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Molecular docking on the phytochemicals from *Catharanthus roseus* L for anticancer activity

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Abstract
This study aims to understand the functional activity and to examine the phytochemical compounds from the plant sample *Catharanthus roseus.* The sample is collected and it will be subjected to phytochemical study. The phytochemical compounds are to be isolated and it will choose for molecular docking with the target receptor. The ligand and receptor binds effectively in the active sites with the binding energy. The active sites of the receptor are to be calculated and the docked structures are validated using bioinformatics tools. From these results, we may observe that the ligand that is effectively docked with the receptor and it could be a responsible compound for drug designing.

Keywords: *Catharanthus roseus*, phytochemical study, Target Receptor, Ligand, Binding Sites, Docking

1. Introduction

Methodology 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 [1]. Diabetes becomes a real problem of public health in developing countries, where its prevalence is increasing steadily. Diabetes mellitus can be found in almost every population in the world. Since the Ayurvedic practice started in India, plants are being used in the cure of diseases. Although the *Catharanthus roseus* have been used for their alleged health benefits and avail their hypoglycemic effect, used as medicine by diabetics. Medicinal plants have rarely been incorporated in food preparations [2].

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 [3]. Several plants of Catharanthus roseus showing phenotype of phytoplasma infection were observed for symptoms of early flowering, virescence, phyllody, and apical clustering of branches. Symptomatic plants were studied for the presence and absence and identity of phytoplasma in flowers. Transcription levels of several genes involved in plants metabolism and development, accumulation of pharmaceutically important terpenoid indole alkaloids in flowers and leaves and variation in the root-associated microbial flora were examined [4]. Iridoids are key intermediates required for the biosynthesis of monoterpenoid indole alkaloids as well as quinoline alkaloids. Although most iridoid biosynthetic genes have been identified, one remaining three step oxidation required to form the carboxyl group of 7-deoxyloganetic acid has yet to be characterized. In Catharanthus roseus, vincristine and vindolidine are highly present and these compounds are essential compounds [5]. In *Catharanthus roseus*, three morphological cum salt-tolerant chemically induced mutants of Mendelian inheritance and their wild-type parent cv Nirmal were characterized for overall cytosine methylation at DNA repeats, expression of 119 protein coding and seven miRNA-coding genes and 50 quantitative traits [6]. Salicylic acid has been reported to ameliorate various stresses in plants. In order to explore the role of SA under nickel (Ni) stress, thirty days old plants of *Catharanthus roseus* were supplied with eight treatments comprising basal applications [7]. We have collected the sample from various locations of Perambalur district. The flowers of the plant were collected and dried under shadow for five days. Then the sample was converted into powdered form using electric blunder. The plant sample was subjected to phytochemical study using Gas Chromatography – Mass Spectrometry. The phytochemical compounds were isolated from

Catharanthus roesus using methanol extract. It shows 38 phytochemical compounds and we have selected the compounds based on peak area such as Hydroxymethyl, Pyran, Cyclohexanetetrol, Cyclo Spermidine and Hexadecanoic acid for docking with the target receptor. The binding sites were calculated for the target receptor using prosite tool. It shows two binding sites which are present in the protein. The target receptor which is responsible for leukemia was retrieved and the structures of the ligand were collected from Protein data bank. The target receptor structure is subjected to docking with the structure of each ligand. The docking was performed using Hex tool and the score values were calculated for the docked structure and the results were discussed. The sequence of *Catharanthus roseus* was retrieved from NCBI database and calculates the sub cellular localization using PSORT tool. The smile values for the ligands were retrieved from drug bank and submit into Swiss Target Prediction tool. Finally, the results were discussed and analyzed.

