



## Flavanones: Potential antidengue targets *in silico* approach

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### ABSTRACT

Dengue is a viral disease caused due to bite of *aedes aegypti* mosquito. There is no approved drug against dengue. Therefore there is need to develop antidengue drug. The docking study of flavanones against dengue virus NS2B/NS3 protease is discussed.

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

### INTRODUCTION

Dengue virus belongs to *flaviviridae* family and is caused by a bite of *Aedes aegypti* mosquito [1]. Dengue is RNA virus having four serotypes viz., DENV 1-4. Dengue virus has three structural proteins and seven nonstructural proteins. Capsid C, envelope E and pre-membrane prM are the structural proteins whereas NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5 are nonstructural proteins [2]. 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. Therefore NS2B/NS3 protease plays a central role in replication of dengue virus [3]. Thus blocking proteolytic activity of dengue virus protease is important. Hence dengue virus NS2B/NS3 protease is targeted for designing new antidengue cores. The catalytic triad of dengue virus protease is located in region His51, Asp75, and Ser135 [4].

There is no approved drug against dengue and therefore there is need to design and develop safe and effective antidengue drug.

Flavanones are known to exhibit anti HIV [5], antimalarial [6], anticancer [7] and antibacterial [8] activities. Flavanones like *rutin*, *fisetin* are reported to exhibit antidengue activity [9]. Moreover flavones have potential antidengue characteristics *in silico* is also reported.[10] In the present work flavanones are docked against dengue virus NS2B/NS3 protease (PDB ID 2FOM) to find out potent antidengue characteristics features *in silico*.

### EXPERIMENTAL SECTION

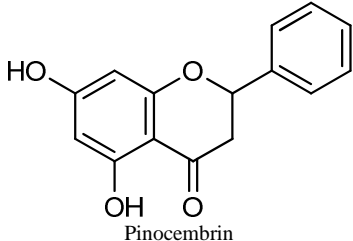
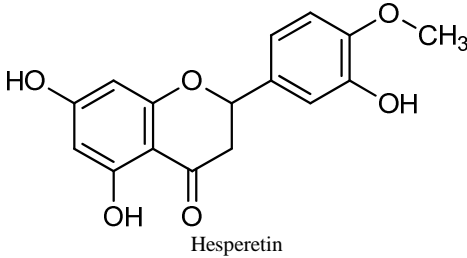
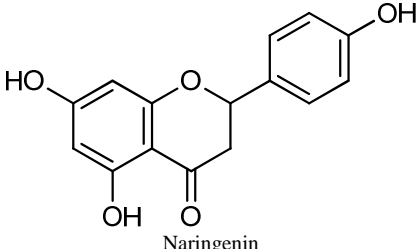
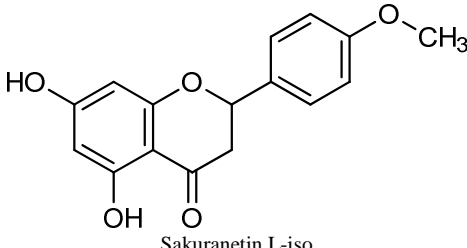
The docking studies were performed on *glide* docking software [11]. The dengue virus NS2B/NS3 protease structure was obtained from Protein Data Bank ([www.rcsb.org/pdb](http://www.rcsb.org/pdb)) having accession code 2FOM. *Protein Preparation Wizard* is used for receptor preparation. The residual chlorine atoms, glycerol molecules and water molecules were removed. The ligands were built in *Maestero* in required format. The OPLS 2005 force field is applied. By using *receptor grid generation* the receptor *grid* was generated at active site that is at catalytic triad of dengue virus NS2B/NS3 protease. For docking studies *Extra Precision (XP)* mode was used. The docked flavanone molecules are presented in Table 1. The docking poses of representative molecules are presented in Figure 1.

