

News Release

Marijuana's Active Ingredient Shown to Inhibit Primary Marker of Alzheimer's Disease

Discovery Could Lead to More Effective Treatments

LA JOLLA, CA, August 9, 2006 - Scientists at The Scripps Research Institute have found that the active ingredient in marijuana, tetrahydrocannabinol or THC, inhibits the formation of amyloid plaque, the primary pathological marker for Alzheimer's disease. In fact, the study said, THC is "a considerably superior inhibitor of [amyloid plaque] aggregation" to several currently approved drugs for treating the disease.

The study was published online August 9 in the journal *Molecular Pharmaceutics*, a publication of the American Chemical Society.

According to the new Scripps Research study, which used both computer modeling and biochemical assays, THC inhibits the enzyme acetylcholinesterase (AChE), which acts as a "molecular chaperone" to accelerate the formation of amyloid plaque in the brains of Alzheimer victims. Although experts disagree on whether the presence of beta-amyloid plaques in those areas critical to memory and cognition is a symptom or cause, it remains a significant hallmark of the disease. With its strong inhibitory abilities, the study said, THC "may provide an improved therapeutic for Alzheimer's disease" that would treat "both the symptoms and progression" of the disease.

"While we are certainly not advocating the use of illegal drugs, these findings offer convincing evidence that THC possesses remarkable inhibitory qualities, especially when compared to AChE inhibitors currently available to patients," said Kim Janda, Ph.D., who is Ely R. Callaway, Jr. Professor of Chemistry at Scripps Research, a member of The Skaggs Institute for Chemical Biology, and director of the Worm Institute of Research and Medicine. "In a test against propidium, one of the most effective inhibitors reported to date, THC blocked AChE-induced aggregation completely, while the propidium did not. Although our study is far from final, it does show that there is a previously unrecognized molecular mechanism through which THC may directly affect the progression of Alzheimer's disease."

As the new study points out, any new treatment that could halt or even slow the progression of Alzheimer's disease would have a major impact on the quality of life for patients, as well as reducing the staggering health care costs associated with the disease.

Alzheimer's disease is the leading cause of dementia among the elderly, and the numbers are growing. The Alzheimer's Association estimates 4.5 million Americans have the disease, a figure that could reach as high as 16 million by 2050. A survey by the National Center for Health Statistics noted that half of all nursing home residents have Alzheimer's disease or a related disorder. The costs of caring for Alzheimer's patients are at least \$100 billion annually, according to the National Institute on Aging.

Over the last two decades, the causes of Alzheimer's disease have been clarified through extensive biochemical and neurobiological studies, leading to an assortment of possible therapeutic strategies including interference with beta amyloid metabolism, the focus of the Scripps Research study.

The cholinergic system - the nerve cell system in the brain that uses acetylcholine (ACh) as a neurotransmitter - is the most dramatic of the neurotransmitter systems affected by Alzheimer's disease. Levels of acetylcholine, which was first identified in 1914, are abnormally low in the brains of Alzheimer's patients. Currently, there are four FDA-approved drugs that treat the symptoms of Alzheimer's disease by inhibiting the active site of acetylcholinesterase, the enzyme responsible for the degradation of acetylcholine.

"When we investigated the power of THC to inhibit the aggregation of beta-amyloid," Janda said, "we found that THC was a very effective inhibitor of acetylcholinesterase. In addition to propidium, we also found that THC was considerably more effective than two of the approved drugs for Alzheimer's disease treatment, donepezil (Aricept®) and tacrine (Cognex®), which reduced amyloid aggregation by only 22 percent and 7 percent, respectively, at twice the concentration used in our studies. Our results are conclusive enough to warrant further investigation."

Other authors of the study, titled "A Molecular Link Between the Active Component of Marijuana and Alzheimer's Disease Pathology," include Lisa M. Eubanks, Claude J. Rogers, and Tobin J. Dickerson of The Scripps Research Institute, the Skaggs Institute for Chemical Biology, and the Worm Institute for Research and Medicine; and

Albert E. Beuscher IV, George F. Koob, and Arthur J. Olson of The Scripps Research Institute.

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For more information contact:

Office of Communications
10550 North Torrey Pines Road
La Jolla, California 92037
press@scripps.edu