ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2015; 1(7): 142-148
www.allresearchjournal.com
Received: 25-04-2015
Accepted: 25-05-2015

R. Vasanthi
Department of Biotechnology, Thanthai Hans Roever College, Perambalur- 621 212 Tamil Nadu, India.

C. Subashini
Department of Biotechnology, Thanthai Hans Roever College, Perambalur- 621 212 Tamil Nadu, India.

K. Ramanathan
Department of Bioinformatics, Thanthai Hans Roever College, Perambalur- 621 212 Tamil Nadu, India.

Correspondence:
K. Ramanathan
Department of Bioinformatics, Thanthai Hans Roever College, Perambalur- 621 212 Tamil Nadu, India.

Identification of Target Classes for the ligands using Swiss Target Prediction

R. Vasanthi, C. Subashini, K. Ramanathan

Abstract
The aim of the work is to identify the strongly coupled target classes for the ligands derived from the phytochemical study for the sample *Catharanthus roseus*. The smile values for the ligands were retrieved and submitted in to swiss target prediction for the identification of target enzymes and proteins. The sequence was also subjected for the analysis of sub cellular localization in the sample *Catharanthus roseus.* From these results, we have observed that the pyran and n-hexadecanoic acid may be strongly coupled with the number of essential enzymes and proteins. The composition of sub cellular.

Keywords: *Catharanthus roseus*, swiss target prediction, Target classes, ligands, sub cellular localization

1. Introduction
Physics based computational approaches to predicting the structure of macromolecules such as proteins are gaining increased use, but there are remaining challenges. The energy-based prediction methods, the degree of optimization of the sampled structures can influence the prediction results. In particular, discrepancies in the degree of local sampling can bias the predictions in favor of the oversampled structures by shifting the local probability distributions of the minimum sampled energies. In simple systems, it is shown that the magnitude of the errors can be calculated from the energy surface, and for certain model systems, derived analytically [1].

Plants in their life cycle are usually exposed to various kinds of non-biological stresses including heavy metals. One of these heavy metals is nickel which affects many physiological processes of plants. Studies have shown that the changes in planting conditions can affect the qualitative and quantitative features of *Catharanthus roseus* and therefore, creating stressful conditions [2].

Bioactive small molecules such as drugs or metabolites, bind to proteins or other macro-molecular targets to modulate their activity, which in turn results in the observed phenotypic effects. For this reason, mapping the targets of bioactive small molecules is a key step toward unraveling the molecular mechanisms underlying their bioactivity and predicting potential side effects or cross-reactivity. Recently, large datasets of protein-small molecule interactions have become available, providing a unique source of information for the development of knowledge based approaches to computationally identify new targets for uncharacterized molecules or secondary targets for known molecules [3].

Cells respond to chemokine stimulation by losing their round shape in a process called polarization, and by altering the sub cellular localization of many proteins. Classic imaging techniques have been used to study these phenomena. However, they required the manual acquisition of many cells followed by time consuming quantification of the morphology and the co-localization of the staining of tens of cells [4].

Environmental pressures forced plants to diversify specialized metabolisms to accumulate noxious molecules such as alkaloids constituting one of the largest classes of defense metabolites. Catharanthus roseus produces monoterpene indole alkaloids via a highly elaborated biosynthetic pathway whose characterization greatly progressed with the recent expansion of transcriptomic resources [5]

Background Tandem repetition of structural motifs in proteins is frequently observed across all forms of life. The topology of the repeating unit and its frequency of occurrence are associated to a wide range of structural and functional roles in diverse proteins, and defects in repeat proteins have been associated with a number of diseases. It is thus desirable to accurately identify the specific repeat type and its copy number. Weak evolutionary constraints on the repeat units and insertions/deletions between them make their identification difficult at the sequence level and structure based approaches are desired [6].

