REVISTA PERUANA DE INVESTIGACIÓN EN SALUD
https://doi.org/10.35839/repis.5.2.928
IDEAS AND OPINIONS
http://revistas.unheval.edu.pe/index.php/repis/

Isatin, an endogenous compound to consider in Parkinson's disease

Isatina, un compuesto endógeno a considerar en la Enfermedad de Parkinson

Lorenzo A. Justo-Cousiño[1,*], Lilian Faro[1], Rafael Durán[1]

[1]Universidad de Vigo, Pontevedra, España

ORCID:
*https://orcid.org/0000-0002-1787-4017

Corresponding author:
Dr. Lorenzo A. Justo Cousiño

Postal Address: Facultad de Fisioterapia. Universidad de Vigo. Campus A Xunqueira s/n, 36005 Pontevedra. Galicia. España. Teléfono: (+34) 986 801 750

Email: lorenzo.antonio.justo@gmail.com

Reception date: january 23, 2021
Approval date: march 20, 2021

Quote as: Justo-Cousiño LA, Faro L, Durán R. Isatin, an endogenous compound to consider in Parkinson's disease. Rev. Peru. Investig. Salud. [Internet]; 5(2): 140-141. Available from: http://revistas.unheval.edu.pe/index.php/repis/article/view/928

Dear Editor

Isatin (indole-2, 3-dione) is an endogenous monoamine oxidase B (MAO B) inhibitor that increases striatal dopamine levels in experimental animals and was proposed as a possible candidate for research in antiparkinsonian pharmacotherapy (1-3).

The isatin-induced increase in dopamine is related to vesicular storage of the neurotransmitter and is dependent on membrane depolarization and extracellular calcium (3). In addition, systemic administration of isatin ameliorates motor deficits in animal models of Parkinson's disease (PD) (1, 2).

As an MAO B inhibitor, isatin could reduce the side effects of long-term treatment with L-DOPA and improve the motor complications of PD. MAO B inhibitors improve the bioavailability of dopamine by inhibiting its main degradative pathway. In addition, it is believed that these compounds may have effects that prevent further neuronal degeneration by preventing the formation of reactive oxygen species derived from dopaminergic metabolism (4).

Despite the incipient research carried out in PD, investigations are focused on determining the efficacy of a drug, ignoring other aspects that could be relevant at the clinical level.

On the one hand, urinary isatin levels could be useful as a biomarker of the clinical severity of PD. In patients with PD from stage III onwards, a significant increase in urinary isatin levels is observed. Likewise, these levels decrease in stage I patients undergoing treatment compared to untreated patients (5).

Recent publications describe a possible neuroprotective action of isatin (6, 7). Furthermore, in cell cultures isatin shows protective effects on dopaminergic neurons and neuroprotection is also described in the mouse model of PD induced by the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) (8). As a neuroprotective agent, isatin acts on glyceraldehyde-3-phosphate dehydrogenase (GAPDH), which is considered a potential therapeutic target in pathologies such as senile dementia, epilepsy and PD (9).

The proteomic profile of isatin reveals that this compound has the capacity to bind to 200 brain proteins in mice, showing a behavior analogous to that of selegiline (9). This opens the door to the possibility that, like selegiline, the possible neuroprotective effect of isatin could be independent of MAO-B inhibition.

Considering that isatin is an endogenous compound and its levels are higher in PD patients, isatin could interact with the antiparkinsonian drugs administered to the patient. Moreover, isatin may also attenuate the effects of other pharmacological agents on specific targets such as MAO or neuroprotective compounds (10).

In this sense, Faro and collaborators have recently analyzed by means of in vivo brain microdialysis in rats the interaction between isatin and various compounds with antiparkinsonian action. The main results observed were that the effects of isatin on extracellular levels of striatal dopamine are similar to those of selegiline and chlorgiline. Furthermore, at the neurochemical level, a positive interaction between isatin and compounds with antiparkinsonian action has been observed. Thus, coadministration of isatin with catechol-O-methyltransferase (COMT) inhibitors, amantadine, L-DOPA and caffeine increases striatal dopamine levels in an additive manner. Only the absence of synergistic effects is described in the coadministration of isatin with the dopaminergic agonist ropinirole (10).

