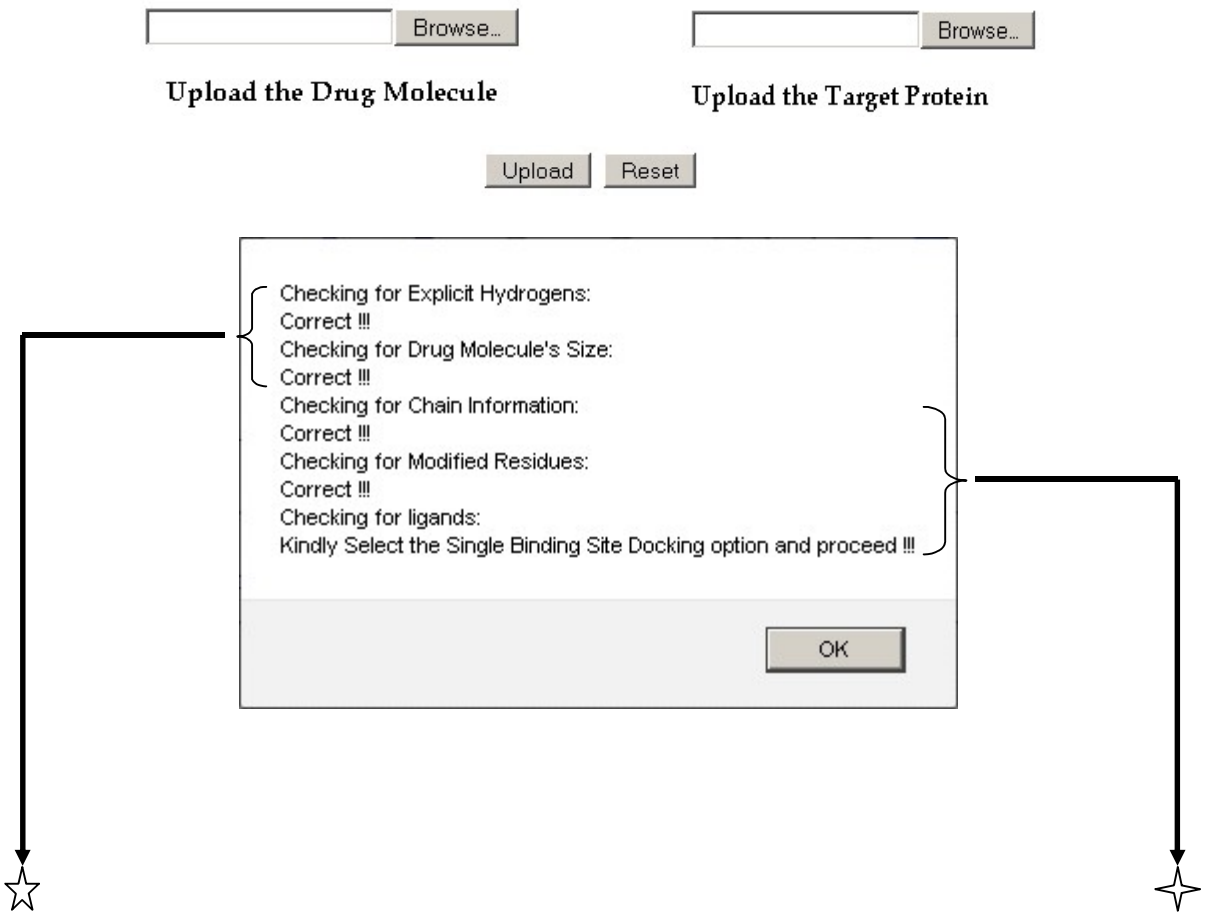
SANJEEVINI - Lead Molecule Design Software

Sanjeevini software has been developed to provide a computational pathway for automating lead design. The user can upload a bimolecular (protein) target and a candidate drug. The software identifies the potential active sites, docks and scores the candidate drug and returns four structures of the candidate drug bound to protein target together with binding free energies.