The prediction of the three-dimensional structure of protein-peptide complexes raises unique challenges for computational algorithms, as exemplified by the recent introduction of protein-peptide targets in the blind international experiment CAPRI (Critical Assessment of Predicted Interactions). Conventional protein-protein docking approaches are often struggling with the high flexibility of peptides whose short sizes impede protocols and scoring functions developed for larger interfaces. On the other side, protein small ligand docking methods are unable to cope with the larger number of degrees of freedom in peptides compared to small molecules and the typically reduced available information to define the binding site [7].

2. Methodology

The sample *Catharanthus roseus* was subjected to phytochemical study and the ligands were identified. The smile values for the ligands were retrieved from drug bank and pubchem compound for the identification of target classes using Swiss Target Prediction. The structures were predicted for the query molecule and the strongly coupled target classes have been identified. The sequence of the plant sample was retrieved and subjected to PSORT tool for the analysis of sub cellular localization.

3. Results

Table 1: Smile values for the Ligands

S. No	Name of the Ligand	Smile Values
1	Hydroxy Methyl	CCOCCOCCOCCOCCOCCOCCOCCOCCO
2	Pyran	[H][C]1(O)C=C(O[C]([H])(OCC(C)C)[C]1([H])NC(C)=O)C(O)=O
3	1,2,3,5 - cyclohexanediol	C1C(CC(C(C1O)O)O)O
4	Methyl ester	COC (=O) CCC (=O) CN
5	n-hexadecanoic acid	CCCCCCCCCCCCCCCC(O)=O

