EDITORIAL

Medicinal Chemistry Studies Against Neurodegenerative Diseases

Medicinal chemistry is a multidisciplinary science combining several specialties such as organic chemistry, biochemistry, physical chemistry, pharmacology, informatics, molecular biology, structural biology, cell biology, *etc*. The Subcommittee on Medicinal Chemistry and Drug Development of the Chemistry and Human Health Division (VII) in the International Union of Pure and Applied Chemistry (IUPAC) states that medicinal chemistry studies the discovery, invention, and preparation of substances with potential biological activity of therapeutic interest. Additionally, it considers molecular factors such as the mode of action of the drugs, their chemical structure-activity relationship (SAR), and pharmacokinetic aspects like absorption, distribution, metabolism, elimination, and toxicity [1-10].

Neurodegenerative diseases include Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), and Huntington's disease. These diseases involve different aspects of reward processing (primary rewards, secondary rewards, reward-based learning, and reward-based decision-making). About 70% of the population with 65 years or more are affected by these progressive neurodegenerative disorders of the central nervous system and characterized by gradual loss of cognitive function, progressive memory loss, disorientation, language impairment, abnormal behavior, personality changes, etc. Medicinal Chemistry studies include current developments in rational drug design, synthetic chemistry, bioorganic chemistry, high-throughput screening, combinatorial chemistry, compound diversity measurements, drug absorption, drug distribution, metabolism, new and emerging drug targets, natural products, pharmacogenomics, and structure-activity relationships. This thematic issue brings together medicinal chemistry studies of different methodologies applied in order to optimize the search for new drugs for the cure and treatment of neurodegenerative diseases [1-10].

Natural products are compounds isolated from plants that provide a variety of lead structures for the development of new drugs by the pharmaceutical industry [2,5-10]. The interest in these substances increases because of their beneficial effects on human health. Alzheimer's disease (AD) affects about 80% of individuals aged 65 years. The most common cause of dementia in the elderly is Alzheimer's disease (AD), which is marked by progressive neurodegenerative changes such as a decrease in cholinergic impulse, increased toxic effects caused by reactive oxygen species, and the inflammatory process in which the amyloid plaque plays a role. *In silico* studies are relevant in drug discovery; through technological advances in the areas of structural characterization of molecules, computational science and molecular biology have contributed to the planning of new drugs used against neurodegenerative diseases. Considering the social impairment caused by an increased incidence of disease and no chemotherapy treatment effective against AD, several compounds are being studied. Natural compounds that have been widely investigated in various Alzheimer's disease models have been used in the search for effective neuroprotectants as potential treatments.Our study entitled **Computer Aided Drug Design Methodologies With Natural Products In The Drug Research Against Alzheimer's Disease r**eviewed articles with *in silico* studies of natural products aimed at potential drugs against Alzheimer's disease (AD) in the period from 2015 to 2021 [11].

The radiation for therapeutic purposes has shown positive effects in different contexts; however, it can increase the risk of many age-related and neurodegenerative diseases such as Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), and Parkinson's disease (PD). These different outcomes highlight a dose-response phenomenon called hormesis. Prevailing studies indicate that high doses of radiation could play several destructive roles in triggering oxidative stress, neuroapoptosis, and neuroinflammation in neurodegeneration. However, there is a lack of effective treatments in combating radiation-induced neurodegeneration, and the present drugs suffer from some drawbacks, including side effects and drug resistance. Among natural entities, polyphenols are suggested as multi-target agents affecting the dysregulated pathogenic mechanisms in neurodegenerative disease. The review of Drs Fakhiri *et al.,* **Phytochemicals targeting oxidative stress, interconnected neuroinflammatory and neuroapoptotic pathways following radiation**, discussed the destructive effects of radiation on the induction of neurodegenerative diseases by dysregulating oxidative stress, apoptosis, and inflammation. The authors also described the promising effects of polyphenols and other candidate phytochemicals in preventing and treating radiation-induced neurodegenerative disorders, aiming to find novel/potential therapeutic compounds against such disorders [12].

Mitochondrial disorders are clinically heterogeneous, resulting from nuclear gene and mitochondrial mutations that disturb the mitochondrial functions and dynamics. There is a lack of evidence linking mtDNA mutations to neurodegenerative disorders, mainly due to the absence of noticeable neuropathological lesions in postmortem samples. In the review entitled **The Role of Mitochondrial Genes in Neurodegenerative Disorders,** Dr. Kumar and co-workers described various gene mutations in Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, and stroke. These abnormalities, including PINK1, Parkin, and SOD1 mutations, seem to reveal mitochondrial dysfunctions due to either mtDNA mutation or deletion, the mechanism of which remains unclear in depth [13].

We, the Guest-Editors, would like to express our gratitude to the many authors who contributed to this special issue, reporting investigations in various aspects of **MEDICINAL CHEMISTRY STUDIES AGAINST NEURODEGENERATIVE DISEASES**.

