosis involves a prolonged study of a combination of antibiotics with toxic side-effects and is associated with poor patient compliance. This has resulted to the multi-drug resistant (MDR) and extensively-drug resistant (XDR) strains of M. tuberculosis. The number of anti-TB drugs currently in the pipeline is insufficient to address this major health challenge. Therefore, there is an urgent need to discover and develop new and efficient drugs against TB. Studying the interaction and functioning of drug components is the first step in the discovery process and Molecular docking is one of the methods that have been used to study drug interaction and functioning. In this study, a molecular dynamics simulation study of ligands (Ethambutol, Isoniazid, Rifampicin, Streptomycin, Pyrazinamides) that are responsible for the effectiveness of Anti-TB/HIV therapy was carried out. Additionally, the Weighted Gamma-Rayleigh distribution (WGRD) is introduced in this research work, and used in testing the stochastic dominance of the binding affinity of the ligands to the Anti-TB/HIV drugs. Results showed that Rifampicin has higher binding affinity as it has (first order stochastically) dominated Streptomycin and Pyrazinamide. Isoniazid has (first order stochastically) dominated Ethambutol. Also, Isoniazid has great power in reducing toxicity of Anti-TB/HIV drug. The results from this study provide an avenue for good health policy and prospective planning, especially in Anti-TB/HIV drug development.

1. INTRODUCTION

Human immunodeficiency virus (HIV) infection is the cogent risk factor in developing tuberculosis and has increased its resurgence, especially in West Africa. An estimated global total of 10.6 million people (95% uncertainty interval [UI]: 9.9–11.4 million) fell ill with TB in 2022, equivalent to 133 incident cases (95% UI: 124–143) per 100 000 population. Among all incident

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TB cases, 6.3% were among people living with HIV [1]. Antiretroviral therapy has strong potential in preventing HIV-associated tuberculosis.

Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis that has become a serious threat for human being given the fact that it has killed approximately 1.5 million people around the world [2]. Pulmonary TB is recognized with continuous three or more-week cough, fever, and great weight loss [3]. Various anti-TB medications have been used and recognized to be effective based on the combinational therapy approach: isoniazid, rifampicin, streptomycin, which are known as first-line medications [4].

The recent treatment for Tuberculosis involves a prolonged study of a combination of antibiotics with toxic side-effects and is associated with poor patient compliance. [2] asserts that this has resulted to the multi-drug resistant (MDR) and extensively-drug resistant (XDR) strains of M. tuberculosis. The number of anti-TB drugs currently in the pipeline is insufficient to address this major health challenge. Therefore, there is an urgent need to discover and develop new and efficient drugs against TB [5]. Studying the interaction and functioning of drug components is the first step in the discovery process and Molecular docking is one of the methods that have been used to study drug interaction and functioning.

A few research works involving molecular docking and simulation abound in literature. [6] reported the molecular study of computational docking of some drugs target against lung cancer and confirm the effectiveness of the drug on lung cancer receptor. As the protein-ligand interaction takes a crucial part in protein function and perturbation, both ligand and its binding site are cogent components for modeling and understanding the protein-ligand complex functions. [7] reviewed and explored molecular docking's application to the study of dietary supplements and disease management. They presented the fundamentals of molecular docking, the various software tools available for docking, and the limitations and difficulties of using molecular docking in nutraceutical research. They also identified the molecular targets for nutraceuticals in numerous disease models. The study of [8] was aimed to identify the possible potent inhibitors of SARS-CoV-2 main proteases $3CL^{pro}$ (6LU7) by selecting 145 phyto-compounds from Kabasura kudineer (KK), a poly-herbal formulation recommended by AYUSH which are effective in combating potential symptoms of COVID-19. Obtained results by molecular docking showed that Acetoside (−153.06), Luteolin 7-rutinoside (−134.6) rutin (−133.06), Chebulagic acid (−124.3), Syrigaresinol (−120.03), Acanthoside (−122.21), Violanthin (−114.9), Andrographidine C (−101.8), myricetin (−99.96), Gingerenone -A (−93.9), Tinosporinone (−83.42), Geraniol (−62.87), Nootkatone (−62.4), Asarianin (−79.94), and Gamma sitosterol (−81.94) are main compounds from KK plants which may inhibit COVID-19 giving the better energy score compared to synthetic drugs..

The main aim of this research work is to investigate the stochastic dominance between ligands that are responsible for efficacy of Anti-TB/HIV therapy based on their binding affinity (kcall/mol). Ligand, coined from the latin word *ligare* meaning “to bind”, is an ion or molecule

which binds to a central atom to form a complex entity. Ligands can be anions, cations, or neutral molecules. Common ligands used in this research work are: Rifampicin, Isoniazid, Ethambutol, Streptomycin and Pyrazinamide. These form the active ingredients of Anti-TB/HIV therapy. On the other hand, Stochastic dominance test is a statistical method of determining the superiority of one distribution over another. It is a statistical means of comparison based on cumulative distribution function. Introducing the Weighted Gamma-Rayleigh distribution and employing it to test the stochastic dominance of the binding affinity of the ligands would make this work novel.

