SciMedCentral

JSM Chemistry

Research Article

Effective Docking Program for Designing Reactivator for Treating Organophosphorus Inhibited AChE

Shibaji Ghosh[1,2], Nellore Bhanu Chandar[1,2], Rabindranath Lo[1], and Bishwajit Ganguly[1,2]*

[1]*Computation and Simulation Unit, CSIR-Central Salt & Marine Chemicals Research Institute, India*

[2]*Academy of Scientific and Innovative Research, CSIR-CSMCRI, India*

***Corresponding author**

Bishwajit Ganguly, Computation and Simulation Unit, CSIR-Central Salt & Marine Chemicals Research Institute, Bhavnagar, Gujarat-364 002, India, Tel: 91-278-2567760; Fax: 91-278-2567562; Email: ganguly@csmcri.org

Submitted: 08 September 2016

Accepted: 30 Septemebr 2016

Published: 03 October 2016

ISSN: 2333-6633

Keywords

- AchE
- Flex-X
- AutoDock
- Docking
- Drug

Abstract

Docking tools are computer-aided simulation process by which appropriate ligand molecules (drugs) are screened for receptor molecules such as protein/enzyme. Molecular docking has become a widely used approach to guide the discovery of drugs in Pharma industry provided the high-resolution structure of the biological system is available to model the study. In this article, we have performed the comparative study of the docking tools Flex-X and AutoDock for screening the ligand/drug as an antidote for Organophosphorus (OP)-inhibited AChE. We have employed both the docking tools for tabun-inhibited *m*AChE with HLö-7 (2JEZ), tabun-inhibited *m*AChE with Ortho-7 (2JF0) and sarin-inhibited *m*AChE with HI-6 (5FPP). Analyzing the docking results obtained from both docking tools, we have confirmed that Flex-X yields better results than AutoDock in these cases. Flex-X has given much lower root mean square deviation (RMSD) values of the docked structures, lower docking scoring and better pose with the corresponding crystal structures. Flex-X seems to be a superior docking tool to screen the antidotes for OP-inhibited AChE.

ABBREVIATIONS

AChE: Acetyl Cholinesterase; ACh: Acetylcholine; PDB: Protein Data Bank; LGA: Lamarckian Genetic Algorithm; GA: Genetic Algorithm; OP: Organophosphorus; RMSD: Root Mean Square Deviation

INTRODUCTION

Docking study was conceptualized in 1980s to study the interaction between small ligand/drug molecules with the macromolecular system like protein/enzyme to predict the ligand protein interaction at molecular level [1-3]. Computer aided docking study can predict the preferred conformation of the ligand/drug molecule inside the protein receptor or enzyme [4]. Computer aided drug design is very important for most of the pharmaceutical companies [4-8]. Most of the commercial drugs available in the market are designed by the computer aided methods [9]. In 2013, three computational chemists Martin Karplus, Michael Levitt and Arieh Warshel won the Nobel Prize for their notable contribution for the development of multiscale modeling for complex chemical systems [10].

To perform docking studies, there are many docking tools available, some of which are free and some of the docking tools can be procured commercially. The most commonly used docking tools are Flex-X, AutoDock, and Gold and Dock [11-14]. In this study, we have employed Flex-X and AutoDock to screen the interaction of ligand with the enzyme. AutoDock is freeware and Flex-x has been procured. It is to note that docking simulations have different algorithms. Flex-X uses incremental reconstruction algorithm and AutoDock uses Lamarckian Genetic Algorithm (LGA) [11-12,15]. AutoDock by using Lamarckian Genetic Algorithm (LGA) explores the conformational space of the ligand. The LGA is a hybrid genetic algorithm (GA) with a local search method [12,16]. In the docking simulation, AutoDock uses two combined methods, viz. (1) rapid grid-based energy evaluation and (2) efficient search of torsional freedom [17]. AutoDock simulation run by mainly four steps: (1) preparation of coordinate files i.e. PDB file format of receptor and ligand are converted into PDBQT format, (2) Auto Grid calculations, wherein atomic affinity potentials of each atom of the ligand molecules are pre-calculated and the receptor is embedded in three-dimensional grid, (3) docking is performed using LGA and it is run many times

