Research Article **www.ijcps.com**

International Journal of
Chemical and Pharmaceutical Sciences
2019, Aug., Vol. 10 (2)

ISSN: 0976-9390
IJCPS

Molecular docking studies on the interaction of different serum albumins with promazine

Thulasidhasan J* and Angeline Jenita L.

Department of Chemistry, School of Arts and Science, Ponnaiyah Ramajayam Institute of Science and Technology (PRIST), Thanjavur, Tamilnadu, India.

***Corresponding Author:** E-Mail**:** drthulasi86@gmail.com

Received: 8th Aug 2019, Revised and Accepted: 9th Aug 2019

ABSTRACT

The interaction processes of two different serum albumins [(bovine serum albumin (BSA) and Human serum albumin (HSA)] with Promazine, as well as their possible interaction types have been investigated theoretically. The binding constant for the promazine-BSA and promazine-HSA were -6.70 and -6.74 kcal/mol, respectively. The docking results showed that drug molecule bind within the binding pocket of sub-domain IIA of both serum molecules. The hydrogen bonding plot was used to explore the hydrogen bonds interactions between drug molecule and BSA/HSA. Polar interaction, hydrophobic interaction, hydrogen bonding, and pi-pi interactions was a predominant intermolecular force in order to stabilize the copolymer.

Keywords: Promazine; BSA; HSA; Molecular docking**.**

1. INTRODUCTION

In recent time a terrific development of research has been observed about the characterization of interaction of various potential drugs with different biological and bio-imitator assemblies. The reason that of the confident prediction of planned assemblies on the biological, photochemical, and photophysical processes [1]. Bovine serum albumin (BSA), the major soluble protein, serves as a transporter of a variety of endogenous and exogenous ligands such as fatty acids, steroids, drugs, metal ions and metabolites [1]. In recent years, BSA has been broadly used as a model protein because of its structural homology with HSA [2]. BSA has 80% similarity to HSA in structure with a major difference in the number of tryptophans: while HSA has only one tryptophan, BSA has two. BSA is usually selected for protein binding studies because of its abundance, low cost, and ease of purification, stability, medical importance and drug binding properties[3-5].

Many drugs, particularly those with local anaesthetic, tranquillizer, antidepressant, and antibiotic, exercise their action by interactions with biological membranes. These compounds must be carried to their site of action and, usually, this function is achieved by globular protein serum albumins (blood carrier proteins) at which they bind with different affinities. Tricyclic antidepressant drugs (TCAs) are one of the largest groups of drugs for the treatment of psychiatric disorders such as depression, mainly endogenous major depressions. The function of these drugs is to block the reuptake of the neurotransmitters and serotonin in the central nervous system [6]. The chemical structure of selected TCA compound is promazine shown in figure 1.

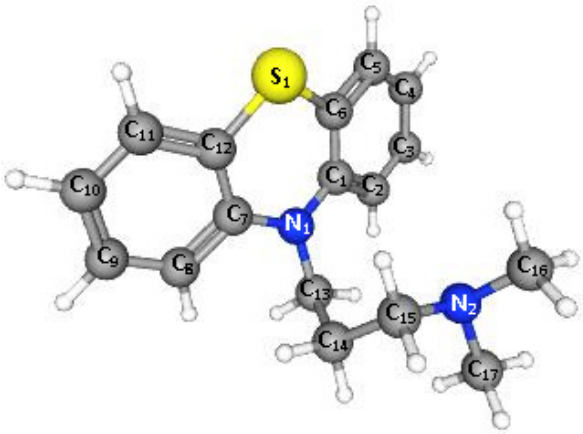

Figure - 1: Optimized structure of promazine.

The importance of TCA is highlighted not only by their therapeutic use for depressive disorders but also by their use in a variety of

diseases with impact on the mental state such as insomnia, anxiety disorder, post-traumatic stress disorder, obsessive compulsive disorder, and chronic pain [7,8]. Furthermore, there is an increasing field for cognitive enhancing and life style use of TCA [9]. Therefore, the analysis of these compounds is important for quality assurance in pharmaceutical preparations and for obtaining optimum therapeutic concentrations to minimize the risk of toxicity.