2. MATERIALS AND METHODS

2.1 Method of Molecular Simulation

In molecular simulation approach, ligands and the targets receptors are separated by small distance and the ligand is therefore allowed to bind the target site after definite time in its conformational space. The conformer Ligands releases energy in every move, in the conforming form. This method is more advantageous because it is easier to accept ligands and targets. The protein-ligand interaction studies are crucial in understanding the mechanisms and pattern of biological regulation, and they provide a theoretical basis for the design and discovery of new drug targets. In this study, we analyzed the molecular interactions of protein-ligand which was docked by AutoDock 4.2 software. Modelling of the drugs were done using Spartan 14 and the best conformer were obtained before DFT calculation which predict the descriptors that explain the toxicity of the drugs on receptors. Edupymol version 1.7.4.4 was used for cleaning TB/HIV receptors obtained from protein data bank (PDB). Bioinformatics softwares (Autodock tools and Vina version 4.2) were used for studying the binding interaction that occur between the ligand and the receptors responsible for tuberculosis and HIV and the simulated output were obtained in kcal/mol. The process involve a MonteCarlo search whereby the drug search for the most stable binding site on the protein receptor thereby changing the conformation and orientation of the receptor which equally stop the growth of the diseases. The resulting binding affinity through Monte Carlo search (Binding affinity of the ligand-receptors interaction) was obtained and the active binding site was viewed using Discovery studio 4.1 visualizer. The obtained binding affinity result was used in this research to study the dynamic behavior of the molecules as they impacted greatly on the protein receptors under investigation.

2.2 Data

Data collected via simulation of molecular dynamics is used in this research work. Since ligands such as Pyrazinamide, Ethambutol, Rifampicin, Isoniazid and Streptomycin are the active ingredients of Anti-TB/HIV interventional therapy (Chemotherapy) and no real life data is

available to study the most active ingredient of this therapy, then there is need to study the behavior of those Ligands using Molecular simulation approach.

Quantum chemical method through density functional theory (DFT) with the use of 6-31G basis set was used to optimize ligands responsible for effectiveness of Anti-TB/HIV therapy. Binding Affinity, highest occupied molecular orbital (E_{HOMO}) energy, lowest unoccupied molecular orbital (E_{LUMO}) energy, band gap, chemical potentials, chemical hardness, dipole moment, hydrogen bond donor (HBD), hydrogen bond acceptor (HBA), were the molecular descriptors obtained with the use of (Spartan 14) by wave function Inc. The results of binding affinity are used for investigating stochastic dominance of the ligands. The investigation was done by employing a newly derived convoluted distribution, the Weighted Gamma-Rayleigh Distribution.

In this study, Excel and R-program was extensively used for data analysis and we analyzed the molecular interactions of protein-ligand. The resulting data used in this research work is shown in the appendix.

2.3 The Weighted Gamma-Rayleigh Distribution

A newly developed convoluted distribution, the Weighted Gamma-Rayleigh distribution (WGRD) will be fitted to the binding affinity of the ligands to be simulated, with a view to investigating the ligand with the highest binding affinity, in relation to their influence on the efficacy of some selected drugs for the treatment of tuberculosis and the human immune virus (TB/HIV). WGRD is a weighted form of the Gamma-Rayleigh distribution (GRD) defined and studied by [9].

The pdf of GRD is given by:

$$f(x) = \frac{2\theta^{\alpha}}{\Gamma(\alpha)} x^{2\alpha-1} e^{-\theta x^2};\ x > 0,\ \alpha,\theta > 0 \tag{1}$$

And the cdf of GRD is given by:

$$F(x) = \frac{\gamma(\alpha,\theta x^2)}{\Gamma(\alpha)} \tag{2}$$

According to [10], the pdf of a weighted distribution is given by

$$g(x;c,\tau) = \frac{w(x;c) f(x;\tau)}{E(w(x;c))}; \tag{3}$$

where X is a non negative random variable with its pdf $f(x;\ \tau)$, τ is its parameter space and $g(x;\ c,\ \tau)$, is a weighted version of $f(x;\ \tau)$; $w(x;c)$ is a non-negative weighting function, the probability of observing a particular value of X and $E[w(x;c)]$ is its expected value, the normalizing factor expected to make the total probability equal to unity.

Using (3), the pdf of the Weighted Gamma-Rayleigh distribution is defined as:

$$f_{WGRD}(x;c,\alpha,\theta) = \frac{2\theta^{\alpha+\frac{c}{2}}}{\Gamma(\alpha+\frac{c}{2})} x^{2\alpha+c-1} e^{-\theta x^2};\ x > 0, \alpha, c, \theta > 0 \tag{4}$$

And the cumulative distribution function is presented below:

$$F_{WGRD}(x;c,\alpha,\theta) = \frac{\gamma(\alpha+\frac{c}{2},\beta_2 x^2)}{\Gamma(\alpha+\frac{c}{2})} \quad (5)$$

The *r*th raw moment is given by:

$$E(X^r) = \frac{1}{\theta^{\frac{r}{2}}\Gamma(\alpha+\frac{c}{2})}\Gamma(\alpha+\frac{r}{2}+\frac{c}{2}) \quad (6)$$

