Molecular Docking Studies of Ubhasanthi Chooranam against the Target enzyme (MAO) - A and (MAO) - B of Parkinson's disease

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Abstract

Background-

Parkinson's Disease (PD) is caused by the progressive loss of dopaminergic neurons. More than 6 million people in the world are affected with a prevalence of 150 in every 100,000 people. Monoamine Oxidase (MAO) exists in two isoforms, MAO-A and MAO-B. Inhibition of Monoamine Oxidase A and B proves to be an effective treatment mechanism for Parkinson's disease.

Objective-

The present study is aimed to assess the potential of Ubhasanthi Chooranam (USC) against Monoamine Oxidase A- (MAO-A) with PDB – 2Z5X and Monoamine Oxidase B- (MAO-B) with PDB – 2V5Z for Parkinson's disease.

Methodology-

Molecular docking was performed using Auto dock and Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method. Docking calculations were carried out for retrieved phytocomponents such as Piperidine, Piperine, Gingerenone-A, Kaempferol, Glycyrrhizin, Quercitin, β-sitosterol, Oleic acid, Cucurbitacin, Kaempferitrin against target enzyme MAO A& B.

Results-

The data shows that the phytocomponents such as Glycyrrhizin, Quercetin, β-sitosterol, Oleic acid, Cucurbitacin, Kaempferitrin and Gingerenone-A reveals maximum of 3 interactions in comparison with STD Clorgyline showing 4 interactions with the core active amino acid residues of MAO- A. The phytocomponents such as Glycyrrhizin, Cucurbitacin and Kaempferitrin reveals 4 interactions with the MAO- B in comparison with standard Selegiline showing 4 interactions with the active site of the enzyme.

Conclusion-

USC possess significant binding against the target MAO A & B by interacting with active amino acid present on the active site and may act effective in management of PD.

Keywords - Ubhasanthi chooranam, Parkinson's, Dopamine, MAO-A, MAO-B.

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INTRODUCTION-

The Siddha system of medicine is one of the traditional medical sciences that aids in the management and treatment of many diseases Siddha medicine originated in the Southern part of India, peculiarly in Tamil Nadu .Our body has three vital life factors exist in the ratio of 4:2:1 in a healthy body; any disturbances in this equilibrium will cause ill- health. Vaatham is one among them responsible for the functioning of locomotor and neurological systems.Derangement in Vaatham leads to muscular rigidity, tremor and dyskinesia. In elderly patients, vitiation of Vaatham and kapham is common and it causes tremors in the head [(1).] Vaatham diseases (vitiated Vaatham humour) like Paanikamba Vaatham, Sirathamba Vaatham and Nadukku Vaatham are clearly explained in Siddha texts expressing symptoms such as difficulty in walking, resting tremor and loss of sensation (chronic state) in the limbs, rigidity and sleeplessness [(2).]Symptoms of Parkinson's disease correlates with that of Nadukku Vaatham aptly [(3).] Among all the NCDs, Neurological disorders contribute in significantly in the universal burden of diseases [(4).]The challenges in dealing the Neurological diseases in developing countries with its limited resources was already reported by the World Health Organization (WHO) and the World Federation of Neurology [(5),(6)] . Razdan *et al*. reported a prevalence rate of 14.1 per 100,000 amongst a population of 63,645 from rural Kashmir in the northern part of India. The prevalence rate over the age of 60 years was 247/100,000. A low prevalence rate of 27/100,000 was reported from Bangalore, in the southern part of India, and 16.1/100,000 from rural Bengal, in the eastern part of India. Bharucha *et al*. reported a high prevalence rate of 328.3/100,000 among a population of 14,010 Parsis living in colonies in Mumbai, Western India [(7).] Degeneration of dopaminergic neurons which are densely packed in substantia nigra and corpus striatum is the hallmark of Pathophysiological changes in Parkinsonism. Degeneration leads to motor dysfunctions and cognitive impairment. However, the loss of non-dopaminergic and associated non-motor functions are results of alterations in neurochemical mechanisms [(8).] Depression, anxiety and cognitive decline are the symptoms of non-motor PD. Herbal based drugs prove effective in showing neuroprotective activity in PD treatment [(9).] The present study was undertaken to scientifically validate the therapeutic efficacy of "Ubhasanthi Chooranam" (USC). The phytocomponents of USC such as Piperidine, Piperine, Gingerenone-A, Kaempferol Glycyrrhizin, Quercitin ,β-sitosterol, Oleic acid, Cucurbitacin, Kaempferitrin are evaluated for its potential against MAO-A & B enzymes for Parkinson's Disease.

Materials and methods-

Ubhasanthi Chooranam (USC) [(10)] is mentioned in Siddha literature *Theran tharu.* It is indicated for Sweat(*Vervai*), Dropsy with Anaemia(*Soobai*), Vomitting(*Vandhi*), Fatigue(*Ilaippu*), Debility(*Soorvu*), Hiccup(*Vikkal*), Bad taste in Mouth(*Vaiilaippu*), Secretion of Saliva (*Vaayil neerooral*),

Tremours(*Nadukal*) and Virulence of Medicine (*Marundhu Vegam*) [11] at a dosage of *1ounce* (30 millilitre) in the form of *Kudineer* with Honey, Butter or Sugar candy. Table.1 represents the ingredients of Ubhasanthi chooranam.

Objective:

Binding of phytocomponents with the core amino acids (Tyr69,Ile335, Tyr407, Tyr444)of the target by forming hydrogen bond will hinder the function of the enzyme Monoamine Oxidase A-(MAO-A) with PDB –2Z5X. Similarly, binding of phytocomponents with the core amino acids (Tyr60, Tyr326, Tyr 398 and Tyr 435) of the target by forming hydrogen bond will hinder the function of the enzyme Monoamine Oxidase B-(MAO-B) with PDB –2V5Z. These amino acid residues are functionally responsible for binding of substrate and further involved in degradation of the neurotransmitter dopamine by MAO-A & B. Thereby phytocomponents which inhibit the target enzyme MAO-A & B may act as a potential therapeutic agent for management of Parkinson's disease. Crystalline structure of the target enzyme Monoamine Oxidase A- (MAO-A) Figure. 1 with PDB –2Z5X and Crystalline structure of the target enzyme Monoamine Oxidase B- (MAO-B) Figure. 2 with PDB –2V5Z were retrieved from protein data bank and protein clean-up process was done and essential missing hydrogen atom were being added. Different orientation of the lead molecules with respect to the target protein was evaluated by Auto dock program and the best dock pose was selected based on the interaction study analysis.