The following modules are present in the software:

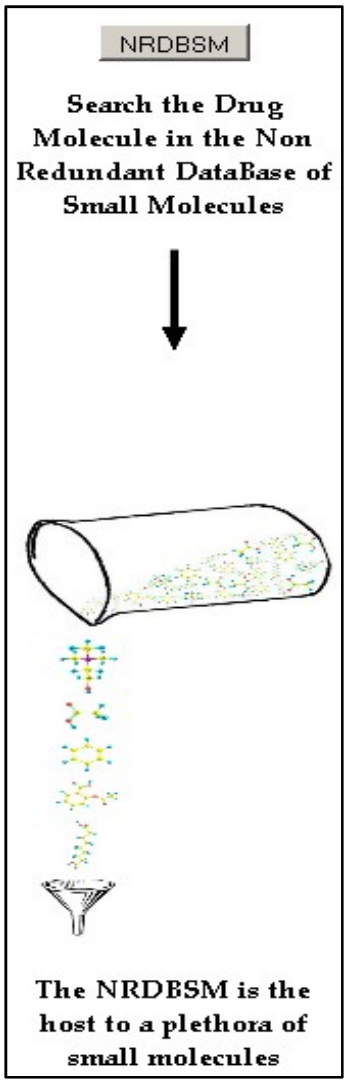
Important Note: Kindly input the Ligand and Protein in .pdb format for all the modules.

The first step in the Sanjeevini protocol is to upload a drug molecule and a target protein. On uploading, Sanjeevini pops-up a window (as shown in the figure below) which displays the results of some essential pre-tests done based on the parameters needed for the acceptable format of the drug and protein files.



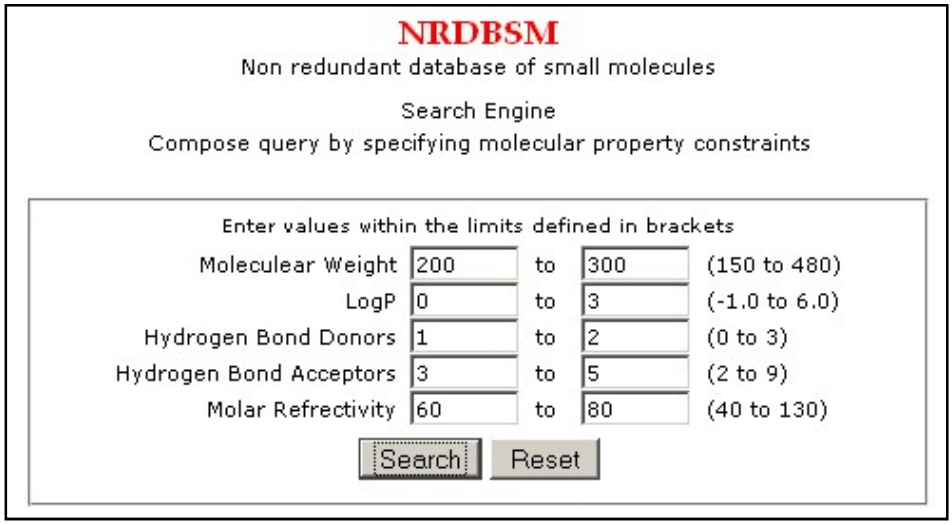
☆ DRUG PREPARATION

You can download the molecule of your interest from the NRDBSM database and upload it for docking and scoring OR upload a self drawn molecule.



NRDBSM database is aimed specifically at virtual high throughput screening of small molecules and their further optimization into successful lead-like candidates. It has been developed giving special consideration to physico-chemical properties and Lipinski's rule of five, which determines the solubility, permeability and transport characteristics across membranes. Some of these are molecular weight, number of hydrogen bond donors and acceptors, logP and molar refractivity. Fixed precincts for these properties have been employed as filters to assemble the database. **NRDBSM database currently holds close to 17000 molecules** with simple structures, low molecular weight, less number of rings and rotatable bonds, low hydrophobicity such that after screening, optimization and consequent increase in molecular complexity, they would show a drift towards **'drug-like' property space**.

