

Researchers design new substances that might help fight Alzheimer's and Parkinson's disease

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University of Granada researchers have tested melatonin analogues in rats that inhibit the enzyme nitric oxide synthase, which is involved in the development of the diseases referred above.

This enzyme is also involved in other conditions as [inflammatory bowel disease](#) or rheumatoid arthritis, as well as in neurodegenerative conditions as Huntington's disease and [amyotrophic lateral sclerosis](#).

University of Granada researchers have tested melatonin analogues in rats as it inhibits the enzyme nitric oxide synthase (NOS), which is involved in the development of conditions as inflammatory bowel disease, [septic shock](#) or [rheumatoid arthritis](#), as well as in [neurodegenerative conditions](#) as Huntington's disease, Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis.

Some of the new analogues developed by the University of Granada have been tested in vivo in rats and present "very interesting pharmacological properties, as they are much more efficient than melatonin" in inhibiting NOS activity in Parkinson models. Most of the results obtained in this study have been published in [Journal of Medicinal Chemistry](#).

Melatonin is a hormone secreted by the pineal gland that inhibits the [central nervous system](#) in rats and humans. Therefore, it is said to have neuroprotective and anticonvulsant properties. These properties give

melatonin the ability to inhibit nitric oxide production, as NO is involved in numerous physiological and pathological processes. Therefore, it is necessary to regulate NO production. At present, researchers are trying to "develop powerful and selective inhibitors of each NOS isoform, which would allow clinicians to control specific pathologies, and would help determine the role of the different isoforms in the [biological system](#)".

New Inhibitors

The University of Granada researchers that participated in this study work at the Department of Pharmaceutical and [Organic Chemistry](#) and the Institute of Biotechnology of the University of Granada. Taking melatonin as a model, the researchers designed and synthesized several families of complexes (kynurenines, kynurenamines and phenyl pyrazolines), which act as NOS inhibitors. The comparative analysis of the structures of these three families of complexes "allows us to determine structure-activity relationships to inhibit the enzyme NOS and develop a model that might be used to design new inhibitors of this enzyme", the researchers state.

Nitric oxide is a very reactive enzyme, has a relatively long mean life and is a non-polar substance, i.e. it easily passes through cell membranes to spread to other tissues and reacts with many different molecules. In addition, it is an important signaling molecule involved in many physiological processes as neurotransmission, blood circulation and pressure, platelet aggregation and inflammation.

A number of studies have confirmed that each NOS isoform is involved in different biological roles. Thus, nNOS is mainly expressed in neural tissue and plays a major role in the production of NO as neurotransmitter; eNOs is mainly found in the vascular endothelium, where it regulates blood pressure and vascular tone. The enzyme iNOS

–which expression is mainly induced by activated macrophages and other types of cells is involved in the body defense system. Finally, the mitochondrial isoforms c-mtNOS and i-mtNOS are involved in NO production within the cell and control cell bioenergetics.

Provided by University of Granada

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