Various studies on serum albumins involving binding of small molecules, in particular fatty acids and drugs, based on different techniques (UV–visible, fluorescence spectroscopy, FTIR, Raman spectroscopy, electrochemistry, NMR, etc.,) have been described [10–20], when these molecules bind to a serum albumin, the intramolecular forces mainly admirable for sustaining the secondary structure can be altered, developing conformational changes in the protein [21].

Drug interactions at protein binding level notably affect important factors such as drug availability, efficacy, transport, elimination rate, etc. Hence, the studies on this aspect can furnish information of the structural features that influence the therapeutic effectiveness of drug and have been an interesting research field in life sciences, chemistry and clinical medicine [22].

2. EXPERIMENTAL

2.1 Molecular Docking

Docking calculations were carried out using Docking Server (http://www.dockingserver.com) [23]. The MMFF94 force field was used for energy minimization of the drug (DOX and DOT) molecules using Docking Server [24]. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of Auto Dock tools [25]. Docking parameter setting- and distance-dependent dielectric functions were used in the calculation of the electrostatic and the van der Waals terms, respectively. Docking studies were performed using the Solis Wets local search and & the Lamarckian genetic algorithm (LGA) method. Initial position, orientation, and torsions of the drug molecules were set randomly. Each docking experiment was derived from 10 different runs that were set to terminate after a maximum of 25 x 10^4 energy evaluations. The population size was set to 150.

3. RESULTS AND DISCUSSION

Molecular docking

Docking is a broadly utilized computational device for the *investigation* of molecular simulation, which goes for anticipating the coupling mode in a complex shaped by at least two constituent particles with known structures. An important type of molecular docking is protein–drug docking because of its therapeutic applications in modern structure-based drug design. The binding site was obtained as LEU463, VAL462, GLN459, ARG197, ASP108, ALA194, TYR148, PRO147, HIS146 and LYS190. The binding constant for the promazine-BSA and promazine-HSA were -6.70 and -6.74 kcal/mol, respectively (Tables 1).

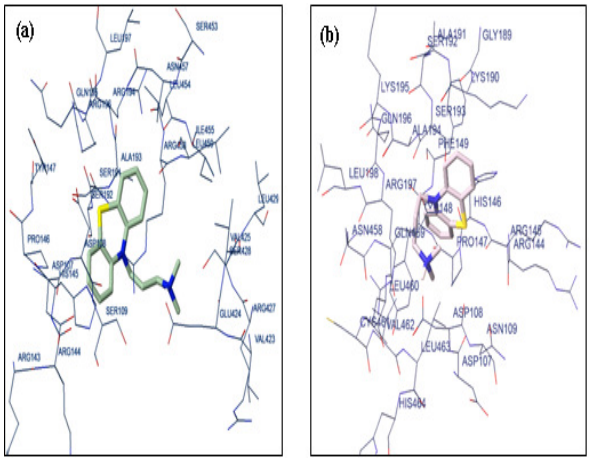

Figure – 2: The binding mode between promazine with (a) BSA and (b) HSA.

