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DOCKING STUDIES OF BENZIMIDAZOLE DERIVATIVES USING HEX 8.0

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Keywords:

Anticonvulsant activity, Benzimidazole derivatives, Hex, Protein-ligand interaction

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ABSTRACT: N-mannich bases of benzimidazole derivatives can work against convulsions. Docking used for virtual screening of database and for the prediction of the strongest binders based on various scoring functions. Docking studies were carried out on different benzimidazole derivaties for better anticonvulsant activity which is important for the development of new class of inhibitors. Protein–ligand interaction plays an important role in structural based drug design. In our research we selected different receptors. The receptors were docked with different imidazole derivatives and the energy values were obtained. Our study reveals that highest minimal energy values were observed with receptors like 4NF8, 4JWY, 4JWX, 3QEK, 3OEK, 3OEL, 3OEM, 3OEN. The results suggests that N-mannich bases of benzimidazole derivatives might be a potential targets of NMDA receptors for effective anticonvulsant activity.

INTRODUCTION: The advent of powerful and inexpensive computers has revolutionized science and medicine. Today, drug design methods are widely used in both industrial and academic environments. It has become popular to carry out in silico screening of drug-receptor candidate interations, known as virtual high-throughput screening (*v*HTS), for future development. The drug-receptor fit and predicted physicochemical properties are used to score and rank compounds according to penalty functions and information filters like molecular weight, number of hydrogen bonds, hydrophobicity, etc. Although medicinal chemists are aware of absorption, distribution, metabolism, elimination, and toxicity (ADMET or ADME/Tox), in recent years, a much more focused approach address these issues in the early design stages. Many of the predictive ADME models use quantitative structure activity relationships (QSAR).

In general, understanding what chemical space descriptors are critical for drug-like molecules helps provide insight into design of chemical libraries for biological evaluation.

With the aid of molecular modeling software, pharmaceutical scientists can modify the structural features of a potential drug candidate in silico and make predictions about its physicochemical properties prior to laboratory synthesis. Crystallographic information about the receptor has allowed the scientists to use structure-based drug design approaches with tangible benefits. Given the difficulty in preparing organic compounds, one can immediately appreciate the power that computer-based methods offer.

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MATERIALS AND METHODS: There are a range of software packages available for molecular docking like Auto Dock, Hex, Schrodinger GLIDE etc.

For our present study we used bioinformatics tools, biological data base PDB (protein data bank) and software like Chem Draw Ultra 12.0, OSIRIS Data Warrior, preADMET, PASS Online, Molinspiration, and Hex 8.0 docking.

Chem Draw Ultra 12.0 is a powerful yet to use tool for producing a nearly unlimited variety of biological and chemical drawings. You can create your own drawings or use those provided in the library of available templates. Having completed a drawing, you can export it to a desktop publishing program, post it on a Web page, or store it in a database. You can calculate predicted values of selected physical and thermodynamic properties for structures of up to 100 atoms.

OSIRIS Data Warrior [1] combines dynamic graphical views and interactive row filtering with chemical intelligence. Data Warrior supports the enumeration of combinatorial libraries as the creation of evolutionary libraries. Compounds can be clustered and diverse subsets can be picked. Calculated compound similarities can be used for multidimensional scaling methods, e.g. Kohonen nets. Physicochemical properties can be calculated, structure activity relationship tables can be created and activity cliffs be visualized. Today, OSIRIS is a vital backbone that enables the entire research process. One component, Data Warrior, specializes as data visualization and analysis tool for chemical and biological data.

PASS[2] (Prediction of Activity Spectra for Substances) is a software product designed as a tool for evaluating the general biological potential of an organic drug-like molecule. PASS provides simultaneous predictions of many types of biological activity based on the structure of organic compounds. Thus, PASS can be used to estimate the biological activity profiles for virtual molecules, prior to their chemical synthesis and biological testing. PASS provides reasonable estimates of structure-activity relationships despite of incompleteness (or some errors in data) of PASS training set. It provides a possibility of simultaneous prediction of about 3,600 kinds of biological activity for drug-like organic compound. Input data represents a structural formula of a compound in MOLfile format. The output file represents a list of activities with two probabilities Pa (probability to be active) and Pi (probability to be inactive).

