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Research Article

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Flavones: Potential antidengue targets in *silico* approach

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ABSTRACT

Dengue is mosquito borne viral disease currently having no approved drug. Thus there is need of safe and potent antidengue drug. The present work describes the docking study of flavones against dengue virus NS2B/NS3 protease.

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

INTRODUCTION

Dengue virus belongs to *flaviviridae* family.[1] Dengue is caused by a bite of *Aedes aegypti* mosquito.[2] There are four serotypes of dengue viz., DENV1, DENV-2, DENV-3 and DENV-4. [3] Dengue virus has three structural proteins and seven nonstructural proteins. The structural proteins are capsid C, envelope E and premembrane prM. The nonstructural proteins are NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5. [4] The replication of dengue virus depends upon correct cleavage of polypeptide which requires both host cell proteases and the virus-encoded two-component protease NS2B-NS3. Thus NS2B/NS3 protease plays a central role in replication of dengue virus. [5] Therefore for designing a new antidengue core NS2B/NS3 protease is targeted the most. The catalytic triad of dengue virus protease is located in region His51, Asp75, and Ser135. [6]

Currently there is neither approved drug nor vaccine against dengue and therefore there is need to design and develop safe and effective antidengue drug.

Flavonoids were known to exhibit antiHIV [7], antimalarial [8], anticancer [9] and antibacterial [10] activities. Flavonoids are reported to exhibit antidengue activity. [11] In present work flavones were docked against dengue virus NS2B/NS3 protease (PDB ID 2FOM).

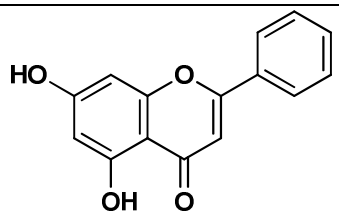
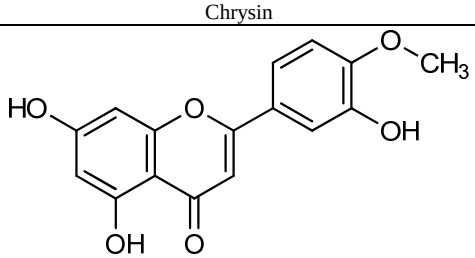
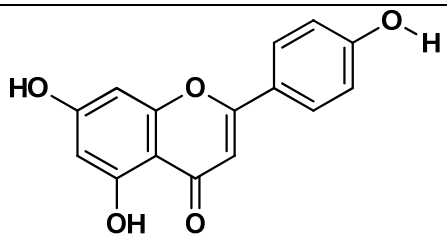
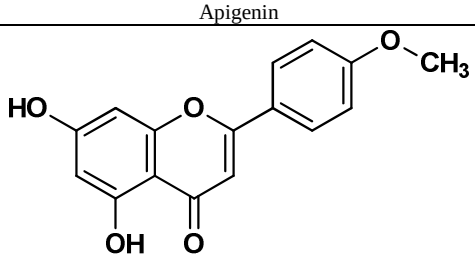
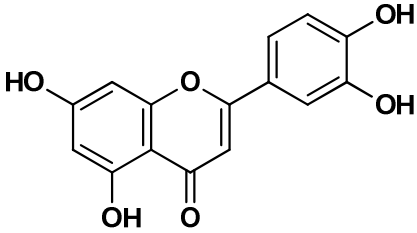
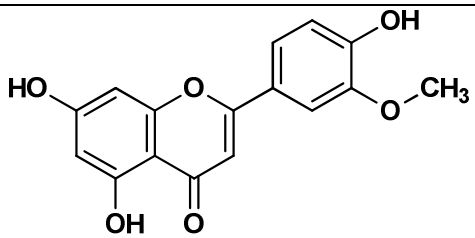
EXPERIMENTAL SECTION