Accordingly, the first 4 raw moments as well as the variance of WGRD are presented below:

$$E(X) = \frac{\Gamma(\alpha+\frac{1}{2}+\frac{c}{2})}{\sqrt{\theta}\,\Gamma(\alpha+\frac{c}{2})}, \quad (7)$$

$$E(X^2) = \frac{1}{\theta}(\alpha+\frac{c}{2}), \quad (8)$$

$$E(X^3) = \frac{\Gamma(\alpha+\frac{3}{2}+\frac{c}{2})}{\theta^{\frac{3}{2}}\Gamma(\alpha+\frac{c}{2})}, \quad (9)$$

$$EX^4 = \frac{(\alpha+\frac{c}{2}+1)(\alpha+\frac{c}{2})}{\theta^2}, \quad (10)$$

$$\text{Var(X)} = \frac{1}{\theta}\left[(\alpha+\frac{c}{2}) - \left(\frac{\Gamma(\alpha+\frac{1}{2}+\frac{c}{2})}{\Gamma(\alpha+\frac{c}{2})}\right)^2\right] \quad (11)$$

Detailed derivations of other properties of WGRD like harmonic mean, central moments, Renyi entropy, Gini coefficient, survival and hazard functions as well as applications are being investigated by the authors.

3. RESULTS

3.1 Molecular Descriptors of Drugs

Table 1 below shows the properties of the drugs used in determine the toxicity, behavior and the general effect of each drugs to the body system. Parameters such as HBA, HBD, PSA, LogP and polarizability are used to determine if a particular compound are good drug candidate. From the result Rifampicin and Streptomycin is not good candidate and they might be very toxic to the body system due to high PSA value, HBA and HBD value. It reveals the active properties of the drugs used in determining the cytotoxicity of each drugs towards the receptor responsible for tuberculosis in HIV patient. Failure of most drugs in clinical experiment is as a result of it poor ADME (Absorption, Distribution, Metabolism and Excretion) properties, hence for a ligand to be chosen as a drug candidate with good ADME properties HBD must be less than five, HBA must be less than ten and it molecular weight in g/mol must be below 500, any ligand that violate this set of rules might result to problem if ingested [11]. We could also observe high molecular weight, high HBD and HBA for Streptomycin and Rifampicin indicating its toxic effect towards the receptors responsible for tuberculosis.

Also, Polar surface area (PSA) gives information about the ability of a drug-like compound to penetrate into the cell membrane. It has been established that ligands with high PSA value greater

than 140Å^2 will have poor penetrating power into the cell membrane. On the other hand, molecules with PSA value below 60Å^2 will have high penetrating power [12]. Hence, we are expecting high penetrating power into the cell membrane from Ethambutol, Isoniazid and pyrazinamide as compared to streptomycin and rifampicin polarizability are used to determine if a particular compound are good drug candidate. From the result Rifampicin and Streptomycin are not good candidate and they might be very toxic to the cell due to high PSA value, HBA and HBD value. The docking result used for stochastic dominance in order to determine the most effective drugs that perform actively in curing the diseases shows better binding affinity and inhibition constant from Streptomycin and rifampicin indicating that the two drugs are responsible for curing the diseases. While the other three drugs shows lower binding effect towards the receptor. Therefore, we can then infer that the three drugs (Ethambutol, Isoniazid and Pyrazinamide) are used as a suppressant so as to reduce the toxic effect that might result from Streptomycin and Rifampicin.

Table 1: Molecular Descriptors of the Drugs under Study

Descriptors	**Ethambutol**	**Isoniazid**	**Pyrazinamide**	**Streptomycin**	**Rifampicin**
Formula	$C_{10}H_{24}N_2O_2$	$C_6H_7N_3O$	$C_5H_5N_3O$	$C_{21}H_{39}N_7O_{12}$	$C_{43}H_{48}N_4O_{12}$
Molecular weight	204.31	197.14	123.12	581.58	822.95
Area	278.01	160.28	139.84	552.42	816.49
Volume	239.31	136.02	117.77	521.30	819.27
Polarizability	58.97	51.11	50.24	64.27	71.25
Hydrogen Bond Donor (HBD)	2	2	1	11	6
Hydrogen Bond Acceptor (HBA)	4	4	4	19	15
Polar Surface Area (PSA)	60.25	62.28	52.54	282.61	149.72
Ovality	1.49	1.25	1.2	1.79	1.93
Log P	0.06	0.92	0.89		4.9
Dipole Moment	1.25	1.88	4.62	3.63	4.41