Pa (probability "to be active") estimates the chance that the studied compound is belonging to the sub-class of active compounds (resembles the structures of molecules, which are the most typical in a sub-set of "actives" in PASS training set).

Pi (probability "to be inactive") estimates the chance that the studied compound is belonging to the sub-class of inactive compounds (resembles the structures of molecules, which are the most typical in a sub-set of "inactives" in PASS training set).

PreADMET [3] is a web-based application for predicting ADME data and building drug-like library using in silico method. PreADMET consists of four main parts as following:

1. Molecular Descriptor Calculation: The ADME/Tox properties are closely related to physico-chemical descriptors such as lipophilicity (logP), molecular weight, polar surface area, and water solubility. The TOPOMOL module calculates more than 2500 molecular descriptors including constitutional, topological, electrostatic, physico-chemical, and geometrical descriptors for ADME/Tox prediction from 2D and 3D chemical structure: TOPOMOL reads MDL mol or sd files and provides a rapid means to calculate all 2D descriptors of 1,000,000 compounds in less than 1 hour using Pentium IV 3.4GHz PC.

2. Drug-likeness Prediction: The most well known rule relating the chemical structures to their biological activities is Lipinski's rule, it is called the 'rule of five'. Another well known rule is the Lead-like rule, i.e. starting from a quantitative survey based upon 18 lead and drug pairs of structure. PreADMET contains drug-likeness prediction module based on these rules. Also, it is possible to use several drug-like rules that several researchers defined drug-like characteristics of drug DB such as CMC (covering more than 80% of

the compounds), WDI (world drug index), and MDDR DB.

3. ADME Prediction: Numerous *in vitro* methods have been used in the drug selection process for assessing the intestinal absorption of drug candidates. Among them, Caco2-cell model and MDCK (Madin-Darby canine kidney) cell model has been recommended as a reliable *in vitro* model for the prediction of oral drug absorption. In absorption, this module provides prediction models for *in vitro* Caco2-cell and MDCK cell assay. Additionally, in silico HIA (human intestinal absorption) model and skin permeability model can predict and identify potential drug for oral delivery and transdermal delivery. In distribution, BBB (blood brain barrier) penetration can give information of therapeutic drug in the central nervous system (CNS), plasma protein binding model in its disposition and efficacy. In order to build these QSAR models, genetic functional approximation is used to select relevant descriptors from all 2D descriptors that calculated by Topomol module, followed by Resilient back-propagation (Rprop) neural network to develop successful nonlinear model.

4. Toxicity prediction: *In silico* toxicity prediction will have more and more importance in early drug discovery since 30% of drug candidates fail owing to these issues.

Ligands:

TABLE 1: THE STRUCTURES WERE DRAWN IN CHEM DRAW ULTRA 12.0 AND FURTHER FOR DOCKING STUDIES

S.no	Molecular Formula	Ligand and its IUPAC Name
P1	$C_{18}H_{19}N_3O$	
P2	$C_{18}H_{20}N_4$	
P3	$C_{19}H_{21}N_3$	

P4	$C_{18}H_{20}N_4$
P5	$C_{18}H_{19}N_5$
P6	$C_{17}H_{18}N_4O$
P7	$C_{18}H_{19}N_3O_2$
P8	$C_{19}H_{21}N_3O$

P9	$C_{18}H_{20}N_4O$
P10	$C_{18}H_{19}N_4Cl$
P11	$C_{19}H_{20}N_4Cl$
P12	$C_{18}H_{18}N_3OCl$
P13	$C_{18}H_{20}N_4O$

P14	$C_{19}H_{22}N_4$
P15	$C_{18}H_{21}N_5$

Docking studies: Hex 8.0.0 protein docking uses spherical polar Fourier Correlations [4]. Hex is an interactive molecular graphics program for calculating and displaying feasible docking modes of pairs of protein and DNA molecules. Hex can also calculate protein-ligand docking, assuming the ligand is rigid, and it can superpose pairs of molecules using only knowledge of their 3D shapes. It is the first protein docking program to be able to use modern graphics processor units (GPUs) to accelerate the calculations.