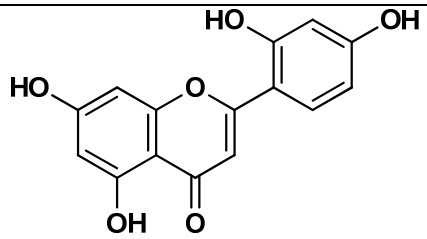
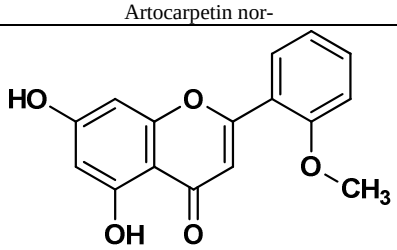
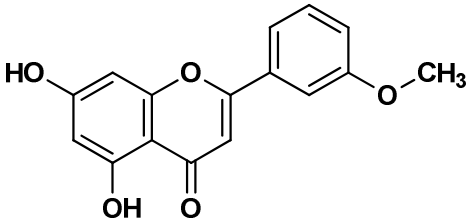
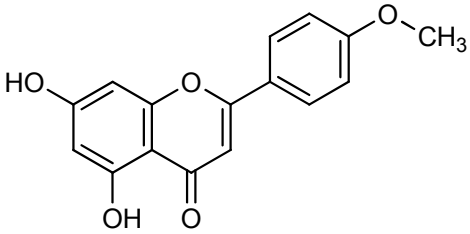
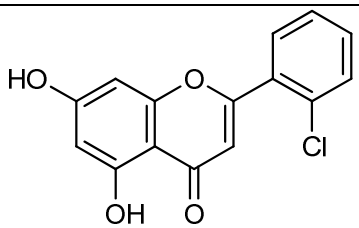
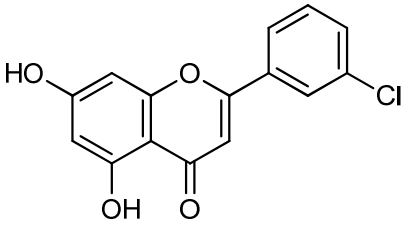
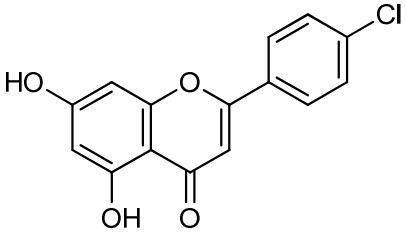
Glide [12] was used for performing docking studies. The dengue virus NS2B/NS3 protease structure was obtained from Protein Data Bank (www.rcsb.org/pdb) having accession code 2FOM. During receptor preparation, using *Protein Preparation Wizard*, residual chlorine atoms, glycerol molecules and water molecules 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. The docking poses of representative molecules are presented in Figure 1.

RESULTS AND DISCUSSION

A number of flavones were docked against dengue virus NS2B/NS3 protease. The docked flavones gave good dock score. The reported antidengue compounds were found to interact with Leu 149, Lys74, Trp83, Asn152 and Ser135.[13] The docked flavones also showed binding interactions with these amino acid residues hence have the potential to exhibit antidengue activity.

Table 1

No	Name and structure of molecule	Docking score (Glide Score)
1	 Chrysin	-5.06
2	 Diosmetin	-6.71
3	 Apigenin	-6.43
4	 Acaetin	-6.37
5	 Luteolin	-6.17
6	 Chrysoeriol	-6.39

7	 Artocarpetin nor-	-6.41
8	 5,7-dihydroxy-2-(2-methoxyphenyl)-4H-chromen-4-one	-5.55
9	 5,7-dihydroxy-2-(3-methoxyphenyl)-4H-chromen-4-one	-5.47
10	 5,7-dihydroxy-2-(4-methoxyphenyl)-4H-chromen-4-one	-5.30
11	 2-(2-chlorophenyl)-5,7-dihydroxy-4H-chromen-4-one	-5.79
12	 2-(3-chlorophenyl)-5,7-dihydroxy-4H-chromen-4-one	-5.36
13	 2-(4-chlorophenyl)-5,7-dihydroxy-4H-chromen-4-one	-5.39

