

Review of data on reputed neurodegeneration toxins

June 18 2021



Researchers process dried chips from the seeds of Guam's native cycad tree in preparation of foods for experimental mammal consumption. The status of knowledge about toxins in cycad seeds is discussed in a joint publication by University of Guam and University of British Columbia researchers. Credit: University of British Columbia

Identifying the causes of human neurodegenerative diseases is a global research priority, warranting frequent reviews of the accumulating knowledge. In doing just that, biologists from the Plant Physiology Laboratory at the University of Guam and neuroscientists from the Experimental Medicine Program at The University of British Columbia have published an update on the reputed environmental toxins that have been suspected of being involved in mammal neurodegeneration. Their summary was published in April in the book *Spectrums of Amyotrophic Lateral Sclerosis*, which is available online from the publisher Wiley Blackwell.

A decades-long search for a dementia-causing toxin

Interest in the correlations between [environmental toxins](#) and neurodegeneration focused the world's magnifying glass on the island of Guam in the 1950s due to an unexpected increase in cases of neurodegenerative cases among the indigenous CHamoru population. The specific condition that temporarily affected Guam is known as amyotrophic lateral sclerosis-parkinsonism dementia (ALS-PDC) and known locally by the CHamoru term lytico-bodig.

A focus on this isolated cluster of cases led to decades of pursuit of causal toxins found in seeds of Guam's native cycad tree. These seeds were components of the local cuisine at the time, and increased reliance on this form of food starch during World War II was a plausible hypothesis to explain the increase in neurodegeneration cases shortly after the war.

Several factors likely coalesce

An ebb and flow of sequential disappointments has evolved since the 1950s because the identification of a single causal cycad toxin remains

elusive.

But these disappointments have been countered by successes. It is now understood that several factors likely coalesce into a synchronized perfect storm to generate an unusual increase in localized neurodegenerative cases, such as what temporarily happened on Guam. These co-factors may include exposure to high doses of the environmental toxin by the most susceptible gender with the most susceptible genes at the most susceptible age, followed by a latency period before the neuronal damage begins to express itself.

The UOG-UBC collaboration has lasted more than two decades, and various members of the team have authored more than 100 journal articles on various aspects of cycad biology during that time. The toxicology of Guam cycad seeds was the subject of 14 of these publications.

"When I began collaborating with UOG, we had the benefit of building on the foundation of decades of research from Guam," said co-author Christopher Shaw, UBC neuroscientist. "We used the fact that no plant scientist had been directly involved in any of the previously published research to secure funds to revisit various issues concerning cycad seed toxins."



University of Guam cycad biologist Benjamin Deloso inspects seeds on a *Cycas micronesica* plant at the Montgomery Botanical Center in Miami. University of Guam biologists collected Guam seeds in 2006 to establish this Miami collection where pollination research is ongoing to benefit Guam's conservation efforts. Credit: Michael Calonje

Difference between acute and slow-acting toxins

One of the many confusing aspects of this research is that acute toxins, which cause immediate poison reactions following cycad seed ingestion, are distinct from slow-acting toxins, which lead to neurodegeneration.

"The distinctions between these two forms of toxins are often confused, and scientists are constantly reminding the public that many years need to elapse after the exposure to a slow plant toxin before negative health outcomes develop," said Benjamin Deloso, a cycad biologist with UOG.

Claims of cyanide poisoning inaccurate

Another benefit from the marathon pursuit of the causal cycad toxin is that an enormous body of literature has developed that uncovered which biomolecules are not at play. "This is how science works," Shaw said. "The aggressive empirical look at each candidate toxin was justified and refined the development of superseding hypotheses that were vigorously tested."

For example, cassava roots contain sugar-based molecules that liberate cyanide after ingestion by mammals, and cycad seeds contain similar molecules, but cycad seeds contain no free cyanide and the identified sugar-based cycad molecules in cycads are incapable of liberating toxic levels of cyanide following ingestion by mammals. The meticulous research revealed the claims of cyanide as a potential cycad [toxin](#) and that cycad seed consumption could cause cyanide poisoning were inaccurate.

"Throwing around fear-mongering buzzwords, like cyanide, is a classic example of a repetition of false information in order to drive a personal agenda," Deloso said. "There are even petitions being circulated that falsely claim that cycad plants contain cyanide in attempts to force retail nurseries to stop selling cycad plants to pet owners."

The research team contends that scientists are not immune from the mistake of repeating these sorts of false claims about cycads. This tends to happen when scientists get their information from the gray literature or online encyclopedia style websites that are not vetted by cycad

experts.

The authors hope that one outcome of their new publication is a decline in the spread of false information about cycad poisoning, as these untruthful statements damage the international community's attempts to improve cycad conservation.

More information: Christopher A. Shaw et al, The Lessons of ALS-PDC – Environmental Factors in ALS Etiology, *Spectrums of Amyotrophic Lateral Sclerosis* (2021). [DOI: 10.1002/9781119745532.ch4](https://doi.org/10.1002/9781119745532.ch4)

Provided by University of Guam

Citation: Review of data on reputed neurodegeneration toxins (2021, June 18) retrieved 27 April 2024 from <https://medicalxpress.com/news/2021-06-reputed-neurodegeneration-toxins.html>

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