The PDB (Protein Data Bank) is the single world wide archive of Structural data of Biological macromolecules, established in Brookhaven National Laboratories (BNL) in 1971 [5]. It contains Structural information of the macromolecules determined by X-ray crystallographic, NMR methods etc.

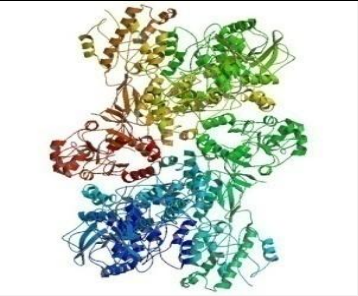
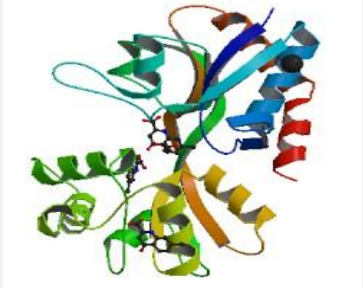
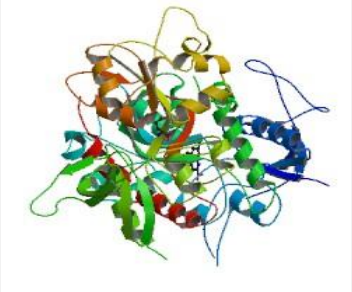
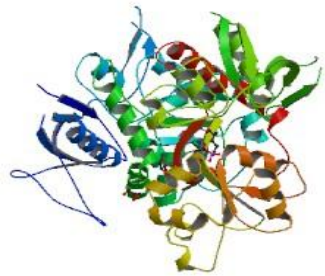
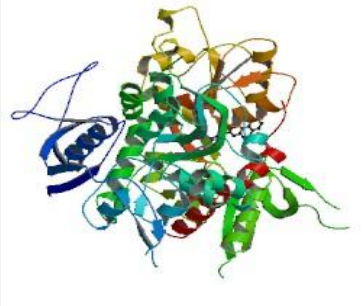
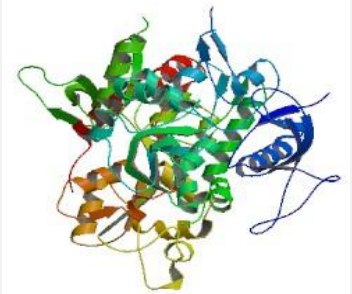
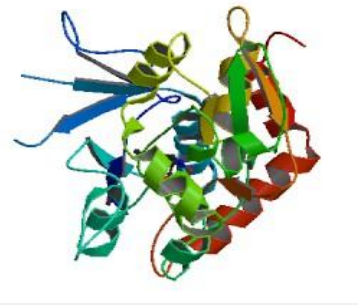
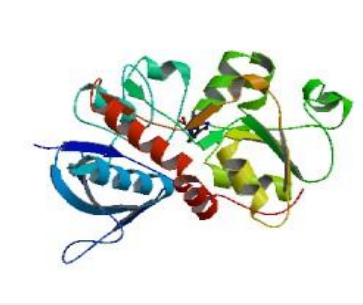
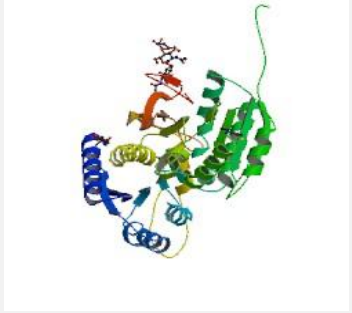
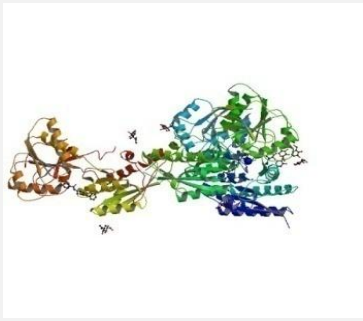
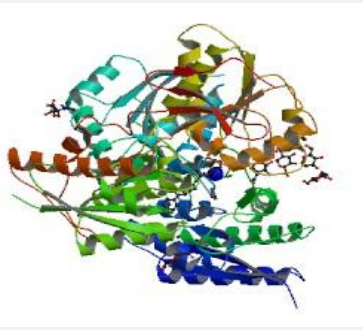
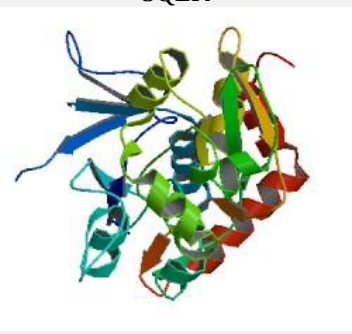
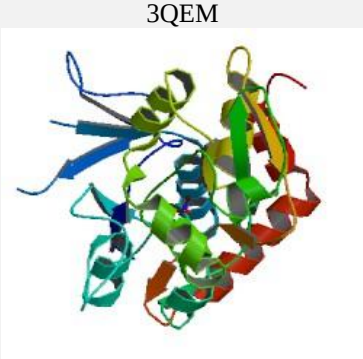
For docking studies Ligand structures and targets are converted to pdb file using Open Babel Graphical User Interface. Generally, most actions cause an immediate effect on the display so that once you've loaded a protein and the ligand. Docking allows the scientist to virtually screen a database of compounds and predict the strongest binders based on various scoring functions. It explores ways in which two molecules, such as drugs and an enzyme NMDA receptor fit together and dock to each other well, like pieces of a three-dimensional jigsaw puzzle. The molecules binding to a receptor, inhibit its function, and thus act as drug.