Important Note: Use the NRDBSM if you want small molecules irrespective of the target protein.



The above page gets displayed. Enter the query by specifying molecular properties of the lead molecule you would like to dock to your target. A list of the molecules falling under the above property constraints gets displayed.

NRDBSM

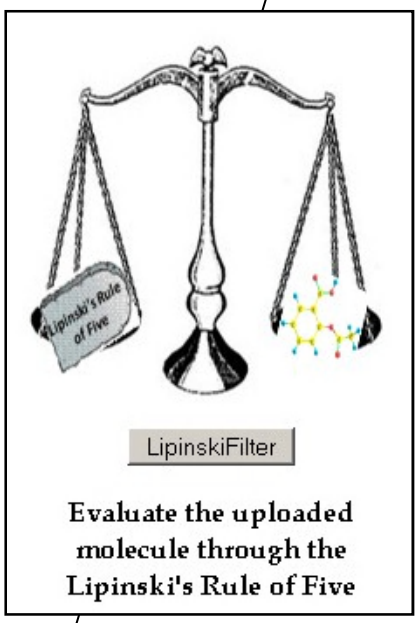
Non redundant database of small molecules

Back to Search Page
Total record found - 1079
1 Page of total 11 Pages
1 Search

S. No.	IUPAC NAME	Molecular Weight	Hydrogen Bond Acceptor	Hydrogen Bond Donor	LogP	Moral Refractivity
1	1- [(2- chlorothiazol- 5- yl)methyl]- 4- methyl- piperazine	233	3	2	2.0	62.724
2	1- benzyl- 2,4- dioxo- 1H- pyrimidine- 5- carbonitrile	227	5	1	0.3	61.584
3	1- (4- chlorophenyl)- 2,4- dioxo- 1H- pyrimidine- 5- carbonitrile	247	5	1	1.0	63.530
4	1- (6- chloropyridazin- 3- yl)piperidine- 4- carboxamide	240	5	2	0.8	61.174
5	difluoro- methyl- BLAHone	235	4	1	2.2	65.325
6	difluoroBLAHone	221	4	2	2.1	60.545
7	2- (1H- benzoimidazol- 2- yl)phenol	210	3	2	2.5	62.021
8	(2- chloro- 3- pyridyl)amino- phenylamino- methanone	247	4	2	2.7	67.942
9	2- [4- (4- fluorophenyl)thiazol- 2- yl]- 2- hydroxyimino- acetonitrile	247	4	1	2.4	67.685
10	N',N'- dimethyl- 5- phenyl- pyrimidine- 2,4- diamine	214	4	2	1.4	64.886
11	2- fluoro- N- (3- pyridyl)benzamide	216	3	1	2.7	62.489
12	2- (2- pyridyliminomethyl)benzene- 1,5- diol	214	4	2	2.2	61.261

Click on the molecule you would like to download and upload it for further docking and scoring.

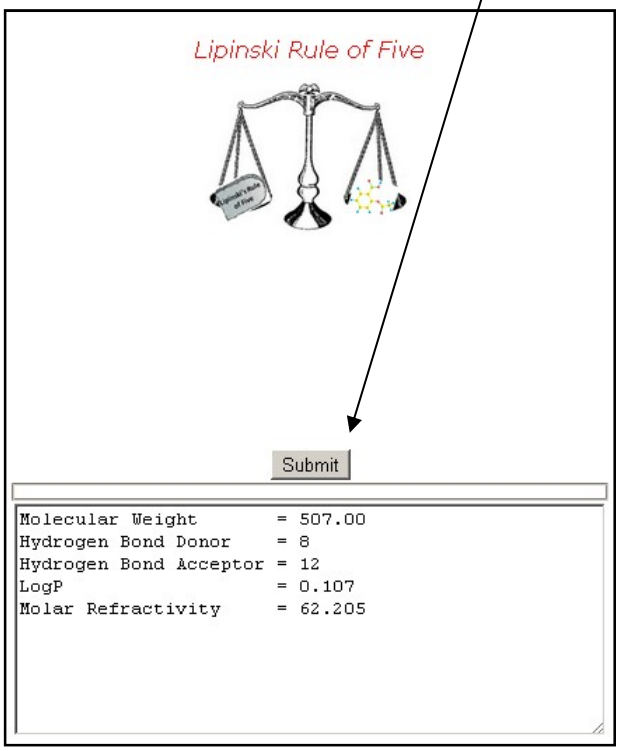
The molecule in the NRDBSM follows the **Lipinski Rule of Five**. However for a self drawn molecule you can check it by **clicking on Lipinski Filter button and then on Submit button in the upcoming pop up window**.