Methodology-

Docking calculations were carried out for retrieved phytocomponents Table. 2 against target enzymes Monoamine Oxidase A & B. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of Auto Dock tools (*Morris, Goodsell et al., 1998*) [12].Affinity (grid) maps of ×× Å grid points and 0.375 Å spacing were generated using the Auto grid program (*Morris, Goodsell et al., 1998*). Auto Dock parameter set- and distance-dependent dielectric functions were used in the calculation of the van der Waals and the electrostatic terms respectively [13]. Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (*Solis and Wets, 1981*). Initial position, orientation, and torsions of the Ligand molecules were set randomly [14]. All rotatable torsions were released during docking. Each docking experiment was derived from 2 different runs that were set to terminate after a maximum of 250000 energy evaluations. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied.

Observation and Inference

Total of 10 bioactive lead compounds were retrieved from the herbs present in the Siddha formulation. From reported data of the formulation, the phytocomponents such as Glycyrrhizin, Quercetin, β-sitosterol, Oleic acid, Cucurbitacin, Kaempferitrin and Gingerenone-A reveals maximum of 3 interactions with the core active amino acid residues present on the target protein enzyme Monoamine

Oxidase A in comparison with STD Clorgyline which reveals maximum of 4 interactions. The phytocomponents such as Glycyrrhizin, Cucurbitacin and Kaempferitrin reveals maximum of 4 interactions with the core active amino acid residues present on the target protein enzyme Monoamine Oxidase B. Followed by this the compounds such as Piperidine, Piperine, Gingerenone-A, Kaempferol, Quercetin, B-sitosterol and Oleic acid ranked second with the maximum of 2-3 interactions with the active site of the target enzyme Monoamine Oxidase B when compared with standard Selegiline which impose 4 interactions with the active site of the enzyme. Table iii, Ligand Properties of the Compounds Selected for Docking Analysis against MAO-Aand Table iv, Ligand Properties of the Compounds Selected for Docking Analysis against MAO-B. Table v, Summary of the molecular docking studies of compounds against Monoamine Oxidase A- (MAO-A) with PDB – 2Z5X.Table vi, Summary of the molecular docking studies of compounds against Monoamine Oxidase B- (MAO-B) with PDB – 2V5Z.Table vii, Amino acid Residue Interaction of Lead against Monoamine oxidase A- (MAO-A) with PDB – 2Z5X.Table viii, Amino acid Residue Interaction of Lead against Monoamine oxidase B- (MAO-B) with PDB – 2V5Z.Table ix, 2 D and 3 D Structures of Phytocomponents having contents of Figure3i,Piperidine, Figure3ii,Piperine, Figure3iii, Gingerenone-A, Figure3iv, Kaempferol, Figure3v,Glycyrrhizin, Figure3vi,Quercetin,Figure3vii, β-sitosterol, Figure 3viii, Oleic acid, Figure 3ix, Cucurbitacin, ,Figure 3x, Kaempferitrin , Figure 3xi, Clorgyline ,Figure 3xii, Selegiline .Table x, Docking pose of phytocomponents with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis. Figure 4 a-c denotes Docking pose of Piperidine with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 5 a-c denotes Docking pose of Piperine with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 6 a-c denotes Docking pose of Gingerenone-A with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 7 a-c denotes Docking pose of Kaempferol with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 8 a-c denotes Docking pose of Glycyrrhizin with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 9 a-c denotes Docking pose of Quercetin with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 10 a-c denotes Docking pose of β-sitosterol with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.

Figure 11 a-c denotes Docking pose of Oleic acid with Monoamine *oxidase A-(MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 12 a-c denotes Docking pose of Cucurbitacin with Monoamine *oxidase A-(MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. . Figure 13 a-c denotes Docking pose of Kaempferitrin with Monoamine *oxidase A-(MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Figure 14 a-c denotes Docking pose of Clorgyline with Monoamine *oxidase A-(MAO-A) – 2Z5X, 2D* Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively. Table xi, Docking pose of phytocomponents with *Monoamine oxidase B (PDB) - 2V5Z, 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis*. Figure 15a-c, denotes docking pose of Piperine with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 16a-c, denotes docking pose of Piperidine with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 17 a-c, denotes docking pose of Gingerenone-A with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 18a-c, denotes docking pose of kaempferol with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* . Figure 19a-c, denotes docking pose of Glycyrrhizin with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure20 a-c, denotes docking pose of Quercetin with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 21a-c, denotes docking pose of β-sitosterol with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 22a-c, denotes docking pose of Oleic acid with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 23a-c, denotes docking pose of Cucurbitacin with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* . Figure 24a-c, denotes docking pose of *Kaempferitrin* with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.* Figure 25a-c, denotes docking pose of Selegiline with *Monoamine oxidase B (PDB) - 2V5Z 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis respectively.*

Conclusion-

Based on the results of the computational analysis it was concluded that the bio-active compounds like Glycyrrhizin, Quercetin, β-sitosterol, Oleic acid, Cucurbitacin, Kaempferitrin and Gingerenone-A present in the Siddha formulation possess significant binding against the target Monoamine oxidase A by interacting with active amino acid present on the active site and the bio-active compounds like Glycyrrhizin ,Cucurbitacin , Kaempferitrin, Piperidine, Piperine, Gingerenone-A, Kaempferol, Quercetin, B-sitosterol and Oleic acid present in the Siddha formulation possess significant binding against the target Monoamine oxidase B by interacting with active amino acid present on the active site. Thereby, it was concluded that these compounds may exert promising anti-Parkinson's activity by inhibiting the enzyme Monoamine oxidase A & B possibly by preventing the degradation of the vital neurotransmitter dopamine essential for neuromotor function. Ubhasanthi Chooranam may perform efficiently in the treatment of Parkinson's disease. Further studies are needed to determine its safety and efficacy.

Acknowledgement-

The author wish to acknowledge sincere thanks to The Noble Research Solutions, Chennai for their technical and analytical support in this research work.

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Table **I.** Ingredients of Ubhasanthi chooranam

Vernacular name (Tamil)	Botanical Name
Milagu	Piper nigrum
Thipilli	Piper longum
Inji	Zingeber officinale
Lavangam	Syzygium aromaticum
Saathikkai	Myristica fragrans
Seeragam	Cuminum cyminum
Athimathuram	Glycyrrhiza glabra
Sembarutthi	Hibiscus rosa sinensis
Thulasi	Ocimum sanctum
Vasambu	Acorus calamus
Aadathodai	Justicia adathoda
Thenkai	Cocus nucifera
Thamarai	Nelumbo nucifera
Perunkaayam	Ferulo asafoetida
Arugu	Cynodon dactylon
Koorai kizhangu	Cyperus rotundus
Neermulli	Hygrofila auriculata
Surai	Lagenaria siceraria
Parangi pattai	Smilax china
Indhuppu	Sodium chloride impura

Table II. List of Phytocomponents Selected for docking

Botanical Name	**Phytocomponents**
Piper nigrum	Piperidine [15]
Piper longum	Piperine [16]
Zingeber officinale	Gingerenone-A [17]
Syzygium aromaticum	kaempferol [18]
Glycyrrhiza glabra	Glycyrrhizin [19]
Hibiscus rosa sinensis	*Quercetin [20]*
Ocimum sanctum	β-sitosterol [21]
Cynodon dactylon	Oleic acid [22]
Lagenaria siceraria	Cucurbitacin [23]
Smilax china	Kaempferitrin [24]