to get the several docked conformations and (4) analysis of the results using AutoDock tools [17]. There are mainly four steps for docking simulation using Flex-X: (1) receptor definition, (2) ligand and docking library composition, (3) docking and (4) analysis [18]. The docking tools in general functions with an aim at positioning of a flexible ligand/drug molecule inside the rigid binding site [19]. The selection of docking tools for screening of ligand/drug molecule with the protein/enzyme is largely empirical and hence the comparative study is required. There are reports, where such comparisons have been carried with specific proteins and ligand molecules.

In serine hydrolase, acetylcholinesterase (AChE, acetylcholine acetylhydrolase, E C 3.1.1.7) is an essential enzyme that terminates nerve impulses at cholinergic synapses found at neuromuscular junctions. Acetylcholine (ACh) is hydrolysed by the serine residue of acetylcholinesterase (AChE) enzyme and produce acetic acid and choline. Due to this process ACh transmits information from one neuron to another neuron [20-24]. The higher second-order rate constant [>108 (mol/L)-1·s-1] of the AChE catalytic hydrolysis activity is remarkable for its enzymatic activity [25-27]. Inhibition of the AChE by Organophosphorus (OP) compounds has severe effect to the human due to the formation of covalent conjugate by phosphylation. The formation of conjugate due to the phosphylation stop the normal activity of AChE, resulting in accumulation of Ach which may lead to death [20,26,28-30]. The normal activity of AChE can be restored by introducing a nucleophilic reactivator such as oxime compounds to eliminate the OP from the conjugate [29,31]. Till date there is no universal drug like candidate which can treat OP-inhibited AChE and therefore this is an active field of research [31-35].

Reports are scarce in the literature on the screening of antidotes with OPs-inhibited AChE with docking tools. In this article, we have performed docking study between Organophosphorus (OP) inhibited AChE as protein and HLö-7, Ortho-7 and HI-6 as antidotes using two widely used docking tools Flex-X and AutoDock. The main objective of this study is to identify the more accurate docking tool for screening the antidote for the reactivation of the OP inhibited AChE.

MATERIALS AND METHODS

For all the docking studies, receptor molecules were taken as a rigid body with a grid potential to evaluate the scoring functions. Docking simulations were done using flexible ligands for the employed docking tools. In the case of AutoDock, both the receptor and ligand were taken as PDB format. Crystals of tabun-inhibited *m*AChE with HLö-7 (2JEZ), tabun-inhibited *m*AChE with Ortho-7 (2JF0) and sarin-inhibited *m*AChE with HI-6 (5FPP) were docked with the crystals of HLö-7, Ortho-7and HI-6 respectively using Flex-X and AutoDock.

We have considered tabun-inhibited *m*AChE with HLö-7 and Ortho-7 and sarin-inhibited *m*AChE with HI-6 for the docking studies using a grid based AutoDock 4.2 program [36]. To explore the grid space and to execute energy assessment on the position of the ligand with respect to the target energy grids Lamarckian Genetic Algorithm (LGA) is utilized by the AutoDock. The grid box dimension of 70-70-70 Å was kept during the Autogrid simulation to keep the receptor and ligand in the grid map preparation. During docking simulation, all the receptor molecules explore six spatial degrees of freedom along with the associated torsion. The interaction energy is calculated at each step of the docking simulation until the global minimum is energy reached.

For Flex-X (LeadIT 2.0.2) all the receptor molecules viz. tabun-inhibited *m*AChE with HLö-7 and Ortho-7and sarin-inhibited *m*AChE with HI-6were taken in PDB format for docking simulation. Ligand molecules were taken in the mol2 format. The default settings provided in the Flex-X was used for the docking simulation. After uploading the receptor molecule, 6.5Å cut-off distance was selected from the defined reference ligand. The crystal structure of the ligand in mol2 format was uploaded and docking simulations were run.