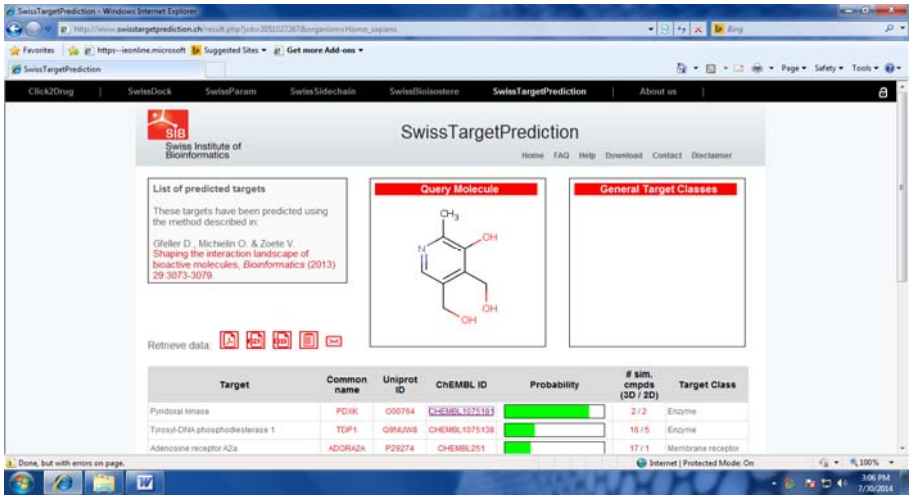


Fig 1: Structure for hydroxymethyl for Target Prediction

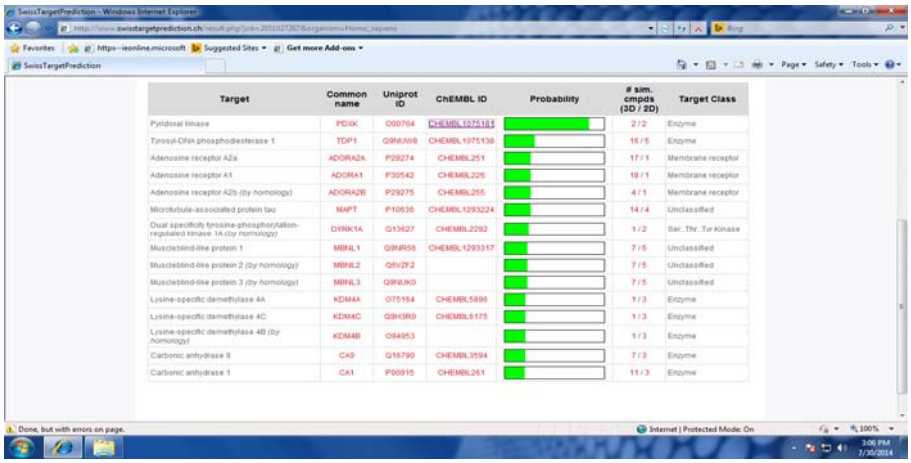


Fig 2: hydroxymethyl strongly coupled with pyridoxal kinase enzyme

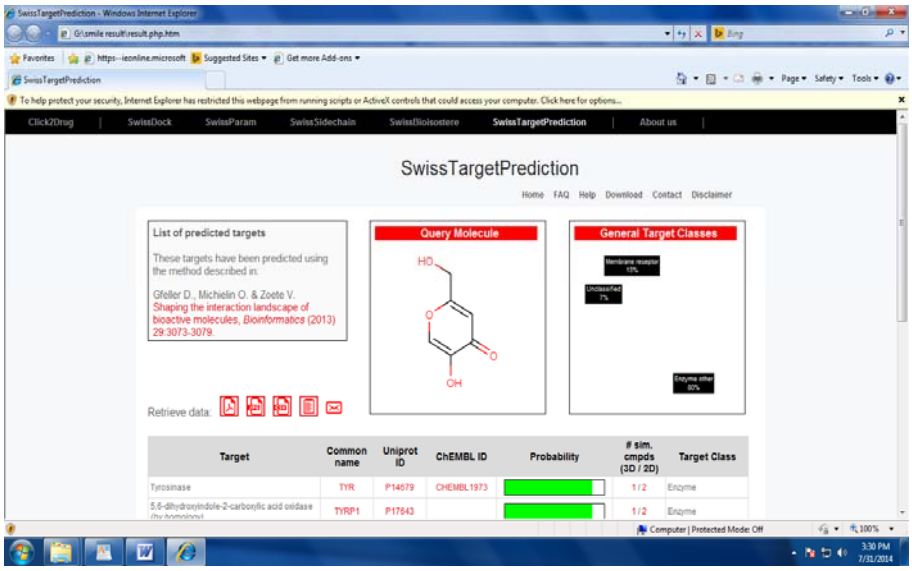


Fig 3: Structure for pyran for Target Prediction

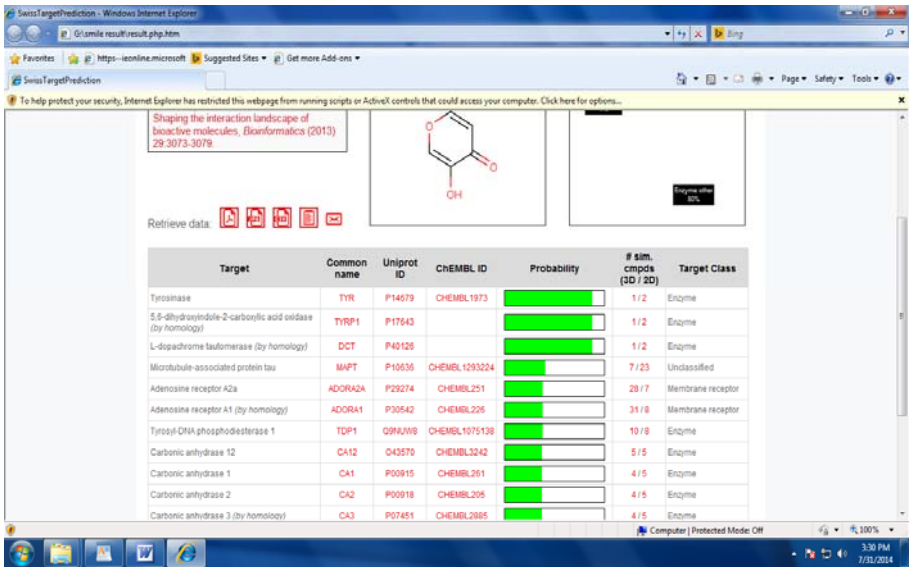


Fig 4: Pyran effectively coupled with Tyrosinase, Carboxylic acid oxidase and tautomerase