Table III. **Ligand Properties of the Compounds Selected for Docking Analysis against**

Compound	**Molar weight g/mol**	**Molecular Formula**	**H Bond Donor**	**H Bond Acceptor**	**Rotatable bonds**
Piperidine	85.15 g/mol	$C_5H_{11}N$	1	1	0
Piperine	285.34 g/mol	$C_{17}H_{19}NO_3$	0	3	3
Gingerenone-A	356.4 g/mol	$C_{21}H_{24}O_5$	2	5	9
Kaempferol	286.24 g/mol	$C_{15}H_{10}O_6$	4	6	1
Glycyrrhizin	822.9 g/mol	$C_{42}H_{62}O_{16}$	8	16	7
Quercetin	302.23 g/mol	$C_{15}H_{10}O_7$	5	7	1
β-sitosterol	414.7g/mol	$C_{29}H_{50}O$	1	1	6
Oleic acid	282.5 g/mol	$C_{18}H_{34}O_2$	1	2	15
Cucurbitacin	558.7 g/mol	$C_{32}H_{46}O_8$	3	8	6
Kaempferitrin	578.5 g/mol	$C_{27}H_{30}O_{14}$	8	14	5
Clorgyline	272.17 g/mol	$C_{13}H_{15}Cl_{l2}NO$	0	2	6

MAO-A

Table IV**. Ligand Properties of the Compounds Selected for Docking Analysis against MAO-B**

Compound	**Molar weight g/mol**	**Molecular Formula**	**H Bond Donor**	**H Bond Acceptor**	**Rotatable bonds**
Piperidine	85.15 g/mol	$C_5H_{11}N$	1	1	0
Piperine	285.34 g/mol	$C_{17}H_{19}NO_3$	0	3	3
Gingerenone-A	356.4 g/mol	$C_{21}H_{24}O_5$	2	5	9
Kaempferol	286.24 g/mol	$C_{15}H_{10}O_6$	4	6	1
Glycyrrhizin	822.9 g/mol	$C_{42}H_{62}O_{16}$	8	16	7
Quercetin	302.23 g/mol	$C_{15}H_{10}O_7$	5	7	1
β-sitosterol	414.7g/mol	$C_{29}H_{50}O$	1	1	6
Oleic acid	282.5 g/mol	$C_{18}H_{34}O_2$	1	2	15
Cucurbitacin	558.7 g/mol	$C_{32}H_{46}O_8$	3	8	6
Kaempferitrin	578.5 g/mol	$C_{27}H_{30}O_{14}$	8	14	5
Selegiline	187.28 g/mol	$C_{13}H_{17}N$	0	1	4

Table V. **Summary of the molecular docking studies of compounds against Monoamine oxidase A- (MAO-A) with PDB – 2Z5X**

Compound	Est. Free Energy of Binding	Est. Inhibition Constant, Ki	Electrostatic Energy	Total Intermo lec. Energy	Interact. Surface
Piperidine	-7.51 kcal/mol	3.14 uM	-0.48 kcal/mol	-8.40 kcal/mol	585.082
Piperine	-9.60 kcal/mol	91.92 nM	-0.07 kcal/mol	-10.00 kcal/mol	697.441
Gingerenone-A	-10.34 kcal/mol	26.14 nM	-0.09 kcal/mol	-11.58 kcal/mol	853.993
Kaempferol	-8.07 kcal/mol	1.22 uM	-0.27 kcal/mol	-8.43 kcal/mol	675.036
Glycyrrhizin	-7.88 kcal/mol	1.68 uM	-0.11 kcal/mol	-9.52 kcal/mol	699.716
Quercetin	-8.69 kcal/mol	423.27 nM	-0.04 kcal/mol	-7.90 kcal/mol	706.645
β-sitosterol	-12.52 kcal/mol	667.56 pM	-0.02 kcal/mol	-14.21 kcal/mol	1010.102
Oleic acid	-5.03 kcal/mol	205.71 uM	-0.77 kcal/mol	-5.33 kcal/mol	371.446
Cucurbitacin	-7.98 kcal/mol	1.41 uM	-0.06 kcal/mol	-8.67 kcal/mol	716.583
Kaempferitrin	-7.57 kcal/mol	2.80 uM	-0.07 kcal/mol	-9.66 kcal/mol	748.403
Clorgyline	-8.46 kcal/mol	631.47 nM	-0.05 kcal/mol	-9.39 kcal/mol	711.724

Table VI. **Summary of the molecular docking studies of compounds against Monoamine oxidase B- (MAO-B) with PDB – 2V5Z**

Compound	Est. Free Energy of Binding	Est. Inhibition Constant, Ki	Electrostatic Energy	Total Intermolec. Energy	Interact. Surface
Piperidine	-7.33 kcal/mol	4.24 Um	-1.06 kcal/mol	-8.21 kcal/mol	694.574
Piperine	-10.06 kcal/mol	42.46 nM	-0.04 kcal/mol	-10.47 kcal/mol	715.576
Gingerenone-A	-10.27 kcal/mol	29.52 nM	-0.01 kcal/mol	-11.13 kcal/mol	962.512
Kaempferol	-8.07 kcal/mol	1.21 uM	-0.04 kcal/mol	-8.43 kcal/mol	672.416
Glycyrrhizin	-8.82 kcal/mol	341.53 nM	-0.15 kcal/mol	-8.13 kcal/mol	852.097

Quercetin	-8.86 kcal/mol	320.32 nM	-0.04 kcal/mol	-8.12 kcal/mol	827.331
β-sitosterol	-13.62 kcal/mol	103.40 pM	-0.03 kcal/mol	-15.56 kcal/mol	1049.603
Oleic acid	-4.90 kcal/mol	256.59 uM	-1.02 kcal/mol	-5.20 kcal/mol	374.116
Cucurbitacin	-0.66 kcal/mol	327.67 mM	-0.03 kcal/mol	-1.13 kcal/mol	1117.371
Kaempferitrin	-3.95 kcal/mol	1.27 mM	-0.32 kcal/mol	-6.27 kcal/mol	1052.179
Selegiline	-6.74 kcal/mol	11.56 uM	-0.79 kcal/mol	-8.20 kcal/mol	566.262

Table **VII.** Amino Acid Residue Interaction Of Lead Against Monoamine Oxidase A- (Mao-A) With Pdb – 2z5x