2. Results

Prosite Results

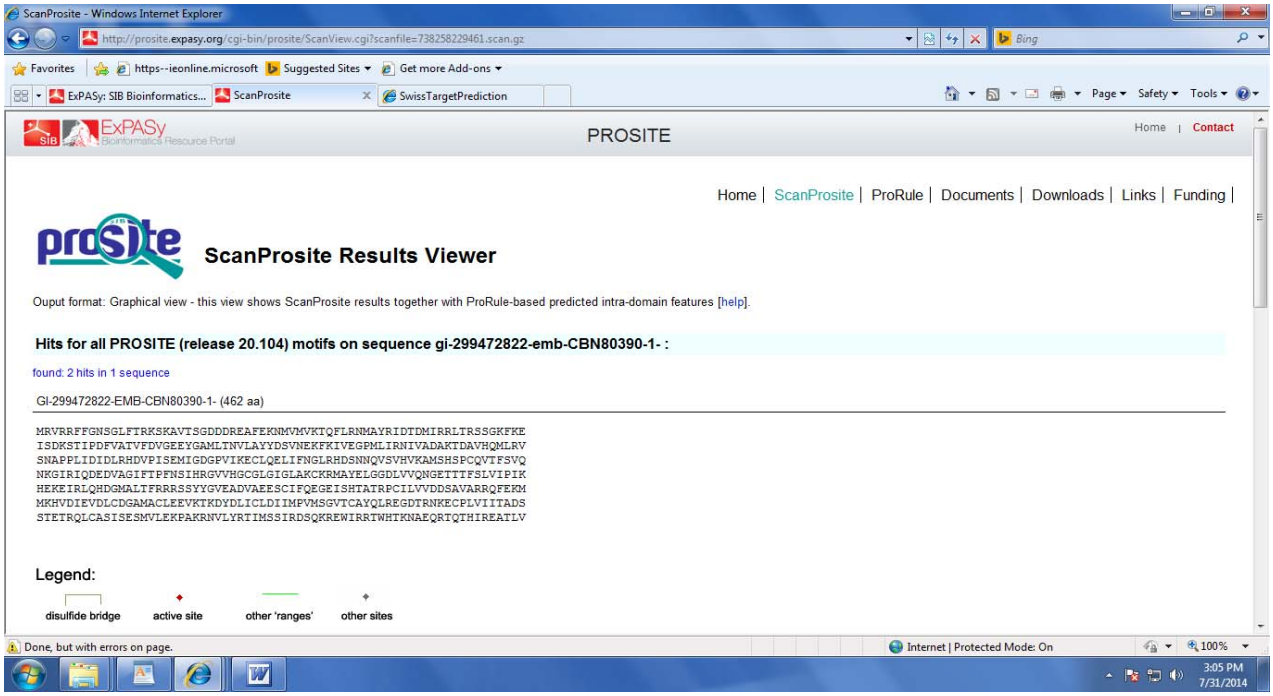

Fig 1: Submission of Histone Protein Sequence into Prosite Tool

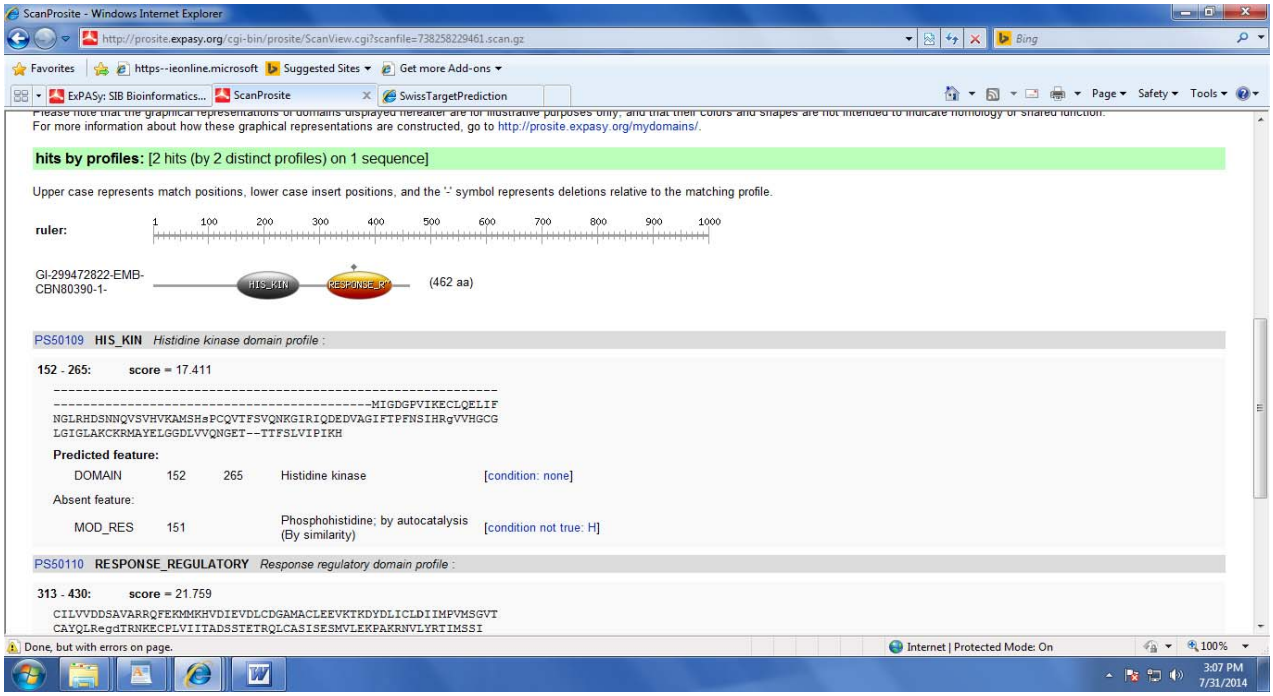

Fig 2: Calculation of Binding Sites in the Target Protein

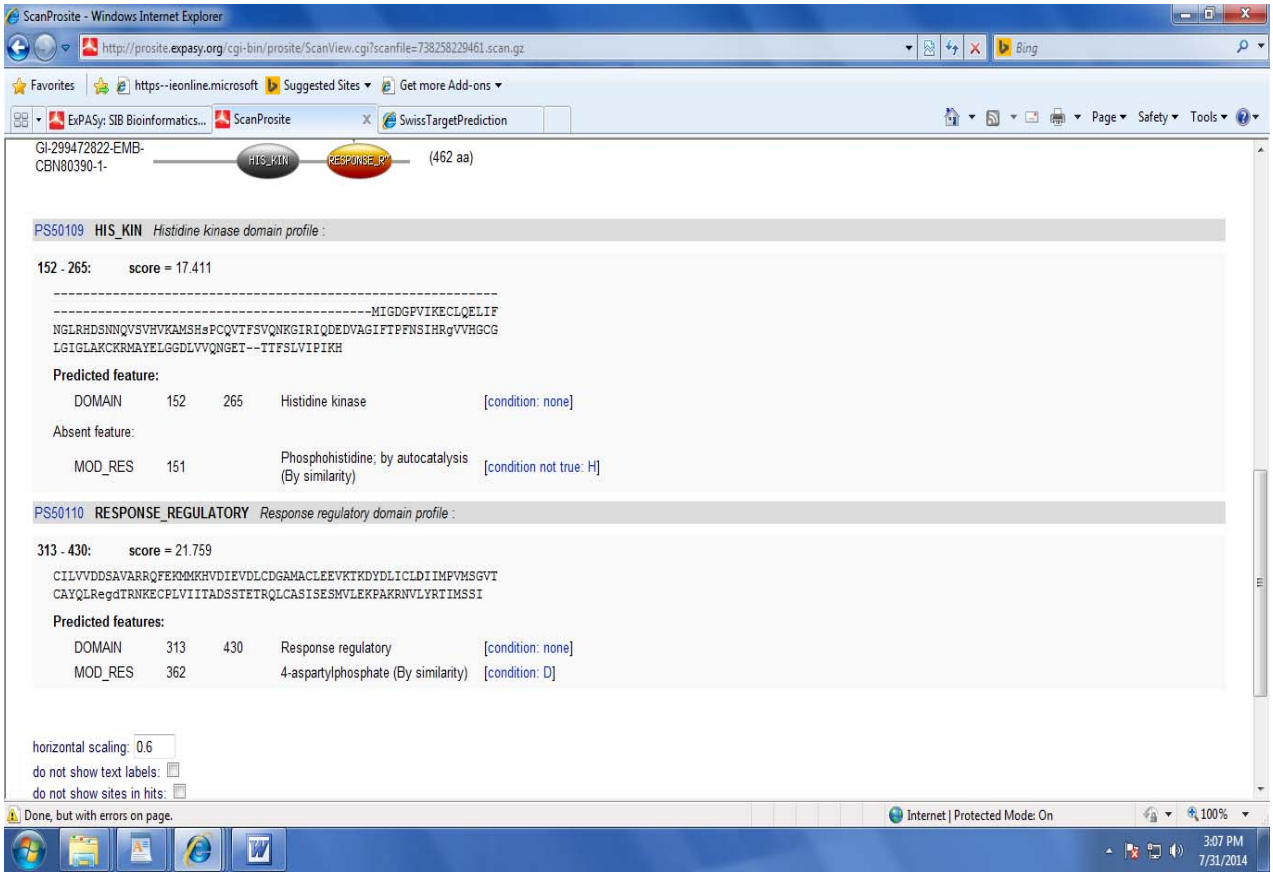

Fig 3: Identification of Position of Binding Sites in the Target Protein

Docking results

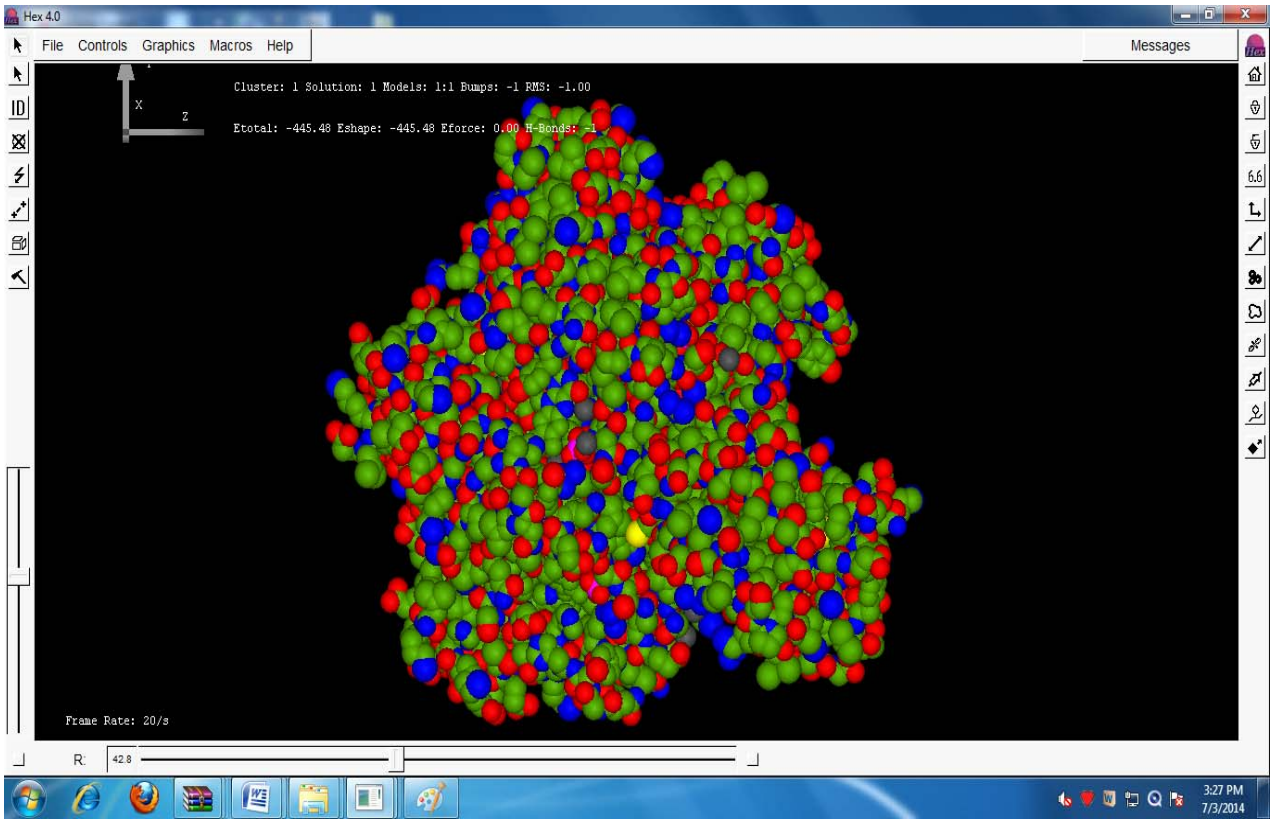

Fig 4: Target Receptor docked with the Ligand hydroxymethyl

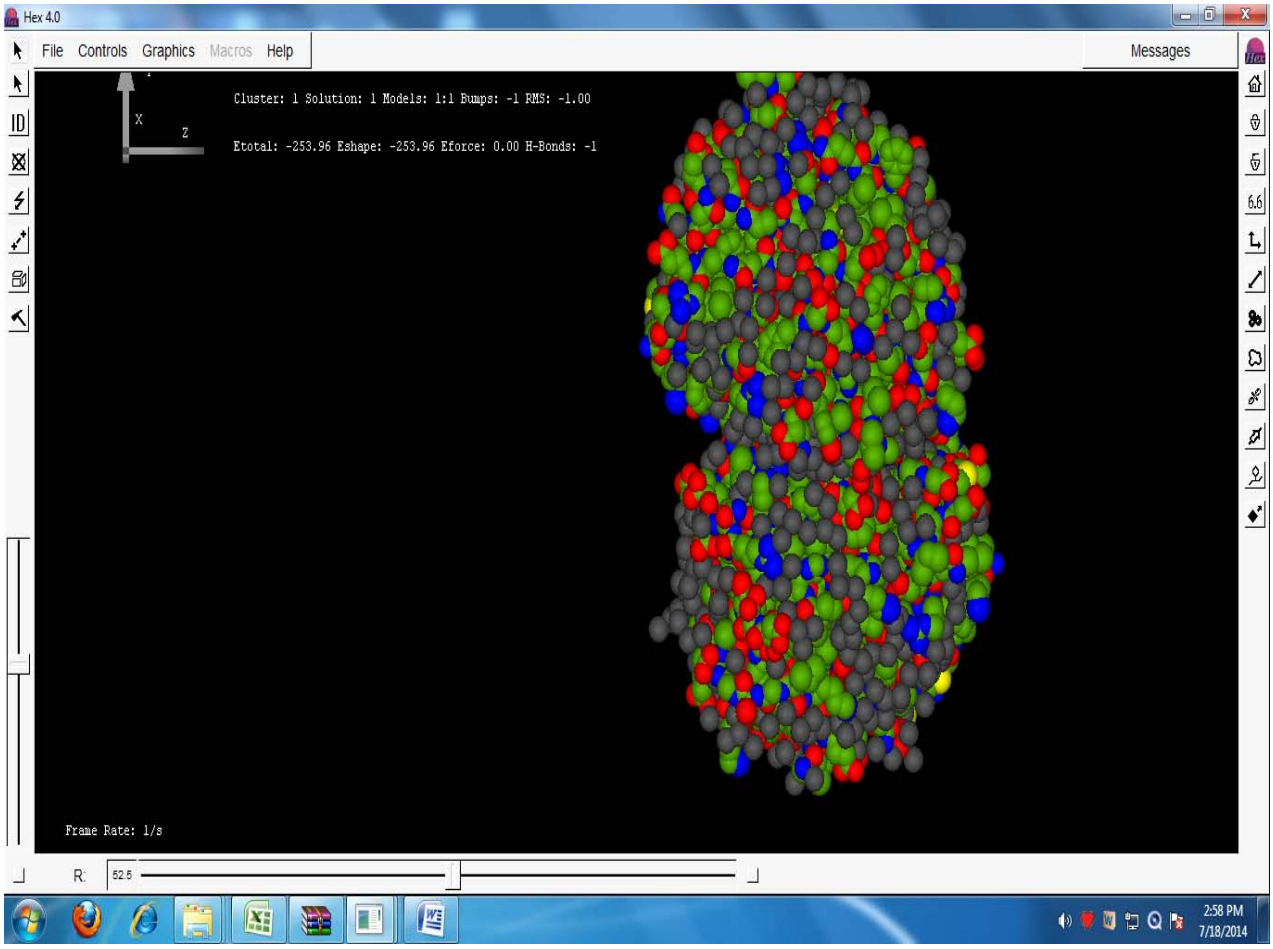

Fig 5: Target Receptor docked with the Ligand Pyran

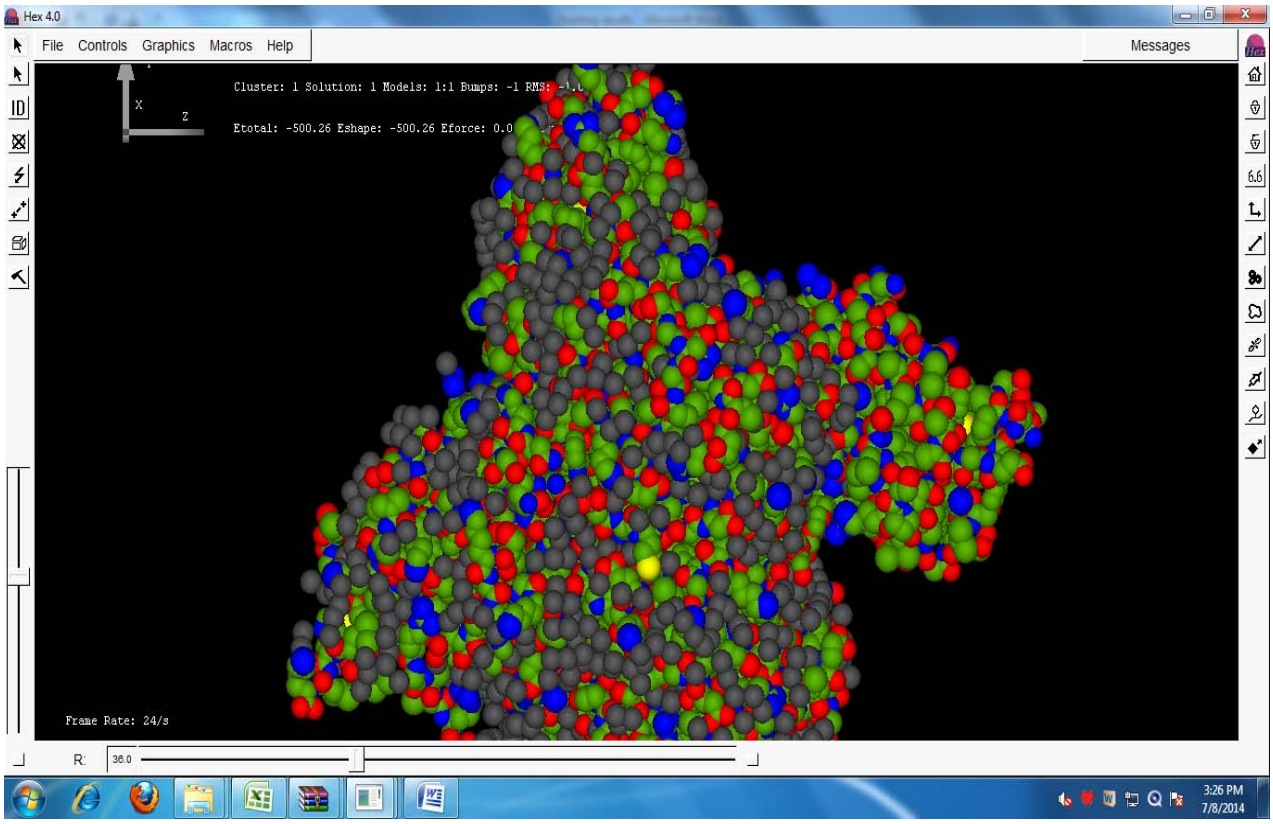

Fig 6: Target Receptor docked with the Ligand Cyclohexanetetrol

