INTRODUCTION

The avocado (Persea americana) also termed as alligator pear or bitter fruit, with its origin in Mexico, Central, or South America ages back to 500 B.C [1,2]. Classified as a member of the flowering plant family Lauraceae, it has long been used as a traditional herbal medicine for the treatment of stomachache, diarrhea, hypertension, and diabetes [3]. A great source of Vitamin C, E, K, B6, riboflavin, niacin, folate, pantothenic acid, magnesium, potassium, lutein, beta-carotene, omega 3, 6, fatty acids preventing free radical damage mostly exhibited in such disorders. It is also found to be rich in Vitamin E and unsaturated fatty acids, which in turn depends on their fatty acid composition. Dietary consumption of avocado that’s rich in linoleic acid and alpha-linoleic acid-like fatty acids has proven to improvise membrane fluidity, synaptic plasticity, neural function, and neuroprotection [19]. Combinations of avocados and soybean fats have been shown to prevent oxidation and formation of ROS, elevating the flexibility of neuronal cells when exposed to low-oxygen conditions [20]. The polyphenolic and monounsaturated fatty acids found in avocado have been evident in inhibiting fibril and Lewy body formation. Steroids in the form of stigmasterol, sitosterol, brassicasterol, and campesterol have also been shown to reduce amyloidogenic processing that may be advantageous in delaying the progression of Parkinson’s disease [21,22]. In addition, the phenolic extracts of avocado seeds have been shown to have high levels of B-type procyanidins and epicatechin exhibiting antioxidant property that may serve the purpose of treating neurodegenerative disorders. It is also found to be rich in Vitamin E and unsaturated fatty acids preventing free radical damage mostly exhibited in such disorders. Rich in extracts such as peptone, B-galactoside, cytochrome P-450, polyuronoids, and volatile oils slow down the process of cellular degeneration and prevent neuronal cell death. The polyphenolic activity of avocados has shown alpha-synuclein to be associated with the modulation of dopamine release and promoting membrane curvature [17,18].

In this context, traditional herbal products found in avocado have long been used to treat memory-related disorders. Neuronal cells require proper electrical impulses and gradient channels for their function which in turn depends on their fatty acid composition. In this study, the inhibitory potential of Hesperidin on the interaction of Parkinson-synuclein was investigated. The results indicate the potential of a Parkinson-synuclein extract from avocado to inhibit fibril and Lewy body formation. Steroids in the form of stigmasterol, sitosterol, brassicasterol, and campesterol have also been shown to reduce amyloidogenic processing that may be advantageous in delaying the progression of Parkinson’s disease [21,22]. In addition, the phenolic extracts of avocado seeds have been shown to have high levels of B-type procyanidins and epicatechin exhibiting antioxidant property that may serve the purpose of treating neurodegenerative disorders. It is also found to be rich in Vitamin E and unsaturated fatty acids preventing free radical damage mostly exhibited in such disorders. Rich in extracts such as peptone, B-galactoside, cytochrome P-450, polyuronoids, and volatile oils slow down the process of cellular degeneration and prevent neuronal cell death. The polyphenolic activity of avocados has shown alpha-synuclein to be associated with the modulation of dopamine release and promoting membrane curvature [17,18].
PBP2a of the bacterial cell wall serving as an antibacterial drug [25]. Further in-vitro and in-silico studies have shown the hydroxyl group of proanthocyanidins in avocado chelating with the catalytic center of the enzyme tyrosine inhibiting its activity further laying a foundation in agriculture, food and nutrition industries [26]. With this context, this paper aims in taking an in-silico approach for understanding the interaction of various phytochemicals present in avocado to the oxidation pathways and amyloid formation in neurodegenerative Parkinson’s disease; serving the possibility of therapeutics to treat it, respectively.

METHODS

The chemical structures of the phytochemicals identified from the extracts of P. americana were retrieved from the PubChem website (https://pubchem.ncbi.nlm.nih.gov/). The protein structure of alpha-synuclein was retrieved from the protein data bank (PDB) website (www.rcsb.org) with a PDB ID: 1XQ8. The protein-ligand docking study was performed using AutoDock 4 software and the results are visualized using the PyMOL tool [27-32].