COMPOUND	Interactions	Amino Acid Residues																		
PIPERIDINE	1	51	52	303	305	352	397	406	407	435	448									
		ARG	THR	VAL	LYS	PHE	TRP	CYS	TYR	THR	ALA									
PIPERINE	1	51	303	305	352	397	406	407	443	445										
		ARG	VAL	LYS	PHE	TRP	CYS	TYR	GLY	MET										
GINGERENONE-A	3	23	51	52	69	215	305	352	397	406	407	435	444	448						
		ILE	ARG	THR	TYR	GLN	LYS	PHE	TRP	CYS	TYR	THR	TYR	ALA						
KAEMPFEROL	1	51	52	305	352	397	406	407	435											
		ARG	THR	LYS	PHE	TRP	CYS	TYR	THR											
GLYCYRRHIZIN	3	23	51	52	69	74	180	181	207	208	215	337	352	406	407	435	441	444	445	448
		ILE	ARG	THR	TYR	GLN	ILE	ASN	ILE	PHE	GLN	LEU	PHE	CYS	TYR	THR	TRP	TYR	MET	ALA
QUERCETIN	3	69	180	181	215	305	352	406	407	444										
		TYR	ILE	ASN	GLN	LYS	PHE	CYS	TYR	TYR										
B-SITOSTEROL	3	51	52	69	180	215	352	407	435	444	445	448								
		ARG	THR	TYR	ILE	GLN	PHE	TYR	THR	TYR	MET	ALA								

OLEIC ACID	3	68	69	303	305	352	397	406	407										
		ALA	TYR	VAL	LYS	PHE	TRP	CYS	TYR										
CUCURBITACIN	3	51	52	69	180	181	207	215	352	406	444								
		ARG	THR	TYR	ILE	ASN	ILE	GLN	PHE	CYS	TYR	TYR	MET	ALA					
KAEMPFERITRIN	3	23	24	51	52	69	215	303	305	352	397	406	407	435	444	445	448		
		ILE	SER	ARG	THR	TYR	GLN	VAL	LYS	PHE	TRP	CYS	TYR	THR	TYR	MET	ALA		

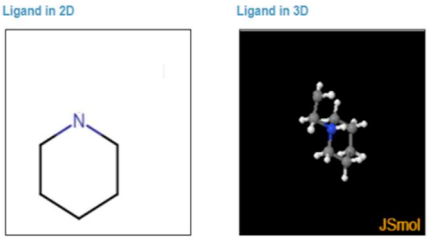
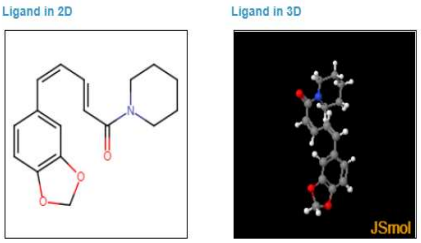
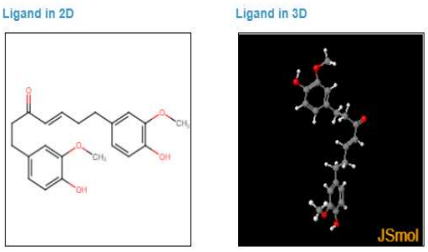
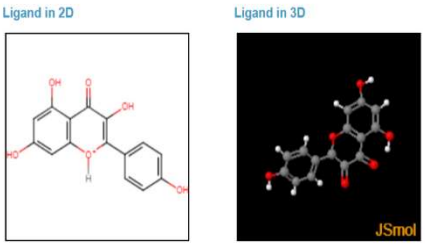
Clorgyline	4	69 TYR	180 ILE	181 ASN	208 PHE	215 GLN	335 ILE	352 PHE	407 TYR	444 TYR

TABLE **VIII.** AMINO ACID RESIDUE INTERACTION OF LEAD AGAINST MONOAMINE OXIDASE B- (MAO-B) WITH PDB – 2V5Z

COMPOUNDS	Interaction	Amino Acid Residues																	
PIPERIDINE	2	59	60	171	172	199	206	296	343	398									
		SER	TYR	LEU	CYS	ILE	GLN	LYS	PHE	TYR									
PIPERINE	2	103	104	119	168	171	172	199	206	316	326	398							
		PHE	PRO	TRP	PHE	LEU	CYS	ILE	GLN	ILE	TYR	TYR							
GINGERENONE-A	3	60	188	296	343	397	398	435	436										
		TYR	TYR	LYS	PHE	CYS	TYR	TYR	MET										
KAEMPFEROL	2	88	119	168	171	172	199	206	316	326	435								
		LEU	TRP	PHE	LEU	CYS	ILE	GLN	ILE	TYR	TYR								
GLYCYRRHIZIN	4	42	59	60	65	167	168	171	172	188	199	206	316	326	343	397	398	435	436
		ARG	SER	TYR	GLN	LEU	PHE	LEU	CYS	TYR	ILE	GLN	ILE	TYR	PHE	CYS	TYR	TYR	MET
QUERCETIN	3	42	60	188	343	397	398	435											
		ARG	TYR	TYR	PHE	CYS	TYR	TYR											
B-SITOSTERO	3	119	167	168	171	172	199	206	326	398	435	436							

L																		
		TRP	LEU	PHE	LEU	CYS	ILE	GLN	TYR	TYR	TYR	MET						
OLEIC ACID	2	60	296	343	388	397	398											
		TYR	LYS	PHE	TRP	CYS	TYR											
CUCURBITACIN	4	60	168	171	172	198	199	206	296	326	343	397	398	435				
		TYR	PHE	LEU	CYS	ILE	ILE	GLN	LYS	TYR	PHE	CYS	TYR	TYR				
KAEMPFERITRIN	4	59	60	167	168	171	172	198	199	206	296	316	326	343	398	435		
		SER	TYR	LEU	PHE	LEU	CYS	ILE	ILE	GLN	LYS	ILE	TYR	PHE	TYR	TYR		
SELEGILINE	4	59	60	168	171	172	199	206	326	343	388	397	398	435	436			171:00:00
		SER	TYR	PHE	LEU	CYS	ILE	GLN	TYR	PHE	TRP	CYS	TYR	TYR	MET			LEU

Table IX. **2D nad 3D Structure of phytocomponents**

2D and 3D Structure of Phytocomponents
 **Figure3 i , Piperidine**
 **Figure 3 ii. Piperine**
 Figure 3 iii, **Gingerenone-A**
 Figure 3 iv, **Kaempferol**

