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GALANTAMINE AS ACETYL CHOLINESTERASE INHIBITOR FOR TREATMENT OF ALZHEIMER'S DISEASE: AN ARTIFICIAL INTELLIGENCE APPROACH

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ABSTRACT

Artificial intelligence (AI) is an emerging field and it has been disseminated in all areas of research. Its importance in medical sciences is also very crucial. The aim of this study was to evaluate the efficacy of Galantamine for Alzheimer's disease as acetyl cholinesterase inhibitor. Protein for study was retrieved through protein databank (PDB ID - 1B41) and ligand was removed using Discovery Studio. Analogs for docking were chosen from zinc database and docking was performed using Auto dock tool and auto dock vine, after docking ADMET properties were calculated against the possible inhibitors using MedChem designer. Drug scoring was done using DSX Online forum. ZINC39293199 has good affinity as compared to other analogs of galantamine.

***Keywords*:** AD (Alzheimer's disease), Acetylcholine esterase, Galantamine, Discovery studio, Auto Dock tool, Auto dock Vine

Introduction

Artificial intelligence (AI) technique is improving and advancing the different fields in the world. Artificial intelligence make medical field very important providing novel solutions to improve patient health during all curing processes. During COVID-19, artificial intelligence was used to get data of any location and any traveller to reduce the risk of spread of coronavirus pandemic[1].

A neurodegenerative disorder was first characterized by a German scientist, Alois Alzheimer in 1907. It is a short term memory loss which may lead to incapability of reading, speaking and thinking. Millions of people suffered from this disease worldwide [2].

Acetylcholine is primary neurotransmitter involved in cholinergic transmission. Acetylcholine esterase enzyme play a role in hydrolysis of neurotransmitter which may deposited in neurofibrils and plaques of amyloid protein associated with Alzheimer disease[3]. Acetylcholine esterase inhibitors are used as cure of this disease. Galantmine is one of the effective therapeutic agents for Alzheimer disease.

Methodology

Acetylcholine esterase protein structure was obtained from the data bank (PDB ID - 1B41). Then ligand was removed from protein structure using Discovery Studio. The program Discovery Studio was designed to visualize and analyze the structure of protein (Figure 1).

