S.Asifa Sulthana et al /J. Pharm. Sci. & Res. Vol. 12(2), 2020, 279-281

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

An *In silico* Evaluation Of Levodopa Present in Mucuna prurience for Anti Parkinsonism Activity

S.Asifa Sulthana*,G. Jasmine Joy Bell, Rupitha N S, Merlin N J, Shaiju S Dharan
Department of Pharmacology, Ezhuthachan College of Pharmaceutcial Sciences, Marayamuttom, Neyyattinkara, 695124, TVM

Abstract

Parkinsonism is a neurodegenerative disorder that causes a group of movement abnormalities. It is also known as movement disorder. Parkinsonism is an extrapyramidal motor disorder and it is characterised by rigidity, tremor and hypokinesia with certain secondary manifestations like defective posture and gait, mask like face and sialorrhoea , dementia may accompany. If this condition is untreated the symptoms progress over several years to end stage disease in which the patient is rigid , unable to move, unable to breathe properly, succumbs mostly to chest infection or embolism. L-dopa present in *Mucuna pruriens* has shown to posses anti parkinsonism activity The powdered seeds of *Mucuna pruriens* contain L-dopa. The L-dopa present in *Mucuna pruriens* has the same effect as that of the synthetic levodopa. The drug interaction was investigated using insilico studies . The insilico studies provides evidence for the interaction of L- dopa with dopamine receptors. The interaction is presumably vital in exerting anti parkinsonism activity. The present study clearly elucidates that L-dopa present in *Mucuna pruriens* posses anti parkinsonism property.

Key words : Parkinsonism, *Mucuna pruriens*, L-dopa, hypokinesia, sialorrhoea

INTRODUCTION:

Parkinsonism is a chronic progressive neurodegenerative disorder mostly affecting older people.. Majority of the cases are idiopathic , some are atheriosclerotic while postencephalitic are now rare. The most consistent lesion in parkinsonism is the degeneration of neurones in the substantia nigra pars compacta and the nigrostriatal tract. This results in the deficiency of dopamine in the striatum which controls muscle tone and coordinates movements. An imbalance between dopaminergic and cholinergic system in the striatum occurs giving rise to the motor defect. Though the cholinergic system is not affected , its suppression by anticholinergics tend to restore balance.[1]

Parkinsoniam Symptoms[1]

MOTOR SYMPTOMS	NON MOTOR SYMPTOMS
Tremor, bradykinesia, rigidity, postural instability	Cognitive impairment , bradykinesia
Hypomimia, dysarthria, dysphagia, sialorrhoea	Depression, fatigue, behavioural and psychiatric problems
Decreased arm swing, shuffling gait, festination difficulty arising from chair, turning in bed	Anosmia ,pain , parathesis, urinary dysfunction, sexual dysfunction, weight loss, constipation
Micrographia, cutting food, feeding, hygiene, slow activities of daily living	Sleep disorders

The etiological factors which results in parkinsonism include ageing, genetic predisposition, oxidative generation of free radicals , MPTP like environmental toxins and excitotoxic neuronal death due to NMDA receptors due to calcium overload.

Genetic factors include mutations in LRRK2, alpha synuclein gene, parkin gene, GBA gene, DJ-1 gene.[2,3]

Enviornmental factors include continous exposure to certain pesticides such as insecticide permethrin, beta-hexa chlorocyclohexane, herbicides, paraquat, 2,4 – dichloro phenoxy acetic acid and fungicide maneb. MPTP (Methyl Phenyl Tetra hydropyridine) is a synthetic neurotoxin which cause immediate and permanent damage. Certain cases reported that individuals injected with synthetic form of heroin contaminated with MPTP are affected by parkinsonism, solvents, head injuries during an accidents . But the cases reported due to environmental factors are not clear because the time passes between the exposure to an environmental factor and occurrence of the parkinsonism symptoms. The main risk factor is age ,elderly are more affected than the younger along with men are more affected than the women. [4]

Molecular docking is a type of bioinformatic tool in the field of molecular biology and computer assisted drug design. Molecular docking involves the interaction of two or more molecules to give stable adduct. Receptors used are proteins and ligands are small organic compounds. Molecular docking computationally predicts the 3D structure of the complex, orientation of the complex and conformation of the complex. Molecular docking can be used to perform virtual screening on large libraries of compounds, rank the results and propose structural hypothesis of how the ligands inhibit the target which is invaluable in lead optimization. The distance between the groups are generally expressed in angstrom. Molecular docking helps to save the problem in a reasonable time frame. Docking mainly requires two components, and they are searching and scoring.[5]

Mucuna pruriens is a climbing legumuinous plant , traditionally used in the Indian system of medicine for treating disease like parkinsonism. *Mucuna pruriens* is also known by the name cowhage, velvet bean and atmagupta. In ayurvedic system of medicine parkinsonism is known by the name Kampavata, a nervous malady bearing similarities of parkinsonism, responding to atmagupta. Levadopa was first isolated from the seeds of

Mucuna pruriens, when the use of levodopa was known to the scientific world its demand increased .[6]

MATERIALS AND METHODS

Docking

The interaction between the ligand and protein was determined by using Auto-dock vina Pyrx virtual screening tool.

- **Preparation of Ligand**

The 3D structure of the compound was obtained from Pubchem, which contains information about the small molecule and their biological activities.

- **Preparation of Protein**

Proteins are the macromolecule contains one or more amino acid residues. The 3D structure of the protein was obtained from PDB (Protein data bank).