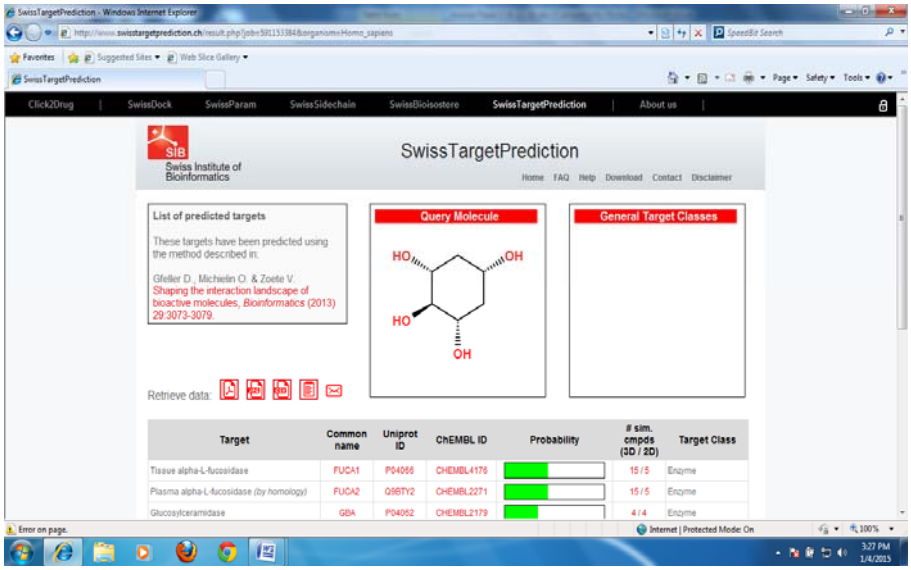
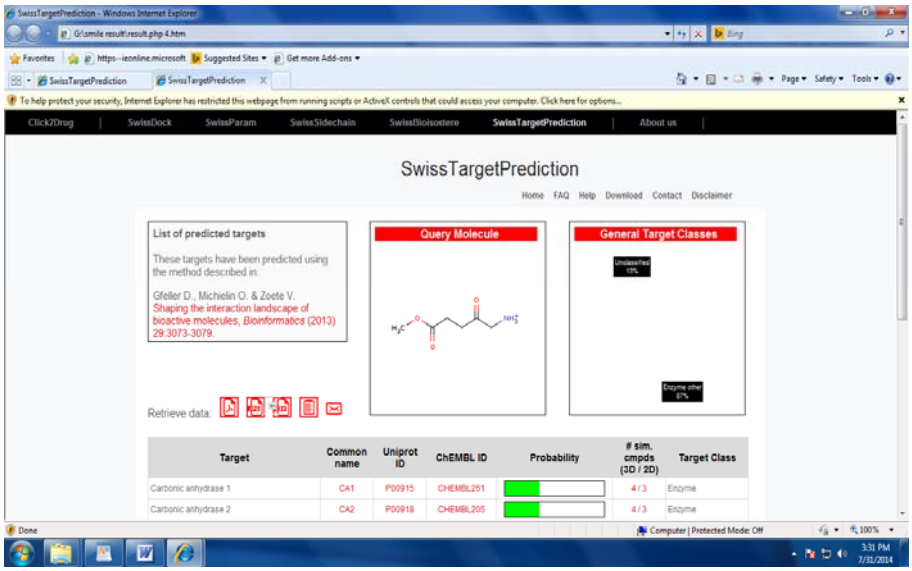