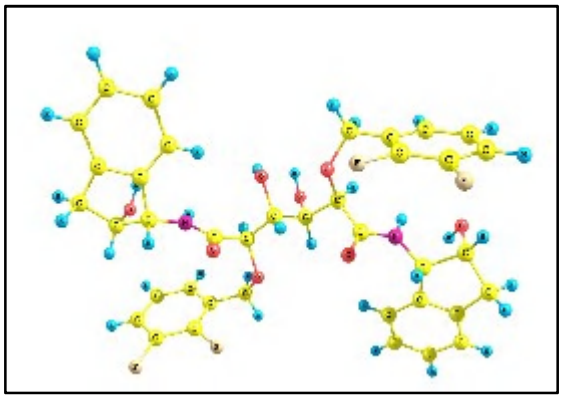


Lipinski rule of 5 helps in distinguishing between drug like and non drug like molecules. It predicts high probability of success or failure due to drug likeness for molecules complying with 2 or more of the following rules

- Molecular mass less than 500 Dalton
- High lipophilicity (expressed as LogP less than 5)
- Less than 5 hydrogen bond donors
- Less than 10 hydrogen bond acceptors
- Molar refractivity should be between 40-130

These filters help in early preclinical development and could help avoid costly late-stage preclinical and clinical failures





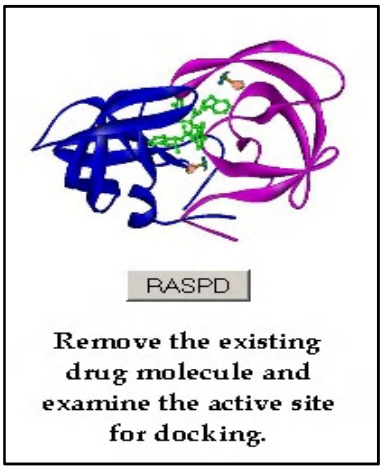
The drug molecule is considered ready for docking after following the above steps.

✧ PROTEIN PREPARATION

Upload the target protein. The target protein can contain either a single binding site or multiple binding sites. Sanjeevini automatically determines the protein type and suggests the user to select either one of the following pathways for docking.