## RESULTS AND DISCUSSION

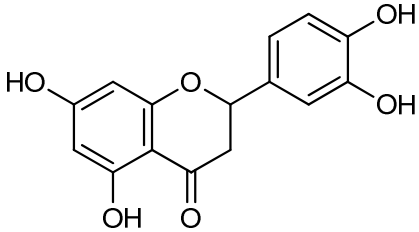
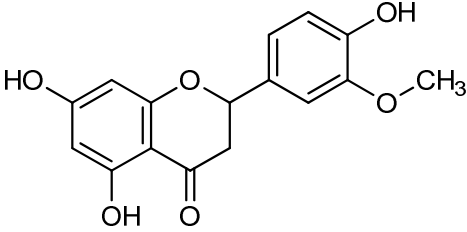
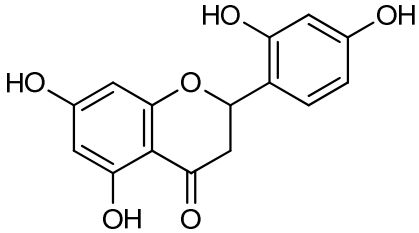
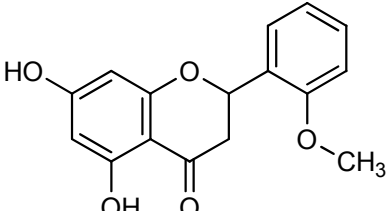
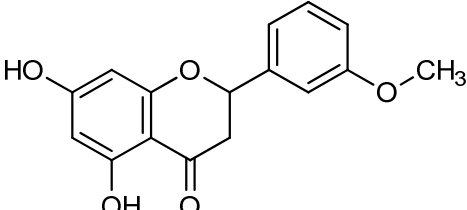
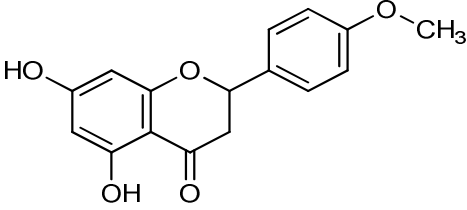
A number of flavanones were docked against dengue virus NS2B/NS3 protease. The flavanones gave dock score comparable with dock score of reported antidengue compounds. The reported antidengue compounds were found to interact with Leu 149, Lys74, Trp83, Asn152 and Ser135 [12]. The Lys74 is bonded directly to with one of catalytic triad Asp75, which brings conformational changes in active site of dengue virus NS2B/NS3 protease. The docked flavanones also showed binding interactions with these amino acid residues and hence have the potential to exhibit antidengue activity.

Pinocembrin [12], pinostrobin and naringenin [9] are known to exhibit antidengue activity. All docked flavanones show comparable dock score with respect to pinocembrin, pinostrobin and naringenin. **Figure 1** shows hydrogen binding interaction between receptor and docked flavanone. Flavanone (Entry 16, Table 1) was designed from reported tricyclic antidengue compound *ARDP 0009*. [13].The designed compound 2-(2, 4-dihydroxy-6-methylphenyl)-5, 7-dihydroxychroman-4-one forms hydrogen bonding interaction with Asp 75 and Asn 152. Therefore it has potential to exhibit antidengue characteristics in *silico*. On similar way eriodicytol shows hydrogen bonding interaction with Leu 149 and Asn152. The hydrogen binding interaction with Leu 149 influence the electron transfer process at catalytic triad site. Thus eriodicytol possess antidengue characteristics in *silico*.

Table 1

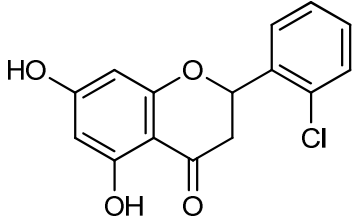
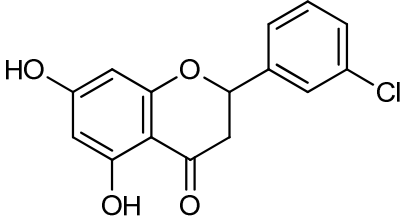
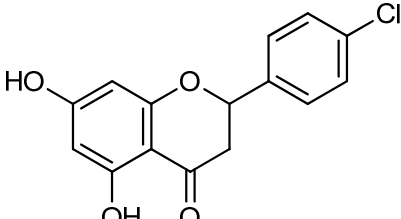
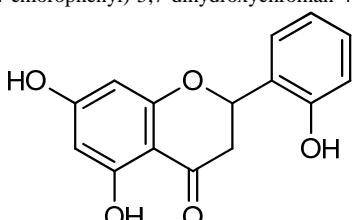
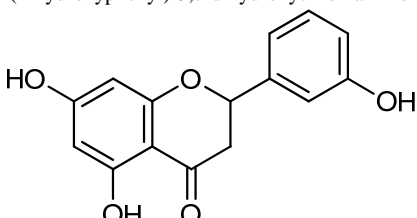
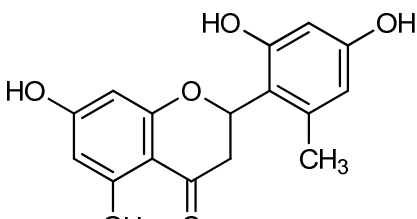
Entry No	Name and structure of flavanone	Docking score (Glide Score)
1	 Pinocembrin	-5.44
2	 Hesperetin	-5.82
3	 Naringenin	-6.91
4	 Sakuranetin L-iso	-5.91

