**IJPSR (2018), Volume 9, Issue 6** **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 August, 2017; received in revised form, 28 December, 2017; accepted, 06 January, 2018; published 01 June, 2018

# COMPARATIVE MOLECULAR DOCKING STUDIES AND STRUCTURAL PREDICTION OF PLANT COMPOUNDS ON LRRK2

P. Jayanthi * and K. Vijayalakshmi

Department of Biochemistry, Bharathi Women's College, Chennai - 600108, Tamil Nadu, India.

**Keywords:**

L-DOPA, LRRK2, Theaflavin, Baicalein, Sesamol, Tenuigenin, Gastrodin, Phloroglucinol

**Correspondence to Author:**
**K. Vijayalakshmi**

Department of Biochemistry,
Bharathi Women's College,
Chennai - 600108, Tamil Nadu, India.

**E-mail:** jayanthip290@gmail.com

**ABSTRACT:** Neurodegenerative disease is the condition of brain cells that lose of its ability to generate the neurotransmitters and this leads to the accumulation of proteins in the brain. These condition causes memory loss and problems in the cognitive functions. Neurological diseases are characterized by four major types such as Alzheimer's disease, Parkinson's disease, Huntington disease, Amyotrophic lateral sclerosis. Parkinson's disease is a second neurological disorder, characterized by a selective loss of dopaminergic neurons in the substantianigra, causing a subsequent reduction of dopamine levels in the striatum. Loss of dopaminergic neurons in striatum causes imbalance of neurotransmitters like acetylcholine and dopamine, resulting in the Parkinson's disease. Tremor, rigidity, dyskinesia are the primary symptoms and memory loss, sleeps disorders, cognitive impairments are the secondary symptoms of Parkinson's. **Aim:** To investigate the structural changes *in silico* docking was performedwith target protein LRRK2 with the following compounds theaflavin, baicalein, sesamol, tenuigenin, gastrodin, phloroglucinol and L-DOPA. **Methods:** The *in silico* docking was carried out using autodock version 4.2. Rasmol tool was used to visualize the protein structures. **Results:** The docking energy of L-DOPA with LRRK2 showed binding energy-4.97 Kcal/mol, theaflavin-7.19 Kcal/mol, baicalein-7.4 Kcal/mol, sesamol-4.99Kcal/mol, tenuigenin-7.9 Kcal/mol, gastrodin-6.02 Kcal/mol and phloroglucinol as binding energy-4.99 Kcal/mol. **Conclusion:** These results indicate that the natural plant compounds have more affinity and interact with LRRK2 in a better manner compared to the L-DOPA the standard drug. Therefore natural plant compounds may be helpful in the treatment of Parkinson's disease.

**INTRODUCTION:** The aggregation of proteins in the nerve ending of the human brain, known as lewy bodies. This formation of the lewy Bodies leads to the loss of neurons and this cause Parkinson's disease [1]. Parkinson's disease is the most common neurodegenerative disease, which affects life span of the elder people. Parkinson's disease is a chronic neurodegenerative disease caused by loss of dopamine producing neurons in substanianigra.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.9(6).2258-65

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(6).2258-65

Among the World wide populations, 1 percent of the above 65 years older people are affected by the Parkinson's disease [2]. It is slow progressive disease; it affects mainly movements of the body, muscle control, memory and concentration.

Tremor, bradykinesia, rigidity and postural imbalance are primary symptoms of Parkinson's disease. Large fractions of patients with Parkinson's disease have cognitive impairments as the most common primary symptoms. Depression, insecurity, confusion, monotone voice, erectile dysfunction are the common secondary symptoms of Parkinson's disease [3]. Parkinson's disease remains poorly understood, although a broad range of studies were conducted over the past few decades. The mutation in LRRK2 causes sporadic late-onset form of Parkinson's diseases [4].

LRRK2 is a large multidomain protein. It contains 2,527 amino acids. The functional domain of LRRK2 are Ank (ankyrin-like), LRR (leucine rich repeat), Roc (Ras-of-complex proteins), Cor(C-terminal of Roc), kinase, wD40 UBL (ubiquitin-like), RING 1, IBR (in-between-ring), RING 2. LRRK2 is the autosomal dominant inherited gene and its mutations may affect the diverse proteins functions [5]. LRRK2 mutations cause early onset of Parkinson's disease, with a clinical profile identical to sporadic late-onset Parkinson's disease.

The putative function of LRRK2 remains unknown. The normal function of LRRK2 is the regulation of kinase and GTPase activities, binding partners, phosphosubstrates. Mutation inLRRK2 leads to enchancedkinase activity and GTP binding that result in cell death [6]. The important pathophysiologys of PD are aggregation of alpha synuclein and the formation of lewy bodies [7]. Parkinson's diseaseis still unclear, because it results due to number of genetic and environmental factors.