3.2 Investigating First Order Stochastic Dominance

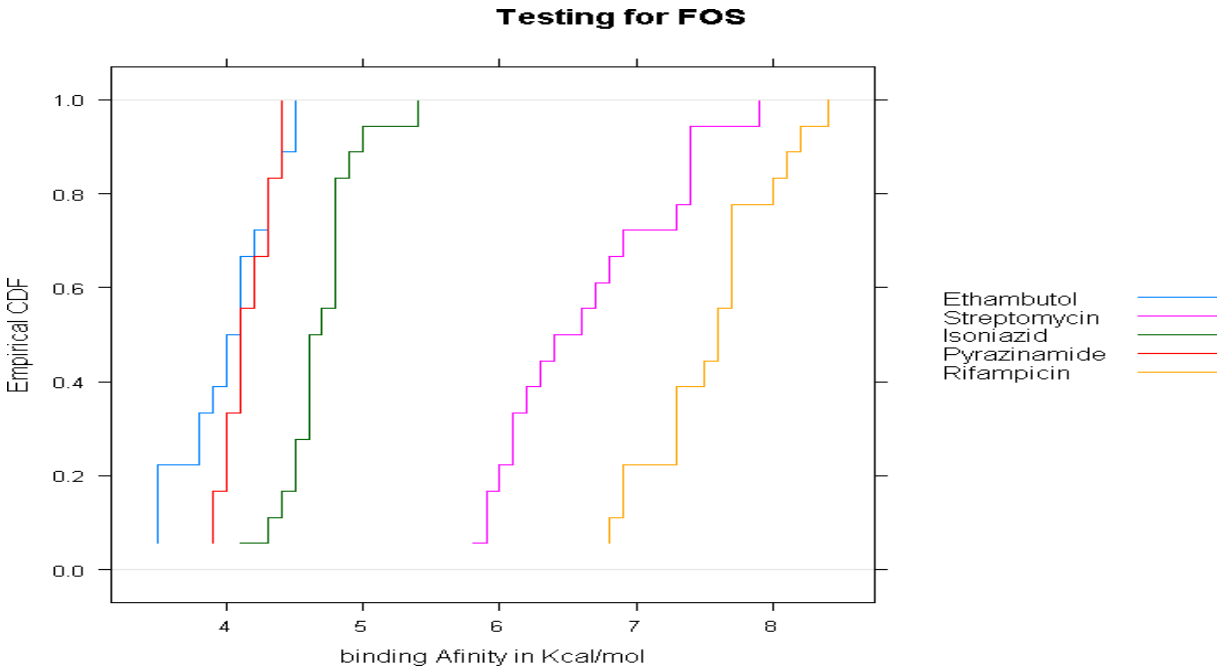


Fig 1: Testing First Order Stochastic Dominance between the all Ligands under investigation

From fig 1 above, we can say that Rifampicin has first order stochastically (FOS) dominated Streptomycin and Streptomycin has FOS dominated Pyrazinamide.

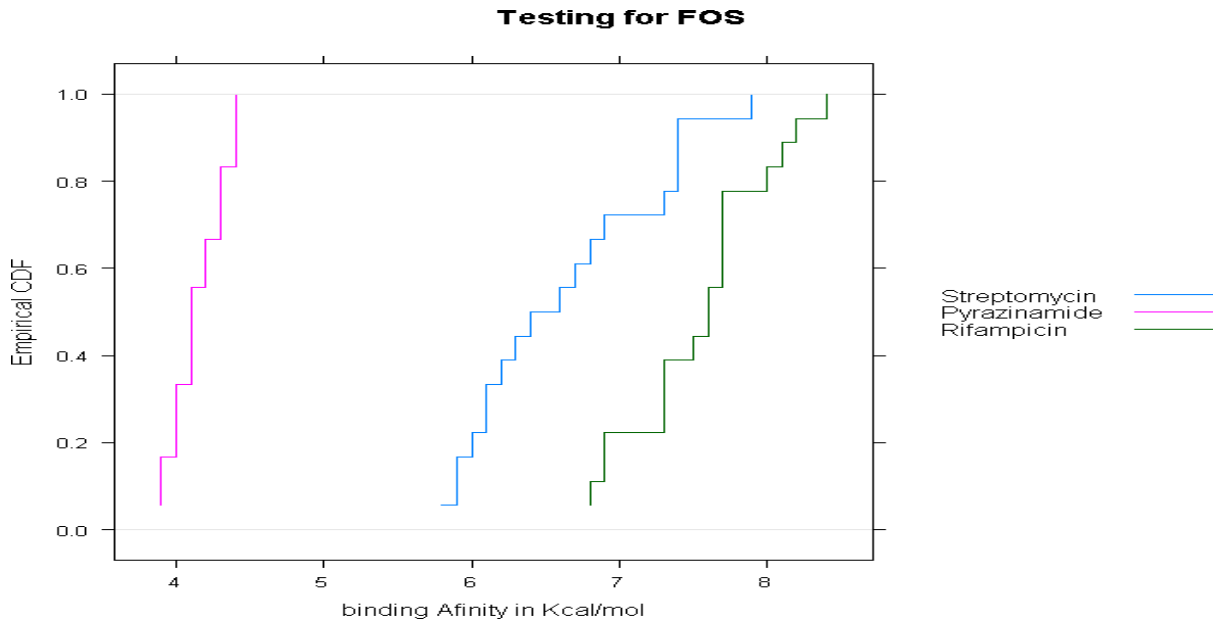


Fig 2: Testing First Order Stochastic Dominance of Three Ligands

From fig 2 above, we can say that Rifampicin has first order stochastically (FOS) dominated Streptomycin and Streptomycin has FOS dominated Pyrazinamide. From this the Rifampicin has higher binding affinity as compared to Streptomycin. And, Streptomycin has higher binding affinity as compared to Pyrazinamide.