Fig 5: Structure for cyclohexanediol for Target Prediction

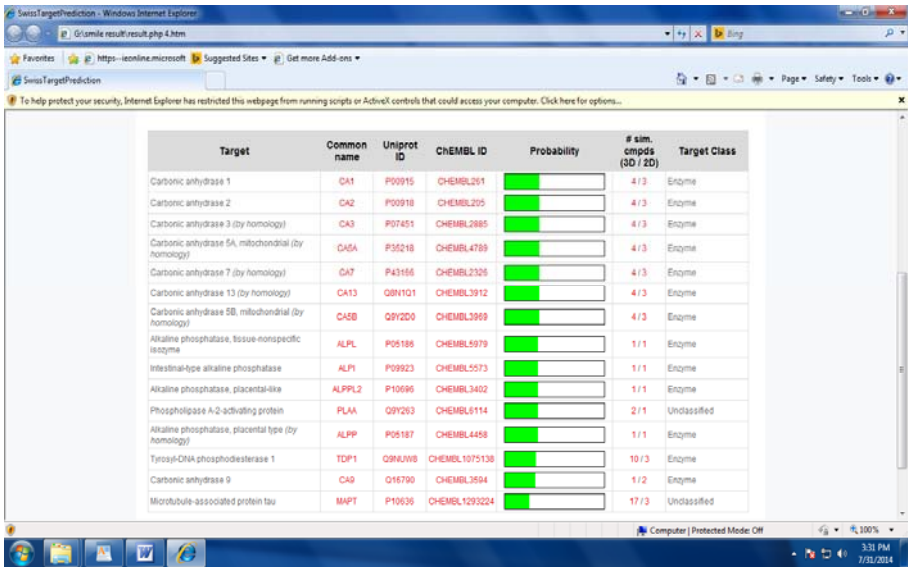
Target	Common name	Uniprot ID	ChEMBL ID	Probability	# sim. cmpds (3D / 2D)	Target Class
Tissue alpha-L-fucosidase	FUCA1	P04066	CHEMBL4175		15 / 5	Enzyme
Plasma alpha-L-fucosidase (by homology)	FUCA2	Q9BTY2	CHEMBL2271		15 / 5	Enzyme
Glucosylceramidase	GBA	P04062	CHEMBL2179		4 / 4	Enzyme
Oxysterols receptor LXR-beta	NR1H2	P55055	CHEMBL4093		0 / 2	Transcription Factor
Oxysterols receptor LXR-alpha	NR1H3	Q13133	CHEMBL2808		0 / 2	Transcription Factor
Glucoamylase	MGAM	O43451	CHEMBL2074		3 / 3	Enzyme
Sucrase	SI	P14410	CHEMBL2748		3 / 3	Enzyme
Uncharacterized protein (by homology)		Q3UNQ2			3 / 2	Enzyme
Tyrosyl-DNA phosphodiesterase 1	TDP1	Q9NUW8	CHEMBL1075138		2 / 5	Enzyme
Lysosomal alpha-glucosidase	GAA	P10253	CHEMBL2608		1 / 1	Enzyme
DNA polymerase alpha catalytic subunit	POLA1	P09884	CHEMBL1828		0 / 1	Enzyme
Desert hedgehog protein C-product (by homology)	DHH	O43323			0 / 10	Unclassified
Indian hedgehog protein N-product (by homology)	IHH	Q14623			0 / 10	Unclassified
Sonic hedgehog protein C-product (by homology)	SHH	Q15465	CHEMBL5602		0 / 10	Unclassified
Carbonic anhydrase 1	CA1	P00915	CHEMBL261		0 / 2	Enzyme

Fig 6: cyclohexanediol strongly coupled with Tissue alpha L-Fucosidase enzyme



Target	Common name	Uniprot ID	ChEMBL ID	Probability	# sim. cmpds (3D / 2D)	Target Class
Carbonic anhydrase 1	CA1	P00915	CHEMBL261		4 / 3	Enzyme
Carbonic anhydrase 2	CA2	P00918	CHEMBL205		4 / 3	Enzyme

