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Synthesis of Designed Dextromethorphan Derivatives as Potential Neuroprotective Agents

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Research in neuroprotection is essential and eager for the development of therapies for neurodegenerative diseases such Alzheimer's disease and Parkinson's disease (PD) important on age-related diseases. Since the primary machinery for the production of neurotoxic factor and pro-inflammatory such as ROS, which cause dopamine (DA) neuron damage in microglia is NADPH oxidase (also called phagocyte oxidase, or PHOX), researches indicated that vital to the neuroprotective effect of DM acts on the NADPH oxidase activity.

Dextromethorphan (DM) is originally a dextrorotary morphinan antitussive drug, which has been proven as a potential neuroprotective drug. 3-Hydroxymorphinan (3-HM) has shown the most potency for protect DA neurons among DM and DM's metabolite family, dextrophan (DX), 3-methoxymorphinan (3-MM), and 3-hydroxymorphinan (3-HM). Not only does 3-HM effectively inhibit microglia to reduce neurotoxicity, but also it stimulates astrocyte secretion neurotrophic factors to protect DA neurons.

This newly discovered capacity to reduce microglial activation may pave a new path for potential use of DM-related compounds in treating neurodegenerative diseases. In search of neuroprotective agents the structural modification of DM was substantially conducted in our laboratories. Those target compounds are under pharmacological evaluations by *in vitro* suppressing the production of nitric oxide (NO) and reactive oxygen species (ROS) in LPS-elicited microglia cells and for further a SAR study.