The collection of ligands and receptor complexes was identified via docking and their relative stabilities were evaluated using molecular dynamics and their binding affinities, using free energy simulations [6]. The parameters used for the docking process were

- Correlation type – Shape only
- FFT Mode – 3D fast lite
- Grid Dimension – 0.6
- Receptor range – 180
- Ligand Range – 180
- Twist range – 360
- Distance Range – 40

The drug and its analogues were docked with the receptor using the above parameters.

TABLE 2: ALL THE 15 TARGETS OF NMDA RECEPTORS

 5FXG	 5CC2	 4NF4
 4NF5	 4NF6	 4NF8
 4JWY	 4JWX	 3QEK
 3QEL	 3QEM	 3OEK
 3OEL	 3OEM	 3OEN

RESULTS AND DISCUSSION:

TABLE 3: PHYSICOCHEMICAL PROPERTIES

Molecular properties of Ligands in Molinspirsation Tool									
Ligand	**logP**	**TPSA**	**n atoms**	**MW**	**nON**	**nOHNH**	**nviolations**	**nrtob**	**volume**
P1	3.48	30.3	22	249.37	4	0	0	3	275.59
P2	2.93	33.09	22	292.39	4	1	0	3	279.01
P3	4.54	21.06	22	291.4	3	0	0	3	283.41
P4	3.47	33.96	22	292.39	4	0	0	3	279.25
P5	1.85	45.98	22	293.37	5	1	0	3	274.85
P6	2.4	43.19	22	294.36	5	0	0	3	271.43
P7	3	50.53	23	309.37	5	1	0	3	283.61
P8	4.06	41.29	23	307.4	4	1	0	3	291.43
P9	2.45	53.32	23	308.38	5	2	0	3	287.03
P10	3.6	33.09	23	326.83	4	1	0	3	292.54
P11	5.22	21.06	23	325.84	3	0	1	3	296.94
P12	4.15	30.3	23	327.81	4	0	0	3	289.13
P13	2.55	56.32	23	308.38	5	2	0	3	286.88
P14	3.61	47.09	23	306.41	4	2	0	3	294.7
P15	2	59.11	23	307.4	5	3	0	3	290.3