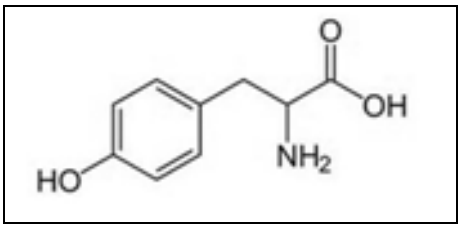


**FIG. 1: MOLECULAR STRUCTURE OF L-DOPA**

L-Dopa **(Fig.1)** (L-3, 4-dihydroxyphenyl alanine) is a synthetic drug and precursor to the neurotransmitter dopamine, nor-epinephrine and epinephrine. L-DOPA increases the reduced level of neurogenesis, which is caused by the 6-OHDA lesion, in the hippocampal dentate gyrusand in the layer of olfactory bulb [8]. The trade name of L-Dopa is sinemet, stalevo and prolopa. L-Dopa is converted into dopamine by the enzyme DOPA decarboxylase in CNS. Pyridoxal phosphate (Vit B6) is the cofactor for these reactions. Prolongedintake of L-DOPA causes side effects for the Parkinson's disease patients. Over dosage of L-DOPA cause's hypertension, extreme emotional states, gastro intestinal bleeding.

L-DOPA gradually increases the abnormal in-voluntary movements, which is known dyskinesias [9]. Other than L-DOPA treatment, the geno typing is used found the impulse control in PD patients and its improvement predicted by the drug ropinirole, the dopamine agonists [10]. Plants are rich in antioxidants and flavonoids may protect neural junction and stimulate the neuronal regeneration [11].

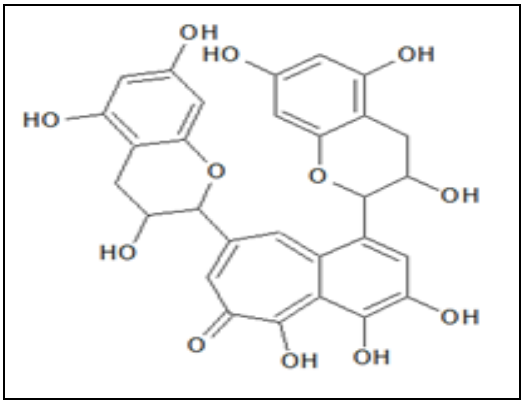


**FIG. 2: MOLECULAR STRUCTURE OF THEAFLAVIN**

Theaflavin **(Fig. 2)** is formed from the black tea processing methods and it has antioxidant and anti microbial activity [12]. Theaflavin gives colour and flavor to black tea. The chemical structure of theaflavin has four types they are theaflavin (TF1), Theaflavin-3-gallate (TF2A and TF2B), Theaflavin-3, 3'digallate (TF3) [13]. Theaflavin protects DNA from oxidative damage. The catechins from the processed Green tea have the antioxidant property and it can scavenge the hydroxy radicals [14].

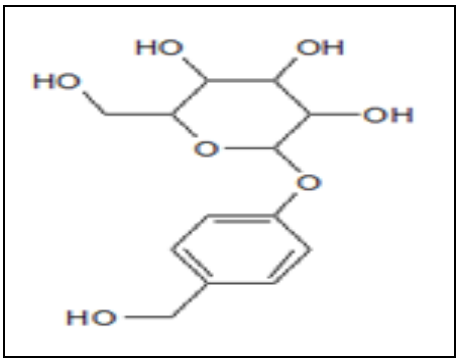


**FIG. 3: MOLECULAR STRUCTURE OF GASTRODIN**

Gastrodin **(Fig. 3)** is a glucoside of gastrodigenin. It was isolated from the orchid Gastrodiaelata and from the rhizome of Galeolafaberi. It has neuro protective effect. Gastrodin shows neuronal death in the MPTP induced PD models [15]. The molecular formula of gastrodin is $C_{13}H_{18}0_7$. *Rhizoma Gastrodiae,* extract of Tianma, chinese herb show the neuroprotective effects, and it may be due to the attenuated apoptosis pathway [16]. Gastrodin improves the cognitive functions in PD patients and also it prevents the increasing level of serotonin transporter [17].

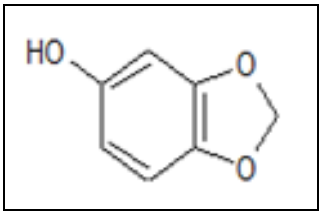


**FIG. 4: MOLECULAR STRUCTURE OF SESAMOL**

Sesamol **(Fig. 4)** is a water soluble lignin. It has antioxidant and anti cancer property [18]. Its molecular formula is $C_7H_6O_3$. Its molecular mass is 38.12g/mol. Sesame oil is used in Ayurvedic medicine. Sesamol is a derivative of phenol and it is soluble in water. It has antioxidant property and also antifungal property. Sesamol has anti photo activity. Administration of sesamol with folic acid shows neroprotective effect in the 6-OHDA parkinsonian animals [19]. Sesamol prevents the cognitive impairments in Alzheimer's disease animal models and also prevents neuroinflammation [20].