Single Binding Site Docking ▾ Multiple Binding Site Docking ▾

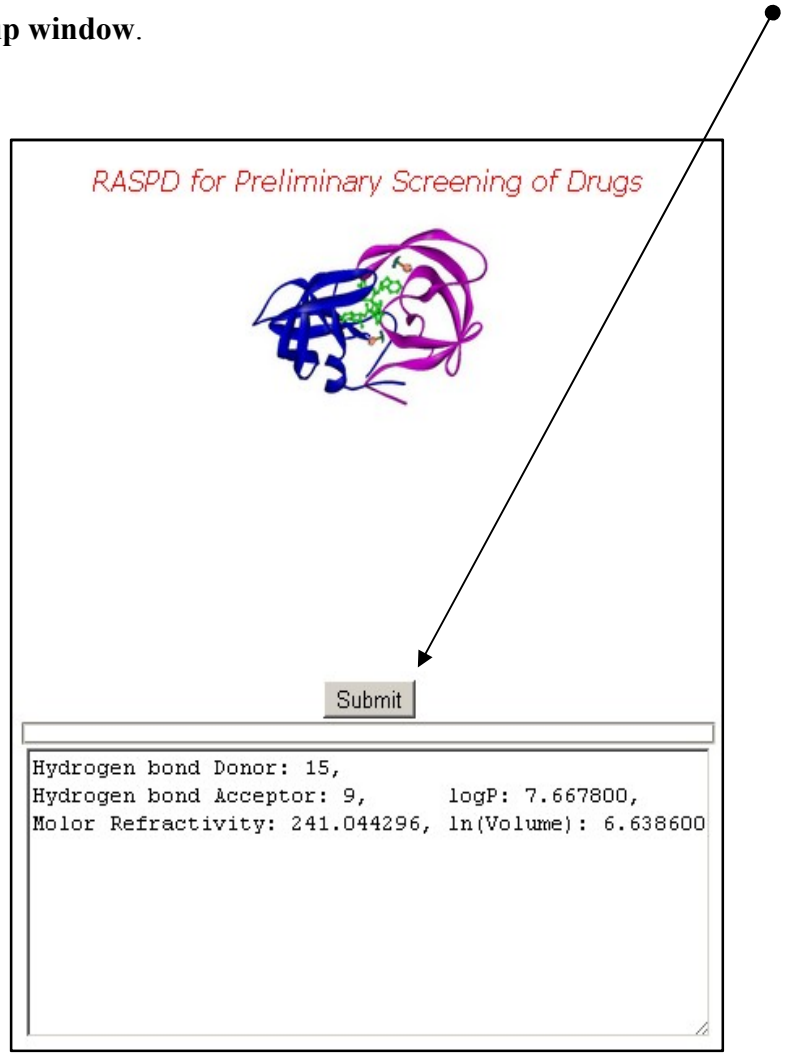
CASE 1: When the target protein has a Single Binding Site



We developed here a new methodology christened **RASPD** (A Rapid Scoring Methodology Based on Physico-Chemical Descriptors of Million Molecules), by using various molecular descriptors of candidate drug like molecules/active site of proteins for computation of binding free energy of target protein with significantly reduced time and cost. This is done by predicting the highly possible candidates for binding from a large data set (millions) and using a reduced set of likely candidate molecules to

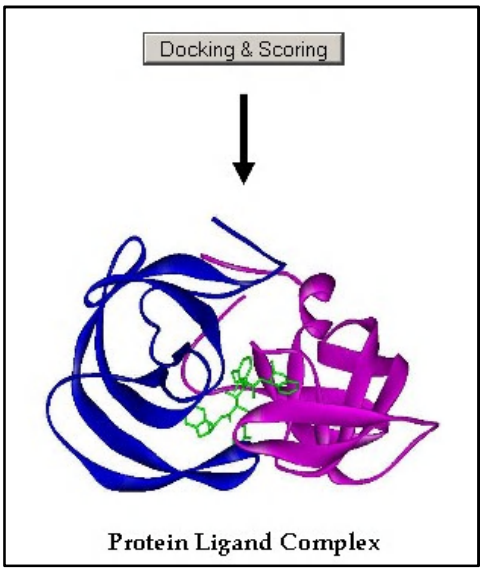
achieve the same result as done in traditional techniques. The most interesting feature of this methodology is that it takes fraction of a second for calculating the binding free energy of the protein-ligand complexes as opposed to minutes in known art today, whereas the accuracy of this method is comparable with the conventional techniques.