RESULTS AND DISCUSSION

In this study, we have considered the approach of re-docking to examine the reliability of two docking programs especially for OPs-inhibited AChE. Re-docking is the first step in any virtual screening analysisfor the discovery of ligands, inhibitors and drug candidates. The total number and percentage of docked pose of the HLö-7 from Flex-X and AutoDock results are plotted in Figure (1) with respect to the root mean square deviation (RMSD) values from the original crystallographic conformation. Flex-X has given total 199 numbers of docked poses and AutoDock has given total 100 docked poses. Among the two docking tools, Flex-X has given lowest RMSD value (1.40) for HLö-7 with respect to crystallographic conformation. Lowest RMSD value obtained for HLö-7 using AutoDock is 6.75, which is significantly higher than the value obtained using Flex-X. There are significant number (21) of docked poses having RMSD values <2 for Flex-X. This lower RMSD value with respect to the crystallographic structure reveals the better accuracy of the docking tool. Since the number of docked poses is different for Flex-X and AutoDock, we have drawn the percentage number of docked poses against RMSD values (Figure 1). Around 10.6% of the total docked poses are <2 RMSD value for HLö-7 in the case of Flex-X.

In the case of Ortho-7 and tabun-inhibited *m*AChE, there are no docked poses under the RMSD value<2 for the docking tools Flex-X and AutoDock (Figure 2). For Flex-X total 20 docked poses and for AutoDock total 101 docked poses have been obtained. For Ortho-7, the lowest RMSD value 3.70 is observed in the case of Flex-X, whereas the lowest RMSD value given by the AutoDock is 5.07. In Flex-X, 10% of the docked poses are having <4 RMSD value, whereas only 1% docked poses have <6 RMSD value in the case of AutoDock.

In the case of HI-6 and sarin-inhibited *m*AChE, observed RMSD values in AutoDock simulations are higher than that of the values obtained for HLö-7 and Ortho-7 (Figure 3). The lowest RMSD value 1.87 is observed in the case of Flex-X and for AutoDock the lowest value is 5.99. There are total 4, 47 and 55 docked poses having less than >2, >4 and >6 RMSD values respectively in the case of Flex-X. There is only one pose having <6 RMSD value in the case of AutoDock. Most of the docked poses 98.7% (88.2% + 6.6% + 3.9 5%) of AutoDock are having more than 6 RMSD values, whereas 99.5% (1.8% + 21.5% + 25.1% + 51.1%) of the docked structure are having < 6 RMSD values in the case of Flex-X.

Scoring function plays a vital role for the screening of

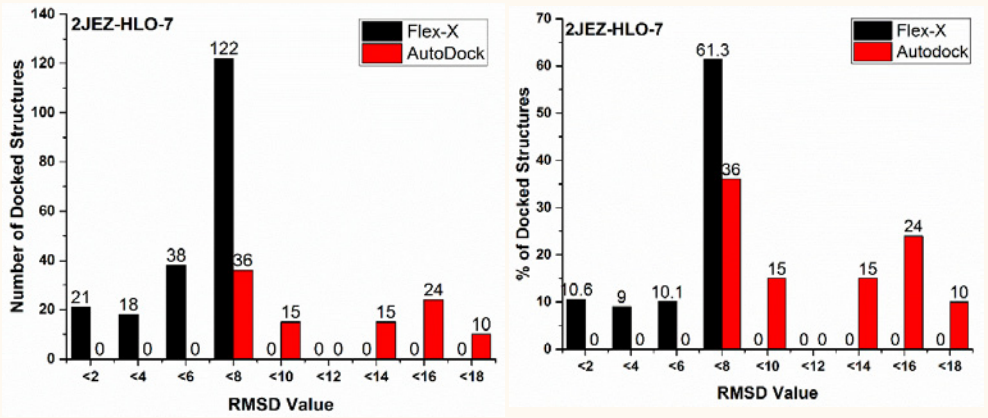

Figure 1 Docking pose of HLö-7 in the tabun-inhibited mAChE with reference to crystallographic pose.

