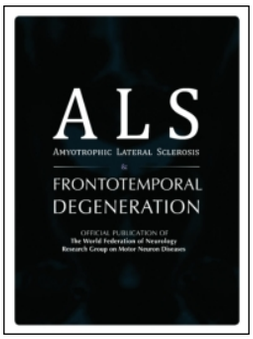
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The ALSUntangled Group

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REPORT

ALSUntangled No. 9: Blue-green algae (Spirulina) as a treatment for ALS

The ALSUntangled Group

Now 22 months old, ALSUntangled (www.alsuntangled.org) has 315 twitter followers. Our NING consists of 72 ALS clinician scientists from across seven countries, participating in more than 30 active discussions. New discussions opened since our last publication include BuNaoGao (BNG), Dean Kraft, Dr. Shahriar Vaziritabar and 'The Healing Code Solution'. We have published eight investigations on nine different alternative and off-label treatment options and are collaborating with Quackwatch (www.quackwatch.org), Patients Like Me (www.patientslikeme.com) and ALS Worldwide (www.alsworldwide.org). At the request of multiple PALS, we here investigate the use of a blue-green algae product called Spirulina as a treatment for ALS.

What is Spirulina?

According to its website, Spirulina is a commercially cultivated, dried form of the cyanobacterium Arthrospira platensis (1). Arthrospira are a specific kind of blue-green algae from alkaline lakes; the high pH in such lakes supposedly prevents other algae from growing and contaminating the product. It is said to consist mainly of protein, pro-vitamin A, mixed carotenoids, phycocyaninin, chlorophyll and gamma linoleic acid (1).

What is the rationale for using Spirulina in ALS?

Promoters claim that Spirulina has nutritional benefits, modulates immune function and has "strong antioxidant and anti-inflammatory activities" (1). Spirulina extract appears to protect mouse embryo fibroblasts from DPPH- or ABTS-induced apoptotic cell death, although the effect seen is less than that obtained with vitamin C (2). Small animal and human studies suggest that Spirulina extracts may lower cholesterol (3), alter interleukin and interferon levels (3,4), increase SOD1 activity (3,5), and enhance natural killer cell (4,6) and macrophage phagocytic activity (7).

Immune dysregulation, oxidative stress, neuroinflammation and apoptotic cell death are all potential parts of ALS pathophysiology (8). Thus, if these purported actions of Spirulina are accurate, there is at least a theoretical basis for its use in ALS.

What are the data for use of Spirulina in ALS?

In the recent paper, 'Neuroprotective Effect of Spirulina in a Mouse Model of ALS', authors Svitlana Garbuzova-Davis and Paula Bickford test their hypothesis that adding Spirulina to the diet can slow down or stop motor neuron degeneration in the mutant SOD1 mouse model of ALS (9). Mutant SOD1 mice were given a diet supplemented with 0.1% Spirulina powder for 10 weeks, starting at five weeks of age, and compared to mutant SOD1 mice on an unsupplemented diet. At 15 weeks of age, the authors 1) weighed the mice; 2) assessed the extent of the hindlimb splay reflex, a widely used assay of motor strength; 3) measured the mRNA levels of selected cytokines (typically involved in inflammation); and 4) sacrificed the animals and used histological techniques to observe motor neuron degeneration and glial cell proliferation. The mice on the diet with Spirulina gained more weight than the non-treated mice, had a slightly greater splay ability in the right hindlimb but not the left, had reduced cytokine levels in a few regions of the brain and spinal cord, and displayed fewer degenerating neurons and reactive glia in sample histological sections of the spinal cord. The authors concluded that "Spirulina slowed the onset of motor symptoms and disease progression" and that "a Spirulina supplemented diet may have future clinical benefit in treating ALS as an alternative or adjunctive therapy".

At best, this paper can be considered an introduction to the authors' hypothesis. It is not clear that the conclusions are supported by the authors' data. Spirulina was associated with improved weight gain, but it is no way proven that this was due to an effect

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on motor neurons. It may simply be that Spirulina-treated mice took in more calories. In this context, the improved nutrition in Spirulina-treated animals might account for any effect on slowed disease progression, rather than a more exotic immunomodulatory or anti-oxidant mechanism. The paper does not provide data to suggest that there was slowing of onset of motor symptoms, because it did not report onset of motor symptoms. The unilateral effect on hindlimb splay is odd; why would a true effect be seen only on one side? The authors did not count motor neurons to see if in fact fewer were degenerating; rather, they qualitatively looked at the slides to obtain an impression. Finally, they ended the experiment when the mice were 105 days old, essentially preventing determination of whether the treated mice actually survived longer than non-treated mice (the SOD1 mutant mice live to about 130 days). The authors acknowledged these deficits in the paper, and indicated their intent to carry out follow-up experiments. However, one of the authors of this paper is a cofounder of a company that sells nutritional supplements; this creates a potential conflict of interest and possible source of bias when reporting subjective measurements as was done here.