log P: Octanol-water coefficient, TPSA: Polar surface area, MW: Molecular weight, nON: No. of hydrogen bond acceptors (O & N atoms), nOHNH: No. of hydrogen bond donars (OH & NH groups), nviolations: No. of rule of 5 violation , nrtob: No. of rotatable bonds, Volume: Molecular volume, Among 15 compounds except P11, all follows Lipinski's rule.

Lipinski's rule of five also known as the Pfizer's rule of five or simply the Rule of five (RO5) is a rule of thumb to evaluate drug likeness or determine if a chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally active drug in humans. The rule was formulated by Christopher A. Lipinski in 1997, based on the observation that most medication drugs are relatively small and lipophilic molecules. P11 which is having a logp > 5 violated this Lipinski's rule which means absorption and bioavailability are likely to be poor (this is for oral drugs only).

TABLE 4: ADME PROPERTIES OF P1 – P8 LIGANDS

ID	P1	P2	P3	P4	P5	P6	P7	P8
BBB	2.82	0.38	0.58	3.77	0.022	0.02	0.056	1.037
Buffer solubility (mg/L)	363.6	1081.6	50.96	109.5	2325.5	2325.55	439.81	61.65
Caco2	51.05	50.5	56.83	55.62	40.86	40.86	50.59	55.67
CYP 2C19 inhibition	-	-	-	-	-	-	-	-
CYP 2C9 inhibition	-	-	-	-	-	-	-	-
CYP 2D6 inhibition	+	+	+	+	+	+	+	+
CYP 2D6 substrate	+	+	+	+	+	+	+	+
CYP 3A4 inhibition	-	-	-	-	-	-	-	-
CYP 3A4 substrate	Weakly	Weakly	Weakly	+	Weakly	Weakly	Weakly	+
HIA	99.94	96.71	100	98.78	96.07	96.07	95.95	96.26
MDCK	189.53	83.31	2.23	20.8	36.69	36.69	75.93	2.99
Pgp inhibition	-	-	-	-	-	-	-	-
Plasma Protein Binding	66.1	56.47	85.8	78.68	40.99	40.99	67.59	82.54
Pure water solubility (mg/L)	147.9	102.9	40.13	699.3	1794.27	1794.27	426.18	115.65
Skin Permeability	-3.37	-3.29	-2.74	-3.38	-3.86	-3.86	-3.63	-3.13
SK log D value	1.76	1.58	2.9	1.81	0.48	0.48	1.34	2.48
SK log P value	3.32	2.92	4.47	3.38	1.83	1.83	2.9	4.05
SK log S buffer	-2.9	-2.43	-3.75	-3.42	-2.1	-2.1	-2.84	-3.69
SK log S pure	-3.29	-3.45	-3.86	-2.62	-2.21	-2.21	-2.86	-3.42