The role of isatin in PD is still unclear; it is not known whether it is formed endogenously to counteract the

dopaminergic deficit or whether it could be involved as a causative agent of PD.

The potential clinical application of isatin requires an extensive research process, as published studies on this compound have been conducted mainly in animals. Nevertheless, considering the effects on dopaminergic neurotransmission, the results in animal models of PD, the diversity of proteins with which it could interact and its potential as a neuroprotective agent, it would be interesting to have more lines of research on isatin.

Finally, the present work shows that in PD there are multiple unknowns that should not be ignored and to which neuroscience should provide answers. An excessively reductionist approach will never allow a complete understanding of the idiosyncrasy of this neurodegenerative disorder and that of other pathologies.

Deepening the knowledge of isatin would help to unravel a pathology as complex as PD, since only by considering all the pieces will it be possible to assemble the puzzle that today represents the second neurodegenerative disease worldwide.

Contribution of the authors

Single authorship.

Interest conflict

We declare that we have no conflict of interest.

Financing sources

The study was self-financed.

References

1. Hamaue N, Minami M, Terado M, Hirafuji M, Endo T, Machida M, et al. Comparative Study of the Effects of Isatin, an Endogenous MAO-Inhibitor, and Selegiline on Bradykinesia and Dopamine Levels in a Rat Model of Parkinson's Disease Induced by the Japanese Encephalitis Virus. Neurotoxicology. 2004; 25(1-2): 205-13.
2. Xu H, Wang D, Zhang W, Zhu W, Yamamoto K, Jin L. Determination of isatin and monoamine neurotransmitters in rat brain with liquid chromatography using palladium hexacyanoferrate modified electrode. Anal Chim Acta. 2006; 577(2): 207-13.
3. Justo LA, Durán R, Alfonso M, Fajardo D, Faro LRF. Effects and mechanism of action of isatin, a MAO inhibitor, on in vivo striatal dopamine release. Neurochem Int. 2016; 99: 147-57.
4. Szökő É, Tábi T, Riederer P, Vécsei L, Magyar K. Pharmacological aspects of the neuroprotective effects of irreversible MAO-B inhibitors, selegiline and rasagiline, in Parkinson's disease. J Neural Transm. 2018; 125(11): 1735-49.
5. Hamaue N. Pharmacological Role of Isatin, an Endogenous MAO Inhibitor. Yakugaku Zasshi. 2000; 120(4): 352-62.
6. Buneeva O, Medvedeva M, Kopylov A, Medvedev A. Ubiquitin Subproteome of Brain Mitochondria and Its Changes Induced by Experimental Parkinsonism and Action of Neuroprotectors. Biochemistry Mosc. 2019; 84(11): 1359-74.
7. Medvedev A, Kopylov A, Buneeva O, Kurbatov L, Tikhonova O, Ivanov A, et al. A Neuroprotective Dose of Isatin Causes Multilevel Changes Involving the Brain Proteome: Prospects for Further Research. Int J Mol Sci. 2020; 21(11): 4187.
8. Zhang J, Zhang F, Qiu Y, Yue W. Isatin decreases Bax protein expression in the substantia nigra of a mouse model of Parkinson's disease. Neural Regen Res. 2011; 6(26): 2022-5.
9. Buneeva OA, Kapitsa IG, Ivanova EA, Kopylov AT, Zgoda VG, Medvedev AE. The effect of a neuroprotective dose of isatin or deprenyl to mice on the profile of brain isatin-binding proteins. Biochem Mosc Suppl B Biomed Chem. 2020; 14(2): 116-26.
10. Faro LRF, Justo LA, Alfonso M, Durán R. Possible synergies between isatin, an endogenous MAO inhibitor, and antiparkinsonian agents on the dopamine release from striatum of freely moving rats. Neuropharmacology. 2020; 171:108083.