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5		-7.32
	Eriodicytol	
6		-6.28
	Eriodicytol homo-	
7		-6.52
	Steppogenin	
8		-6.01
	5,7-dihydroxy-2-(2-methoxyphenyl)-chroman-4-one	
9		-6.35
	5,7-dihydroxy-2-(3-methoxyphenyl)-chroman-4-one	
10		-5.91
	5,7-dihydroxy-2-(4-methoxyphenyl)-chroman-4-one	

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11		-5.63
	2-(2-chlorophenyl)-5,7-dihydroxychroman-4-one	
12		-5.70
	2-(3-chlorophenyl)-5,7-dihydroxychroman-4-one	
13		-5.31
	2-(4-chlorophenyl)-5,7-dihydroxychroman-4-one	
14		-6.02
	2-(2-hydroxyphenyl)-5,7-dihydroxychroman-4-one	
15		-6.36
	2-(3-hydroxyphenyl)-5,7-dihydroxychroman-4-one	
16		-7.31
	2-(2,4-dihydroxy-6-methylphenyl)-5,7-dihydroxychroman-4-one	

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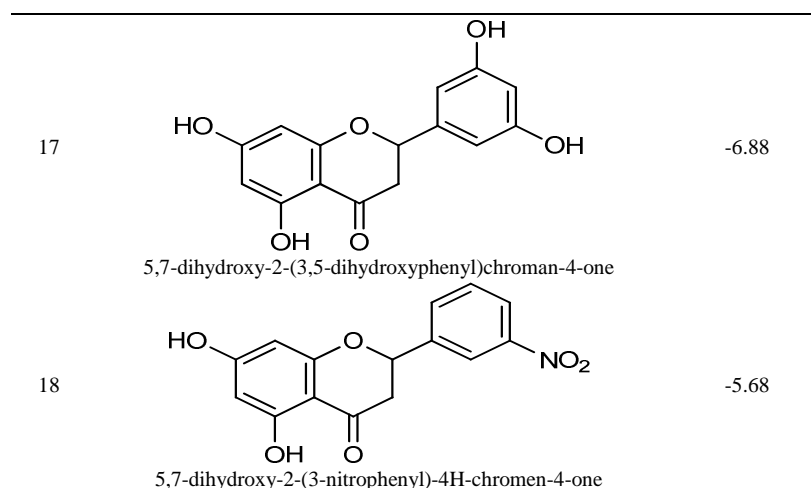
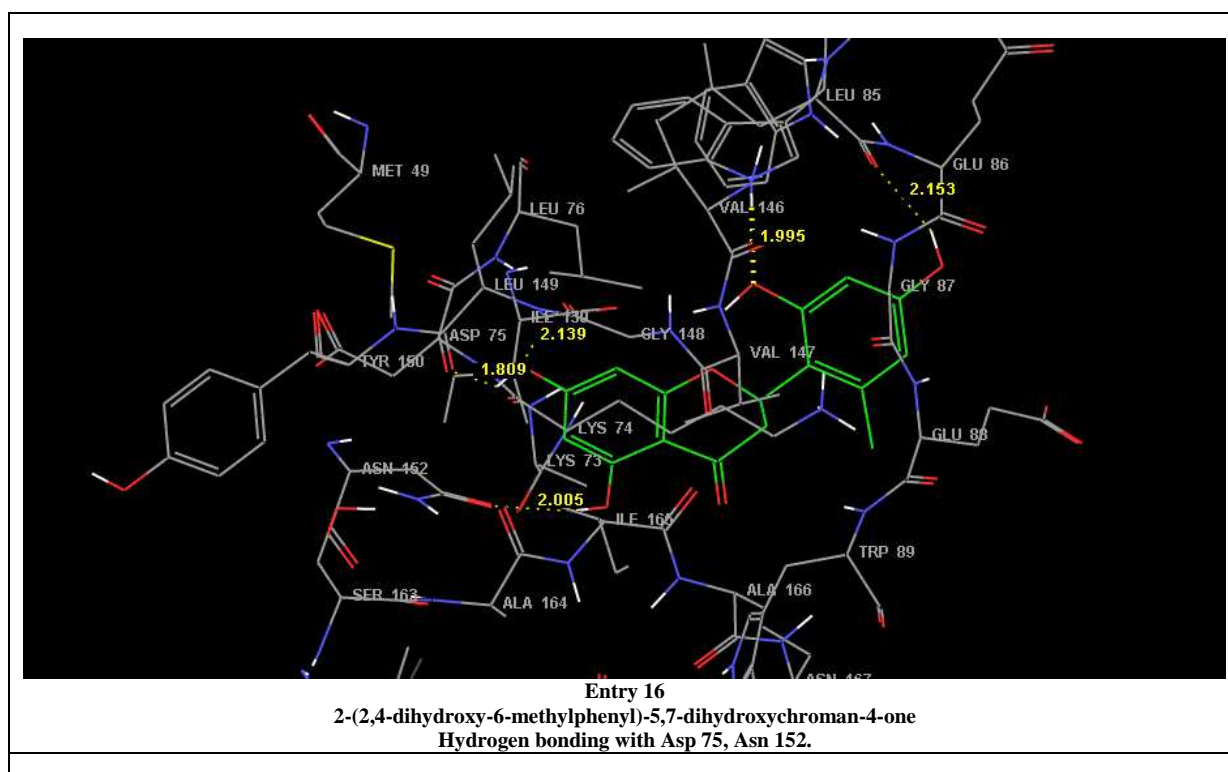
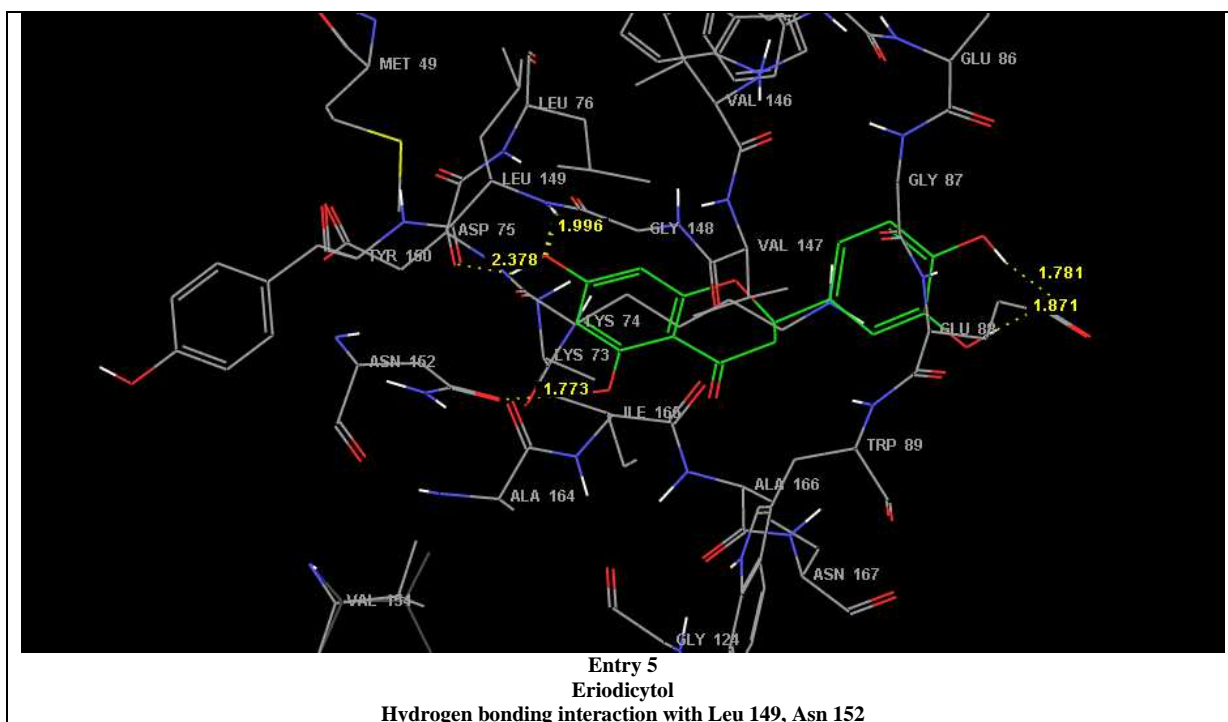


Figure 1





### CONCLUSION

Based on docking results, all flavanones possess potential antidengue characteristics *in silico*. Leu 149 and Asn 152 are involved in hydrogen bonding interaction between receptor and flavanones suggesting potential antidengue characteristics.

### Acknowledgement:

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