TABLE 5: ADME PROPERTIES OF P9 – P15 LIGANDS

ID	P9	P10	P11	P12	P13	P14	P15
BBB	0.35	0.54	1.19	0.13	0.021	0.12	0.05
Buffer solubility mg/L	1308.28	657.1	30.97	220.8	472.32	66.2	1404.95
Caco2	48.95	55.43	57.57	57.14	42.43	55.66	44.62
CYP 2C19 inhibition	-	-	-	-	-	-	-
CYP 2C9 inhibition	-	-	-	-	-	-	-
CYP 2D6 inhibition	+	+	+	+	+	+	+
CYP 2D6 substrate	+	+	+	+	+	+	+
CYP 3A4 inhibition	-	-	-	-	-	-	-
CYP 3A4 substrate	Weakly	Weakly	+	Weakly	+	+	Weakly
HIA	94.45	97	100	100	96.26	96.42	94.84
MDCK	40.68	47.72	0.81	120.47	81.53	7.32	42.74
Pgp inhibition	-	+	+	+	-	-	-
Plasma Protein Binding	60.6	74.53	83.72	77.94	51.68	77.49	42.94
Pure water solubility mg/L	296.66	14.82	5.78	21.29	164.08	44.52	114.21
Skin Permeability	-3.67	-3.35	-2.82	-3.43	-3.65	-3.04	-3.57
SK log D value	1.15	2.25	3.58	2.43	1.06	2.2	0.88
SK log P value	2.5	3.59	5.14	4	2.62	3.77	2.22
SK log S buffer	-2.37	-2.69	-4.02	-3.17	-2.81	-3.66	-2.34
SK log S pure	-3.01	-4.34	-4.75	-4.18	-3.27	-3.83	-3.42

TABLE 6: SOLUBILITY, DRUGLIKENESS AND TOXICITY PROPERTIES ACCORDING TO OSIRIS DATA WARRIOR

Ligand	cLogS	Drug likeness	Toxicity			
			Mutagenic	Tumerigenic	Reproductive effect	Irritant
P1	-3.358	1.9358	None of the 15 Ligands are toxic			
P2	-3.222	3.5687				
P3	-4.247	1.4258				
P4	-3.452	1.4258				
P5	-2.427	3.5687				
P6	-2.563	1.9358				
P7	-3.053	4.7078				
P8	-3.951	1.2878				
P9	-2.926	3.4673				
P10	-3.958	3.5871				
P11	-4.983	1.4252				
P12	-4.049	1.9725				
P13	-3.434	1.8965				
P14	-4.323	1.3423				
P15	-3.298	3.5042				

These toxicity studies are again conformed by mcule studies where it showed all 15 compounds are non toxic.

TABLE 7: ACTIVITY PREDICTION USING PASS ONLINE

Ligand	Pa	Pi	Activity	Ligand	Pa	Pi	Activity
P1	0.797	0.035	Phobic disorders treatment	P9	0.707	0.054	Mucomembranous protector
	0.715	0.009	Anticonvulsant		0.603	0.039	Kidney function stimulant
	0.689	0.007	Antiviral		0.538	0.011	Antihelmintic
	0.605	0.003	Interleukin agonist		0.465	0.044	Anticonvulsant
P2	0.704	0.026	Nicotinic α2 β2 receptor agonist	P10	0.706	0.009	Anticonvulsant
	0.633	0.0005	5-hydroxy tryptamine 1 antagonist		0.61	0.005	GABA agonist
	0.632	0.015	Anticonvulsant		0.668	0.071	Mucomembranous protector
	0.62	0.005	Antiadrenergic		0.57	0.026	Antiviral
P3	0.612	0.017	Antiviral	P11	0.762	0.007	Anticonvulsant
	0.536	0.006	GABA agonist		0.657	0.01	Antiviral
	0.529	0.029	Anticonvulsant		0.619	0.004	Gaba agonist
P4	0.728	0.005	6-hydroxy nicotine oxidase inhibotor	P12	0.864	0.013	Phobic disorders treatment
	0.612	0.017	Antiviral		0.787	0.005	Anticonvulsant

	0.536	0.006	GABA agonist		0.665	0.009	Antiviral
	0.529	0.029	Anticonvulsant		0.657	0.004	GABA agonist
P5	0.824	0.007	Nicotinic α2 β2 receptor agonist	P13	0.789	0.005	Anticonvulsant
	0.526	0.007	GABA agonist		0.753	0.004	Antiviral
	0.472	0.023	Antimicrobial		0.7	0.076	Phobic disorders treatment
	0.47	0.042	Anticonvulsant		0.576	0.005	GABA agonist
p6	0.686	0.029	Nicotinic α2 β2 receptor agonist	P14	0.765	0.007	Anticonvulsant
	0.622	0.015	Antiviral		0.745	0.004	Antiviral
	0.572	0.005	GABA agonist		0.562	0.012	Antimycobacterial
	0.569	0.023	Anticonvulsant		0.541	0.006	GABA agonist
p7	0.632	0.013	Antiviral	P15	0.7	0.01	Anticonvulsant
	0.57	0.017	Vasodilator		0.671	0.008	Antiviral
	0.564	0.024	Anticonvulsant		0.626	0.009	Antimycobacterial
	0.616	0.115	Phobic disorders treatment		0.558	0.013	Octopamine antagonist
P8	0.623	0.015	Antiviral				
	0.59	0.022	Alopecia treatment				
	0.569	0.056	Kidney function stimulant				
	0.524	0.03	Anticonvulsant				