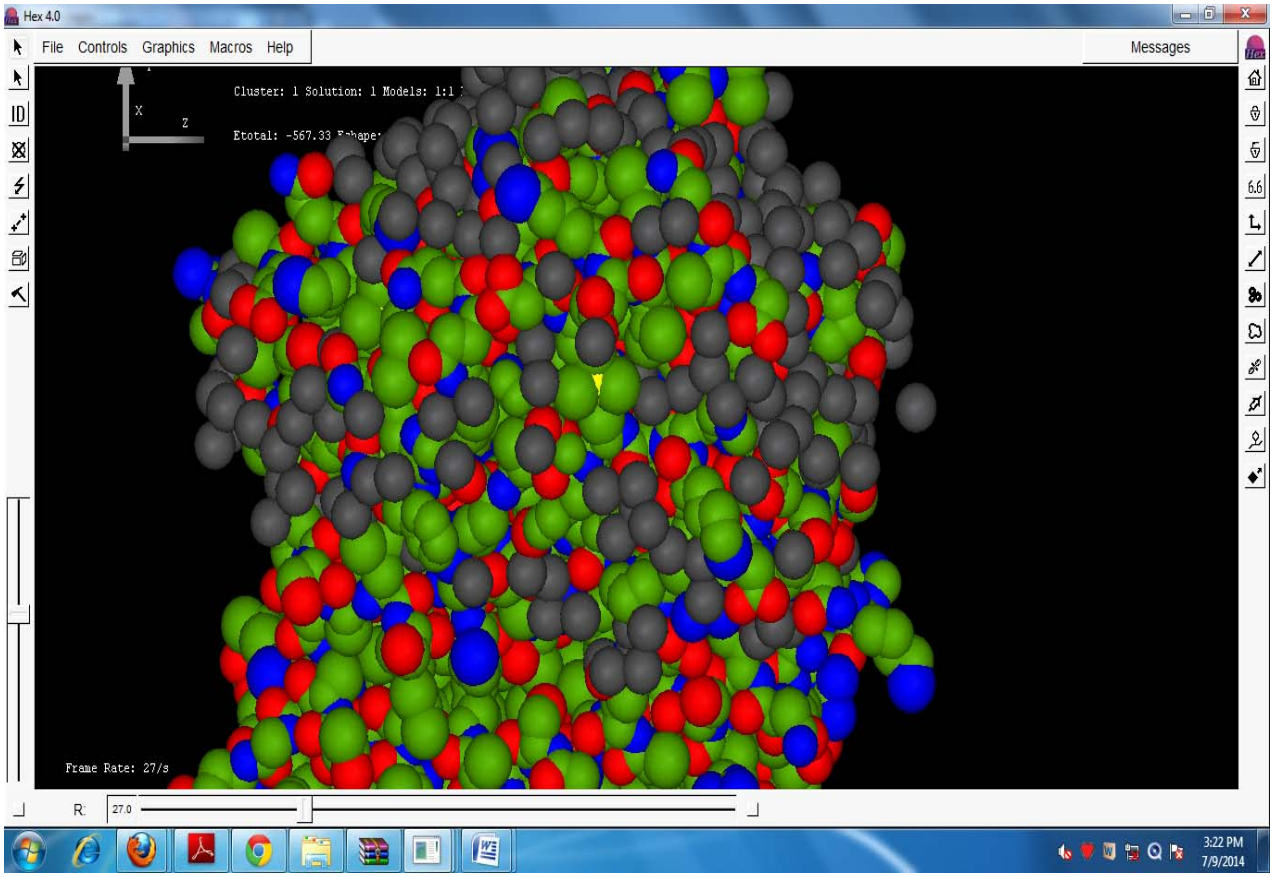

Fig 7: Target Receptor docked with the Ligand methyl ester

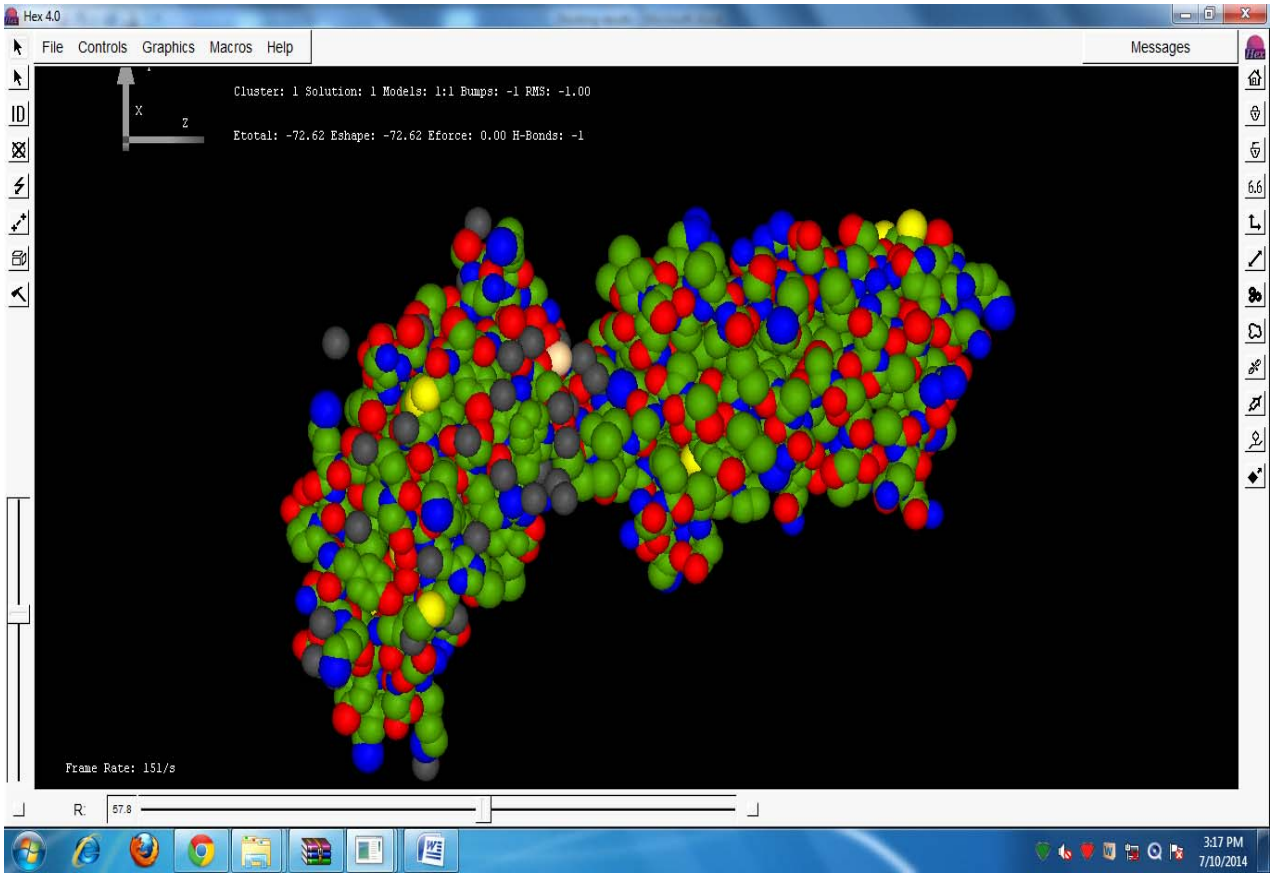

Fig 8: Target Receptor docked with the Ligand n-hexaadecanoic acid

Table 1: Parameters for the docked structures

Receptor – Ligand Interaction	E total	Eshape	Emax	Emin	Residues in the receptor	Atoms in the Ligand
Structure 1	-445.48	-445.48	-142.93	-445.48	476	1517
Structure 2	-253.96	-253.96	-68.99	-253.96	476	4172
Structure 3	-500.26	-500.26	-293.98	-500.26	476	9178
Structure 4	-567.33	-567.33	-355.13	-567.33	476	1732
Structure 5	-72.62	-72.62	-34.36	-72.62	476	991

Table 2: Score values for the docked structures

