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Bisphosphonates: Future perspective for neurological disorders

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Abstract

Neurodegenerative disorders and osteoporosis share some common underlying pathological features including calcium overload, accumulation of toxic chemicals, inflammation and impaired protein prenylation by isoprenoids (farnesyl pyrophosphate and geranylgeranyl pyrophosphate) appear later stage of life. Substantial number of pre-clinical and clinical reports as well as *in vitro* data univocally acknowledged the negative impact of altered post-translational modification (prenylation) of proteins like small GTPases (Rffhes, Rho, Rac etc) and cholesterol levels in both serum and brain on CNS integrity. Bisphosphonates (BPs), referred to as gold standard for osteoporosis treatment, have well established role in attenuation of bone resorption and osteoclast apoptosis by inhibition of farnesyl pyrophosphate synthase enzyme (FPPS) in mevalonate pathway. BPs mainly nitrogen containing BPs (NBPs) have potential to offer new therapeutic targets for neurological disorders and received increasing attention in recent years. A year back clinical and pre-clinical studies revealed that NBPs have the potential to alleviate the symptoms of neurological disorders like brain calcification, Alzheimer's disease and Huntington's disease by targeting mevalonate pathway. Though these drugs have well developed