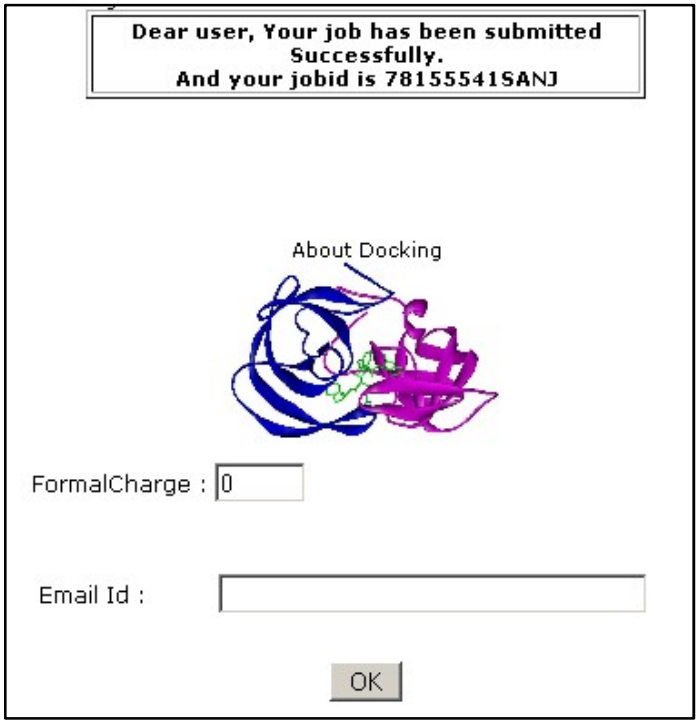
For checking the protein active site information and determining the binding affinity of you drug molecule to the target protein, **click on RASPD button and then on Submit button in the upcoming pop up window**.



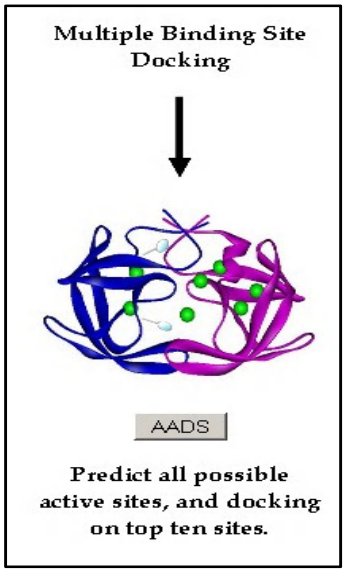
Docking and Scoring with Case 1

After you have selected the drug and target protein-ligand complex by screening them through Lipinski's filter and RASPD respectively, **click on the Docking and Scoring button**. On doing so, in a pop-up window you'll be asked to give the total formal charge of the chosen drug molecule along with your e-mail id and then submit the job. Four docked structures along with their predicted binding affinity values will be sent back to you via e-mail.