Receptor – Ligand Interaction	Net charge		Top average energy			Docking score
	+ve	-ve	10	100	1000	
Structure 1	10	17	-413.44	-353.52	-296.12	42.75
Structure 2	32	68	-226.79	-192.97	-157.76	52.50
Structure 3	106	126	-470.65	-404.73	-352.59	36.98
Structure 4	27	28	-529.25	-466.94	-395.76	44.25
Structure 5	3	15	-61.24	-51.82	-40.28	57.75

3. Discussion

Nowadays, most of the people affected by leukemia. Leukemia is the type of blood cancer and it is the challengeable problem in the society. There are number of herbs are having medicinal property. One of the most important herbal medicine is that *Catharanthus roseus*. We have collected the sample from various locations of Perambalur district. The flowers of the plant were collected and dried under shadow for five days. Then the sample was converted into powdered form using electric blunder. The plant sample was subjected to phytochemical study using Gas Chromatography – Mass Spectrometry. Table 1 showed that 38 phytochemicals which are isolated from *Catharanthus roesus* using methanol extract and Graph 1 shows that the chromatogram for the phytochemical studies. The compounds were selected based on peak area for docking with the target receptor. The compounds such as hydroxy methyl, Pyran, Cyclohexanetetrol, Cyclo Spermidine and Hexadecanoic acid