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A COMPARATIVE STUDY ON *IN SILICO* SOFTWARES IN STATISTICAL RELATION TO MOLECULAR DOCKING SCORES

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ABSTRACT

In the recent day, Computational drug discovery technique in Pharmaceutical research has successfully used with different algorithm programing software's. Commonly used to search algorithms in docking analysis are based on Genetic Algorithm, Monte Carlo, Fragment-based, Molecular Dynamics etc. In the aim of present study was to compare the docking score with Protein and Ligand interaction using various molecular docking software's. Four different algorithm used as Autodock vina, iGemdock, Hex and LeDock for molecular docking with Rutin, Stigmasterol, Quercetin, Gallic acid and Coumarin. To find on strong relationship between Autodock vina vs iGemdock r = 0.99831, Autodock vina vs Hex r = 0.94002, iGemdock vs Hex r = 0.93189, Autodock vina vs LeDock r = 97283, iGemdock vs LeDock r = 96132 and Hex vs LeDock r = 96627. Phytocompounds binding scores was a strong relationship on between the algorithm based Molecular docking software's, they are phytocompounds active scores were each software finds out on Rutin < Stigmasterol < Quercetin < Gallic acid < Coumarin active score was reported in 1HD2 protein. Overall that docking scores are similarly strong relationship in all four software's between the scores according to algorithm based program thereby may use any software for protein and ligand interactions.

Keywords: Computational analysis, Molecular docking, Statistical analysis, Docking scores relationship, 1HD2, Phytocompounds.

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INTRODUCTION

Molecular docking is one of the most used methods in Structure Based Drug Design of ability to predict of ligands binding with macromolecule binding site (Meng *et al.,* 2011). Current pharmaceutical research was successfully molecular modeling methods, within a variety of computational drug discovery program to the biological and chemical systems. The computational and experimental strategies has been of great value in the identification and development of novel compounds, variety of docking algorithms are available in each methods of fundamental importance in the development of effective strategies and the generation (Leonardo *et al.,* 2015). Understanding the Structure Based Drug Design principles which small-molecule ligands recognize and interact with macromolecules is of great importance in pharmaceutical research and development (Blaney, 2012).

Molecular docking method helps in predicting the bound conformation of a protein to ligand, docking algorithms targets to finding best orientation of these ligand and macromolecules such that have the minimum energy as scored by a predefined scoring function (Atilgan and Hu, 2011). Docking algorithm relies on predicting the correct placement of ligands within the receptor binding pocket of protein. Molecular docking program the interaction of chemical compounds with the macromolecule by scoring functions, calculates the free energy of binding between a ligand and macromolecule, which based on the estimates of the total energy of intermolecular forces of Van der Waals, hydrogen bonding, electrostatic, and hydrophobic etc., In the present study statistically relationship between the molecular docking score to find on correlation matrix analysis in 1HD2 (Human peroxiredoxin 5) protein binding on Quercetin, Coumarin, Gallic acid, Stigmasterol and Rutin Phytocompounds.

COMPUTATIONAL ANALYSIS

Ligand and protein preparation

Ligands (Quercetin, Coumarin, Gallic acid, Stigmasterol and Rutin) were obtained from Pubchem database, ligands were converted in to other format using Open bable software and Protein obtained from PDB database. 1HD2 protein preparation was generally to have a remove of all water molecules and any other Ligand molecules prior to docking; using Pymol software.

Molecular docking

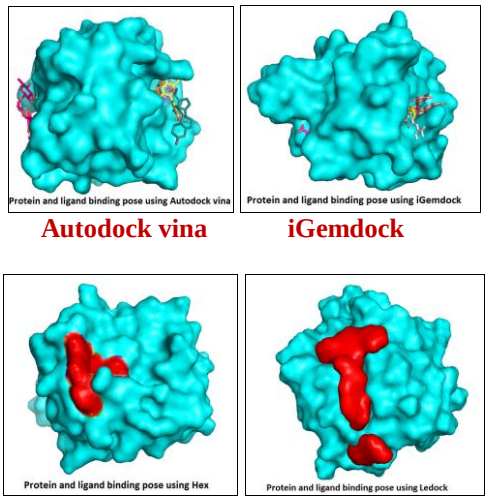
Molecular docking software used in PyRx 0.8, iGemdock 2.1, Hex 8.0.0 and LeDock. PyRx virtual screening tool (Autodock vina program) software for grid dimension prepared (Center x = 6.75, center y = 43.14 and center z = 19.55) (Trott and Olson, 2010). iGemdock application first we have to select the protein binding site and ligands, Virtual screening procedure of iGemdock consists of four main steps (Population size = 200, Generations = 70, Number of solutions = 2 and Default setting = Standard docking) (Hsu *et al.*, 2011). Hex is an interactive molecular graphics program, it used for small molecules (Ligand) docking with macromolecules (Protein), Hex software parameters were (Correlation type = Shape only, FFT mode = 3D fast line, Grid dimension = 0.6, Receptor range = 180, Ligand range = 180, Twist range = 360, Distance range = 40) used, the receptor was docked (http://www.hex.loria.fr/dist50). Graphic interface of LeDock contains is two tabs, one tabs of LePro used for protein process and another one is LeDock used for docking study (Zhang and Zhao, 2016). Protein and ligand interaction analysis used in Pymol software.