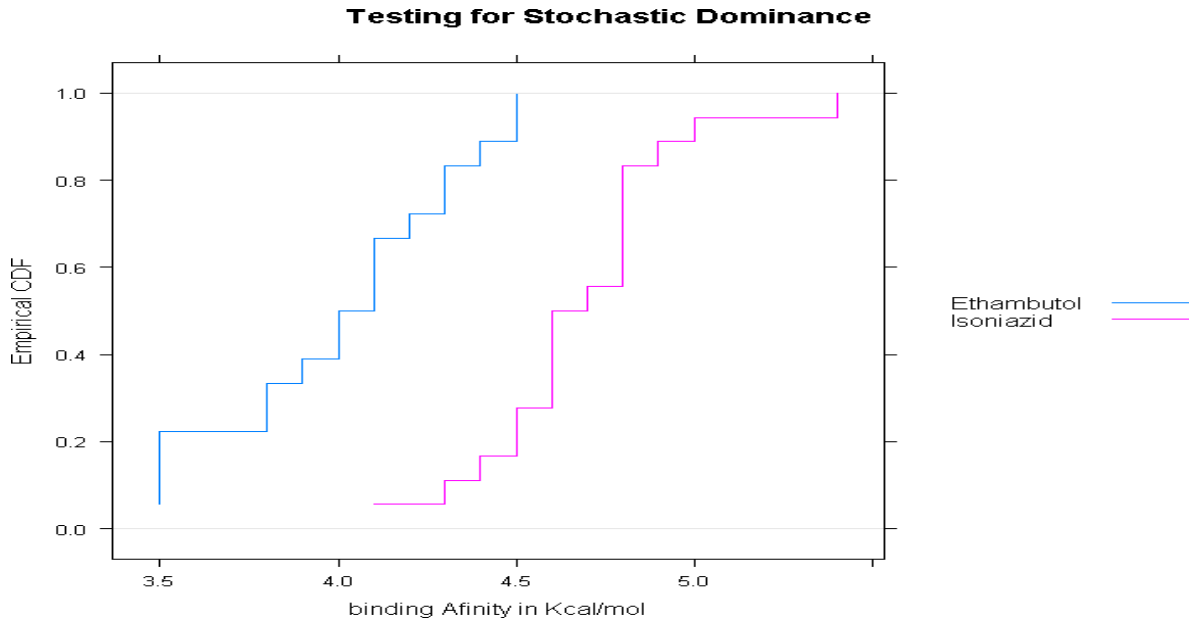


Fig 3: Testing First Order Stochastic Dominance of Two Ligands

From fig 3 above, we can say that Isoniazid has first order stochastically (FOS) dominated Ethambutol. We can therefore conclude that Isoniazid has higher efficiency in reducing the toxicity and facilitating high binding affinity of Ligands.

3.3 Fitting WGRD to Data Obtained Via Molecular Dynamics Simulation

Table 2: Fitting WGRD to Binding Affinity Data

Ligands	WGRD($\hat{\alpha}, \hat{c}, \theta$)	mean	Std dev
Streptomycin	WGRD(2.68,1.048,3.2)	5.71	0.27
Ethambutol	WGRD(0.70,0.98,1.30)	0.73	0.41
Isoniazid	WGRD(0.25,0.96,0.851)	1.23	0.23
Pyrazinamide	WGRD(0.024,1.21,1.62)	1.05	0.12
Rifampicin	WGRD(1.56,1.20,3.162)	8.15	0.19

From the table 2 above, we can deduce that Rifampicin has high mean binding affinity as compared to others; we therefore conclude that Rifampicin has higher effect in Anti-TB/HIV therapy. Streptomycin and Isoniazid dominated Ethambutol and Pyrazinamide.

The above result is consistent with the results in 3.2 where the first order stochastic dominance was investigated. Both results show that Rifampicin has high binding affinity as compared to others and therefore higher effect in Anti-TB/HIV therapy.