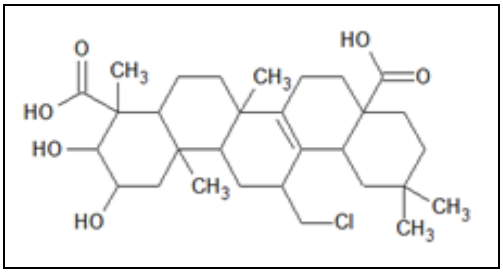


**FIG. 5: MOLECULAR STRUCTURE OF TENUIGENIN**

Tenuigenin **(Fig. 5)** is an active component extracted from achinese herb *Polygala tenuifolia* root. It is used to treat memory loss and cognitive function in Chinese medicine [21]. Tenuigenin protects the PC 12 cells from $Mpp^+$ induced neuronal death [22]. Tenuigenin shows neuroprotective effect on neuro inflammation from a single intranigral dose of LPS in adult male rat. Tenuigenin protects the neurons by inhibiting the LPS-induced inflammation in microglia cells [23].

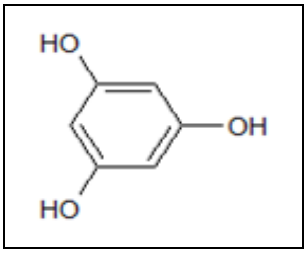


**FIG. 6: MOLECULAR STRUCTURE OF PHLOROG-LUCINOL**

Phloroglucinol **(Fig. 6)** are secondary metabolites that occur naturally in certain plant species. It is also produced by organisms that are not plants, such as algae or bacteria. Phlorotannin is one of the forms of phloroglucinol and it is abundantely present in *Ecklonia cava* (edible brown algae). Phloroglucinal treated cells shows attenuation of $H_2O_2$ induced cell damage through an activation of antioxidant system inside the cell [24]. Phloroglucinol has anti-inflammatory activity. Phlorotannins have acetylcholinesterase inhibitory activity [25].

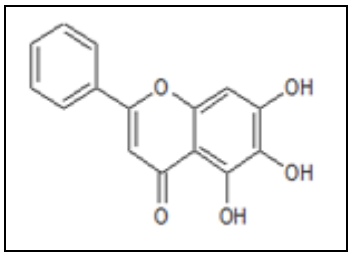


**FIG. 7: MOLECULAR STRUCTURE OF BAICALEIN**

Baicalein **(Fig: 7)** is type of flavanoid, isolated, from the root of *Scutellaria baicaleinsis* and *Scutellaria lateriflora*. It is used in Chinese medicine and has antiallergic, anticarcinogenic and antioxidant activity [26]. Baicalein interacts with alpha-synclein and form quinones during oxidation and it inhibits fibrillation. Baicalein prevents damage made by 6-OHDA or MPTP in both *in-vivo* and *in-vitro* models of Parkinson's disease. Roteone induced mitochondrial damage, production of ROS, swelling of brain mitochondria is prevented by baicalein [27].

The new drug development and its designing are most challenging tasks. In advance science, production of new and effective drugs is more important. Docking studies helps to find out effective drug interactions before they are tested with human. The known structure of protein (LRRK2) and ligands are docked using Autodock 4.0. In this study, we have docked the plant compounds and L-DOPA with LRRK2.

## MATERIALS AND METHODS:

**Preparation of Target Protein:** The sequence of LRRK2 protein was taken from PDB files. The receptor file used by AutoDock must be in "pdbqs" format which is pdb plus 'q' charge and 's' solvation parameters, AtVol, the atomic fragmental volume, and AtSolPar, the atomic solvation parameter which are used to calculate the energy contributions of desolvation of the macromolecule by ligand binding.

**Preparation of Ligand Structure:** Before docking partial atomic charges are laid to each atom of the ligand. We also distinguish between aliphatic and aromatic carbons, names for aromatic carbons start with 'A' instead of 'C'. Auto Dock ligands are written in files with special keywords recognized by Auto Dock. The root is a rigid set of atoms, while the branches are rotatable groups of atoms connected to the rigid root. The TORSDOF for a ligand is the total number of possible torsions in the ligand minus the number of torsions that only rotate hydrogens. TORSDOF is used in calculating the change in free energy caused by the loss of torsional degrees of freedom upon binding. After all the above conditions are set the ligand is saved in "pdbq" format.

**AutoDock 4.0-Running:** AutoDock Tool was used for creating PDBQT files from traditional PDB files. The preparation of the target protein (unbound target) with the Auto Dock Tools software involved adding all hydrogen atoms to the macromolecule, which is a step necessary for correct calculation of partial atomic charges. Gasteiger charges are calculated for each atom of the macromolecule in Auto Dock 4.2 instead of Kollman charges which were used in the previous versions of this program.

Auto Dock was run several times to get various docked conformations, and used to analyze the predicted docking energy. The binding sites for these molecules were selected based on the ligand-binding pocket of the templates [28]. AutoDock Tools provide various methods to analyze the results of docking simulations such as, conformational similarity, visualizing the binding site and its energy and other parameters like intermolecular energy and inhibition constant. Discovery Studio Visualizer was used to visualize the structure**.** Molecular visualization is a key aspect of the analysis and communication of modeling studies.

**RESULTS AND DISCUSSION:** The plant compounds were docked with the target protein LRRK2 and the best docking poses were identified. Majority of the plant compounds had greater binding affinity with target protein. The best binding configuration measured in Kcal/mol. The binding configuration and their docking energy are listed below.