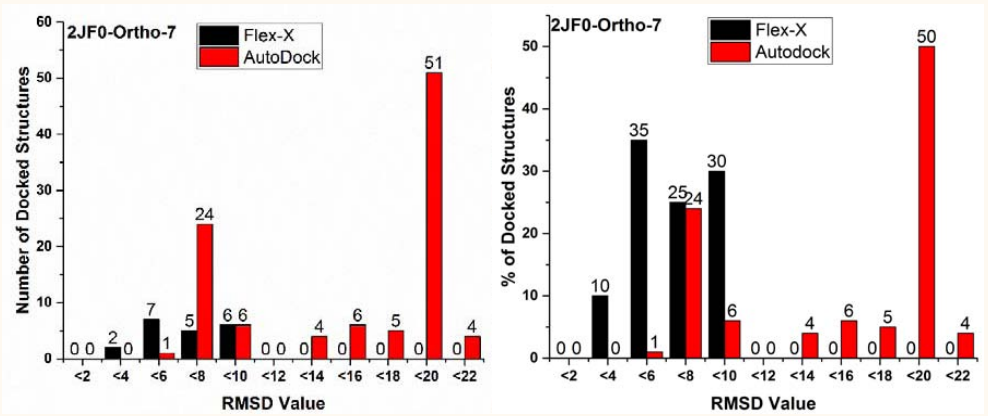

Figure 2 Docking pose of Ortho-7 in the tabun-inhibited mAChE with reference to crystallographic pose.

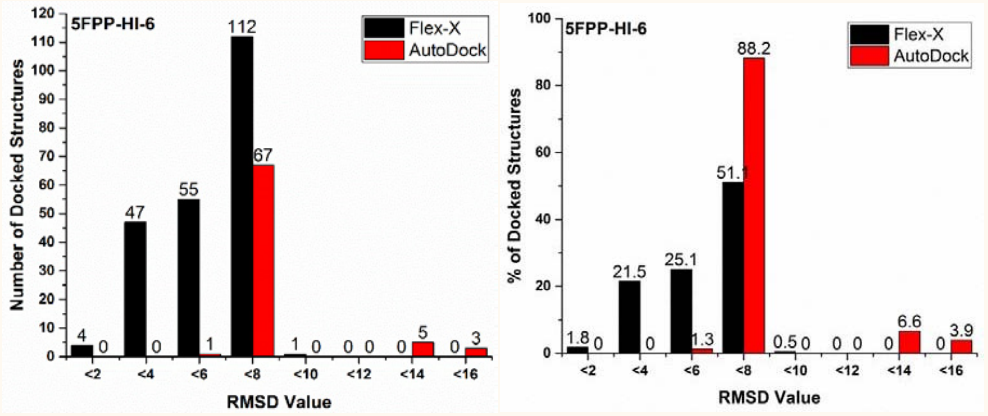

Figure 3 Docking pose of HI-6 in the sarin-inhibited mAChE with reference to crystallographic pose.

ligand molecules for interaction with protein/enzyme. Scoring function estimates the interaction energies of the ligand and receptor molecules and based on the relative binding affinities of the ligand, rank the docked structures [37]. The scoring function is influenced by many parameters such as concerning input preparation, docking algorithm and the terms of the scoring functions [37]. The scoring in Flex-X is done by using Böhm scoring function which consists of entropy loss for ligand binding, hydrogen bonding, electrostatic interaction, interaction between the aromatic groups and hydrophobic interactions [38]. AutoDock uses energy based scoring function which consists of short-ranged van der Waals and electrostatic interactions, entropy loss for ligand binding, hydrogen bonding and solvation energy [38].

The scoring obtained for tabun-inhibited *m*AChE with HLö-7 (2JEZ), tabun-inhibited *m*AChE with Ortho-7 (2JF0) and sarin-inhibited *m*AChE with HI-6 (5FPP) with Flex-X and AutoDock

suggests that the drug molecules bind strongly with the OPS-inhibited enzyme in the former case compared to the later.

We have also calculated inhibition constant (K_i) of reactivator molecules for docking score i.e. binding free energy of the reactivator molecule using the Equation-1 [39,40].

$$K_i = e^{\frac{\Delta G \times 1000}{R_{cal} \times TK}} \quad (1)$$

Where ΔG is the binding free energy, R_{cal} is 1.98179 and TK is 298 K.

