

MECHANISMS OF PREVENTION OF ALZHEIMER PATHOGENESIS WITH THE TURMERIC EXTRACT, CURCUMIN AND THE OMEGA-3 FATTY ACID, DHA

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Multiple degenerative diseases of aging including Alzheimer's disease (AD) involve oxidative damage and inflammation suggesting that chronic intervention in these pathways for primary prevention might be widely beneficial. However, to date clinical trial results with chronic intervention with vitamin E and cyclooxygenase inhibitors have been disappointing. To look for alternatives, we screened multiple antioxidants, anti-inflammatory and cocktail approaches in AD animal models and found two promising enough to demand further study. One is the yellow curry pigment and NSAID/ phenolic antioxidant curcumin (diferulomethane) which is also a potent anti-carcinogen and anti-amyloid drug with an established safety profile. Oral curcumin inhibited amyloid oligomer and fibril formation and promoted phagocytosis of amyloid in vitro and effectively reduced oxidative damage, inflammation, amyloid and synaptic and cognitive deficits in animal models. A second approach is to increase dietary n-3 (omega-3) and decrease n-6 fatty acids in the diet. Increasing n-6 fatty acids and depleting n-3 dietary DHA increased oxidative damage, caspase activation and synaptic and cognitive deficits in APP transgenic mice while decreasing PI3-kinase pathway signaling. Curcumin or DHA supplementation reversed these effects and reduced amyloid accumulation and combined curcumin and DHA appeared to have a synergistic effect. Clinical trials with curcumin and with omega 3 fatty acid supplements are already underway in AD patients, but our ultimate goal must be primary prevention.