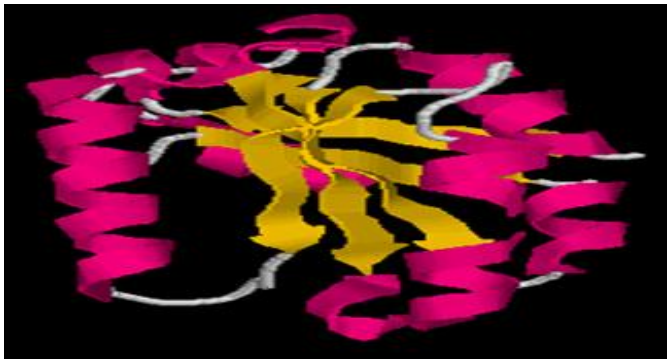

**FIG. 8: THREE DIMENSIONAL STRUCTURE OF LEUCINE RICH REPEAT KINASE 2 USING RASMOL**

**TABLE 1: L-DOPA AND ROC DOMAIN OF LRRK2**

| ROC domain of LRRK2 | | L-DOPA | Distance (Å) | Docking Energy (Kcal/mol) |
|---|---|---|---|---|
| Residue | Atom | | | |
| LEU1474 | O | H | 2.04 | –4.97 |
| LYS1476 | N | O | 3.10 | |
| ILE1482 | N | O | 2.66 | |
| ASN1475 | O | H1 | 1.96 | |
| ARG1477 | N | O | 2.99 | |
| ARG1477 | NH1 | OXT | 2.66 | |

## Binding Configuration and Statistical Docking Results of L-DOPA with LRRK2:

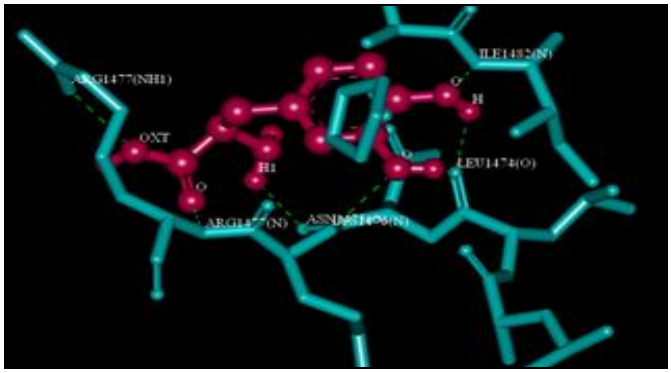


**FIG. 9: INTERACTIONS BETWEEN L-DOPA AND ROC DOMAIN OF LRRK2**

## Binding Configuration and Binding Docking Results of Tenuigenin with LRRK2:

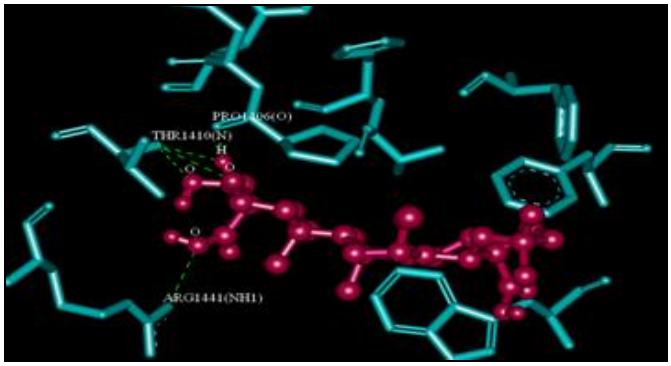


**FIG. 10: INTERACTIONS BETWEEN TENUIGENIN AND ROC DOMAIN OF LRRK2**

**TABLE 2: INTERACTIONS BETWEEN TENUIGENIN AND ROC DOMAIN OF LRRK2**

| ROC domain of LRRK2 | | Tenuigenin | Distance | Docking Energy |
|---|---|---|---|---|
| Residue | Atom | | (Å) | (Kcal/mol) |
| PRO1406 | O | H | 2.06 | –7.91 |
| THR1410 | N | O | 2.38 | |
| THR1410 | N | O | 3.06 | |
| THR1410 | N | O | 2.61 | |
| ARG1441 | NH1 | O | 2.90 | |

## Binding Configuration and Docking Results of Baicalein with LRRK2:

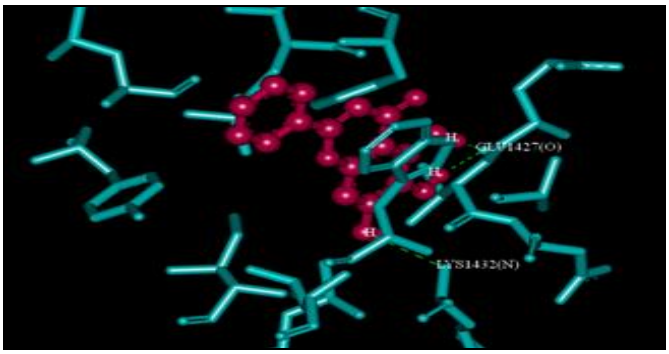


**FIG. 11: INTERACTIONS BETWEEN BAICALEIN AND ROC DOMAIN OF LRRK2**

**TABLE 3: INTERACTIONS BETWEEN BAICALEIN AND ROC DOMAIN OF LRRK2**

| ROC domain of LRRK2 | | Baicalein | Distance (Å) | Docking Energy (Kcal/mol) |
|---|---|---|---|---|
| Residue | Atom | | | |
| GLU1427 | O | H | 1.94 | –7.4 |
| GLU1427 | O | H | 1.85 | |
| LYS1432 | N | O | 3.06 | |