Fig 7: Structure for methyl ester for Target Prediction



Target	Common name	Uniprot ID	ChEMBL ID	Probability	# sim. cmpds (3D / 2D)	Target Class
Carbonic anhydrase 1	CA1	P00915	CHEMBL261		4 / 3	Enzyme
Carbonic anhydrase 2	CA2	P00918	CHEMBL205		4 / 3	Enzyme
Carbonic anhydrase 3 (by homology)	CA3	P07451	CHEMBL2885		4 / 3	Enzyme
Carbonic anhydrase 5A, mitochondrial (by homology)	CA5A	P35218	CHEMBL4789		4 / 3	Enzyme
Carbonic anhydrase 7 (by homology)	CA7	P43166	CHEMBL2326		4 / 3	Enzyme
Carbonic anhydrase 13 (by homology)	CA13	Q8N1Q1	CHEMBL3912		4 / 3	Enzyme
Carbonic anhydrase 5B, mitochondrial (by homology)	CA5B	Q9Y2D0	CHEMBL3969		4 / 3	Enzyme
Alkaline phosphatase, tissue-nonspecific isozyme	ALPL	P05186	CHEMBL5979		1 / 1	Enzyme
Intestinal-type alkaline phosphatase	ALPI	P09923	CHEMBL5573		1 / 1	Enzyme
Alkaline phosphatase, placental-like	ALPPL2	P10696	CHEMBL3402		1 / 1	Enzyme
Phospholipase A-2-activating protein	PLAA	Q9Y263	CHEMBL6114		2 / 1	Unclassified
Alkaline phosphatase, placental type (by homology)	ALPP	P05187	CHEMBL4458		1 / 1	Enzyme
Tyrosyl-DNA phosphodiesterase 1	TDP1	Q9NUW8	CHEMBL1075138		10 / 3	Enzyme
Carbonic anhydrase 9	CA9	Q16790	CHEMBL3594		1 / 2	Enzyme
Microtubule-associated protein tau	MAPT	P10636	CHEMBL1293224		17 / 3	Unclassified

Fig 8: Methyl ester firmly tied with carbonic anhydrase group of enzymes

Fig 9: Structure for n-hexadecanoic acid for Target Prediction

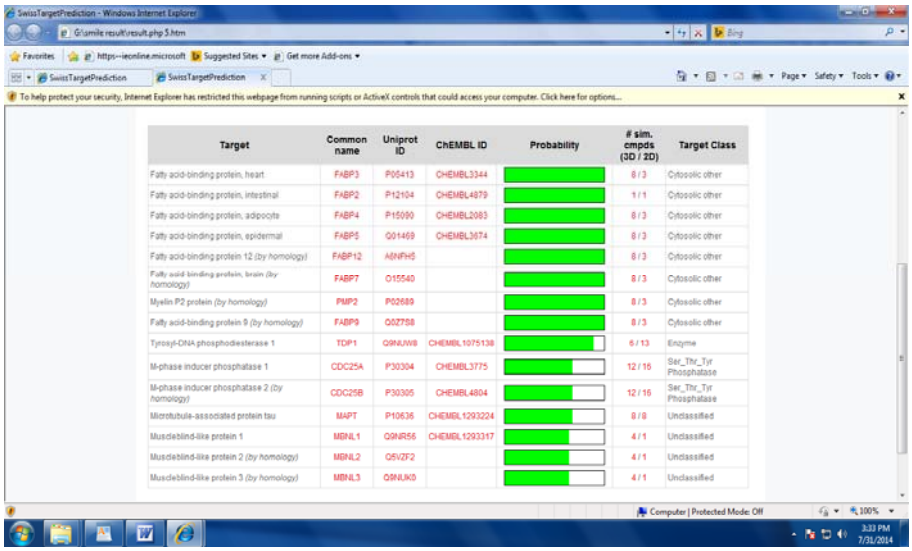


Fig 10: n-hexadecanoic acid strongly coupled with Myelin P2 Protein and fatty acid binding proteins in the heart, intestinal, adipocyte and epidermal