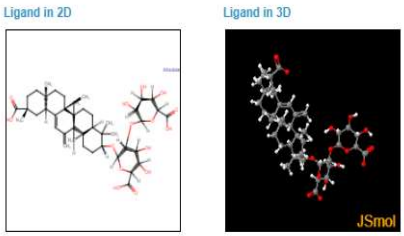


Figure 3v **,Glycyrrhizin**,

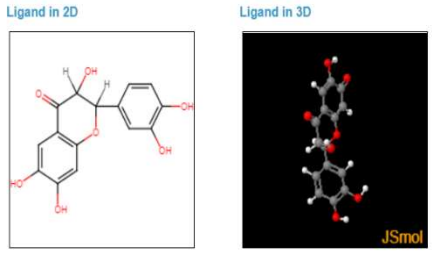


Figure 3vi, **Quercetin**

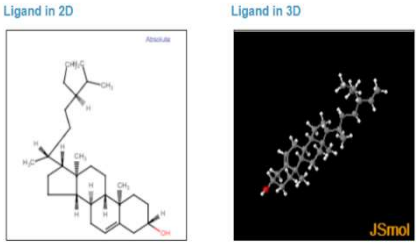


Figure 3vii, **β-sitosterol**

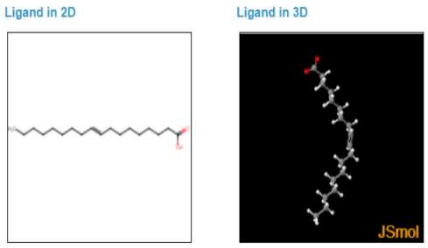


Figure 3viii, **Oleic acid**

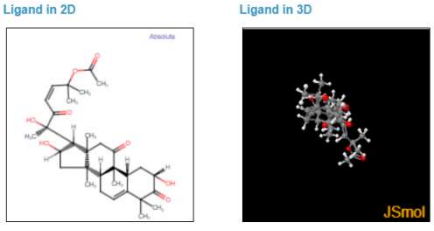


Figure 3ix, **Cucurbitacin**

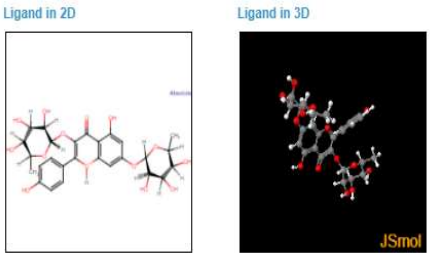


Figure 3x. **Kaempferitrin**

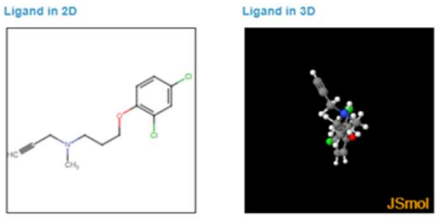


Figure 3xi. **Clorgyline**

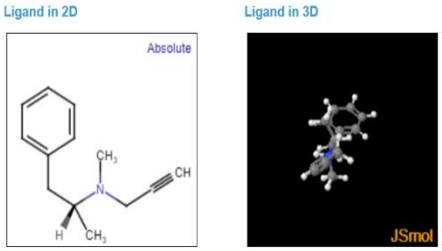
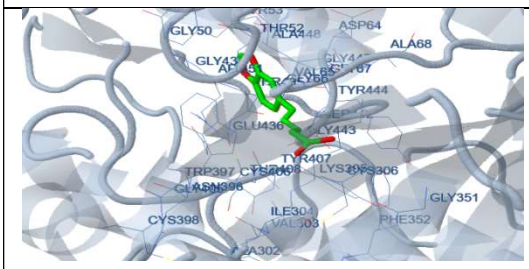
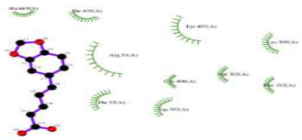
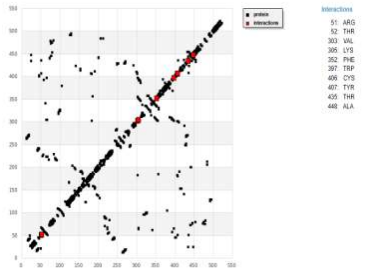
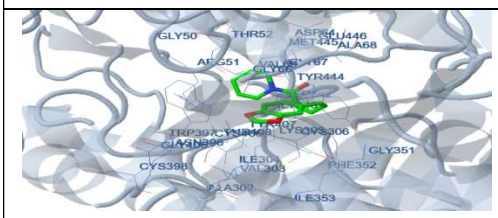
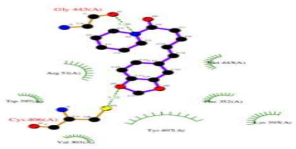
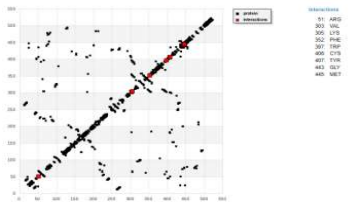
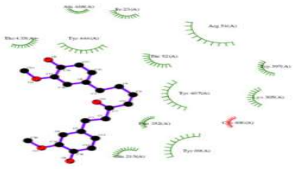
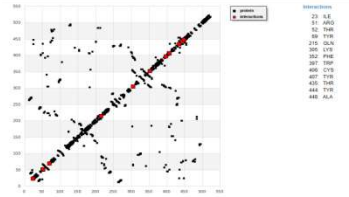
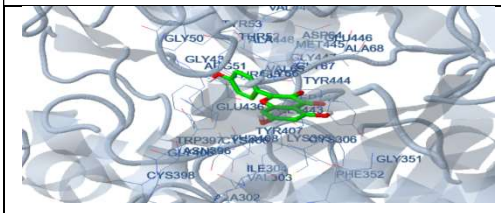
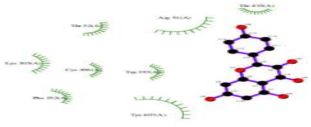
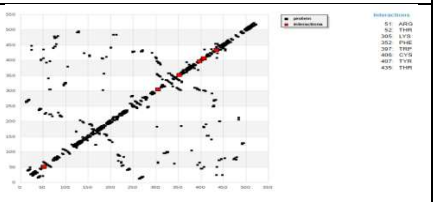


Figure 3xii. **Selegiline**

Table X. **Docking pose of phytocomponents with Monoamine *oxidase A- (MAO-A) – 2Z5X, 2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis***

Docking pose	***2D Interaction Plot Analysis***	***Hydrogen bond plotting with core amino acid Analysis***
 **Figure 4a. Piperidine with Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 4b**	 **Figure 4c**
 **Figure 5a. Piperinewith Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 5b**	 **Figure 5c**
 **Figure 6a. Gingerenone-A with Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 6b**	 **Figure 6c**
 **Figure 7a. Kaempferolwith Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 7b**	 **Figure 7c**