## Binding Configuration and Docking Results of Theaflavin and LRRK2:

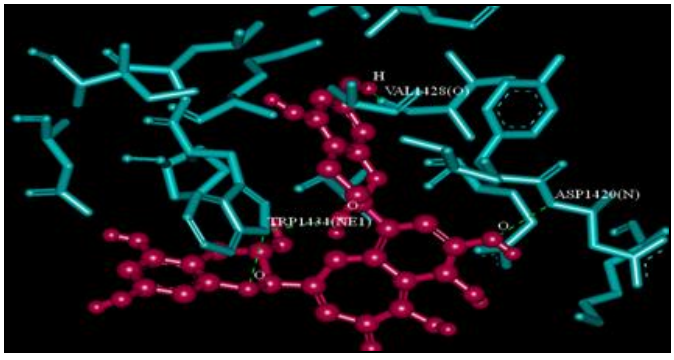


**FIG. 12: INTERACTIONS BETWEEN THEAFLAVIN AND ROC DOMAINOF LRRK2**

**TABLE 4: INTERACTIONS BETWEEN THEAFLAVIN AND ROC DOMAINOF LRRK2**

| ROC domain of LRRK2 | | Theaflavin | Distance (Å) | Docking Energy (Kcal/mol) |
|---|---|---|---|---|
| Residue | Atom | | | |
| ASP1420 | N | O | 2.63 | –7.19 |
| VAL1428 | O | H | 1.85 | |
| TRP1434 | NE1 | O | 2.94 | |
| TRP1434 | NE1 | O | 3.04 | |

## Binding Configuration and Docking Results of Gastrodin and LRRK2:

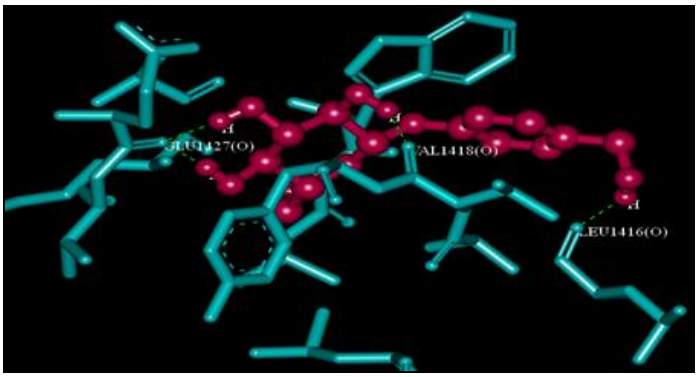


**FIG. 13: INTERACTIONS BETWEEN GASTRODIN AND ROC DOMAIN OF LRRK2**

**TABLE 5: INTERACTIONS BETWEEN GASTRODIN AND ROC DOMAIN OF LRRK2**

| ROC domain of LRRK2 | | Gastrodin | Distance (Å) | Docking Energy (Kcal/mol) |
|---|---|---|---|---|
| Residue | Atom | | | |
| LEU1414 | O | H | 1.77 | –6.02 |
| VAL1418 | O | H | 1.94 | |
| GLU1427 | O | H | 1.69 | |
| GLU1427 | O | H | 1.76 | |

## Binding Configuration and Docking Results of Sesamol and LRRK2:

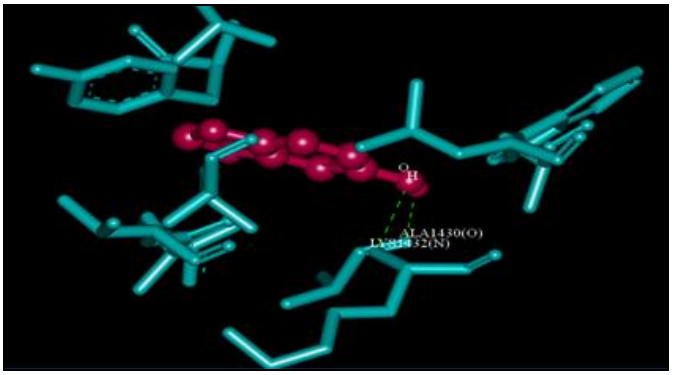


**FIG. 14: INTERACTIONS BETWEEN SESAMOL AND ROC DOMAIN OF LRRK2**

**TABLE 6: INTERACTIONS BETWEEN SESAMOL AND ROC DOMAIN OF LRRK2**

| ROC domain of LRRK2 | | Gastrodin | Distance (Å) | Docking Energy (Kcal/mol) |
|---|---|---|---|---|
| Residue | Atom | | | |
| LYS1432 | N | O | 2.92 | –4.99 |
| ALA1430 | O | H | 2.05 | |

According to the docking results, the docking energy of L-DOPA with LRRK2 showed binding energy as -4.97Kcal/mol. L-DOPA was found to be the standard drug in reducing the symptoms of Parkinson's disease.