REFERENCES

[1] Corsaro, A.; Thellung, S.; Bucciarelli, T.; Scotti, L.; Chiovitti, K.; Villa, V.; D'Arrigo, C.; Aceto, A.; Florio, T. High hydrophobic amino acid exposure is responsible of the neurotoxic effects induced by E200K or D202N disease-related mutations of the human prion protein. *Intl. J. Biochem. Cell Biol.,* **2011**, *43* (3), 372-382. DOI: 10.1016/j.biocel.2010.11.007.

1875-6190/22

[2] de Moura, E. P.; Fernandes, N. D.; Monteiro, A. F. M.; de Medeiros, H. I. R.; Scotti, M. T.; Scotti, L. Machine learning, molecular modeling and Qsar studies of natural products against Alzheimer's Disease. *Curr. Med. Chem.,* **2021**, *28* (38), 7808-7829.
[3] Ishiki, H. M.; Barbosa, J. M.; da Silva, M. S.; Scotti, M. T.; Scotti, L. Computer-aided drug design applied to parkinson targets. *Curr. Neuropharmacol.,***2018**, *16* (6), 865-880.
[4] Lorenzo, V. P.; Alves, M. F.; Scotti, L.; dos Santos, S. G.; Diniz, M.; Scotti, M. T. Computational chemistry study of natural alkaloids and homemade databank to predict inhibitory potential against key enzymes in neurodegenerative diseases. *Curr. Top. Med. Chem.,***2017**, *17* (26), 2926-2934..
[5] Maia, M. D.; Rodrigues, G. C. S.; de Sousa, N. F.; Scotti, M. T.; Scotti, L.; Mendonca, F. J. B. Identification of new targets and the virtual screening of lignans against Alzheimer's Disease. *Oxid. Med. Cell. Longev.,* **2020**, *2020*, 3098673.
[6] Mendonca, F. J. B.; Scotti, M. T.; Muratov, E. N.; Scotti, L.; Nayarisseri, A. Natural bioactive products with antioxidant properties useful in neurodegenerative diseases 2020. *Oxid.Med. Cell. Longev.,* **2021**, *2021*, 6262316..
[7] Mendonca, F. J. B.; Scotti, M. T.; Nayarisseri, A.; Zondegoumba, E. N. T.; Scotti, L. Natural bioactive products with antioxidant properties useful in Neurodegenerative Diseases. *Oxid. Med. Cell. Longev.,* **2019**, *2019*, 7151780.
[8] Monteiro, A. F. M.; Viana, J. D.; Nayarisseri, A.; Zondegoumba, E. N.; Mendonca, F. J. B.; Scotti, M. T.; Scotti, L. Computational studies applied to flavonoids against Alzheimer's and Parkinson's Diseases. *Oxidat. Med. Cell. Longev.,* **2018**, *2018*, 7912765.
[9] Ribeiro, F. F.; Mendonca, F. J. B.; Ghasemi, J. B.; Ishiki, H. M.; Scotti, M. T.; Scotti, L. Docking of Natural Products Against Neurodegenerative Diseases: General Concepts. *Comb. Chem. High Throughput Screen.,* **2018**, *21* (3), 152-160.
[10] Scotti, L.; Scotti, M. T.; Pasqualoto, K. F. M.; Bolzani, V. D.; Ferreira, E. I. Molecular physicochemical parameters predicting antioxidant activity of Brazilian natural products. *Revista Brasileira De Farmacognosia-Brazil. J.Pharmacog.,* **2009**, *19*(4), 908-913.
[11] Sousa, N. F.; Scotti, L.; Moura, É. P.; Maia, M. S.; Soares, G. C. S.; Medeiros, H. I. R.; Lopes, S. M.; Scotti, M. T. Computer aided drug design methodologies with natural products in the drug research against Alzheimer's Disease. *Curr. Neuropharmacol.,* **2022**, *20*(5), 857-885.
[12] Fakhri, S.; Moradi, S. Z.; Khan, H. Phytochemicals targeting oxidative stress, interconnected neuroinflammatory and neuroapoptotic pathways following radiation. *Curr. Neuropharmacol.*, **2022**, *20*(5), 836-856.
[13] Kumar, R.; Harilal, S.; Parambi, D. G. T.; Kanthlal, S. K.; Rahman, M. A.; Alexiou, A.; Batiha, G. E-S.; Mathew, B. The role of mitochondrial Genes in neurodegenerative disorders. *Curr. Neuropharmacol.*, **2022**, *20*(5), 824-835.

Luciana Scotti
(Guest Editor)
Federal University of Paraíba
Postgraduate Program in Natural and Synthetic Bioactive Products
50670-910, João Pessoa, PB
Brazil
Federal University of Paraiba
University Hospital
Paraiba
Brazil

Marcus T. Scotti
(Co-Guest Editor)
Federal University of Paraíba
Postgraduate Program in Natural and Synthetic Bioactive Products
50670-910, João Pessoa, PB
Brazil