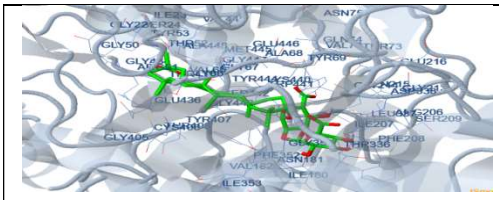


Figure 8a. Glycyrrhizin with Monoamine oxidase A- (MAO-A) – 2Z5X

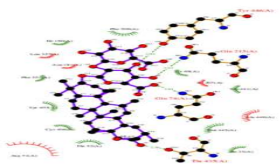


Figure 8b

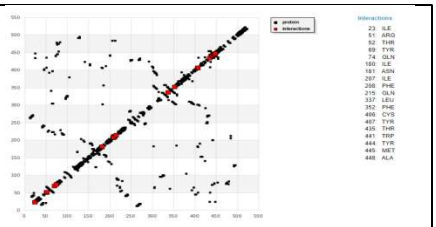


Figure 8c

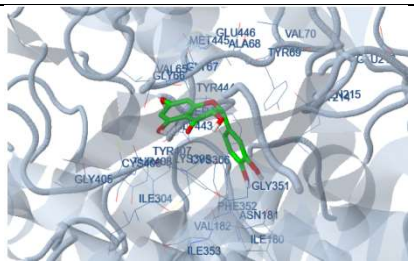


Figure 9a,
Quercetin with Monoamine oxidase A- (MAO-A) – 2Z5X

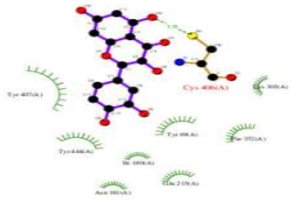


Figure 9b

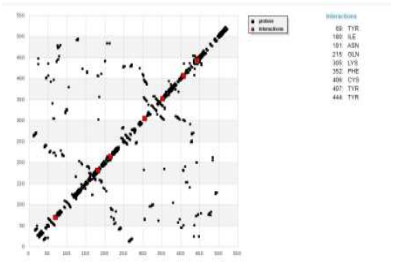


Figure 9c

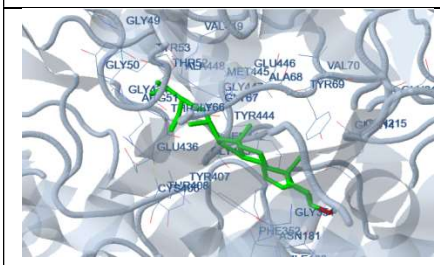


Figure 10a. β-sitosterolwith Monoamine oxidase A- (MAO-A) – 2Z5X

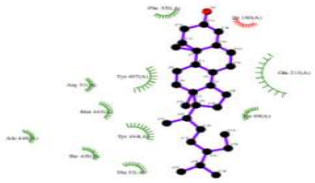


Figure 10b

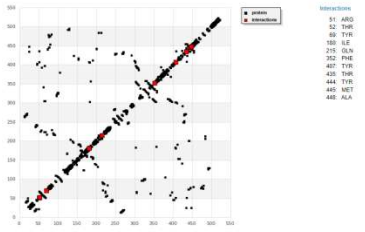


Figure 10c

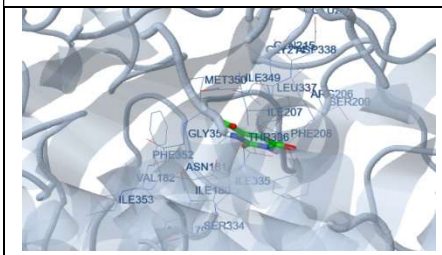
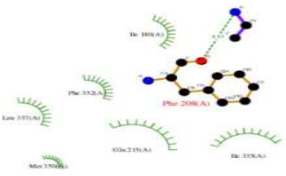