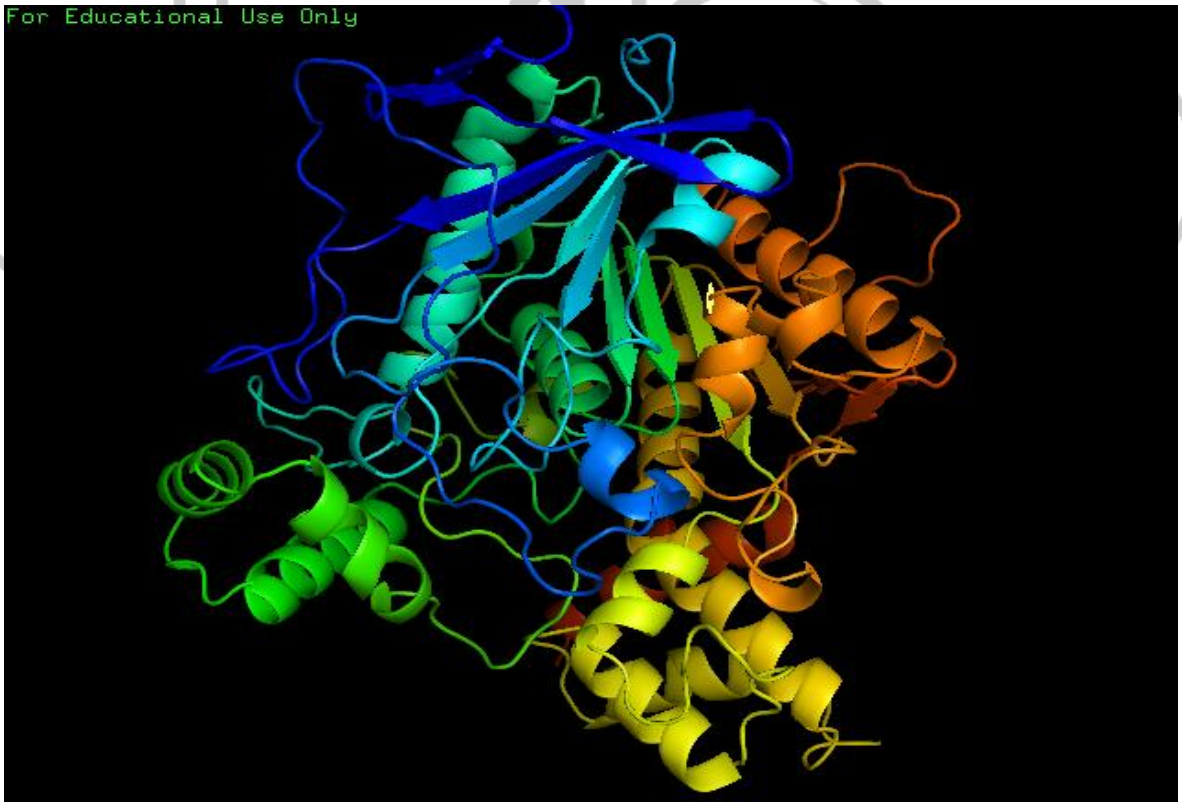

Figure 1: Ribbon structure of acetylcholinesterase

Selection of Inhibitor

For docking purpose Galantamine is chosen as an inhibitor. Its sdf file is saved from PubChem and converted into pdb file using Discovery Studio. Then torsion is applied to the inhibitor in Auto dock tool and its pdbqt file is saved. The structure of galantamine is shown in figure 2.

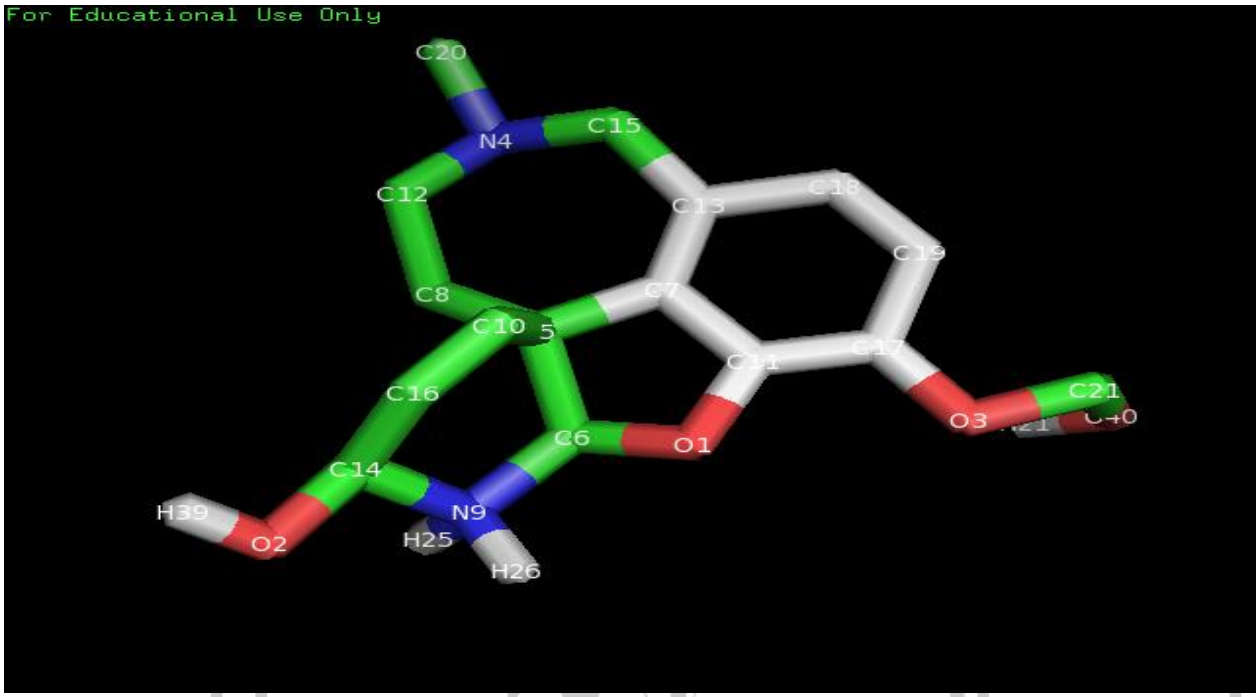

Figure 2: Structure of ligand

Molecular Docking

Artificial intelligence tools (e.g. Auto dock vina) were used for docking purpose [4]. All the parameters of X, Y and Z plane are saved. PDBQT files of ligand and protein will be saved in Vina folder along with configuration file. For docking command is typed on Command prompt.