**Binding Configuration and Docking Results of Phloroglucinol and LRRK2:**

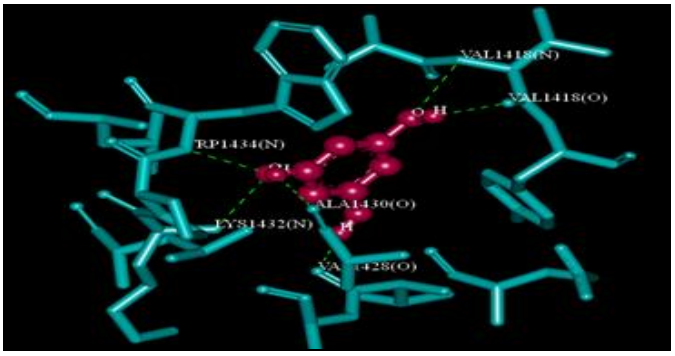


**FIG. 15: INTERACTIONS BETWEEN PHLOROGLUCINOL AND ROC DOMAIN OF LRRK2**

**TABLE 7: INTERACTIONS BETWEEN PHLORO-GLUCINOL AND ROC DOMAIN OF LRRK2**

| ROC domain of LRRK2 | | Phloroglucinol | Distance (Å) | Docking Energy (Kcal/mol) |
|---|---|---|---|---|
| Residue | Atom | | | |
| VAL1428 | O | H | 2.00 | –4.99 |
| VAL1418 | O | H | 2.07 | |
| VAL1418 | N | O | 3.02 | |
| LYS1432 | N | O | 2.82 | |
| ALA1430 | O | H | 1.99 | |
| TRP1434 | N | O | 3.18 | |

Voon *et al*., 2017 suggested that chronic treatment of L-DOPA induces the L-DOPA induced dyskinesias (LID) in nearly 80 % of PD patients [29]. Tenuigenin with LRRK2 showed binding energy as -7.9Kcal/mol, Wei *et al*., 2015 suggested that tenuigenin improves cognitive functions and enchances the basic synaptic transmission by stimulating the pre-synaptic intracellular calcium [30]. Baicalein with LRRK2 showed binding energy as -7.4 Kcal/mol. Sownd-harajan *et al.*, 2017 reported that baicalein has neuroprotective effects and it may be used as therapeutic agent to treat the neurotoxicity-mediated diseases [31]. Theaflavin with LRRK2 showed binding energy as -7.19 Kcal/mol. Dhivya *et al*., 2015 suggested that black tea and increases the neuroprotective activity [32].

Gastrodin with LRRK2 showed binding energy of -6.02 Kcal/mol. This suggests that gastrodin may increase GABA concentration by inhibiting GABA shunt.

Kumar *et al*., 2013 reported that Gastrodin prevents the $Mpp^+$ induced neurotoxicity in SH-SY5Y cells by regulation of free radicals and capcase 3 pathway [33]. Sesamol has protected the neurons from neuronal degeneration by regulating the anti-oxidant profile and improves behavioral activity of rats. Hassanzadeh *et al*., 2014 suggested that sesamol shows ameliorative effects in experimental models of epilepsy and prevent the oxidative drugs and also it may be beneficial to produce antiepileptic drugs [34]. Sesamol with LRRK2 showed binding energy as -4.99 Kcal/mol. Phloroglucinol with LRRK2 showed binding energy of -4.99 Kcal/mol. Phloroglucinol reduces ROS (reactive oxygen species) levels. Kadam *et al*., 2013 suggested that phloroglucinol extracted from marine algae and it has neuroprotective effect [35].

The docking results ofplants compounds compared to L-DOPA, the standard drug shows that tenuigenin, theaflavin, baicalein, gastrodin have higher docking score than L-DOPA, sesamol and pholoroglucinal have equal score to L-DOPA. All plant compounds having hydrogen bond interaction with LRRK2 the target protein.

Comparing all the plant compounds, gastrodin **(Fig. 13)** and phloroglucinol **(Fig. 15)** having more hydrogen bond interactions with LRRK2 protein than other compounds. These results show clearly that like L-DOPA, the plants compounds also have effective binding capacity with ROC domain of LRRK2 protein. The plant compounds may have anti-Parkinson's effect. However *in-vivo* studies may be carried out to confirm the same.

**TABLE 8: NO. OF HYDROGEN BONDS AND DOCKING SCORES OF THE COMPOUNDS**

| Compounds | Molecular Formula | Protein | Docking Energy (Kcal/mol) | No of Hydrogen Bonds |
|---|---|---|---|---|
| L-Dopa | $C_9H_{11}NO_4$ | LRRK2 | -4.97 | 2 |
| Tenuigenin | $C_{30}H_{45}ClO_6$ | LRRK2 | -7.91 | 1 |
| Baicalein | $C_{15}H_{10}O_5$ | LRRK2 | -7.4 | 2 |
| Theaflavin | $C_{29}H_{24}O_{12}$ | LRRK2 | -7.19 | 1 |
| Gastrodin | $C_{13}H_{18}O_7$ | LRRK2 | -6.02 | 4 |
| Phloroglucinol | C6H6O3 | LRRK2 | -4.99 | 3 |
| Sesamol | $C_7H_6O_3$ | LRRK2 | -4.99 | 1 |

**CONCLUSION:** Parkinson's disease is a multi-factorial pathological disease. Currently available conventional treatments are not able to prevent the pathomechanisms.