In the Table (1), we have also reported the K_i values correspond to the best docking score [41-42].

Further, we have also examined the snapshots of the docked ligand based on the best RMSD values with respect to the crystal structure of the ligand in the OP-inhibited AChE to examine the pose deviation.

From the snapshot results (Figure 4) it is observed that the pose of the best docked structure (based on RMSD vales) is similar to the crystal pose of the HLö-7 in the case of Flex-X than that of the AutoDock tools for tabun-inhibited *m*AChE. Moreover, the observed distance between the oxygen atom of the oxime group at the para position of the pyridinium ring of the HLö-7 and phosphorus atom of the active serine (SUN203) is 4.52 Å and 9.8 Å in the case of Flex-X and AutoDock respectively. In the case of 2JEZ crystal, this distance is 5.59 Å. Therefore, it is observed that in the case of AutoDock tool there is a larger deviation from the crystal structure of 2JEZ.

For tabun-inhibited *m*AChE with Ortho-7 (2JF0), snapshot figure (Figure 5) of the best docked structure based on RMSD values shows that the pose of the docked Ortho-7 is close to

Table 1: Top Scoring/Binding energy (in kcal/mol) of the docked conformers obtained by using Flex-X and AutoDock for tabun-inhibited *m*AChE with Ortho-7 (2JF0), tabun-inhibited *m*AChE with HLö-7 (2JEZ) and sarin-inhibited *m*AChE with HI-6 (5FPP).

Docking Tools	Tabun-inhibited *m*AChE with Ortho-7 (2JF0)	Tabun-inhibited *m*AChE with HLö-7 (2JEZ)	Sarin-inhibited *m*AChE with HI-6 (5FPP)
Flex-X	-33.4	-15.5	-20.9
*K_i(μM)	3.19×10^{-19}	4.29×10^{-6}	4.70×10^{-10}
AutoDock	-6.93	-6.61	-7.84
*K_i(μM)	8.27	14.2	1.77

*calculated using Eq-1.
Abbreviations: AChE: Acetylcholinesterase; ACh: Acetylcholine; PDB: Protein Data Bank; LGA: Lamarckian Genetic Algorithm; GA: Genetic Algorithm; OP: Organophosphorus; RMSD: Root Mean Square Deviation

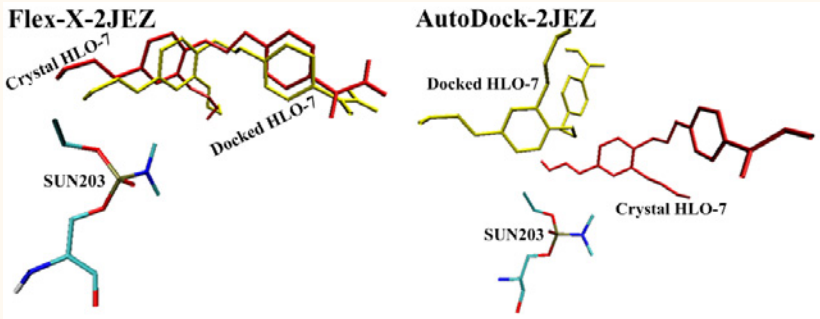

Figure 4 Best docking pose of HLö-7 based on the RMSD values with reference to crystallographic pose in tabun-inhibited mAChE.

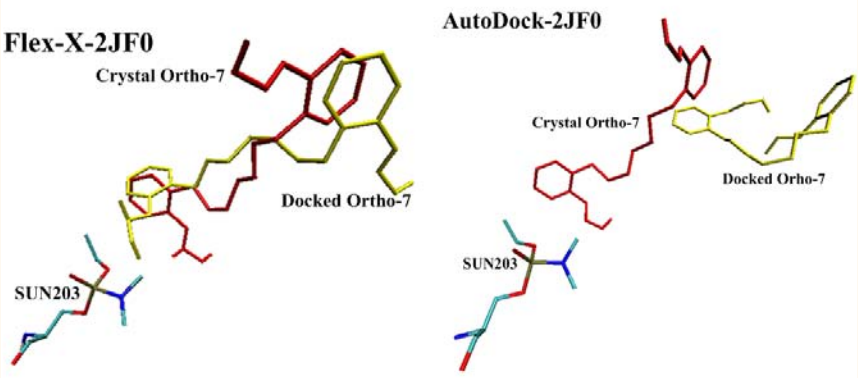

Figure 5 Best docking pose of Ortho-7 based on the RMSD values with reference to crystallographic pose in tabun-inhibited mAChE.