ADMET Properties

After docking the inhibitor and its zinc analogs, ADMET properties were calculated using MedChem designer software. Firstly, pdb file of ligand is converted into Mol file using Discovery Studio. It is uploaded on MedChem Designer to calculate the properties.

Drug Scoring

Drug Score was done using DSX Online forum.PDB file of protein and Mol2 file of ligand was chosen at DSX job.

Result

Artificial intelligence (AI) techniques make easy to solve many complex diagnostic problems. Alzheimer's disease (AD) is a neurodegenerative disorder leading to person incapability because of soluble proteins abnormality. Acetylcholine esterase inhibitors are used for treatment process of Alzheimer disease. Galantamine

is one of acetylcholine esterase inhibitors effective compound against Alzheimer disease. Galantamine and its eight zinc analogs were docked at auto dock vina . Out of 8 analogs zinc39293199 gives suitable result. It has binding affinity -10.3 kcal/mol energy and its drug score is -116.

Table I: Properties of Galantamine and its Zinc analogs taken from Zinc Database

Compound	MOL wt(g/mol)	X Log p	H donor	H acceptor	Rotable bonds
Galantamine	287.35	1.8	1	4	1
zinc_518852	302.394	-2.24	1	4	1
zinc_3881813	288.367	1.54	2	4	1
zinc_4083592	316.421	-1.86	1	4	2
zinc_39293199	358.428	2.42	2	6	2
zinc_39293825	341.432	2.52	2	4	1
zinc_39293827	341.432	2.52	2	4	1
zinc_4102422	276.356	1.32	3	4	1
zinc_5178996	302.394	-2.24	1	4	1

Table II: Docking energy calculated using AutoDock Vina

Compound	Binding Affinity (kcal/mol)								
	1	2	3	4	5	6	7	8	9
Galantamine	-8.2	-7.9	-7.8	-7.4	-7.3	-7.3	-7.2	-7.0	-7.0
Zinc_518852	-9.3	-9.1	-8.5	-7.9	-7.8	-7.7	-7.6	-7.3	-7.2
Zinc_3881813	-9.2	-8.7	-8.0	-7.9	-7.4	-6.9	-6.7	-6.7	-6.7
Zinc_4083592	-9.0	-8.7	-8.2	-8.1	-7.6	-7.5	-7.4	-7.2	-7.0
Zinc_39293199	-10.3	-8.7	-8.4	-8.3	-7.8	-7.8	-7.7	-7.7	-7.5
Zinc_39293825	-9.0	-8.6	-8.5	-7.9	-7.8	-7.8	-7.5	-7.4	-7.3
Zinc_39293827	-8.4	-8.2	-8.2	-8.0	-7.8	-7.5	-7.2	-7.2	-7.2
Zinc_4102422	-9.5	-9.2	-9.1	-9.1	-8.6	-8.0	-7.8	-7.6	-7.1
Zinc_5178996	-9.5	-9.4	-8.9	-8.4	-7.6	-7.5	-7.3	-7.2	-7.1

Table III: ADMET properties calculated for Galantamine and its Zinc analogs using MedChem designer software

Compound Name	M log P	S+ log P	S+ log D	HBDH	M_NO	TPSA	Rule of 5
Galantamine	1.931	1.780	1.012	1.000	4.000	41.930	0.000
Zinc_518852	-1.515	-1.531	-1.531	1.000	4.000	38.690	0.000
Zinc_3881813	1.931	1.780	1.012	1.000	4.000	41.930	0.000
Zinc_4083592	-1.283	-1.326	-1.326	1.000	4.000	38.690	0.000
Zinc_39293199	2.201	1.970	1.970	2.000	6.000	71.030	0.000
Zinc_39293825	3.012	2.872	2.869	2.000	4.000	52.930	0.000
Zinc_39293827	3.012	2.872	2.869	2.000	4.000	52.930	0.000
Zinc_4102422	1.778	1.490	0.056	2.000	4.000	50.720	0.000
Zinc_5178996	-1.515	-1.531	-1.531	1.000	4.000	38.690	0.000

Table IV: Drug Score accounted by DSX-online

Ligand	rank	score
Galantamine	1	-96
Zinc_518852	1	-114
Zinc_3881813	1	-96
Zinc_4083592	1	-130
Zinc_39293199	1	-116
Zinc_39293825	1	-105
Zinc_39293827	1	-109
Zinc_4102422	1	-103
Zinc_5178996	1	-125

