

DIMEBON - A NOVEL THERAPEUTIC CANDIDATE FOR NEURODEGENERATIVE DISEASES

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Dimebon is an oral small molecule that has demonstrated beneficial effects in patients with Alzheimer's disease (AD) and Huntington's disease (HD). In a recently reported AD clinical trial, Dimebon treatment was associated with improvements compared with placebo on cognition and memory, psychiatric symptoms and activities of daily living. Preclinical studies suggest that Dimebon does not exert its clinical benefits via targets typically associated with memory but rather through stabilization and enhancement of mitochondrial and neuronal function. Disruption of mitochondrial membrane potential with the calcium ionophore ionomycin was used to evaluate Dimebon action. Dimebon at picomolar concentrations preserves mitochondrial JC-1 fluorescence in human neuroblastoma cells (SHSY-5Y cells) and primary rat hippocampal cells exposed to ionomycin. In addition, Dimebon is similarly potent at promoting neurite outgrowth of primary rat neurons derived from the hippocampus, cortex or spine comparable to the prototypical neurotrophic factor BDNF. As mitochondrial function is important for neurite outgrowth, these potent effects of Dimebon may share a common mechanism. Mitochondrial dysfunction is a hallmark of neurodegenerative diseases including AD and HD and the clinical effects of Dimebon may involve changes in mitochondrial function.