Journal of Computational Methods in Molecular Design, 2015, 5 (3):104-105

Scholars Research Library
(http://scholarsresearchlibrary.com/archive.html)

ISSN : 2231- 3176
CODEN (USA): JCMMDA

Chalcones: Potential antidengue targets *in silico* approach

M. M. V. Ramana*, Prasanna B. Ranade, Rahul R. Betkar, Amey P. Nimkar, Balaji C. Mundhe and Shanta Bhar

Department of Chemistry, University of Mumbai, Santacruz (E), Mumbai, India
**Corresponding E-mail ramanammv@yahoo.com*

ABSTRACT

Dengue caused by a bite of aedes aegypti mosquito and currently having no approved drug or effective antiviral therapy. Thus there is need to design effective antidengue compound. The docking study of various chalcones against dengue virus NS2B/NS3 protease is discussed.

Keywords: Chalcones, Dengue Virus, NS2B/NS3 Protease, Glide, Docking.

INTRODUCTION

Dengue, a viral disease caused by bite of *aedes aegypti* mosquito. Dengue is RNA virus, falls under *flaviviridae* family. [1] Dengue has four serotypes viz., DENV-1, DENV-2, DENV-3 and DENV-4. [2] It has three structural proteins capsid C, premembrane prM and envelope E while seven nonstructural proteins such as NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5. [3]

Dengue virus protease plays a central role in dengue virus life cycle by cleavage of polypeptide of both host cell and virus encoded two component protease NS2B-NS3. [4]

Currently, there is no effective antiviral therapy or drug is available against dengue, hence there is need to design and develop a safe and potent drug. The catalytic triad of dengue virus protease is located in region His51, Asp75, and Ser135. [5]

Chalcones were known to possess various biological activities including anti HIV [6], anticancer [7], anti-inflammatory [8], antifungal [9] and antibacterial. [10] Trihydroxyhalcones were reported to exhibit antidengue activity. [11] In present work, monohydroxy chalcones and dihydroxy chalcones were docked against dengue virus NS2B/NS3 protease (PDB ID 2FOM).

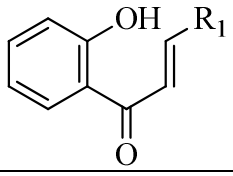
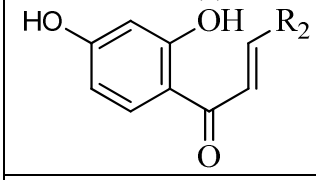
MATERIALS AND METHODS

There are number of software's were used to perform docking study viz., *gold*, [12] *autodock* [13] *etc*. Docking of chalcone molecules were performed on g*lide* docking software. [14] The crystal structure of dengue virus NS2B/NS3 protease (PDB ID 2FOM) was obtained from Protein Data Bank (www.rcsb.org/pdb).During receptor preparation, using *Protein Preparation Wizard*, residual chlorine atoms, glycerol molecules and water molecules were removed. The ligands were built in *maestero* in required format. The OPLS 2005 force field is applied. The receptor grid was generated at catalytic triad of dengue virus NS2B/NS3 protease using *Receptor Grid Generation*. For docking studies *Extra Precision* (XP) mode was used. The docked molecules are presented in Table 1.

RESULTS AND DISCUSSION

Several chalcones were docked against dengue virus NS2B/NS3 protease. Docked chalcones show comparable dock score with respect to reported pinostrobin chalcone. [15] From docking score it can be concluded that several chalcones have dock score comparable with respect to each other. The docking score of each chalcone is presented in Table 1.

Table 1:

