Azolla, BMAA, and Neurodegenerative Diseases

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Azolla is a water fern that forms a symbiosis with nitrogen fixing cyanobacteria. Studies have shown that BMAA, a non-protein amino acid, is present in *Azolla* [1]*. BMAA has been linked to neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) and Parkinsons dementia complex (PDC). Since *Azolla* has been suggested as a food stuff and is used as animal fodder [12] it is relevant to consider the relationship between *Azolla*, BMAA, and neurodegenerative diseases. This document attempts to answer the question wether or not there is reason to be worried about BMAA if *Azolla* is used as food for humans or as animal fodder. The short answer is that there is reason to be sceptical about using great amounts of *Azolla* as food for humans or as animal fodder but probably no reason to worry about consumption of smaller amounts of *Azolla*. However, without further research it is difficult to say anything for certain.

BMAA is produced by cyanobacteria and can be found in water where there are cyanobacteria, on plants living in symbiosis with cyanobacteria, and in animals feeding on sources of BMAA. The link between BMAA and neurodegenerative disease was discovered by studying the diet of Chamorro people on Guam, an island in the south-west Pacific Ocean. Since the 1940s the cause of highly raised occurrence of ALS-PDC within the Chamorro population on Guam has been searched for. In the 1950s incidence of ALS-PDC among the Chamorro was 50-100 times greater than ALS-PDC elsewhere [6] [5], with people contracting ALS-PDC already in their 40s [5]. Causes for this that have been hypothesised and discarded include hereditary causes, environmental causes, infectious agents, prions, and micronutrient deficiency. [5]

In 1967, a new substance, BMAA, was discovered on cycad seeds on Guam [7]. It was later discovered that the BMAA found in cycad seeds is produced by a nitrogen fixating cyanobacteria living in a symbiosis with the cycad seeds (similar to the symbiosis that nitrogen fixating cyanobacteria form with *Azolla)* [11]. After the discovery of BMAA on cycad seeds It was hypothesised that BMAA could be linked to ALS-PDC on Guam since the Chamorro ate flour made from cycad seeds. However, it was argued that the quantities of BMAA were too low in cycad flour to be of concern and the hypothesis was discarded. In the 2000s the hypothesis was brought up again as scientists found that BMAA could accumulate through biomagnification in flying foxes that fed on cycad seeds, and that the Chamorro used to eat flying foxes [7].

Because of hunting and the introduction of new predatory species the flying fox on Guam is extinct since the 1970s [9]. However, when flying foxes were common on Guam they were desirable food served at Chamorro weddings, village fiestas, and religious events. [5] Chamorro who contracted ALS-PDC may also have eaten meat and dairy products from pigs, cattle, sheep, and deer that have grazed on cycad seeds and thus accumulated high levels of BMAA through biomagnification [2][7].

Since the 1990s the number of people with ALS-PDC on Guam has declined rapidly and is now comparable to the Western world (1.9/100 000 in the 1990s vs 179/100 000 in the 1950s) [5]. The Chamorros diet has also changed since the 50s, with less consumption of flying foxes and cycad seed flour because of the extinction of the flying fox and imported flour replacing cycad seed flour [5]. The correlation between the decline of ALS-PDC on Guam and the Chamorros dietary changes since the 1950s support the hypothesis that consumption of BMAA is linked to ALS-PDC on Guam. Further support for the hypothesis is that BMAA has been found in the brains of Chamorro dying of ALS-PDC but not in control brains [2]. BMAA has also been found in people with neurodegenerative diseases outside of Guam [7].

In addition to cycad seeds and *Azolla* high concentrations of BMAA has been found in seafood such as mussels, oysters, crabs [3], shrimps [7], and fish [8] [4]. Elevated occurrences of neurodegenerative diseases have been found in some areas where BMAA may be present in seafood which further support the hypothesis that there is a link between BMAA and neurodegenerative diseases [7]. In addition to seafood and land animals feeding on cycads, BMAA has also on occasion been found in dietary supplements such as Spirulina and in drinking water [7].

Although it is still only a hypothesis these are strong indicators that BMAA is linked to neurodegenerative diseases. However, neurodegenerative diseases are likely related to BMAA in combination with genetic factors [2] and other variables. As one scientist describes it; neurodegeneration is probably caused by a “smorgasbord of bad things that can happen in your life” [7].