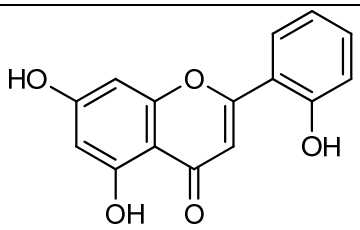
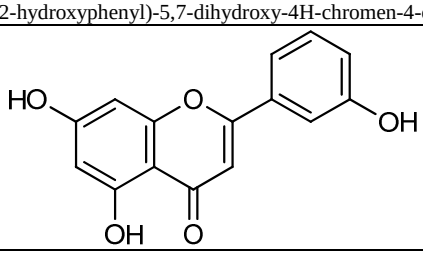
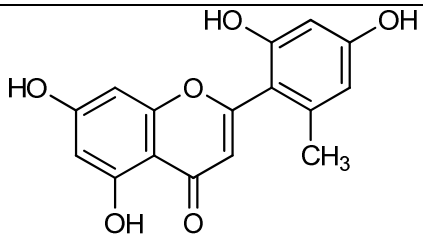
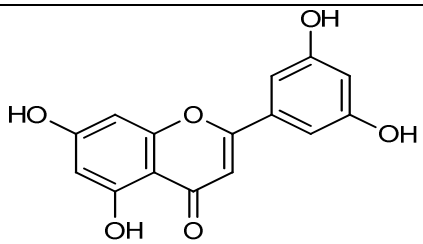
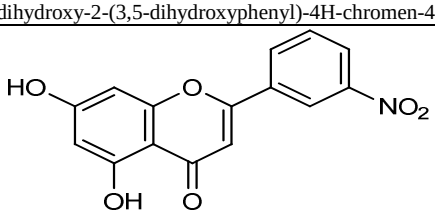
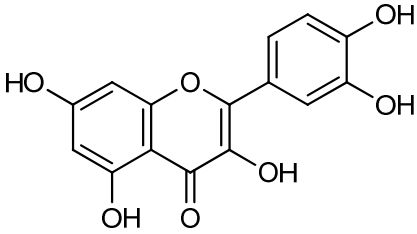
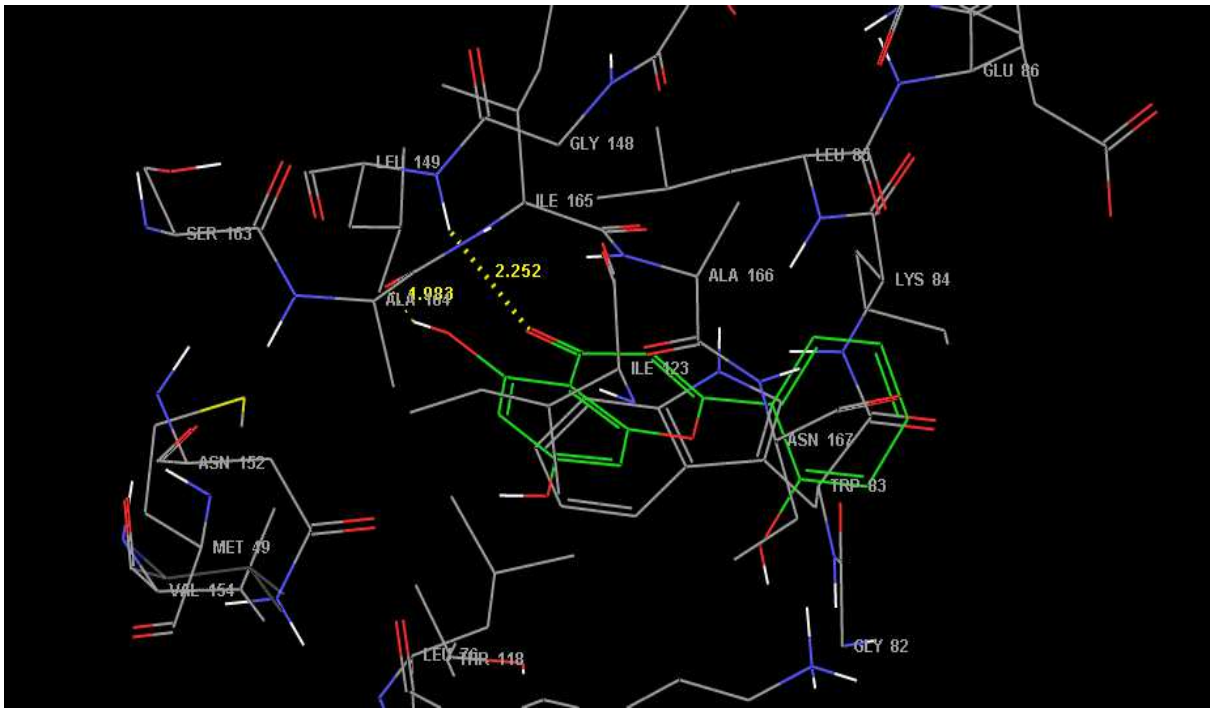
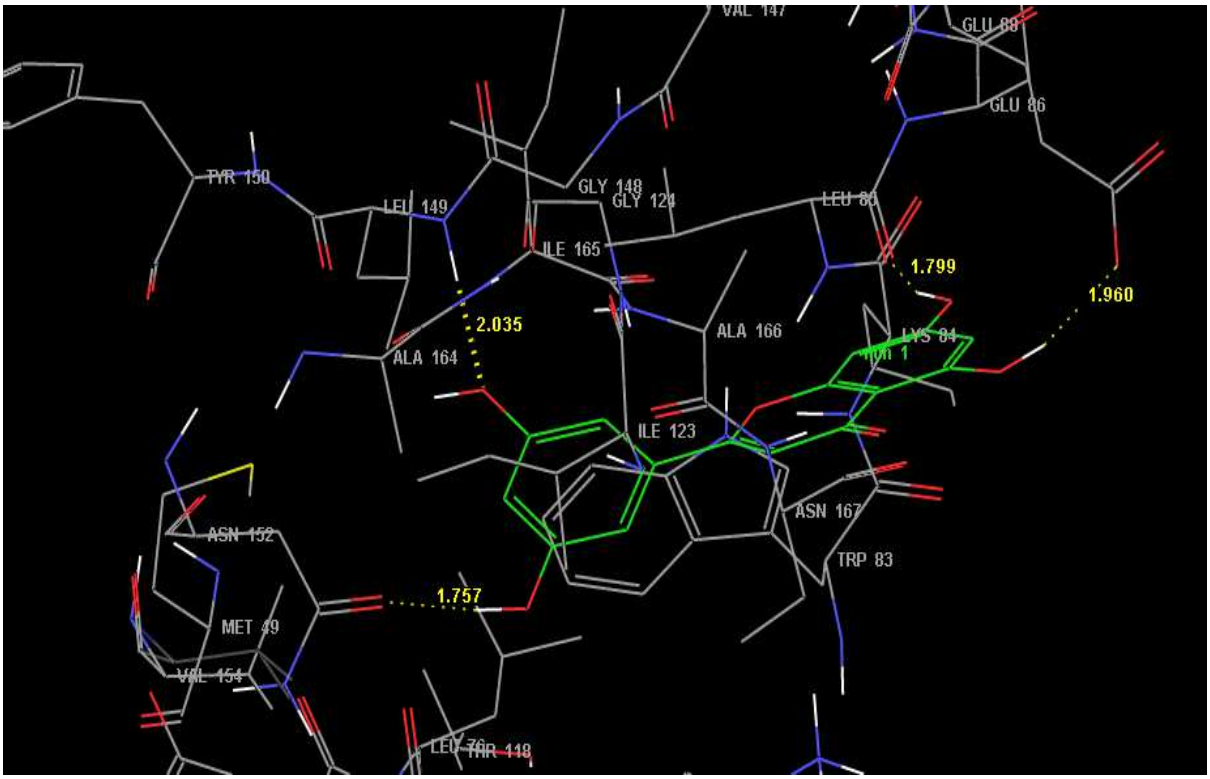
14	 2-(2-hydroxyphenyl)-5,7-dihydroxy-4H-chromen-4-one	-5.79
15		-5.50
16	 2-(2,4-dihydroxy-6-methylphenyl)-5,7-dihydroxy-4H-chromen-4-one	-6.24
17	 5,7-dihydroxy-2-(3,5-dihydroxyphenyl)-4H-chromen-4-one	-6.78
18	 5,7-dihydroxy-2-(3-nitrophenyl)-4H-chromen-4-one	-4.48
19	 Quercetin	-7.71