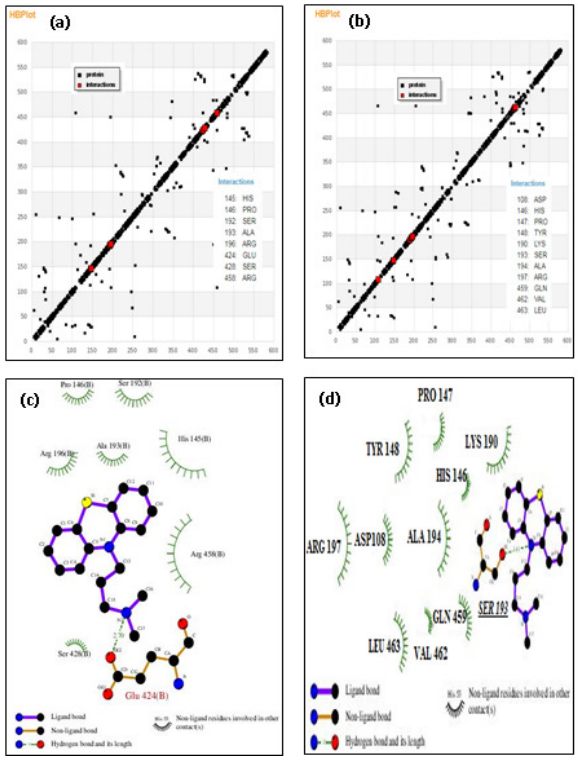

Figure – 3: The Hydrogen bonding plots between promazine with (a) BSA and (b) HSA. Two-dimensional schematic representation of hydrogen bonding and hydrophobic interactions of drug with (c) BSA and (d) HAS.

Table - 1: Estimated free energy, Inhibition constant, Electrostatic energy and Total intermolecular energy of the promazine with BSA and HSA

Protein	Est. Free Energy of Binding kcal/mol	Est. Inhibition Constant,Ki µM	vdW + H-bond + desolv Energy kcal/mol	Electro static Energy kcal/mol	Total Intermolec, Energy kcal/mol	Frequency	Intert Surfce
BSA	-6.70	12.21	-7.66	-0.44	-8.11	10%	696.3
HSA	**-6.74**	**11.46**	**-7.20**	-0.22	-7.41	30%	630.4

The strong interactions are mentioned in bold letters

The docking results showed that drug molecule bind within the binding pocket of sub-domain IIA of serum albumins [Figures. 2]. The binding site of the BSA was studied to understand the nature of the residues defining the site. The hydrogen bonding plot was used to explore the hydrogen bonds interactions between BSA/HSA and promazine as shown in Figures 3a and 3b. Hydrogen bonding interaction of BSA - promazine is observed between the nitrogen atom at N_2 position with OH of GLU424 (–N_2…OH, 2.70 Å - Figure 3c and 3d).

Meanwhile, in HSA - promazine hydrogen bonding is observed between the nitrogen atom at N_1 position of drug molecule act as a hydrogen acceptor to form hydrogen bonds with the group of SER193 (–N_1···· HO, 3.41 Å). However, a series of hydrophobic residues, Ala193, PRO147, 146, VAL462 and HIS145 around the peripheral region of the molecule interacted with the drug molecules through hydrophobic interactions.

4. CONCLUSIONS

Interaction between BSA and HSA with promazine drug has been investigated by using molecular docking studies. Molecular docking studies shows, HSA has more binding affinity than BSA with promazine drug molecule.

5. REFERENCES

1. Z. G. Yasseen, On the Interactions of Bovine Serum Albumin with Some Surfactants: New Insights from conductivity Studies. J. Chem. Pharm. Res., 4 (2012) 3361–3367.
2. X. M. He and D. C. Carter, Atomic structure and chemistry of HSA, Nature, 358 (1992) 209–215.
3. P. Bourassa, C. D. Kanakis, P. Tarantilis, M. G. Pollissiou, H.A. Tajmir-Riahi, Resveratrol, genistein, and curcumin bind bovine serum albumin, J. Phys. Chem. B, 114 (2010) 3348–3354.
4. T. Banerjee, S. K. Singh and N. Kishore, Binding of naproxen and amitriptyline to bovine serum albumin: Biophysical aspects, J. Phys. Chem. B, 110 (2006) 24147–24156.
5. V. Gomathi Sankareswari, D. Vinod, A. Mahalakshmi, M. Alamelu, G Kumaresan, R. Ramaraj and S. Rajagopal, Interaction of oxovanadium(IV)–salphen complexes with bovine serum albumin and their cytotoxicity against cancer, Dalton Trans., , 43 (2014) 3260 – 3272.
6. J. Wang, M. Bonakdar, C. Morgan, Voltammetric measurement of tricyclic antidepressants following interfacial accumulation at carbon electrodes, Anal. Chem. 58 (1986) 1024-1028.
7. M. Moore, H.M. Yuen, N. Dunn, M.A, Mullee, J., Maskell, T. Kendrick, Explaining rise in antidepressant prescribing descriptive study using general practice research database., BMJ 339 (2009) b3999.
8. D.R, Petty, A. House, P. Knapp, T., Raynor, A., Zermansky Prevalence duration and indications for prescribing of antidepressants in primary care, Age Ageing 35 (2006) 523e6.
9. C. Elliott, Pursued by happiness and beaten senseless. Prozac and the American dream. Hastings Cent Rep 30 (2000) 7e12.
10. L.A. Sklar, B.S. Hudson, R.D. Simoni, Conjugated polyene fatty acids on fluorescent probes: spectroscopic characterization. Biochemistry 16 (1977) 813-819.
11. J. Steinhardt., J. Krijn, J.G. Leidy, Differences between bovine and human serum albumins, binding isotherms, optical rotatory dispersion, viscosity, hydrogen ion titration, and fluorescence effects. Biochemistry 10 (1971) 4005-4015.
12. M. Yamasaki, T. Yamashita, H. Yano, K. Tatsumi, K. Aoki, Differential scanning calorimetric studies on bovine serum albumin. Int. J. Biol. Macromol., 19 (1996) 241-246.