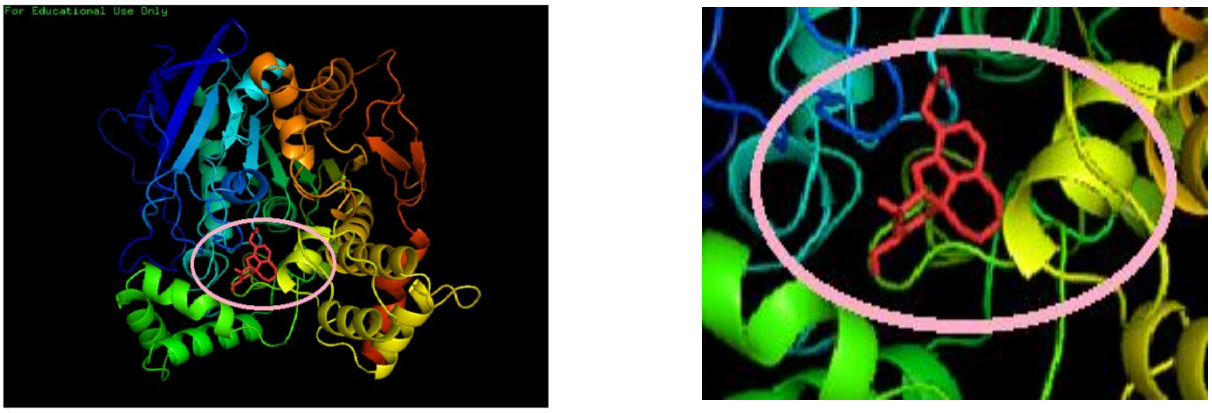

Figure 3 : Interaction of protein and inhibitor on PyMOL

Discussion

Artificial intelligence (AI) technique has becoming most used technique in healthcare for providing complex data. Various artificial intelligence tools are in use by different medical healthcare companies [5]. Artificial intelligence is used for drug design, patient monitoring, medical imaging, treatment analysis, robotic surgery, and the security of healthcare systems etc.

Alzheimer's disease (AD) is a frequent neurodegenerative disorder leading memory loss, dementia, and person incapability. It is caused by abnormal processing of proteins because of environmental factors and alterations, leading to neuronal abnormality. Various treatment process have tried to cure but efficient methods are under development [6].

Acetylcholine is organic naturally and functions as brain neurotransmitter and other functions. Acetylcholine esterase inhibitors enhance synaptic acetylcholine levels and neurotransmitter action in brain. Acetylcholine esterase inhibitors are used for treatment of Alzheimer disease. Galantamine is natural compound containing alkaloid and effective compound against Alzheimer disease[7].

Conclusion

Artificial Intelligence approaches prove that Galantamine is an acetyl cholinesterase inhibitor that can be used for treatment of Alzheimer's disease:

References

1. Basu, Kanadpriya et al. "Artificial Intelligence: How is It Changing Medical Sciences and Its Future?." *Indian journal of dermatology* vol. 65,5 (2020): 365-370.
2. Evans DA, Funkenstein H, Albert MS, Scherr PA, Cook NR, Chown MJ, Hebert LE, Hennekens CH, Taylor JO. JAMA 1989;262:2551
3. Inestrosa NC, Alvare A, Garrido J. In Alzheimer's Disease: Biology, Diagnosis and Therapeutics 1997: John Wiley and Sons, London; 1997. p. 500-10.
4. Goodsell DS, Morris GM, Halliday RS, Huey R, Belew RK, Olson AJ. Automated docking using a lamarckian genetic algorithm and empirical binding free energy function. J Computational Chem 1998;19:1639-62.
5. Davenport, Thomas, and Ravi Kalakota. "The potential for artificial intelligence in healthcare." *Future healthcare journal* vol. 6,2 (2019): 94-98.

6. Tiwari S, Atluri V, Kaushik A, Yndart A, Nair M. Alzheimer's disease: pathogenesis, diagnostics, and therapeutics. International journal of nanomedicine. 2019 Jul 19:5541-54.
7. Santos TC, Gomes TM, Pinto BA, Camara AL, Paes AM. Naturally occurring acetylcholinesterase inhibitors and their potential use for Alzheimer's disease therapy. Frontiers in Pharmacology. 2018 Oct 18;9:1192.