3.4 Empirical Histogram of WGRD using Binding Affinity Data

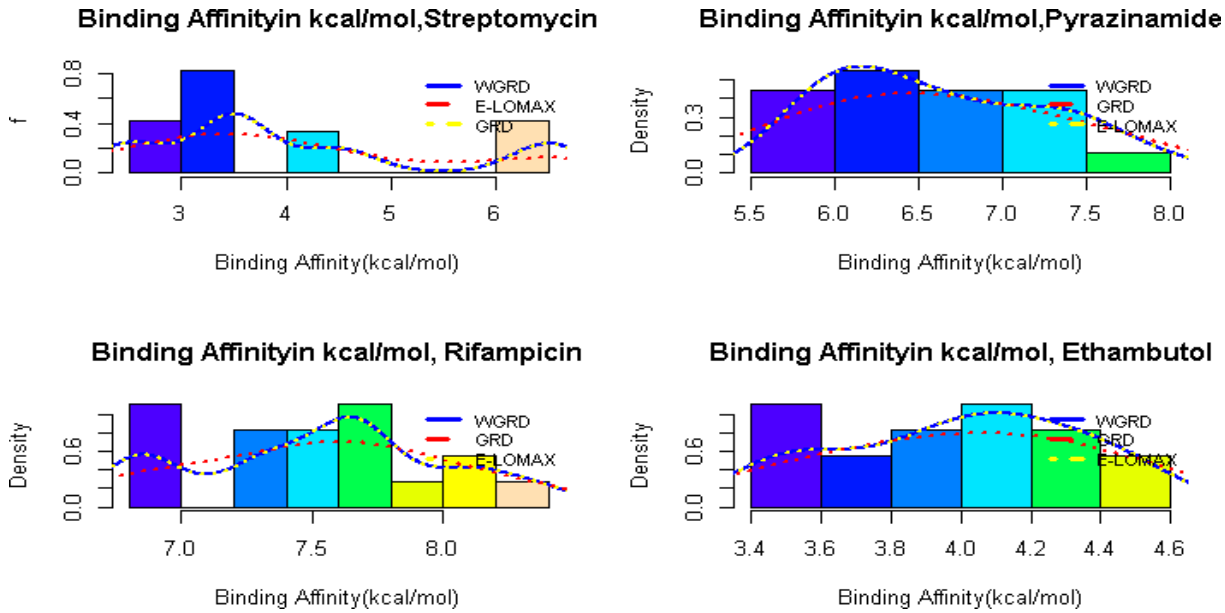
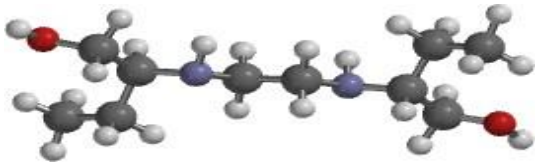


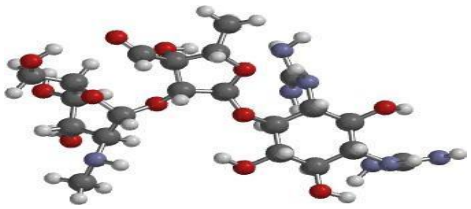
Fig 4: Fitting Convoluted Models to Binding Affinity Data

From Fig 4, we can say that the data approximately follow WGRD

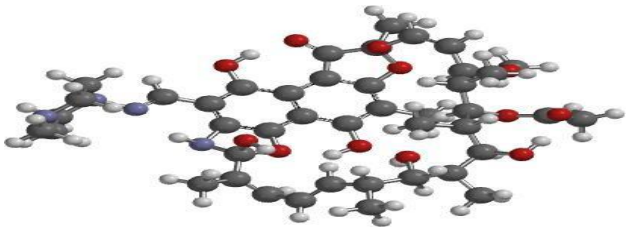
3.5 Simulated Pictures of Ligands



(a) Ethambutol (b) **Isoniazid**



(d) Pyrazinamide **(c) Streptomycin**



Rifampicin (e)

Fig 5: Simulated Ligands used for molecular docking

The Fig 5a-5e shows the Ligand used in this research work and they were optimized using Spartan 14 in order to obtain the best conformer, the best conformer was later used for modecular docking (Autodock). The molecular properties of the ligands were obtain via molecular simulation by studying the binding affinity of the Ligands with TB/HIV protein receptor.