PSORT Predictions

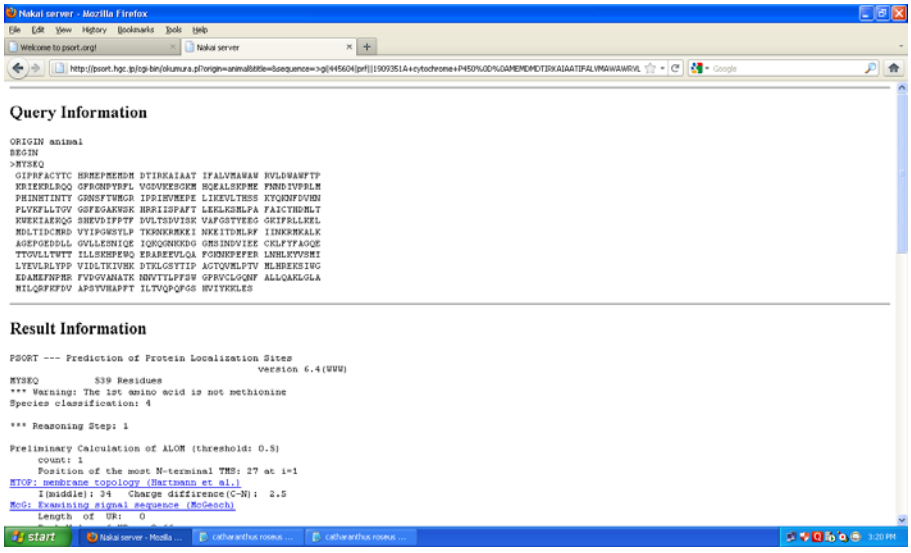


Fig 11: Sequence Submitted to PSORT Tool

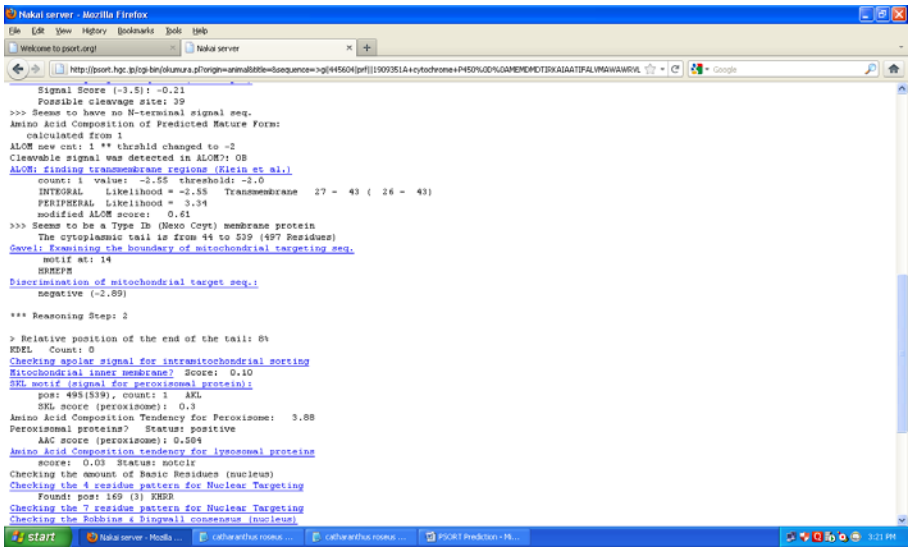


Fig 12: PSORT tool shows Sub cellular Localization

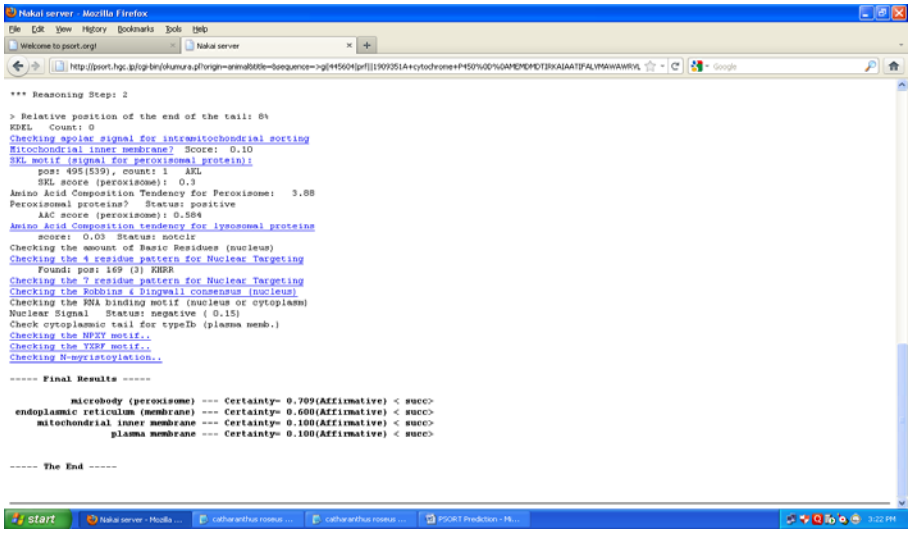


Fig 13: Score values for the sub cellular localization

4. Discussion

The structure prediction and the identification of target classes are to be used for the docking studies. The ligands were identified from the phytochemical study of the sample *Catharanthus rosesus*. The smile values for the liagnds were retrieved from drug bank and pubchem compound. Table 1 represents the smile values for the liagnds and subjected to swiss target prediction tool. Fig 1 shows that the structure for the ligand hydroxymethyl and the strongly coupled target classes represented in the Fig 2. The structure for the pyran was predicted in the Fig 3 and the closely associated receptors shows in the Fig 4. The ligand hydroxy methyl may be effectively coupled with pyridoxal enzyme and the pyran may be effectively coupled with tyrosinase, carboxylic acid oxidase and tautomerase. The Fig 5 shows that the structure for the cyclohexanediol and the target classes represents in the Fig 6. The structure for the methyl ester was predicted in the Fig 7 and the strongly bounded target classes represented in the Fig 8. The cyclohexanediol and methyl ester may be coupled with tissue alpha L-fucosidase enzyme and carbonic anhydrase group of enzymes respectively. The n-hexadecanoic acid structure was predicted in the Fig 9 and the target classes showed in the Fig 10. The n-hexadecanoic acid may be strongly coupled with Myelin P2 Protein and fatty acid binding proteins in the heart, intestinal, adipocyte and epidermal.