The standard drugs L-DOPA cannot be used for prolonged period and over dosage may be produced. Along with L-DOPA these plants compounds may given to the patients. It may reduce the side effects and thereby increase the anti-Parkinson's effect.

**ACKNOWLEDGEMENT:** This study was technically supported by the Mrs. Shoba, Assistant Professor, Department of Biochemistry and Bioinformatics, MGR Janaki college of Arts and Science for Women, Chennai.

**CONFLICT OF INTEREST:** We declare that we have no conflict of interest.

## REFRENCES:

1. Surmeier DJ, Obeso JA and Halliday GM: Selective neuronal vulnerability in Parkinson's disease. Nature review neuroscience 2017; 18(20): 101-113.
2. Harris DM, Rantalainen T, Muthalib M, Johnson and Teo WP: Exergaming as a viable therapeutic tool to improve static and dynamic balance among older adults and people with idiopathic Parkinson's disease, a systematic review and meta-analysis. Frontiers in aging Neuroscience 2015; 7(167): 1-12.
3. Brichta L, Greengard P and Flajolet M: Advances in the pharmacological treatment of Parkinson's disease, targeting neurotransmitter systems. Trends in neuro sciences 2013; 36(9): 543-554.
4. Monfrini E and Fonzo AD: Leucine-rich repeat kinase (LRRK2) genetics and Parkinson's disease. Neurobiology 2017; 14: 3-13.
5. Kalinderi K, Bostantjopoulou S and Fidani L: The genetic background of Parkinson's disease, current progress and future prospects. Neurologica 2016; 134(5): 314-326.
6. Cardona F, Pérez TM and Tur PJ: Structural and functional *in silico* analysis of LRRK2 missense substitutions. Molecular Biology Reports 2014; 41(4): 2529-2542.
7. Heinz R, Moritz DB and Lisa K: The nonmotor features of Parkinson's disease, pathophysiology and management advances. Current Opinion in Neurology 2016; 29(4): 467-473.
8. Chiu WH, Depboylu C, Hermanns G, Maurer L, Windolph A, Oertal WH, Ries V and Hoglinger GU: Long-term treatment with L-DOPA or pramipexole affects adult neurogensis and corresponding non-motor behavior in a mouse model of Parkinson's disease. Neuropharmacology 2015; 95(1): 367-376.
9. Lindenbach D, Palumbo N, Ostock CY, Vilceus N, Conti MM and Bishop C: Side effects profile of 5-HT treatments for Parkinson's disease and L-DOPA-induced dyskinesia in rats. British Journal of Pharmacology 2015; 172(1): 119-130.
10. MacDonald HJ, Stinear CM, Ren A, Coxon JP, Kao J, MacDonald L, Snow B, Cramer SC and Byblow WD: Dopamine gene profiling to predict impulse control and effects of dopamine agonist ropinirole. Journal of Cognitive Neuroscience 2016; 28(7): 909-919.
11. Heffernan N, Smyth TJ, FitzGerald RJ, Soler-Vila A and Brunton N : Antioxidant activity and phenolic content of pressurised liquid and solid-liquid extracts from four Irish origin macroalgae. International Journal of Food Science and Technology 2014; 49(7): 1765-1772.
12. Ustundag OG, Ersan S, Ozcan E, Ozan G Kayra N and Ekinci FY: Black tea processing waste as a source of antioxidant and anti-microbial phenolic compounds. European Food Research and Technology 2016; 242(9): 1523-1532.
13. Teng J, Gong Z, Deng Y, Chen L, Li Q, Shao Y, Lin L and Xiao W: Purification, characterization and enzymatic synthesis of theaflavins of polyphenols oxidase iso-enzymes from tea leaf (*Camellia sinesis*). LWT-Food Science and Technology 2017; 84(1): 263-270.
14. Ananingsih VK, Sharman A and Zhou W: Green tea catechains during food processing and storage, A review on stability and detection. Food Research International 2013; 50(2): 469-479.
15. Kumar H, Kim IS, More SV, Kim BW, Bahk YY and Choi DK: Gastrodin protects apoptotic dopaminergic neurons in a toxin-induced Parkinson's disease Model. Evidence-Based Complementary and Alternative Medicine 2013; 9: 1-13.
16. Xiaohua D, Weili W, Qing LX, Hanwen Y, Rong D and Quig L: Neuroprotective effect of ethyl acetate extract from *Gastrodia elata* against transient focal cerebral ischemia in rats induced by middle cerebral artery occlusion. Journal of Traditional Chinese Medicine 2015; 35(6): 671-678.
17. Wang X, Tan Y and Zhang F: Ameliorative effect of gastrodin on 3,3'-iminodipropionitrile-induced memory impairment in rats. Neuroscience Letter 2015; 594(6): 40-45.
18. Bhardwaj R, Sanyal SN, Vaiphei K, Kakkar V, Deol PK, Kaur IP and Kaur T: Sesamol induces apoptosis by altering expression of Bcl-2 and Bax proteins and modifies skin tumor development in Balb/c mice. Anti-cancer Agents in Medicinal Chemistry 2016; 17(5): 726-733.
19. Khadira S, Vijayalakshmi K, Priya N and Balima S: Effect of sesamol in association with folic acid on 6-OHDA induced parkinsonian animals- Biochemical, Neuro chemical and Histopathological evidence. International Journal of Research in Pharmacy and Science 2014; 5(3): 16-20.
20. Kovacic P: Phenolic antioxidants as drugs for Alzheimer's disease, oxidative stress and selectivity. Novel Approches in Drug Desinging and Development 2017; 2(5): 1-3.
21. Hwang KC: The pharmacology of Chinese herbs, Bola protein, CRL press, Edition 2nd, 2000.
22. Sarrafchi A, Bahmani M, Shirzad H and Kopaei MR: Oxidative stress and Parkinson's disease: New hopes in treatment with herbal antioxidants. Current Pharmaceutical Design 2016; 22(9): 238-246.
23. Wang X, Li M, Cao Y, Wang J, Zhang H, Zhou X, Li Q and Wang L: Tenuigenin inhibits LPS-induced inflammatory responses in microglia *via* activating the Nrf2-mediated $HO^{-1}$ signaling pathway. European Journal of Pharmacology 2017; 809: 196-202.
24. Kang SM, Cha SH, Ko JY, Kang MC, Kim D, Heo SJ and Jeon YJ: Neuroprotective effects of phlorotannins isolated from a brown alga, *Ecklonia cava*, against $H_2O_2$-induced oxidative stress in murine hippocampal HT22 cells. Environmental Toxicology and Pharmacology 2012; 34(1): 96-105.
25. Kannan RRR, Aderogba MA, Ndhlala AR, Stirk WA and Van Staden J: Acetylcholinesterase inhibitory activity of phlorotannins isolated from the brown alga, *Ecklonia maxima* (Osbeck) Papenfuss. Food Research International 2013; 54(1): 1250-1254.