- **Conversion of ligand from SDF to PDB format**

Openbabel-2.3.2/obgui.exe was used.

- **Protein preparation and molecular visualization**

pyMOL is software used for the both purposes. pyMOL can produce high quality 3D images of proteins.

RESULTS AND DISCUSSION

Compounds which has low bioavailability are less effective against disease. To solve this problem predicting the bioavailabilty properties before the drug development will be a great advantage. By using certain computer based methods such as molecular docking it can be studied. Increased hydrogen bond interaction and high binding affinity score express the strong binding of constituents with the selected receptor. Here in the insilico evaluation of levodopa in *Mucuna pruriens*, protein chose from the protein data bank is dopamine receptors and levodopa is the ligand choosed from pubchem.

Since dopamine cannot cross the blood brain barrier it is administered in the form of levodopa. Levodopa act as the precursor and as a dopamine replacing agent to dopamine. It is mainly used to treat the bradykinetic symptoms in parkinsonism. It is also used to treat postencephaltic parkinsonism and symptomatic parkinsonism due to carbonmonoxide intoxication. By performing insilico evaluation by using certain computer based methods it is proved that levodopa present in *Mucuna pruriens* has better binding affinity to dopamine receoptors.[7]

Table 1 shows the hydrogen bond interactions and binding affinity of levodopa with receptor (6cm4).Table 1- 2 gives the physicochemical properties, pharmacokinetics and drug likeness properties of levodopa.

TABLE :1 Physicochemical properties of levodopa

Physicochemical Properties	**Levodopa**
Formula	C9H11NO4
Molecular weight	197.19 g/mol
Num. heavy atoms	14
Num. arom. heavy atoms	6
Fraction Csp3	0.22
Number of rotatable bonds	3
Number of hydrogen bond acceptors	5
Number of hydrogen bond donors	4
Molar refractivity	49.55
TPSA	103.78 Å²

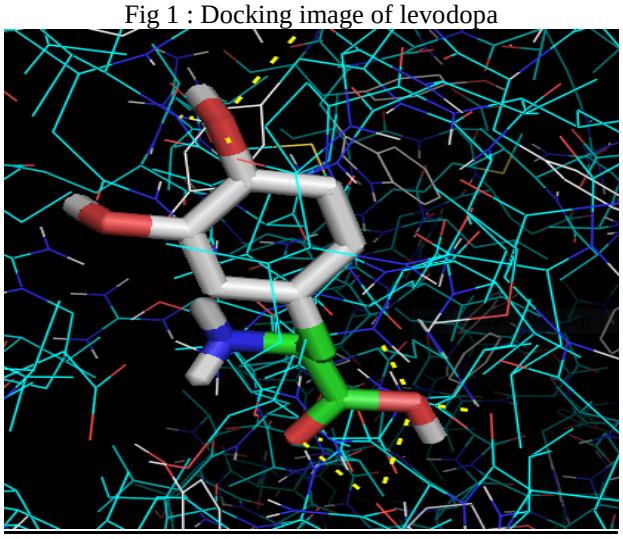
Table 2 : Pharmacokinetics of levodopa

Pharmacokinetic Parameters	Levodopa
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2, 2C9 inhibitor	No
Log K_p (skin permeation)	-9.45 cm/s

Docking images

Molecular docking is a bioinformatic tool in molecular biology and computer assisted drug design. Molecular docking involves the interaction of two or more molecule to form a stable complex. The complex formed will be with non covalent interaction. Through molecular docking the 3D structure , orientation, structure and conformation of the complex can be viewed.

Fig 1 : Docking image of levodopa



Docking score

Drugs	Docking score(kcal/mol)	Hydrogen bond
Levodopa	-7.2	8

CONCLUSION:

The seed of *Mucuna pruriens* contain levodopa . By using certain computational tools the bioavailability properties and the binding affinity of levodopa present in *Mucuna pruriens* is determined. The computational properties shows that levodopa has high affinity towards dopamine receptors (6cm4). Thus we can conclude that levodopa present in *Mucuna pruriens* can be used to treat the bradykinetic of parkinsonism, Postencephalalitic parkinsonism and sympathomimetic parkinsonism.

REFERENCE :

1. J. Jankovic. Parkinson's disease: clinical features and diagnosis. J Neurol Neurosurg Psychiatry 2007; 368-374
2. Feany M.B. New Genetic Insights into Parkinson's disease. The New England Journal of Medicine 2006 ;354: 422-423.
3. Aharon-Peretz.Rosenbaum H and Gershoni-Baruch. Mutation in the Glucocerebrosidase Gene and Parkinson's Disease in Ashkenazi Jews. The New England Journal of Medicine 2004;351:1972-1977.
4. David G. Standaert, John N. Whitaker. Parkinson's Disease Handbook. American Parkinson Association 2019; 4-40.
5. Vincent Zoetea, Aurélien Grosdidier,Olivier Michielin Docking, virtual high throughput screening and in silico fragment-based drug design December 10, 2008; Accepted: January 11, 2009.
6. R Katzenschlager, A Evans, A Manson, P N Patsalos, N Ratnaraj, H Watt, L Timmermann,R Van der Giessen, A J Lees. Mucuna pruriens in Parkinson's disease: a double blind clinical and pharmacological study. J Neurol Neurosurg Psychiatry 2004;75:1672–1677.
7. LeWitt P.A. Levodopa for the treatment of Parkinson's disease. The New England Journal of Medicine 2008;359:2468-2476.