The sequence was retrieved and calculates the sub cellular localization using PSORT tool. (Fig 11). Fig 12 shows the sub cellular organelles such as micro bodies, endoplasmic reticulum, mitochondrial inner membrane and plasma membrane with their values of 0.709, 0.600, 0.100 and 0.100 respectively.

5. Conclusion

The *Catharanthus roseus* was subjected to phytochemical study and it shows various phytochemicals such as hydroxy methyl, pyran, cyclohexanediol, methyl ester and Hexadecanoic acid. These ligands were subjected to structure prediction and identify the strongly coupled target classes. The sub cellular localization occurs in micro bodies, endoplasmic reticulum, mitochondrial inner membrane and plasma membrane. From these results, we observed that the ligand pyran and n-hexadecanoic acid may be effectively coupled with number of essential enzymes and proteins and it could be shows the possible way for docking studies.

6. References

1. Petrella RJ. Optimization Bias in energy based structure prediction J Theor Comput Chem, 2013, 12(8).
2. Arefifard M, Mahdieh M, Amirjani M. Study of the effect of nickel heavy metals on some physiological parameters of Catharanthus roseus, 2014; 28:1-4.
3. Gfeller D, Grosdidier A, Wirth M, Daina A, Michielin O, Zoete V. SwissTargetPrediction: a web server for target prediction of bioactive small molecules. Nucleic Acids Res, 2014, 42(8).
4. Megrelis L, Delon J. Rapid and robust analysis of cellular and molecular polarization induced by chemokine signaling. J Vis Exp 2014; 12:94.
5. Courdavault V, Papon N, Clastre M, Giglioli-Guivarc'h N, St-Pierre B, Burlat V. A look inside an alkaloid multisite plant: the Catharanthus logistics 2014; 19:43-50.
6. Chakrabarty B, Parekh N. Identifying tandem Ankyrin repeats in protein structures. BMC Bioinformatics 2014; 30:15(1):6599.
7. Trellet M, Melquiond AS, Bonvin AM. Information-Driven Modeling of Protein-Peptide Complexes. Methods Mol Biol, 1268, 221-239.