Figure 11a. Oleic acid with Monoamine oxidase A- (MAO-A) – 2Z5X



Figue 11b

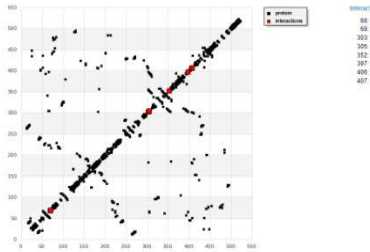


Figure 11c

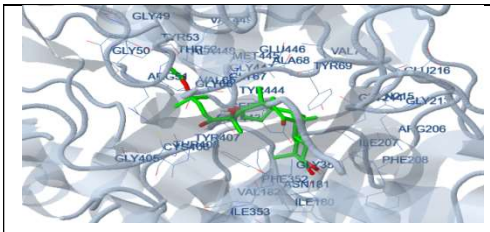
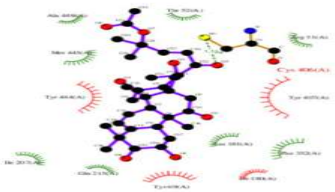
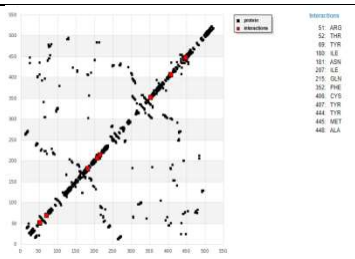
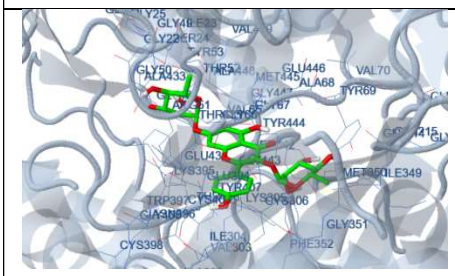
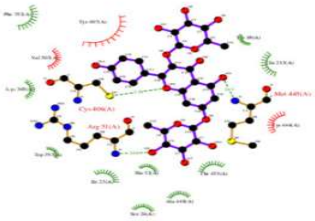
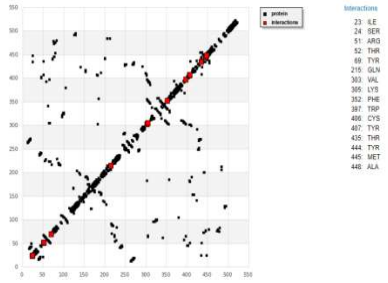
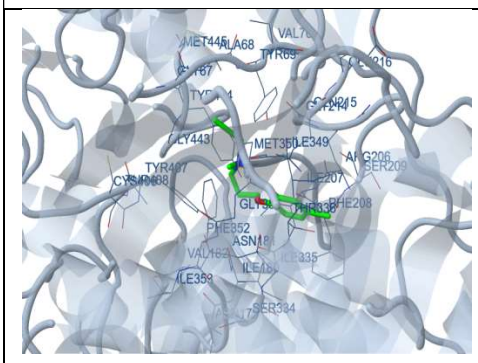
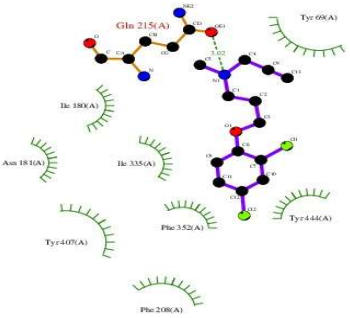
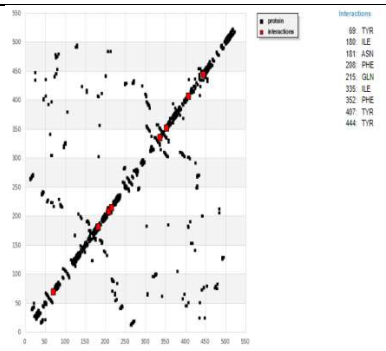
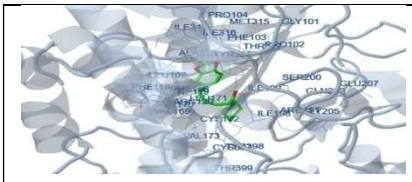
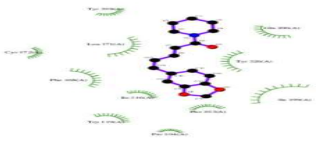
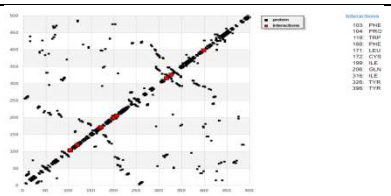
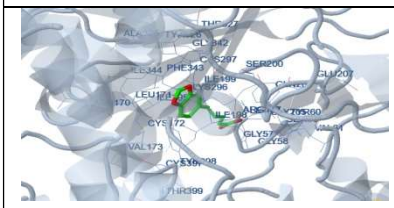
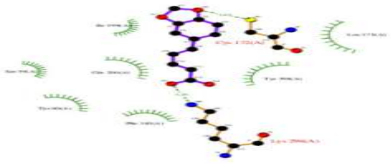
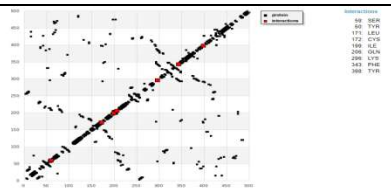
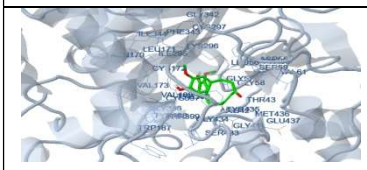
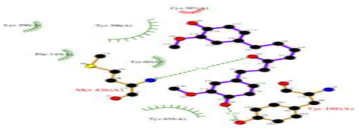
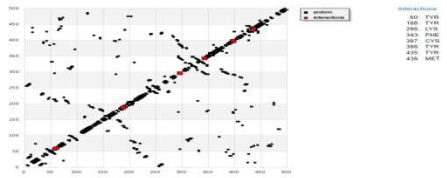
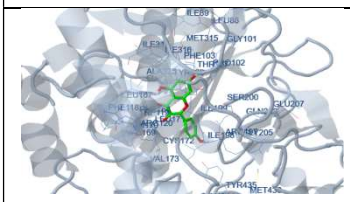
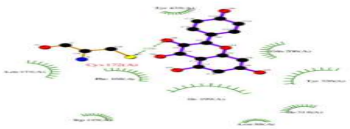
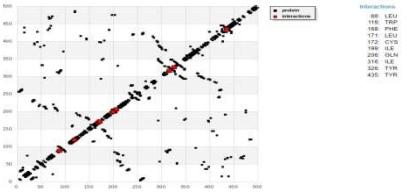
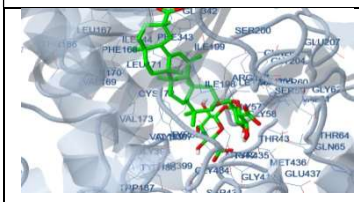
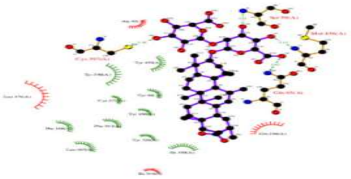
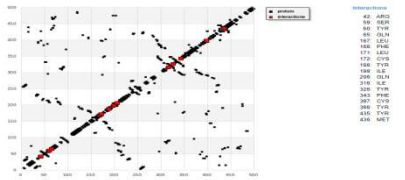
 **Figue 12a. Cucurbitacinwith Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 12b**	 **Figure 12c**
 **Figue 13a, Kaempferitrin with Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 13b**	 **Figure 13c**
 **Figure 14a. Clorgylinewith Monoamine oxidase A- (MAO-A) – 2Z5X**	 **Figure 14 b**	 **Figure 14 c**

Table xi, Docking pose of phytocomponents with *Monoamine oxidase B (PDB) - 2V5Z* *2D Interaction Plot Analysis, Hydrogen bond plotting with core amino acid Analysis*

Docking pose	***2D Interaction Plot Analysis***	***Hydrogen bond plotting with core amino acid Analysis***

 **Figure 15a. Piperine with Monoamine oxidase B (PDB) - 2V5Z**	 **Figure 15 b**	 **Figue 15c**
 **Figure 16 a. Piperidine with Monoamine oxidase B (PDB) - 2V5Z**	 **Figure 16 b**	 **Figure 16c**
 **Figure 17 a, Gingerenone-A with Monoamine oxidase B (PDB) - 2V5Z**	 **Figure 17b**	 **Figure 17c**
 **Figure 18a. kaempferol with Monoamine oxidase B (PDB) - 2V5Z**	 **Figure 18b**	 **Figure 18c**
 **Figure 19a. Glycyrrhizin with Monoamine oxidase B (PDB) - 2V5Z**	 **Figure 19b**	 **Figure 19c**