Even if the authors can someday show that they are able to use Spirulina to delay onset or slow progression in this animal model, it is not clear what this would mean for patients with ALS. It is not currently possible to start treatment in patients before the clinical onset of their motor dysfunction. Furthermore, a number of immunomodulatory and anti-oxidant treatments have already been shown to slow progression in the SOD1 mouse, and have had no similar effect on patients with ALS.

Within the Patients Like Me online community, six members with ALS report taking any form of blue-green algae; two report taking the brand Spirulina and one reports taking the brand Pure Planet Hawaiian Spirulina. Dosages taken ranged from 3 mg to 3000 mg daily, and durations of therapy ranged from three months up to two years or more. Compliance was high, with members reporting either "always" or "usually" taking their selected regimen. No members reported any efficacy or side-effects. All six have stopped taking blue-green algae, with four stating they stopped due to lack of efficacy and two stating they stopped due to cost. Reported out-of-pocket costs ranged from $50 to $200 per month.

What are the potential problems with Spirulina for ALS?

Some types of blue-green algae contain toxins (10); these include microcystins that are toxic to the liver, heavy metals, neurotoxic alkaloids, and the chemical BMAA, which may even be an environmental trigger for ALS (11). Vendors of Spirulina state that their product is free of most or all of these toxins, but assurance of this supplement is up to the manufacturer or vendor, unlike FDA regulated pharmaceuticals. Even if it is toxin free, there are other real and theoretical and safety concerns related to the use of Spirulina in patients with ALS. One website reports possible adverse reactions to Spirulina including upset stomach, diarrhea, and rash and that there is a potential for more serious allergic reactions (12). Spirulina contains pro-vitamin A, and too much vitamin A can be toxic. Worse lipid profiles may be associated with slower ALS progression (13); thus, the purported lipid-lowering effect of Spirulina could theoretically accelerate ALS progression. Similarly, decreasing macrophage phagocytic activity may slow ALS progression and is now being pursued in treatment trials (14); by activating macrophage phagocytic activity Spirulina could theoretically accelerate ALS progression.

Conclusion

At this time, ALSuntangled finds no evidence that Spirulina is effective for ALS and there appear to be real and theoretical toxicities that patients with ALS may encounter with it. Until better efficacy and safety studies are published, we do not support the use of Spirulina in patients with ALS.

The ALSUntangled Group currently consists of the following members: Richard Bedlack, Orla Hardiman, Jeff Dietz, Josep Gamez, Mazen Dimachkie, Yunxia Wang, Paul Wicks, James Heywood, Steven Novella, L.P. Rowland, Merit Cudkowicz, Eric Pioro, Lisa Kinsley, Kathy Mitchell, Jonathan Glass, Sith Sathornsumetee, Hubert Kwiecinski, Jon Baker, Nazem Atassi, Dallas Forshew, John Ravits, Robin Conwit, Carlayne Jackson, Alex Sherman, Kate Dalton, Katherine Tindall, Ginna Gonzalez, Janice Robertson, Larry Phillips, Michael Benatar, Eric Sorenson, Christen Shoesmith, Steven Nash, Nicholas Marigakis, Dan Moore, James Caress, Kevin Boylan, Carmel Armon, Megan Grosso, Bonnie Gerecke, Jim Wymer, Bjorn Oskarsson, Robert Bowser, Vivian Drory, Jeremy Shefner, Terry Heiman-Patterson, Noah Lechtzin, Melanie Leitner, Robert Miller, Hiroshi Mitsumoto, Todd Levine, James Russell, Khema Sharma, David Saperstein, Leo McClusky, Daniel MacGowan, Jonathan Licht, Ashok Verma, Michael Strong, Catherine Lomen-Hoerth, Rup Tandan, Michael Rivner, Steve Kolb, Meraida Polak, Stacy Rudnicki, Pamela Kittrell, Muddasir Quereshi, George Sachs, Gary Pattee, Tahseen Mozaffar, Michael Weiss, John Kissel, Jonathan Goldstein, Jeffrey Rothstein, Dan Pastula.

Note: this paper represents a consensus of those weighing in. The opinions expressed in this paper are not necessarily shared by every investigator in this group.

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