were subjected to docking. The sequence for the target receptor was retrieved and submitted to Prosite tool (Fig 1). Fig 2 shows that the calculation of binding sites and the position of binding sites showed in Fig 3. The position for first binding site is between 152 and 265 with its score 17.411. The second binding site is from 313 to 430 with its score 21.759. The target receptor was docked with the ligand hydroxymethyl and the score value is 42.75(Fig 4). Fig 5 represents that the ligand pyran was docked with the target receptor and shows the score value 52.50. Fig 6 and 7 represents that the compound cyclohexanediol and methyl ester was docked with the receptor and the score values are 36.98 and 44.25 respectively. The ligand n-hexadecanoic acid was docked and shows the score value 57.75 (Fig 8). Table 1 represents that the docking parameters such as Etotal, Eshape, Emax, Emin, Residues in the receptor and the atoms present in the ligands. Table 2 shows that the net charge, average energy and score values for the docked structures.

4. Conclusion

The *Catharanthus roseus* collected from various locations of Perambalur district and the plant sample was subjected to phytochemical study using Gas Chromatography – Mass Spectrometry. It shows various phytochemical compounds which are isolated from the sample *using* methanol extract and the compounds were selected based on peak area for docking with the target receptor. The compounds such as hydroxy methyl, Pyran, Cyclohexanetetrol, Cyclo Spermidine and Hexadecanoic acid were subjected to docking and the target receptor was effectively docked with n-hexadecanoic acid with the score value of 57.75. The Binding sites of the receptor were also calculated using prosite tool. From these results, we observed that n-hexadecanoic acid was effectively docked with the binding sites of the receptor and it could be a responsible ligand for drug designing.

5. References

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