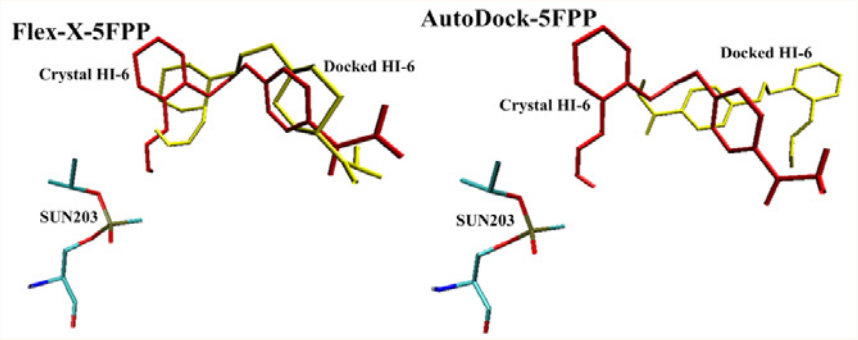

Figure 6 Best docking pose of HI-6 based on the RMSD values with reference to crystallographic pose in sarin-inhibited mAChE.

the crystal pose of Ortho-7 in the case of Flex-X than that of the AutoDock tool. The distance between the oxygen atom of the oxime group near to the active serine (SUN203) and phosphorus atom of the SUN203 is 3.54 Å which is more close to the distance found in the crystal structure (6.74 Å) in the case of Flex-X, whereas the distance measured from the AutoDock tool is 18.53 Å.

From the snapshot (Figure 6) of sarin-inhibited *m*AChE, it is observed that the best docked pose is similar with respect to the crystal structure in the case of Flex-X. The oxime oxygen of the best docked structure is very close (4.84Å) to the phosphorus atom of active serine (SUN203) of the sarin-inhibited *m*AChE with respect to the distance observed in the crystal (3.26Å). There is a large deviation of the docked pose from the crystal pose of HI-6 for AutoDock. Moreover, the oxime group of the HI-6 is situated away from the phosphorus atom of the active serine (SUN203) in the case of AutoDock best docked structure.

CONCLUSION

In the work, we have examined the screening results of ligand/small molecules with enzyme using the docking tools Flex-X and AutoDock. The interaction of antidotes with OP-inhibited AChE has been evaluated using these two docking tools. Flex-X showed superior binding affinity of drug molecules with OP-inhibited AChE. Flex-X takes much less time to give the screen results compared to the AutoDock for similar systems. In terms of RMSD values, Flex-X has given lower values i.e., 1.35, 3.26 and 1.87 for tabun-inhibited *m*AChE with HLö-7 (2JEZ), tabun-inhibited *m*AChE with Ortho-7 (2JF0) and sarin-inhibited *m*AChE with HI-6 (5FPP) respectively, whereas AutoDock has given 6.75, 5.07 and 5.99, respectively for same systems. The scoring observed with these two docking tools also suggests that Flex-X yields better binding of the antidotes with OP-inhibited AChE. Further, the posing of the best docked conformer is much closer to that of the crystal structure for all the three systems in the case of Flex-X. This clearly shows that the commercially available package surpasses the freely available docking program in all parameter examined. Therefore, this study reveals that in the discovery of new antidotes for the treatment of OP-inhibited AChE, Flex-X can perform better than that of AutoDock.