3.6 Binding Affinity of Simulated Ligands

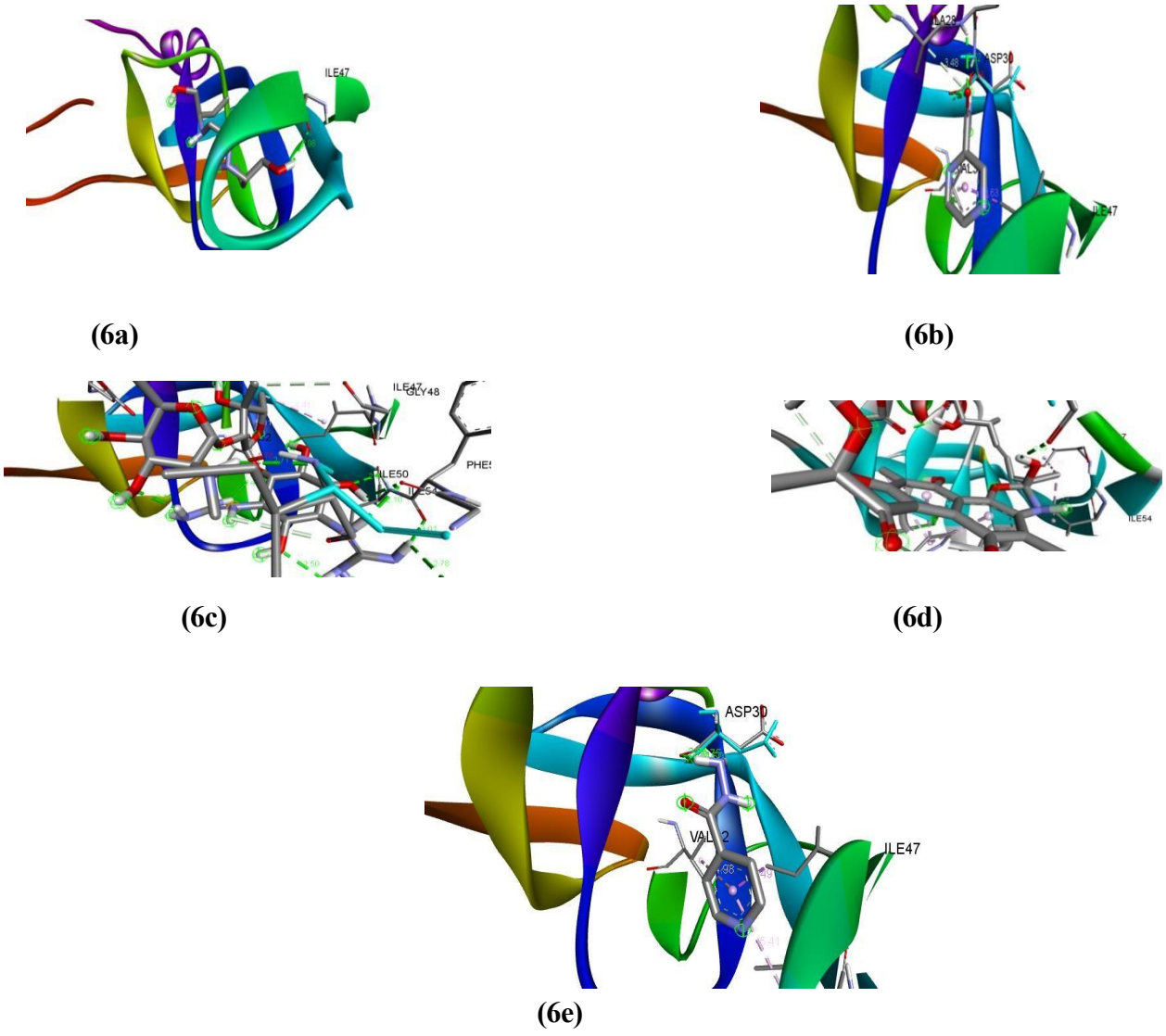


Fig 6: Ethambutol – 3ST5 (6a), Isoniazid – 3ST5 (6b), Pyrazinamide – 3ST5(6c), Streptomycin- 3ST5 (6d) and Rimfampacin – 3ST5 (6e).

The fig (6a-6e) above show the drug ligand interaction for all the Ligands under investigation and TB/HIV protein receptor, the shorter the distance between Ligand and protein receptor, the higher the binding affinity, thereby making the ligands with higher affinity more effective as compared to others in disrupting the structure of TB/HIV protein structure which in turn reduces their activities.

The results show that Rimfampacin has a high binding affinity, which is consistent what earlier results obtained.

4. DISCUSSION

The first order stochastic dominance of the ligands was investigated . The results show that Rifampicin has first order stochastically (FOS) dominated Streptomycin and Streptomycin has FOS dominated Pyrazinamide. This also revealed that Rifampicin has higher binding affinity as compared to Streptomycin. And, Streptomycin has higher binding affinity as compared to Pyrazinamide.

A further test revealed that Isoniazid has first order stochastically (FOS) dominated Ethambutol. We can therefore conclude that Isoniazid has higher efficiency in reducing the toxicity and facilitating high binding affinity of Ligands.

A second aspect of this study involved generating and applying new distribution to data obtained by molecular dynamics simulation of the ligands to test their binding affinity. It was deduced from the results that Rifampicin has high mean binding affinity as compared to others; we therefore conclude that Rifampicin has higher effect in Anti-TB/HIV therapy. Streptomycin and Isoniazid dominated Ethambutol and Pyrazinamide. This result is consistent with earlier results where the first order stochastic dominance was investigated. Both results show that Rifampicin has high binding affinity as compared to others and therefore higher effect in Anti-TB/HIV therapy.

Pictures of the Ligands used in this research work were presented, and they were optimized using Spartan 14 in order to obtain the best conformer, the best conformer was later used for modecular docking (Autodock). The molecular properties of the ligands were obtained via molecular simulation by studying the binding affinity of the Ligands with TB/HIV protein receptor. The aim was to study the drug-ligand interaction for all the Ligands under investigation and TB/HIV protein receptor, the shorter the distance between a Ligand and protein receptor, the higher the binding affinity, thereby making the ligands with higher affinity more effective as compared to others in disrupting the structure of TB/HIV protein structure which in turn reduces their activities. Again, the results show that Rimfampacin has a high binding affinity, which is consistent what earlier results obtained.

5. CONCLUSION

The study investigated the stochastic dominance of the binding affinity of molecular dynamics simulation study of ligands to selected drugs for treatment of TB/HIV.

In investigating stochastic dominance, Rifampicin has first order stochastically (FOS) dominated Streptomycin and Streptomizine has FOS dominated Pyrazinamide. We can therefore say that Rifampicin has first order stochastically (FOS) dominated Streptomycin and Streptomycin has FOS dominated Pyrazinamide. From this the Rifampicin has higher binding affinity as compared to Streptomycin. And, Streptomycin has higher binding affinity as compared to Pyrazinamide. Fitting the binding affinity's data to the convoluted distribution enables us to know that the Rifampicin maintained its average binding affinity and tend to have more effectiveness as compared to streptomycin and pyrazinamide in Anti-TB/HIV therapy.