Sr. No.	Chalcone (A) 	Dock Score	Sr. No.	Chalcone (B) 	Dock Score
	R_1			R_2	
1	4-Nitrophenyl	-5.75	19	2,4-Dihydroxyphenyl	-7.78
2	4-Hydroxy-3-ethoxyphenyl	-5.73	20	3-Hydroxy-4-methoxyphenyl	-7.17
3	3-Hydroxy-4-methoxyphenyl	-5.40	21	4-Chlorophenyl	-6.89
4	4-Hydroxyphenyl	-5.34	22	4-Nitrophenyl	-6.87
5	2-Hydroxyphenyl	-5.24	23	3-Hydroxyphenyl	-6.83
6	2,4-Dihydroxyphenyl	-5.22	24	4-Methylphenyl	-6.38
7	4-Methoxyphenyl	-5.16	25	Phenyl	-6.36
8	1-Napthyl	-5.13	26	2-Hydroxyphenyl	-6.18
9	2-Hydroxyphenyl	-4.9	27	3-Chlorophenyl	-6.04
10	3-Chlorophenyl	-4.81	28	4-Bromophenyl	-6.01
11	2-Napthyl	-4.78	29	4-Hydroxy-3-methoxyphenyl	-6.00
12	2-Chlorophenyl	-4.73	30	4-Methoxyphenyl	-5.71
13	4-Chlorophenyl	-4.68	31	1-Napthyl	-5.7
14	2-Thienyl	-4.62	32	2-Chlorophenyl	-5.7
15	Phenyl	-4.62	33	2-Napthyl	-5.47
16	4-Methylphenyl	-4.6	34	2-Thienyl	-5.44
17	4-Bromophenyl	-4.55	35	4-Hydroxyphenyl	-5.07
18	2-Furyl	-4.32	36	2-Furyl	-4.91

From docking score it is observed that almost all chalcones show comparable dock score to that of pinocembrin chalcone. [15] Therefore it can be concluded that docked chalcones have potential antidengue characteristics in *silico.*

CONCLUSION

From docking study it can be concluded that all docked chalcones possess potential antidengue characteristics in *silico.* Further chalcones (Entries 1, 2, 19 to 32) exhibited better docking score than pinocembrin chalcone. [15]

Acknowledgement
We gratefully acknowledge the financial support from Department of Chemistry, University of Mumbai and University Grants Commission, New Delhi, INDIA for the award of UGC-BSR Fellowship.

REFERENCES

[1] JG. R-P erez; GG.Clark ;DJ. Gubler ; P. Reiter ;EJ,Sanders; AV. Vorndam; *Lancet* **1998,** 352, 971–977.
[2] EA. Henchal; JR. Putnak. *Clin. Microbiol.Rev.* **1990,** 3, 376–396.
[3] TJ. Chambers; RC.Weir;A. Grakoui; DW. McCourt;JF. Bazan; RJ. Fletterick. *Proc. Natl.Acad.Sci.U.S.A.* **1990,** 87, 8898.
[4] HMK. Murthy;S. Clum; R. Padmanabhan. *J. Biol. Chem.* **1999**, 274, 5573–5580.
[5] RI. Brinkworth; DP. Fairlie; D. Leung; PR. Young *J. Gen. Virol.* **1999**,80,1167–77.
[6] H. Sharma; S. Patil; TW. Sanchez; N. Neamati; RF. Schinazi; JK. Buolamwini; *Bioorg. Med. Chem.* **2011,** 19, 2030
[7] S. Shenvi;K. Kumar; KS. Hatti; K. Rijesh; L. Diwakar; GC. Reddy; *Eur. J. Med. Chem.* **2013 ,**62, 435
[8] Z. Nowakowska; *Eur. J Med. Chem.* **2007,** 42,125-137.
[9] M. Subramanian; G. Vanangamudi; G. Thirunarayanan; *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2013**,110,116

[10] BT. Yin; CY. Yan; XM. Peng; SL. Zhang; S. Rasheed; RX. Geng; CH. Zhou; *Eur. J. Med. Chem.* **2014,** 71,148.
[11] TS. Kiat; R.Pippen; R. Yusof; H. Ibrahim;N. Khalid; N. A. Rahman; *Bioorganic & Med. Chem. Lett.* **2006**,16, 3337–3340.
[12] KM. Khalid; A. Wadood; M. Ali; U-H. Zaheer; M. Lodhi; K. Momin; P.Shahnaz; *J. Mol. Graph. & Model.* **2010**, 28,8, 792-798.
[13] GM. Morris; R. Huey; W. Lindstrom; MF. Sanner; RK. Belew; DS. Goodsell; AJ. Olson; *J. Comput. Chem.* **2009**, 30, 2785–2791
[14] Glide: Schroedinger, Portland OR. http://www.schroedinger.com.
[15] R. Othman; TS Kiat; N. Khalid; R. Yusof, EI. Newhouse; JS. Newhouse;NA. Rahman; *J.Chem.Inf. Model.* **2008,** *48*, 1582–1591.