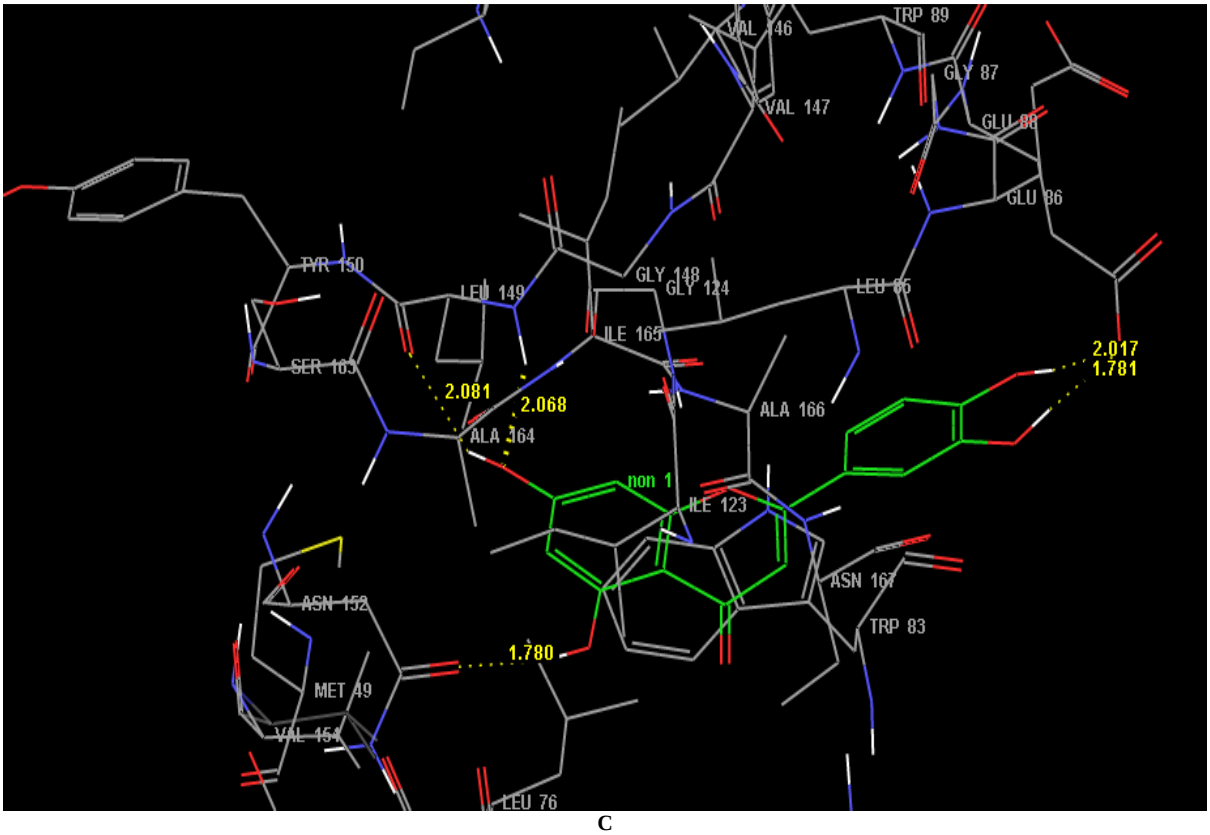
Figure 1



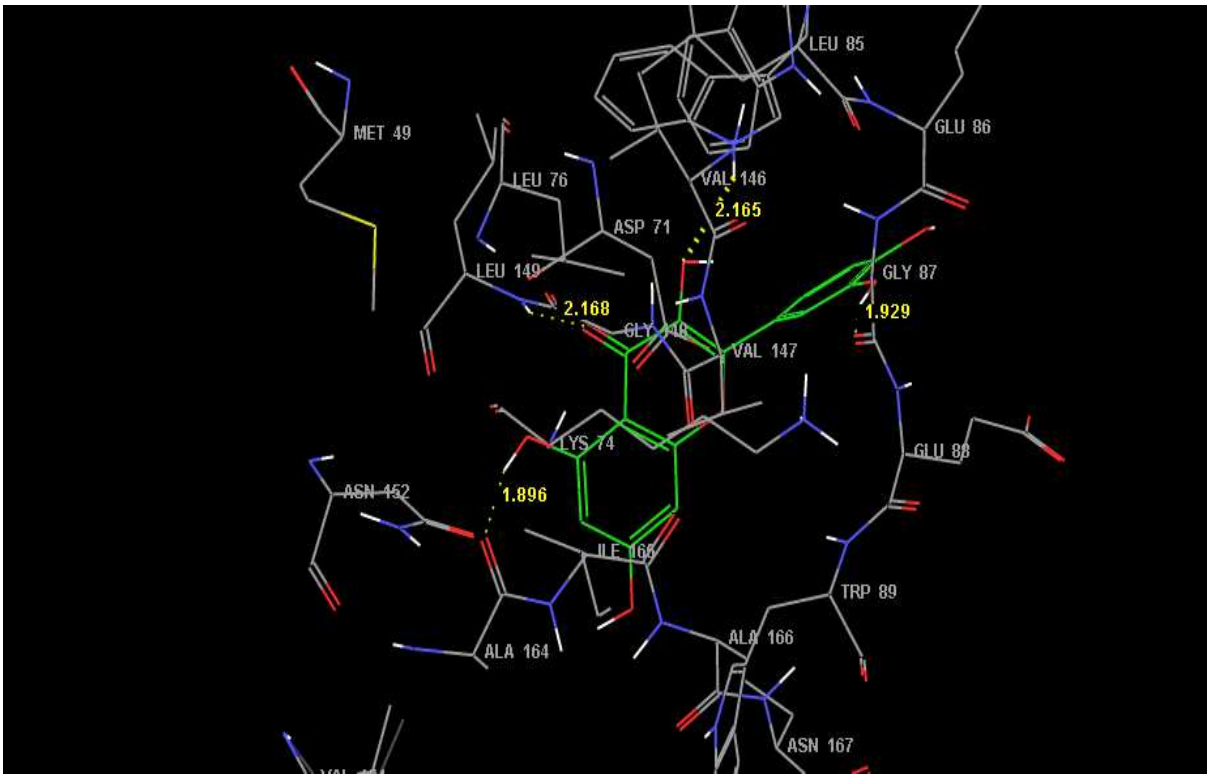
A
Entry 14



B
Entry 17



C
Entry 5 Luteolin



D
Entry 19 Quercetin

To find out the potential antidengue characteristics, the docking of quercetin was performed in order to compare the docking of other flavones with quercetin.

From docking score it is observed that almost all flavones show comparable dock score. From the docking poses of compounds, it is observed that flavones show hydrogen bonding interaction with Leu 149 and Asn152. The conformational change is observed due to binding of flavone with Leu 149. This affects indirectly the catalytic triad of dengue virus protease. Therefore it can be concluded that docked flavones have potential antidengue characteristics in *silico.*

CONCLUSION

From docking study it can be concluded that all docked flavones possess potential antidengue characteristics in *silico.* The Leu 149, Asn 152 show hydrogen bonding interaction with flavone molecules.

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