After careful application of the newly compounded distribution to the data on CD4-counts, Molecular Behavior of Ligand (Docking Results) and Simulated Data, it was found that Rifampicin has very higher binding affinity and toxicity test showed that it is not a better drug candidate. It is then recommended that more researches should be done to reduce the side effect of this most active ingredient of Anti-TB/HIV interventional therapy.

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Authors Contribution. The first author conceived the idea, reviewed all literature and did the write up. The second author did the derivations for the distribution and used Spartan for the molecular docking and simulation. The third author provided the data and provided information about the drug interactions with different ligands.

Authors' Conflicts of interest. None

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REFERENCES

[1] World Health Organization (WHO) (2023). Global Tuberculosis Report. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/tb-disease-burden/1-1-tb-incidence, retrieved 13/10/2024

[2] World Health Organization (WHO) (2014). Malaria Fact Sheet No 94. 2014. Retrieved 25/6/2015.

[3] Ryu, Y. J. (2015). Diagnosis of Pulmonary Tuberculosis: Recent Advances and Diagnostic Algorithms. Tuberc Respir Dis (Seoul). Apr;78(2):64-71. doi: 10.4046/trd.2015.78.2.64. Epub 2015 Apr 2. PMID: 25861338; PMCID: PMC4388902.

[4] Asgharzadeh, M., Kafil, H. S., & Pourostadi, M. (2014). Limited transmission of multidrug-resistant tuberculosis in East Azarbaijan, Iran.*BeniSuef Univ. J. Basic Appl. Sci*. 3, 254–259. doi: 10.1016/j.bjbas.2014. 11.004.

[5] Zumla, A., Nahid, P., & Cole, S.T (2013). Advances in the development of new tuberculosis drugs and treatment regimens.*Nat Rev Drug Discov*, 12(5):388–404.

[6] Kanagaraj, B., Wadhwa, D. and Prakash, A. (2014). Molecular Docking of Lung Cancer Proteins Against Specific Drug Targets. World Journal of Pharmaceutical Research, Volume 3, Issue 3, 4248-4262

[7] Agu, P.C., Afiukwa, C.A., Orji, O.U., Ezeh, E.M., Ofoke, I.H., Ogbu, C.O., Ugwuja, E.I. and Aja, P.M. (2023). Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. *Sci Rep* 13, 13398. https://doi.org/10.1038/s41598-023-40160-2

[8] Vincent S, Arokiyaraj S, Saravanan M and Dhanraj M (2020) Molecular Docking Studies on the Anti-viral Effects of Compounds from Kabasura Kudineer on SARS-CoV-2 $3CL^{pro}$. *Front. Mol. Biosci.* 7:613401. doi: 10.3389/fmolb.2020.613401

[9] Akarawak, E.E.E., Adeleke, A.I., & Okafor, R.O., (2017). Gamma-Rayleigh Distribution with Application to Survival Data, *Nigerian Journal of Basic and Applied Science*, 25(2):130-142.

[10] Patil, G.P. and Rao, C.R. (1978) Weighted Distributions and Size-Biased Sampling with Applications to Wildlife Populations and Human Families. Biometrics, 34, 179-189. http://dx.doi.org/10.2307/2530008

[11] Syed, A., Muhammad, H., Muhammad, U., Rana, M., Shahid, M., Khalid, A., Muhammad, B. & Muhammad, Z. (2019). A Molecular Docking Approach to Evaluate the Pharmacological Properties of Natural and Synthetic Treatment Candidates for Use against Hypertension, *International Journal of Environmental Research and Public Health*, 16:923-956

[12] Adejoro, I.A., Waheed, S.O., & Adeboye O.O. (2016). Molecular Docking Studies of Lonchocarpus cyanescens Triterpenoids as Inhibitors for Malaria; *Journal of Physical Chemistry and Biophysics*, 6: 2; doi:10.4172/2161-0398.1000213.

APPENDIX

The binding affinity (kcal/mol) obtained by docking Anti-TB/HIV drug target with TB/HIV protein receptor.

Receptors Code	Ethambutol	Isoniazid	Pyrazinamide	Streptomycin	Rifampicin
3H5B	4	4.8	4.4	6.4	8.1
	4	4.8	4.3	6.3	7.7
	3.9	4.8	4.3	6.2	7.7
	3.8	4.6	4.2	6.1	7.6
	3.8	4.6	4.1	6.1	7.3
	3.5	4.5	4	6	6.9
	3.5	4.5	3.9	5.9	6.9
	3.5	4.4	3.9	5.9	6.8
	3.5	4.3	3.9	5.8	6.8
3ST5	4.5	5.4	4.4	7.9	8.4
	4.5	4.1	4.4	7.4	8.2
	4.4	5	4.3	7.4	8
	4.3	4.9	4.2	7.4	7.7
	4.3	4.8	4.1	7.3	7.6
	4.2	4.8	4.1	6.9	7.5
	4.1	4.7	4.1	6.8	7.3
	4.1	4.6	4	6.7	7.3
	4.1	4.6	4	6.6	7.7

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