26. Giese EC, Gascon J, Anzelmo G, Barbosa AM, Alvesda CMA and Dekker RFH: Free radical scavenging properties and antioxidant activities of botryosphaeran and some other β-D-glucans. International Journal of Biological Macromolecules 2015; 72: 125-130.
27. Yanwei L, Jinying Z and Christian H: Therapeutic potential of baicalein in Alzheimer's disease and Parkinson's Disease. CNS Drugs 2017; 31(8): 639-652.
28. Chang MW, Ayeni C, Breuer S and Torbett BE: Virtual screening for HIV Protease inhibitors: Acomparison of Auto dock 4 and vina. PLoS ONE 2012; 5: 11955.
29. Voon V, Napier C, Frank MJ, Faure VS, Grace AA, Oroz MR, Obeso J, Bezard E and Fernagut PO: Impulse control disorders and levodopa-induced dyskinesias in Parkinson's disease, an update. The Lancet Neurology 2017; 16(3): 238-250.
30. Wei PJ, Yao LH, Dai D, Huang JN, Liu XW, Peng X and Li CH: Tenuigenin enchances hippocampel schaffer collateral-CA1 synaptic transmission through modulating intracellular calcium. Phytomedicine 2015; 22(9): 807-812.
31. Sowndhararajan K, Deepa P, Kim M, Park SJ and Kim S: Baicalein as a potent neuroprotective agent. A review. Biomedicine and Pharmacotherapy 2017; 95: 1021-1032.
32. Dhivya BM, Justin A, Thenmozhi T and Manivasagam: Protective effect of black tea extract aluminium chloride-induced Alzheimer's disease in rats, Abehavioural, biochemical and molecular approach. Journal of Functional Foods 2015; 16: 423-435.
33. Kumar N, Mudgal J, Parihar VK, Nayak PG, Kutty NG and Rao CM: Sesamol treatment reduces plasma cholesterol and triacylglycerol levels in mouse models of acute and chronic hyperlipidemia. Lipids 2013; 48(6): 633-638.
34. Hassanzadeh P, Arbabi E and Rostami F: The ameliorative effects of sesamol against seizures, cognitive impairment and oxidative stress in the experimental model of epilepsy. Iran Journal of Basic Medical Science 2014; 17(2): 100-107.
35. Kadam SU, Tiwari BK and O'Donnell CP: Application of novel extraction technologies for bioactives from marine algae. Journal of Agricultural and Food chemistry 2013; 61(20): 4667-4675.


**How to cite this article:**
Jayanthi P and Vijayalakshmi K: Comparative molecular docking studies and structural prediction of plant compounds on LRRK2. Int J Pharm Sci Res 2018; 9(6): 2258-65. doi: 10.13040/IJPSR.0975-8232.9(6).2258-65.