Docking studies: The results of the docking pair are as follows

TABLE 8: DOCKING WITH FOUR TARGETS (5FXG, 5CC2, 4NF4, 4NF5) OF NMDA RECEPTORS

Ligand	5FXG		5CC2		4NF4		4NF5	
	E min	E max	E min	E max	E min	E max	E min	E max
P1	-320.27	260.19	-273.4	264.95	-387.99	315.5	-286.27	280.6
P2	-321.08	259.84	-273.9	265.01	-388.46	315.62	-286.55	281.11
P3	-323.36	259.05	-277.39	263.99	-389.76	315.27	-287.43	279.65
P4	-323.19	256.78	-277.5	264.2	-386.88	315.68	-286.71	279.91
P5	-320.9	257.29	-274	265.22	-385.58	316.03	-285.83	281.38
P6	-324.24	289.89	-345.95	481.6	-376.67	352.68	-103.95	121.88
P7	-283.98	254.17	-296.33	253.6	-50.55	71.09	-319.22	284.92
P8	-285.37	253.37	-299.36	253.93	-115.9	0	-319.2	284.7
P9	-284.03	254.15	-297.12	253.69	-50.56	71.13	-319.32	284.92
P10	-285.37	251.22	-296.03	254.4	-49.52	71.31	-318.64	279.98
P11	-287.11	250.11	-298.84	254.29	-50.14	71.51	-318.61	279.81
P12	-285.23	250.41	-296.06	254.43	-50.06	71.31	-318.81	280.05
P13	-283.42	253.9	-296.27	253.37	-50.53	71.08	-319.27	284.67
P14	-284.82	253.09	-299.3	253.7	-50.57	71.39	-319.24	284.45
P15	-283.47	253.88	-297.06	253.46	-50.54	71.12	-319.36	284.67

TABLE 9: DOCKING WITH FOUR TARGETS (4NF6, 4NF8, 4JWY, 4JWX) OF NMDA RECEPTORS

Ligand	4NF6		4NF8		4JWY		4JWX	
	E min	E max	E min	E max	E min	E max	E min	E max
P1	-338.65	311.99	-344.85	338.35	-349.9	453.96	-328.02	330.97
P2	-338.65	312.15	-345.14	340.4	-350.1	453.32	-328.8	330.75
P3	-339.78	315.46	-346.16	339.09	-350.5	451.58	-327.21	332.94
P4	-368.09	318.83	-346.15	339.2	348.9	452.32	-327.23	335.16
P5	-337.11	311.89	-345.13	340.51	-348.5	454.07	-327.86	332.98
P6	-360.85	308.94	-371.31	338.44	-331.3	384.43	-328.85	309.46
P7	-366.9	314.52	-384.58	388.81	-336.52	443.6	-355.2	425.59
P8	-368.05	317.17	-350.01	389.69	-336.02	445.09	-356.59	422.41
P9	-367.25	316.15	-349	389.06	-336.31	445.01	-355.49	424.04
P10	-371.5	315.12	-345.71	389.31	-341.76	438.65	-356.34	423.25
P11	-371.98	314.96	-344.96	391.05	-342.1	440.12	-351.81	419.99
P12	-371.35	314.06	-345.01	389.39	-341.66	439.08	-356.27	424.04
P13	-366.94	316.19	-348.31	387.88	-338.08	441.88	-354.02	426.19
P14	-368.09	318.83	-349.74	388.76	-337.59	443.37	-355.41	423.01
P15	-367.28	317.82	-348.74	388.13	-337.88	443.29	-354.31	424.64