ACKNOWLEDGEMENTS

CSIR-CSMCRI Registration no: 137/2016. Shibaji Ghosh acknowledges AcSIR and CSIR-CSMCRI for providing him the opportunity for the doctoral research program. NBC is thankful to CSIR New Delhi, India and RL is thankful to UGC, New Delhi, India. BG thanks (MSM, SIP, CSIR, and New Delhi) and Department of Atomic Energy-Board of Research in Nuclear Sciences, Mumbai for financial support. We thank the reviewer for valuable suggestions.

REFERENCES

1. Michael L, Christopher E, Paula S. Comparison of current docking tools for the simulation of inhibitor binding by the transmembrane domain of the sarco/endoplasmic reticulum calcium ATPase. Biophys Chem. 2010; 150: 88-97.
2. Taylor RD, Jewsbury PJ, Essex JW. A review of protein-small molecule docking methods. J Comput Aided Mol Des. 2002; 16: 151-166.
3. Lengauer T, Rarey M. Computational methods for biomolecular docking. Curr Opin Struct Biol. 1996; 6: 402-406.
4. Chen YC. Beware of docking! Trends Pharmacol Sci. 2015; 36: 78-95.
5. Warren GL, Do TD, Kelley BP, Nicholls A, Warren SD. Essential considerations for using protein-ligand structures in drug discovery. Drug Discov Today. 2012; 17: 1270-1281.
6. Merz KM, Ringe JD, Reynolds CH. Structure- and Ligand-Based Approaches. Cambridge University Press 2010; 11: 165-178.
7. Zheng M, Liu X, Xu Y, Li H, Luo C, Jiang H. Computational methods for drug design and discovery: focus on China. Trends Pharmacol Sci. 2013; 34: 549-559.
8. Pei J, Yin N, Ma X, Lai L. Systems biology brings new dimensions for structure-based drug design. J Am Chem Soc. 2014; 136: 11556-11565.
9. Sliwoski G, Kothiwale S, Meiler J, Lowe EW. Computational methods in drug discovery. Pharmacol Rev. 2013; 66: 334-395.
10. The Nobel Prize in Chemistry 2013. Nobel Media AB. 2014.
11. Rarey M, Kramer B, Lengauer T, Klebe G. A fast flexible docking method using an incremental construction algorithm. J Mol Biol. 1996; 261: 470-489.
12. Morris GM, Goodsell DS, Halliday RS, Huey R, Hart WE, Belew RK, et al. Automated docking using a Lamarckian genetic algorithm and an empirical binding free energy function. J Comput Chem. 1998; 19: 1639-1662.
13. Jones G, Willett P, Glen RC, Leach AR, Taylor R. Development and validation of a genetic algorithm for flexible docking. J Mol Biol. 1997; 267: 727-748.
14. Kuntz ID, Blaney JM, Oatley SJ, Langridge R, Ferrin TE. A geometric

approach to macromolecule-ligand interactions. J Mol Biol. 1982; 161: 269-288.

15. Osterberg F, Morris GM, Sanner MF, Olson AJ, Goodsell DS. Automated docking to multiple target structures: incorporation of protein mobility and structural water heterogeneity in AutoDock. Proteins. 2002; 46: 34-40.

16. Chikhi A, Bensegueni A. Comparative Study of the Efficiency of Three Protein-Ligand Docking Programs. J Proteomics Bioinformatics. 2008; 1: 161-165.

17. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, et al. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. J Comput Chem. 2009; 30: 2785-2791.

18. Katrin Stierand, Marcus Gastreich. Pose View. 2011.

19. Nabuurs SB, Wagener M, de Vlieg J. A flexible approach to induced fit docking. J Med Chem. 2007; 50: 6507-6518.

20. Sussman JL, Harel M, Frolow F, Oefner C, Goldman A, Toker L, et al. Atomic structure of acetylcholinesterase from Torpedo californica: a prototypic acetylcholine-binding protein. Science. 1991; 253: 872-879.

21. Barnard EA. The Peripheral Nervous System. New York. 1974; 201-224.

22. Katz B. Nerve, Muscle, and Synapse. New York. 1966.

23. Lo R, Chandar NB, Ghosh S, Ganguly B. The reactivation of tabun-inhibited mutant AChE with Ortho-7: steered molecular dynamics and quantum chemical studies. Mol Biosyst. 2016; 12: 1224-1231.