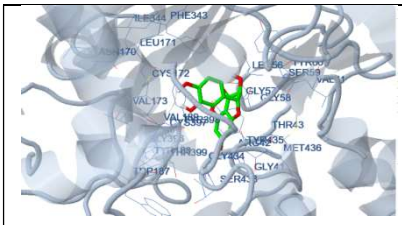


Figure 20a.
Quercetin with Monoamine oxidase B (PDB) - 2V5Z

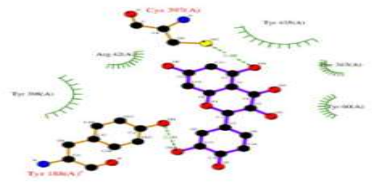


Figure 20b

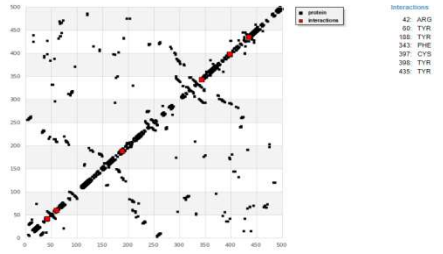


Figure 20c

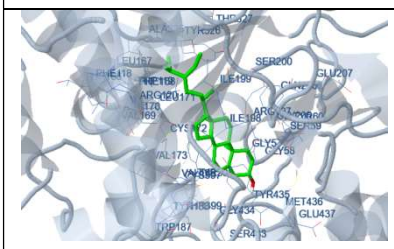


Figure 21 a.
β-sitosterolwith Monoamine oxidase B (PDB) - 2V5Z

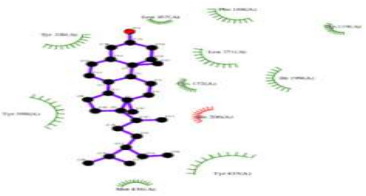


Figure 21b

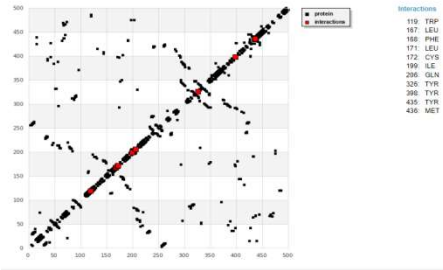


Figure 21c

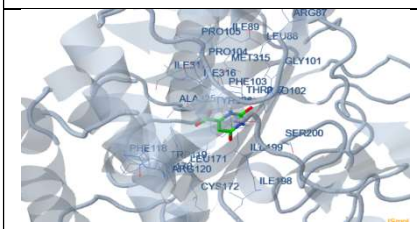


Figure 22 a.
Oleic acid with Monoamine oxidase B (PDB) - 2V5Z

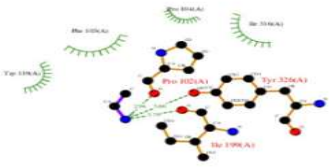


Figure 22b.

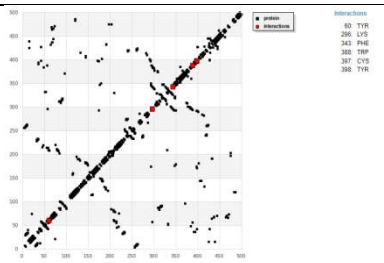


Figure 22c.

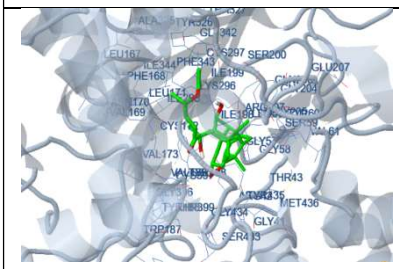


Figure 23a. Cucurbitacinwith Monoamine oxidase B (PDB) - 2V5Z

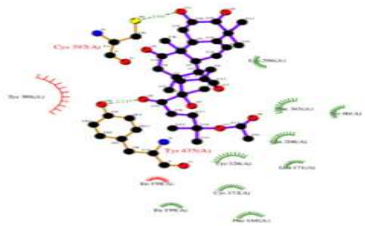


Figure 23b

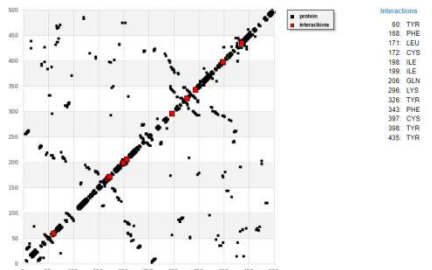
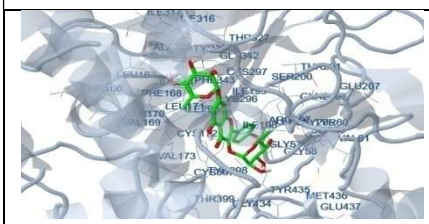
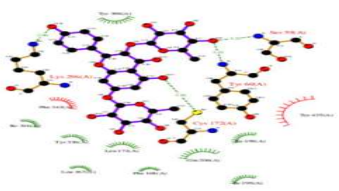


Figure 23c





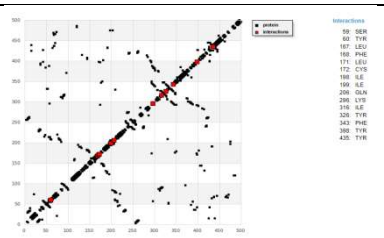


Figure 24a. Kaempferitrin with Monoamine oxidase B (PDB) - 2V5Z	Figure 24b	Figure 24c

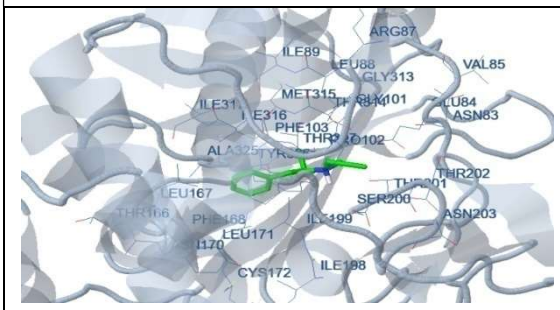
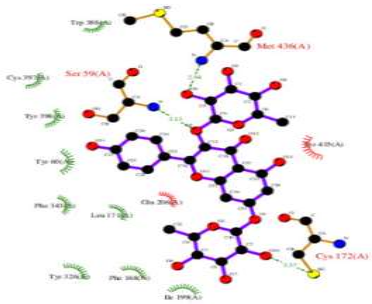
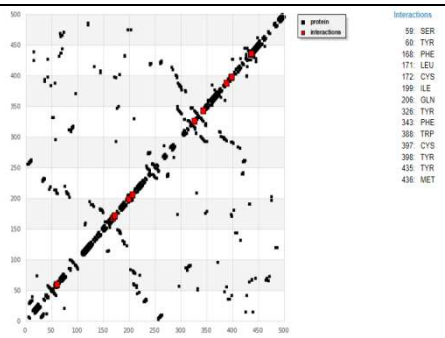
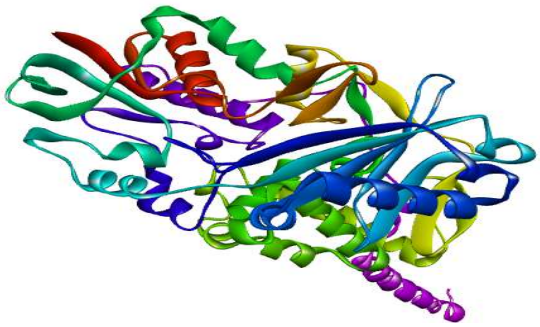

		

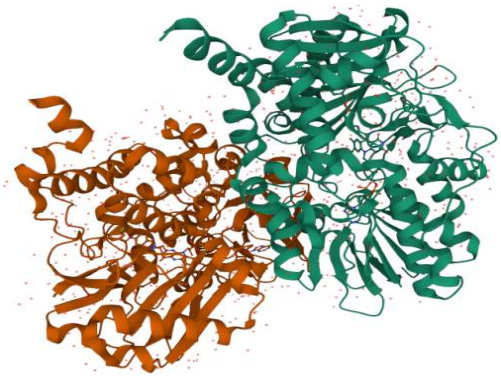
Figure 25a. Selegiline with Monoamine oxidase B (PDB) - 2V5Z	Figure 25b	Figure 25c

Figure1. 3D- Structure of Monoamine oxidase A (PDB) - 2Z5X



RECEPTOR STRUCTURE

Figure2. 3D- Structure of Monoamine oxidase B(PDB)-2V5Z



RECEPTOR STRUCTURE