I have only been able to find one study that indicates that BMAA is present in *Azolla* [1] and one mentioning of the amount of BMAA in Azolla [5]. The study that showed BMAA being present in *Azolla* can be questioned since new analysis methods show that earlier methods may have mistaken the common, non-toxic, isomers DAB and AEG for BMAA. According to scientist at Stockholm University where the study was made it is likely that this mixup was the case in this analysis of *Azolla*. Furthermore the study found that BMAA was produced in *Azolla* in absence of cyanobacteria. This would indicate that BMAA is not produced exclusively by cyanobacteria in *Azolla*, or that it is produced exclusively by the fern or by other bacteria in *Azolla*. Since, as far as I am aware, no other study has found that BMAA is produced by any organisms other than cyanobacteria, this supports the idea that BMAA was mistaken for DAB or AEG.

The mentioning of the amount of BMAA in *Azolla* (2 mg/kg) is in a credible report. However no reference to the analysis is made. It is possible that this figure is derived from an analysis made with the same methods as the questionable study at Stockholm University and therefore is wrong. It is also possible that the BMAA came from another source than the Azolla, such as from cyanobacteria in the water Azolla was grown in. However, without further conclusive evidence of the amount, if any, of BMAA in *Azolla* I have assumed the mentioning of 2 mg/kg of free BMAA in *Azolla* to be correct.

2 mg/kg of free BMAA [5] in *Azolla* can be put in relation to the concentrations of BMAA in plants and animals that have been suspected to cause ALS-PDC on Guam. Cycad seeds on Guam contain 750 - 1 200 mg/kg of free BMAA [5]. Flying foxes on Guam who have fed on cycad seeds contain just over 3 500 mg/kg [6]. The BMAA dose derived from eating a single flying fox (with a body weight of around 150 g [9]) is equivalent to eating around 1 kg of cycad flour [6]. Assuming a content of 750 mg / kg of free BMAA in cycad seed flour, and 2mg / kg in *Azolla*, one flying fox, or one kilo of cycad seed flour, would be equivalent to eating about 375 kg of *Azolla*.

Animals such as cattle, sheep, horses, and pigs who grace on cycads on Guam are know to occasionally develop paralysis from cycad poisoning. It is not known which substance causes the paralysis but BMAA has been been suggested by some investigators [5]. Studies have also reported that high doses of BMAA can cause shaking and paralysis in animals [7]. The levels of BMAA present in the amount of cycads known to cause cycad poisoning in animals on Guam corresponds to 0.56 mg/kg body weight [5]. For a person weighing 70 kg that would equal a dose of 39.2 mg of BMAA. To be exposed to the same dose of BMAA that potentially causes paralysis in animals a person weighing 70 kg would have to eat 19.6 kg of *Azolla* (again assuming 2mg/kg of BMAA in *Azolla*). No studies appear to have been done on the concentration of BMAA in animals fed with *Azolla*. However because of the ability of BMAA to biomagnify it is likely that animals, such as poultry, fish, or cattle, who are fed with *Azolla* contain levels of BMAA higher than those in *Azolla*.

There is little research available on *Azolla* and BMAA but what is available suggests that the risk of developing neurodegenerative diseases from BMAA in *Azolla* or meat and produce from animals fed with *Azolla* is not likely to be greater than that of developing neurodegenerative diseases from BMAA in common seafoods or other food stuffs. The risk of acute poisoning from BMAA in *Azolla* is negligible since one would have to eat tens of kilos of Azolla. To be subjected to the same amounts of BMAA as the Chamorro people on Guam who contracted ALS-PDC a person would have to eat many, possible even hundreds, of kilos of *Azolla* or products from animals fed with *Azolla* for many years, even decades, and starting at an early age.

In conclusion, until new analyses are made the presence of BMAA in *Azolla* cannot be ruled out. Because of the potential presence of BMAA in *Azolla*, the ability of BMAA to biomagnify in animals, and the strong link between BMAA and neurodegenerative diseases there is reason to be sceptical about using great amounts of *Azolla* as food for humans or as animal fodder. Hopefully further research will arrive at a more conclusive answer as to weather there is BMAA present in *Azolla* and BMAA is a cause of neurodegenerative diseases.

References

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