TABLE 10: DOCKING WITH FOUR TARGETS (3QEK, 3QEL, 3QEM, 3OEK) OF NMDA RECEPTORS

Ligand	3QEK		3QEL		3QEM		3OEK	
	E min	E max	E min	E max	E min	E max	E min	E max
P1	-292.32	353.14	-158.83	147.44	-151.58	152.18	-375.07	464.29
P2	-292.48	353.8	-159.38	147.65	-151.85	152.6	-376.22	463.94
P3	-292.05	354.16	-163.86	145.9	-154.97	153.98	-377.26	463.82
P4	-293.57	354.59	-162.26	145.62	-153.7	153.59	-375.43	462.09
P5	-292	354.23	-158	147.36	-150.58	152.64	-374.4	462.21
P6	-46.45	88.92	-37.73	59.8	-37.87	53.66	-364.43	436.79
P7	-317.7	274.23	-187.86	190.95	-185.54	190.91	-362.28	460.41
P8	-317.09	273.66	-186.84	191.12	-187.03	189.54	-363.35	461.95
P9	-317.07	274.27	-187.9	191.36	-185.96	190.46	-362.36	461
P10	-359.42	270.99	-192.76	178.77	-184.34	180.15	-364.76	463.32
P11	-359	271.44	-193.16	177.6	-185.23	179.21	-366.49	464.28
P12	-359.9	271.44	-192.78	178.95	-184.09	180.11	-364.54	462.95
P13	-317.82	274.09	-188.53	190.98	-185.53	190.99	-362.5	460.47
P14	-317.81	273.52	-188.9	191.16	-187.02	189.61	-363.56	462.02
P15	-317.79	274.13	-188.57	191.39	-185.95	190.54	-362.58	461.06

TABLE 11: DOCKING WITH FOUR TARGETS (3OEL, 3OEM, 3OEN) OF NMDA RECEPTORS

Ligand	3OEL		3OEM		3OEN	
	E min	E max	E min	E max	E min	E max
P1	-363.64	411.86	-363.51	426.82	-341.85	507.48
P2	-365.01	411.59	-364.14	426.62	-342.23	507.28
P3	-367.33	411.21	-367.87	424.07	-344.39	508.98
P4	-366.57	408.6	-367.13	422.76	-341.46	508.66
P5	-364.25	408.99	-362.29	425.31	-339.29	506.97
P6	-343.4	464.28	-349.09	406.54	-356.79	383.14
P7	-372	493.15	-373.82	439.56	-373.89	415.61
P8	-374.91	492.76	-374.77	443.33	-375.63	416.91
P9	-372	492.89	-372.9	441.13	-374.36	451.65
P10	-377.64	486.5	-373.03	438.95	-375.91	422.62
P11	-380.05	845.5	-376.53	441.53	-374.67	423.31
P12	-376.71	485.99	-373.74	439.18	-374.67	421.57
P13	-373.04	492.14	-373.9	439.55	-373.82	417.06
P14	-375.95	491.75	-374.85	443.31	-375.56	418.36
P15	-373.04	491.88	-372.98	441.11	-374.28	417.11

CONCLUSION: The Protein-Ligand interaction plays a significant role in structural based drug designing. In the present work we have taken the NMDA receptors and identified the drugs that were used against convulsions. When the receptors like 4NF8, 4JWY, 4JWX, 3QEK, 3OEK, 3OEL, 3OEM, 3OEN docked with molecules we observed a minimal energy values. From this we can conclude that NMDA receptors can be used as drug targets against convulsions. In future research work the ADME/T (Absorption, Distribution, Metabolism, Excretion/Toxicity) properties of these compounds can be calculated using the commercial ADME/T tools available thus reducing the time and cost in drug discovery process.

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