24. Chandar NB, Ghosh S, Lo R, Banjo S, Ganguly B. In silico studies on the role of mutant Y337A to reactivate tabun inhibited mAChE with K048. Chem Biol Interact. 2015; 242: 299-306.

25. Kesharwani MK, Ganguly B, Das A, Bandyopadhyay T. Differential binding of bispyridinium oxime drugs with acetylcholinesterase. Acta Pharmacol Sin. 2010; 31: 313-328.

26. Quinn DM. Acetylcholinesterase: enzyme structure, reaction dynamics, and virtual transition states. Chem Rev. 1987; 87: 955-979.

27. Voet D, Voet JG. Biochemistry. 2nd Edn. Wiley & Sons.1995.

28. Sussman JL, Harel M, Silman I. Three-dimensional structure of acetylcholinesterase and of its complexes with anticholinesterase drugs. Chem Biol Interact. 1993; 87: 187-197.

29. Musilek K, Kuca K, Jun D, Dolezal M. Progress in synthesis of new acetylcholinesterase reactivators during the period 1990-2004. Current Organic Chem. 2007; 11: 229-238.

30. Marrs TC. Organophosphate poisoning. Pharmacol Ther. 1993; 58: 51-66.

31. Kassa J. Review of oximes in the antidotal treatment of poisoning by organophosphorus nerve agents. J Toxicol Clin Toxicol. 2002; 40: 803-816.

32. Worek F, Wille T, Koller M, Thiermann H. Structural requirements for effective oximes-Evaluation of kinetic in vitro data with phosphylated human AChE and structurally different oximes. Chem. Biol. Interact. 2013; 203: 125-128.

33. Kassa J, Karasova JZ, Sepsova V, Bajgar J. A comparison of the reactivating and therapeutic efficacy of the newly developed bispyridinium oxime K203 with currently available oximes, in sarin poisoned rats and mice. J Appl Biomed. 2011; 9: 225-230.

34. Kassa J, Karasova JZ, Kuca K, Musilek K. A comparison of the reactivating and therapeutic efficacy of newly developed oximes (K347, K628) with commonly used oximes (obidoxime, HI-6) against tabun in rats and mice. Drug Chem Toxicol. 2010; 33: 227-232.

35. Bajgar J, Fusek J, Kuca K, Bartosova L, Jun D. Treatment of organophosphate intoxication using cholinesterase reactivators: Facts and fiction. Mini Rev Med Chem. 2007; 7: 461-466.

36. Autodock. Edn 4.2. The Scripps Research Institute. 2007.

37. Schulz-Gasch T, Stahl M. Scoring functions for protein-ligand interactions: a critical perspective. Drug Discov Today Technol. 2004; 1: 231-239.

38. Bursulaya BD, Totrov M, Abagyan R, Brooks CL. Comparative study of several algorithms for flexible ligand docking. J Comput Aided Mol Des. 2003; 17: 755-763.

39. Iman M, Saadabadi A, Davood A. Docking studies of phthalimide pharmacophore as a sodium channel blocker. Iran J Basic Med Sci. 2013; 16: 1016-1021.

40. Iman M, Saadabadi A, Davood A. Molecular docking analysis and molecular dynamics simulation study of ameltolide analogous as a sodium channel blocker. Turk J Chem. 2015; 39: 306-316.

41. AzamF, MadiAM, AliHI. Molecular docking and prediction of pharmacokinetic properties of dual mechanism drugs that block MAO-B and adenosine A2A receptors for the treatment of parkinson's disease. J Young Pharm. 2012; 4: 184-192.

42. Bhattacharjee AK, Kuca K, Musilek K, Gordon RK. In silico pharmacophore model for tabun-inhibited acetylcholinesterase reactivators: a study of their stereoelectronic properties. Chem Res Toxicol. 2010; 23: 26-36.

Cite this article

Ghosh S, Chandar NB, Lo R, Ganguly B (2016) Effective Docking Program for Designing Reactivator for Treating Organophosphorus Inhibited AChE. JSM Chem 4(4): 1032.