Statistical analysis

Molecular docking score was analysis on correlation coefficient (r) statistic, relationship between the docking software using MS-excel ver. 2013, statistically significant $P<0.05$ (Two tail).

RESULTS AND DISCUSSION

Computational technique of Molecular modeling that fits a small molecule (Ligand/Inhibitors) into a target's binding sites of macromolecules. In the present study relationship between docking scores, associated on Autodock vina, iGemdock, Hex and LeDock between the molecular docking software. In this study, the four algorithm based software such as Autodock vina (New generation of Auto Dock, Autodock as Lamarckian Genetic Algorithm), iGemdock (Generic evolutionary method), Hex (Spherical Polar Fourier correlations) and LeDock (Evolutionary algorithm) result output scores were reported on table 1 and best binding pose visual represent in plate 1. Commonly used search algorithms used in docking analysis are based on Genetic Algorithm, Monte Carlo, Fragment-based, Molecular Dynamics etc., (Mohan *et al.*, 2005).



Autodock vina **iGemdock**

Hex **LeDock**

Plate.1: Best binding pose on Ligands with 1HD2 protein

Table.1: Ligands binding with 1HD2 protein molecular docking scores

Phytocompounds	Molecular docking scores			
	Autodock vina (Binding affinity (Kcal/mol))	**iGemdock** (Total energy (Kcal/mol))	**Hex** (Energy values (Kcal/mol))	**LeDock** (Binding affinity (Kcal/mol))
Coumarin	-5.50	-74.81	-147.80	-2.90
Gallic acid	-5.70	-78.20	-147.99	-3.50
Quercetin	-6.80	-124.31	-213.35	-4.35
Rutin	-7.30	-141.35	-317.31	-5.66
Stigmasterol	-7.10	-136.13	-250.81	-5.18

The Genetic algorithms high computational cost associated with stochastic methods of the theory of evolution and natural selection applying concepts. They are Autodock vina was new generation of Autodock, Autodock as Lamarckian Genetic Algorithm, Autodock vina output score evaluates on Rutin was -7.30, Stigmasterol was -7.10, Quercetin was -6.80, Gallic acid was -5.70 and Coumarin -5.50 Binding affinity (Kcal/mol) was reported on 1HD2 protein binding scores. Genetic algorithms are an interesting application have used successfully for molecular docking programs such as AutoDock and Gold (Jones *et al.*, 1997).

iGemdock suite is an automated docking/screening tool used a generic evolutionary method for molecular docking and empirical scoring function. The search algorithm is taken as iGemdock consists of four main steps such as Population size 200, Generations 70, Number of solutions 2 and Default setting as standard docking to run. iGemdock output scores evaluate on Rutin was -141.35, Stigmasterol was -136.13, Quercetin was -124.31, Gallic acid was -78.20 and Coumarin was -74.81 Total energy (Kcal/mol) was reported on 1HD2 protein binding scores. iGemdock useful tool for molecular recognition and used to systematically evaluate and improve docking scoring function (Jinn-Moon Yang and Chun-Chen Chen, 2004).

Hex (Interactive Molecular Graphics Program) for calculating and displaying feasible docking modes of pairs of macromolecules, calculate ligand with protein docking assuming the ligand is rigid and it can superpose pairs of molecules using only 3D shapes knowledge. Spherical polar Fourier correlations were used to accelerate the calculations, and still one of few docking programs. Hex program docking parameters on Correlation type as Shape only, FFT mode 3D fast line, Grid dimension 0.6, Receptor range 180, Ligand range 180, Twist range 360, and Distance range 40 as receptor and ligands were docked in Hex program. Hex output score evaluate on Rutin was -317.31, Stigmasterol was -250.81, Quercetin was -213.35, Gallic acid was -147.99 and Coumarin was -147.80 Energy values (Kcal/mol) was reported on 1HD2 protein binding scores.

LeDock is evolutionary algorithm is first generation of docking pose is adopted in combination with simulated annealing search. It is flexible of small-molecule with macromolecule docking software (Zhang and Zhao, 2016). LeDock to study docking parameters in binding pocked on Xmin = -17.13 and Xmax = 23.88, Ymin = 1.75 and Ymax = 41.38 while Zmin = -10.80 and Zmax = 30.35 where Number of binding poses on 20 and then Start docking. LeDock reported on Rutin was -5.66, Stigmasterol was -5.18, Quercetin was -4.35, Gallic acid was -3.50 and Coumarin was -2.90 binding affinity (Kcal/mol) was reported on 1HD2 protein.

