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# Targeting Calcium Dysregulation for Treatment of Dementia in Alzheimer's Disease

**Authors :** Huafeng Wei

**Abstract :** Dementia in Alzheimer's Disease (AD) is the number one cause of dementia internationally, without effective treatments. Increasing evidence suggest that disruption of intracellular calcium homeostasis, primarily pathological elevation of cytosol and mitochondria but reduction of endoplasmic reticulum (ER) calcium concentrations, play critical upstream roles on multiple pathologies and associated neurodegeneration, impaired neurogenesis, synapse, and cognitive dysfunction in various AD preclinical studies. The last federal drug agency (FDA) approved drug for AD dementia treatment, memantine, exert its therapeutic effects by ameliorating N-methyl-D-aspartate (NMDA) glutamate receptor overactivation and subsequent calcium dysregulation. More research works are needed to develop other drugs targeting calcium dysregulation at multiple pharmacological acting sites for future effective AD dementia treatment. Particularly, calcium channel blockers for the treatment of hypertension and dantrolene for the treatment of muscle spasm and malignant hyperthermia can be repurposed for this purpose. In our own research work, intranasal administration of dantrolene significantly increased its brain concentrations and durations, rendering it a more effective therapeutic drug with less side effects for chronic AD dementia treatment. This review summarizesthe progress of various studies repurposing drugs targeting calcium dysregulation for future effective AD dementia treatment as potentially disease-modifying drugs.

**Keywords :** alzheimer, calcium, cognitive dysfunction, dementia, neurodegeneration, neurogenesis
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