New therapeutic property of dimebon as a neuroprotective agent

Ustyugov A.

Shevtsova E.

Barreto G.E.

Ashraf G.M.

Bachurin S.O.

Aliev G.

Dimebon (or Latrepirdine) was initially used as an anti-histamergic drug but later new therapeutic properties were rediscovered, adding to a growing body of "old" agents with prominent neuroprotective effects. In the present manuscript, we are focusing on our latest study on Dimebon with regard to brain's pathological processes using in vivo proteinopathy models. In the study, neurodegenerative pathology has been attributed to a group of aggregate-prone proteins: hyperphosphorylated tau, fused in sarcoma and ?-synuclein , which are involved in a number of neurological disorders. We have also presented our in vitro model based on overexpression of an aberrant mutant form of transactive response DNA binding 43 kDa protein in cultured SH-SY5Y neuroblastoma cells. Dimebon treatment followed by the activation of autophagy markers resulted in reduced number of inclusion containing cells. The most significant effects of Dimebon appeared to be on the improving cellular energy balance, mitochondria stability by increasing the threshold for nonselective mitochondrial pore opening as well as on increased calcium retention capacity while reducing lipid peroxidation. The therapeutic potential of Dimebon and newly designed analogs show disease modifying properties and could be used to treat neurodegenerative disorders. In addition, new data hint on a possible anti-aging effect and potential application of Dimebon for treatment of anxiety, ischemia and depression. Overall, our findings suggest that the most pronounced effect of Dimebon was observed when treatment was started at the early stages of disease onset and this factor needs to be taken into account while planning future clinical trials.

Dimebon

Latrepirdine

Mitochondrial permeability transition

Neuroprotection

Proteinopathy

dimebon

DNA

gamma synuclein

neuroprotective agent

RNA binding protein FUS

synuclein

tau protein

dimebon

indole derivative

neuroprotective agent

RNA binding protein FUS

tau protein

autophagy

cell energy

cell function

degenerative disease

DNA binding

drug mechanism

in vitro study

lifespan

lipid peroxidation

mitochondrial permeability

mitochondrion

neuroblastoma cell

neuroblastoma cell line

neuroprotection

nonhuman

Review

tauopathy

animal

chemistry

degenerative disease

drug effect

genetics

human

metabolism

pathology

Animals

Autophagy

Humans

Indoles

Mitochondria

Neurodegenerative Diseases

Neuroprotective Agents

RNA-Binding Protein FUS

tau Proteins