Overall binding scores were evaluated on Autodock, iGemdock, Hex and LeDock molecular docking software carried on each docking score was found to be in the following order Rutin < Stigmasterol < Quercetin < Gallic acid < Coumarin.

Table.2: Find out on Correlation coefficient (r) matrix (N=5)

Molecular docking scores	Autodock vina	Gemdock	Hex	Ledock
Autodock vina	1			
Gemdock	0.99831**	1		
Hex	0.94002*	0.93189*	1	
Ledock	0.97283**	0.96132**	0.96627**	1

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).
N=5 (Coumarin, Gallic acid, Quercetin, Rutin and Stigmasterol).

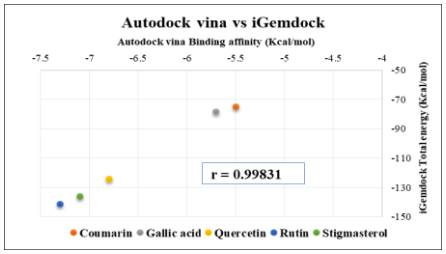


Fig.1: Autodock vina vs iGemdock

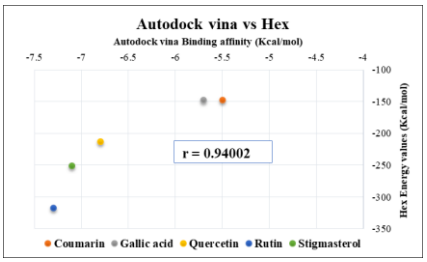


Fig.2: Autodock vina vs Hex

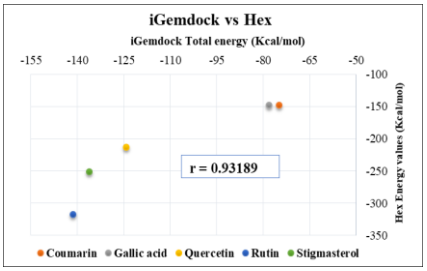


Fig.3: iGemdock vs Hex

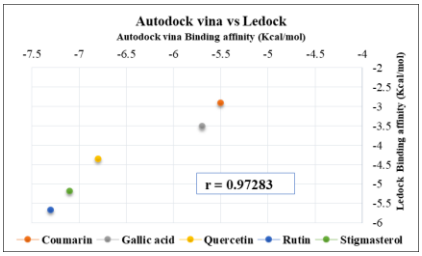


Fig.4: Autodock vs LeDock

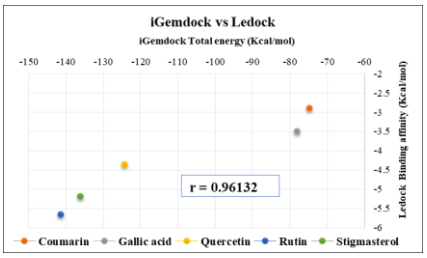


Fig.5: iGemdock vs LeDock

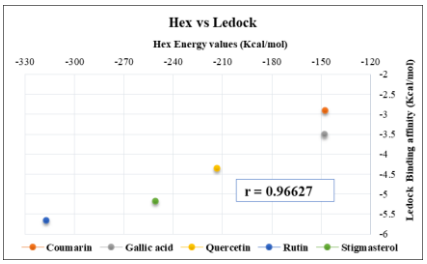


Fig.6: Hex vs LeDock

The correlation matrix represented in table 2. Docking scores relationship analysis in correlation coefficient methods were used. The correlation value was strong relationship the between the docking program. Figure 1 Autodock vina vs iGemdock r = 0.99831**, figure 2 Autodock vina vs Hex r = 0.94002*, figure 3 iGemdock vs Hex r = 0.93189*, figure 4 Autodock vina vs LeDock r = 0.97283**, figure 5 iGemdock vs LeDock r = 0.96132** and figure 6 Hex vs LeDock r = 0.96627** in the correlation coefficient (r) value was statistically significant at 0.05 for two tailed. Molecular docking scores were each phytocompound active score were strong relationship with binding on 1HD2 protein. Tanguenyongwatana and Nathjanan Jongkon (2016) correlated with the inhibitory concentrations (IC_{50}) vs docking score performed. Ligand K_i values with correlated on binding scores were reported (Jun *et al.*, 2015). Overall final output scores strong relationship between in the algorithm based docking programs find in this study on phytocompounds docking with Human peroxiredoxin 5 protein (1HD2).

CONCLUSION

The protein and ligand interaction plays a strong relationship role in algorithm based molecular modeling program. Present study concluded that docking scores are similarly strong relationship in all four software's between the scores according to algorithm and thereby may use any software for protein and ligand interactions for best results.

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