Nitrone derivatives with antioxidant and neuroprotective activity for the treatment of Ictus and Ischemia

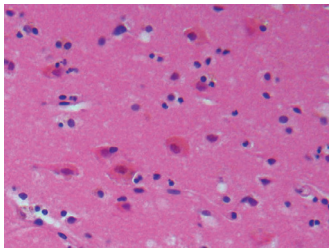
Researchers from CSIC, the Universidad Complutense de Madrid and the public Hospital Ramón y Cajal have synthesized new nitrone derivatives with high permeability and neuroprotective activity. These compounds present antioxidant and neuroprotective activity higher than known nitrones like phenyl-t-buthyl nitrone (PBN), and are candidates to be used as drugs for Ictus, Ischemia and other neurodegenerative diseases. We are looking for a pharmaceutical company interested in further development and patent licence.

An offer for Patent Licensing and/or R+D collaboration

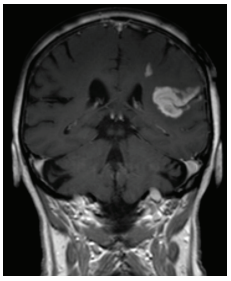
A new approach to the treatment of Ictus and Ischemia

The use of nitrone derivates represents a new and interesting approach for the treatment of diseases like Ictus or Ischemia, related with the oxidation of lipid membranes in neurones. The nitrone group acts as a radical scavenger and reduces oxidative stress. Known nitrones like phenyl-t-butyl nitrone (PBN) and NXY-059, show a high activity as antioxidant agents, however, at low dose, their in vivo efficacy is limited, probably due to low cell permeability. Taking into account the excellent antioxidant characteristics of nitrone compounds, the search of new derivatives with major activity and better permeability is of great interest in the area of neurodegenerative diseases.

New quinoline nitrone derivatives with elevated antioxidant activity against hydroxyl radicals and lipidic peroxidation, have been prepared. The presence of a quinoline group in the structure of the molecules increases their lipophilicity and can improve their cell permeability. In vitro assays in cell cultures show that new compounds have also high neuroprotective activity. Furthermore, the compounds are able to cross the blood-brain barrier, which, together with their antioxidant activity, make them especially useful as drugs for the treatment of CNS diseases.



Microphotography of brain tissue after an ictus (M. Hasselblatt)



Brain injured after an ictus (Hellerhoff)

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Main applications and advantages

- The new compounds are able to inhibit lipidic peroxidation and show an activity as antioxidant agents against free radicals (at 100 µM, 95-100% of scavenging activity for hydroxyl radicals) higher than PBN (90%) and the antioxidant trolox (73%)
- Neuroprotective effect on cells exposed to oxygen-glucose deprivation (70% of neuroprotection at 1 µM) higher than PBN (68% at 100 µM)
- In vitro assays show that the compounds are able to cross the blood-brain barrier with good permeability values (P_e= 15 10^{-6} cm s^{-1}), similar to those reported for verapamil (P_e= 16 10^{-6} cm s^{-1}), that is generally used as a high permeability standard
- All the compounds are prepared in a single synthetic step from commercially available starting materials in a rapid and straightforward process

Patent Status

Priority patent application filed

For further information please contact

Luis Miguel Lozano, Ph.D.
Institute for General Organic Chemistry / Deputy Vice-Presidency for Knowledge Transfer of CSIC

Tel.: + 34 – 91 562 29 00
E-mail: lml@iqog.csic.es