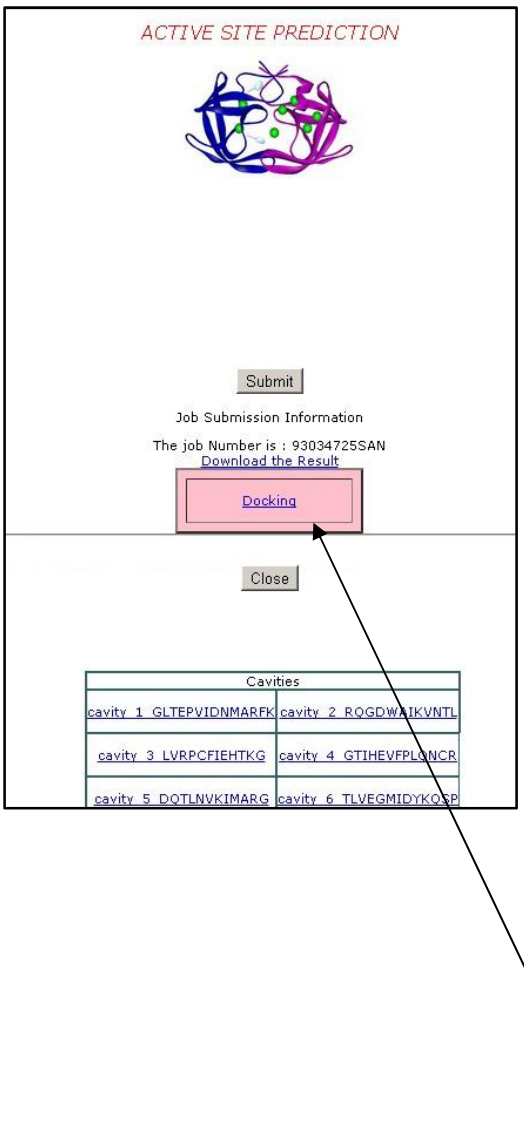




CASE 2: When the target protein has a Multiple Binding Site

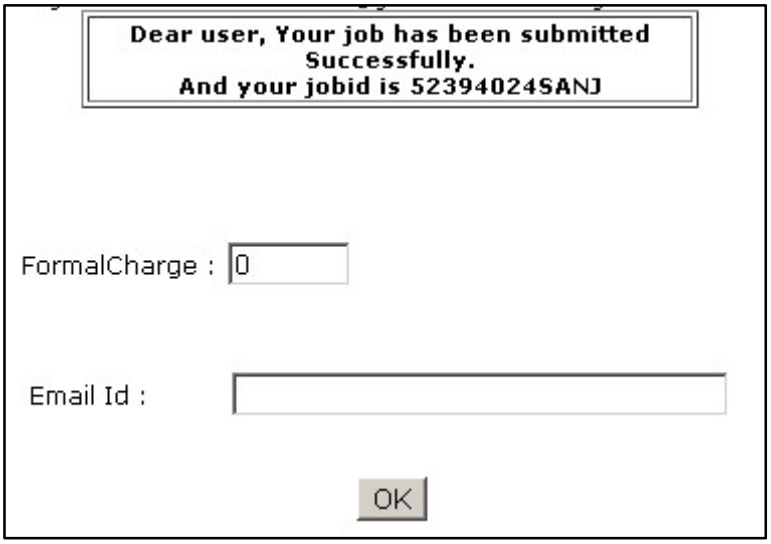


AADS (Active Site identification followed by docking and scoring) methodology predicts binding sites in a protein. The top ten binding sites reported by the above algorithm have an accuracy of 100%. The top ten binding sites predicted by the above algorithm are submitted for an automated docking and scoring. The candidate drug molecule is docked at all the ten binding sites predicted by the above algorithm and the docked structures are finally scored using an in house developed scoring function christened *BAPPL*. Finally ten docked structures along with their predicted binding free energy values are reported back to the user via e-mail.



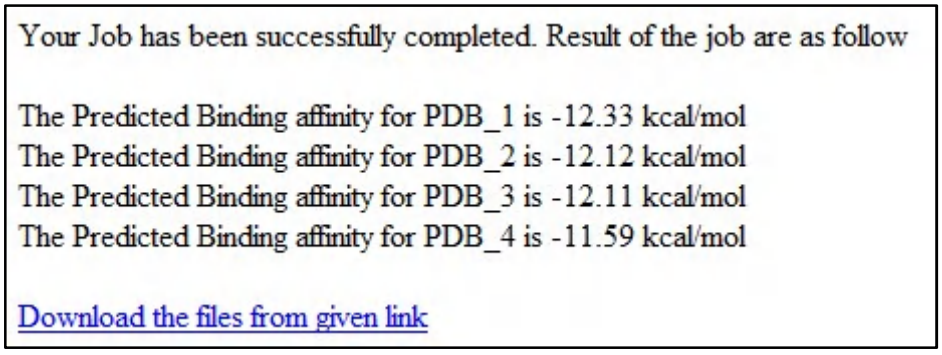
Docking and Scoring with Case 2

After you obtain the cavity points through AADS, **click on the Click here for Docking button**. On doing so, in a pop-up window you'll be asked to give the total formal charge of the chosen drug molecule along with your e-mail id and then submit the job. Ten docked structures along with their predicted binding affinity values will be sent back to you via e-mail.



RESULTS

You will obtain four or ten (depending upon the pathway chosen) docked protein-ligand complexes along with their predicted binding affinities in the e-mail specified during job submission. Additionally will be present a link, which will guide you to our web server from where you can download the docked structure files.



Important Note: Kindly refresh the Sanjeevini page before submitting another job.

For any queries and further suggestions kindly contact:

tanya@scfbio-iitd.res.in, **abhinav@scfbio-iitd.res.in** **or** **goutam@scfbio-iitd.res.in**

For other drug design utilities kindly go to the following link:

http://www.scfbio-iitd.res.in/bioinformatics/drugdesign.htm

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