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Cocoa Extract May Counter Specific Mechanisms of Alzheimer's Disease

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New York - A specific preparation of cocoa-extract called Lavado may reduce damage to nerve pathways seen in Alzheimer's disease patients' brains long before they develop symptoms, according to a study conducted at the Icahn School of Medicine at Mount Sinai and published June 20 in the *Journal of Alzheimer's Disease (JAD)*.

Specifically, the study results, using mice genetically engineered to mimic Alzheimer's disease, suggest that Lavado cocoa extract prevents the protein β -amyloid- $(A\beta)$ from gradually forming sticky clumps in the brain, which are known to damage nerve cells as Alzheimer's disease progresses.

Lavado cocoa is primarily composed of polyphenols, antioxidants also found in fruits and vegetables, with past studies suggesting that they prevent degenerative diseases of the brain.

The Mount Sinai study results revolve around synapses, the gaps between nerve cells. Within healthy nerve pathways, each nerve cell sends an electric pulse down itself until it reaches a synapse where it triggers the release of chemicals called neurotransmitters that float across the gap and cause the downstream nerve cell to "fire" and pass on the message.

The disease-causing formation of Aβ oligomers – groups of molecules loosely attracted to

each other – build up around synapses. The theory is that these sticky clumps physically interfere with synaptic structures and disrupt mechanisms that maintain memory circuits' fitness. In addition, $A\beta$ triggers immune inflammatory responses, like an infection, bringing an on a rush of chemicals and cells meant to destroy invaders but that damage our own cells instead.

"Our data suggest that Lavado cocoa extract prevents the abnormal formation of Aβ into clumped oligomeric structures, to prevent synaptic insult and eventually cognitive decline," says lead investigator Giulio Maria Pasinetti, MD, PhD, Saunders Family Chair and Professor of Neurology at the Icahn School of Medicine at Mount Sinai. "Given that cognitive decline in Alzheimer's disease is thought to start decades before symptoms appear, we believe our results have broad implications for the prevention of Alzheimer's disease and dementia.

Evidence in the current study is the first to suggest that adequate quantities of specific cocoa polyphenols in the diet over time may prevent the glomming together of $A\beta$ into oligomers that damage the brain, as a means to prevent Alzheimer's disease.

The research team led by Dr. Pasinetti tested the effects of extracts from Dutched, Natural, and Lavado cocoa, which contain different levels of polyphenols. Each cocoa type was evaluated for its ability to reduce the formation of A β oligomers and to rescue synaptic function. Lavado extract, which has the highest polyphenol content and anti-inflammatory activity among the three, was also the most effective in both reducing formation of A β oligomers and reversing damage to synapses in the study mice.

"There have been some inconsistencies in medical literature regarding the potential benefit of cocoa polyphenols on cognitive function," says Dr. Pasinetti. "Our finding of protection against synaptic deficits by Lavado cocoa extract, but not Dutched cocoa extract, strongly suggests that polyphenols are the active component that rescue synaptic transmission, since much of the polyphenol content is lost by the high alkalinity in the Dutching process."

Because loss of synaptic function may have a greater role in memory loss than the loss of nerve cells, rescue of synaptic function may serve as a more reliable target for an effective Alzheimer's disease drug, said Dr. Pasinetti.

The new study provides experimental evidence that Lavado cocoa extract may influence Alzheimer's disease mechanisms by modifying the physical structure of $A\beta$ oligomers. It also strongly supports further studies to identify the metabolites of Lavado cocoa extract that are active in the brain and identify potential drug targets.

In addition, turning cocoa-based Lavado into a dietary supplement may provide a safe, inexpensive and easily accessible means to prevent Alzheimer's disease, even in its earliest, asymptomatic stages.

Researchers from Kanazawa University in Japan contributed to the study and the cocoa used in the study was a gift from Dr. Jeffrey Hurst of the Hershey Company.

Article:

Wang J, Varghese M, Ono K, Yamada M, Levine S, Tzavaras N, Gong B, Hurst WJ, Blitzer RD, Pasinetti GM (2014) Cocoa Extracts Reduce Oligomerization of Amyloid-β: Implications for Cognitive Improvement in Alzheimer's Disease. *J Alzheimers Dis*, doi: 10.3233/JAD-132231.