RESULTS

Phytochemicals of P. americana

Based on the previous study by Rachael et al. (2020) (unpublished data), the list of phytochemicals present in the ethanol, water, and ethyl acetate extract of P. americana seed was obtained and the chemical structures of these list of chemicals were retrieved from PubChem database. A total of 30 ligands were identified and retrieved from the PubChem database and were used for docking analysis.

Anti-Parkinson’s docking analysis

The 30 ligand molecules were subjected to protein-ligand docking study to predict their Anti-Parkinson potential by inhibition of alpha-synuclein protein. AutoDock 4 was used for this purpose. The free binding energy of all the retrieved phytochemicals against the alpha-synuclein protein is tabulated in Table 1. Among the 30 ligand molecules, the highest significance was exhibited by Hesperidin with a free binding energy of −6.8 kcal/mol and formation of five hydrogen bonds (Lys-043, Lys-032, Val-040). The graphical representation of the interaction between Hesperidin and alpha-synuclein is shown in Fig. 1. The second highest significance was demonstrated by Biphenyl 4-(4-diethylaminobenzylidenamino) with a free binding energy of −5.9 kcal/mol with the formation of two hydrogen bonds (Val-040, Lys-043). Interactions of Biphenyl 4-(4-diethylaminobenzylidenamino) with alpha-synuclein are shown in Fig. 2. The third highest significance was demonstrated by the aldosterone molecule with a free binding energy of −5.8 kcal/mol. The interaction between aldosterone and alpha-synuclein is shown in Fig. 3. All three analyzed ligands show the same binding site interaction with the alpha-synuclein protein. Among the three extracts that are analyzed in this protein-ligand docking study, it is predicted that the aqueous extract of P. americana has the potential to be applied as an Anti-Parkinson agent, by inhibition of alpha-synuclein.

DISCUSSION AND CONCLUSION

Molecular docking is a frequently used approach in molecular drug designing, providing easy access to understand ligand-receptor interaction. Previous studies have shown these computation techniques to unravel and design potent new drugs by understanding the mechanism of drug-receptor interaction. Computer-aided drug design aids in recognizing small molecules by orienting and scoring them in the active binding site of the protein [33,34]. The protein alpha-synuclein has its active binding site for the formation of Lewy bodies and synucleinopathies. Three forms of extracts taken from P. americana were studied through docking for its potential binding affinity to the active site of the protein and inhibition of Synuclein activity. The highest significant value was evaluated for Hesperidin in the aqueous extract of the plant with a binding energy of −6.8 kcal/mol. It was found to be a more suitable ligand, confounding a greater ability to bind to the active site of the synuclein protein, thus preventing its aggregation and serving as a potential drug to treat Parkinson’s. Moreover, previous reports have shown lower solubility of the drug.

Table 1: The binding energy of phytochemicals from Persea americana with alpha-synuclein protein

| Extract               | Compound name                                      | Protein data bank ID | Binding energy (kcal/mol) |
|-----------------------|----------------------------------------------------|----------------------|--------------------------|
| Ethanol extract       | Androsta-1,4-dien-3-one, 17-hydroxy-17-methyl-isopropyl myristate | 6300                 | −5.7                     |
| Aqueous extract       | 1-Eicosanol                                        | 12400                | −3.2                     |
| Ethyl acetate extract | 1,14-Eicosadienoic acid, methyl ester             | 5365566              | −3.8                     |
|                      | Cyclohexane, 1-ethyl-1-methyl-2,4-bis (1 methylthienyl) | 641756              | −4.0                     |
|                      | Methacrylic acid, hexadecyl ester                 | 17235                | −3.5                     |
|                      | n-Heptacosanol                                     | 74822                | −3.0                     |
|                      | Octadecanoic acid                                  | 5281                 | −2.9                     |
|                      | Palmitoyl oleate                                   | 5377655              | −2.8                     |
|                      | Tridecanediol                                      | 544162               | −3.5                     |
|                      | Z, Z-4,15-Octadecadien-1-ol acetate                | 5363119              | −3.6                     |

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