13. H. Yuan, W.E. Antholine, W.K. Subczynski, M.A. Green, Release of Cu PTSM from human serum albumin after addition of fatty acids. J. Inorg. Biochem. 61 (1996) 251-259.
14. J. Thulasidhasan, R. Anandhi, G. Venkat Kumar Binding Interaction of Azo Dye Derivatives with BSA: Molecular Dynamic Study - International Journal of Innovative Research & Studies 8 (IX), 1-7 , 2018
15. N. Rajendiran, J.Thulasidhasan, R. Anandhi, G. Venkat Kumar, Interaction of Fast Garnet GBC with bovine serum albumin: Spectral, Electrochemical and Molecular Docking Methods International Journal of Innovative Research & Studies 8 (7), 111-119, 2018
16. N. Rajendiran, J. Thulasidhasan, M Suresh, Interaction of Azo Dyes with BSA and Adenine: Spectral, Electrochemical and Molecular Docking Methods –Der Pharma Chemica 10 (2), 2018
17. N. Rajendiran, J. Thulasidhasan, Effects of interaction between non-steroidal anti-inflammatory drugs with BSA and DNA base: Spectral, electrochemical and molecular docking methods –J. Indian Chem. Soc 94 (1), 83-93, 2017
18. N. Rajendiran, J. Thulasidhasan, Spectroscopic, electrochemical and molecular docking studies of dothiepin and doxepin with bovine serum albumin and DNA base Luminescence 31 (8), 1438-1447, 2016
19. N. Rajendiran, J. Thulasidhasan, Spectral, electrochemical and molecular docking methods to get an understanding of supramolecular chemistry of sulfa drugs to biomolecules Journal of Molecular Liquids 212, 857-864, 2015
20. N. Rajendiran, J. Thulasidhasan, Interaction of sulfanilamide and sulfamethoxazole with bovine serum albumin and adenine: Spectroscopic and molecular docking investigations Spectrochimica Acta Part A: 144, 183-191, 2015
21. W. Parker, P.S. Song, Protein structures in SDS micelle-protein complexes. Biophys. J. 61 (1992) 1435-1439.
22. L. Jiaquin, T. Jianniao, J. Zhang, Z. Hu, C. Xingguo, Interaction of magnolol with bovine serum albumin: a fluorescence-quenching study, Anal. Bioanal. Chem. 376 (2003) 864-867.
23. Z. Bikadi, E. Hazai, Application of the PM6 semi-empirical method to modelling proteins enhances docking accuracy of Auto Dock. J. Chem. inf. 1 (2009) 1-15.
24. T.A. Halgren. Merck molecular force field. I. Basis, form, scope, parametrization, and performance of MMFF94. J Comput. Chem. 17 (1998) 490-519.
25. G.M, Morris, D.S. Goodsell, Automated docking using LGA and an empirical binding free energy function, J Comput. Chem., 19 (1998) 1639-1662.